



**Co-funded by  
the Health Programme  
of the European Union**

*“This Deliverable is a part of the joint action “724161/JARC” which has received funding from the European Union’s Health Programme (2014-2020)”.*



D4.1-4.2

List of rare cancers and list of differences and commonalities between cancers registration and rare diseases registration

## RARECAREnet list of rare cancers vs Orphanet

The list of cancer types provided by RARECAREnet was produced by a group of pathologists, haematologists, clinicians and epidemiologists and emerged after a consultation process during which the developing list and its rationale were available at <http://www.rarecare.eu>. The list, endorsed by major European cancer organisations, is organised into three tiers as exemplified in Table 1. The bottom tier corresponds to the WHO names of individual cancer entities (<http://www.iarc.fr/en/publications/pdfs-online/pat-gen/>) and their corresponding ICD-O-3 codes. Bottom tier entities were grouped into categories (middle tier) considered to require similar clinical management and research. Middle tier entities were grouped into general categories (top tier) considered to involve the same clinical expertise and patient referral structure.

Table 1. The three-tier structure of the RARECAREnet list of cancers illustrated for epithelial cancers of nasal cavity and sinuses

| Tier | Tumour   | ICD-O-3 Topography code | ICD-O-3 Morphology code   |
|------|--|-------------------------|---|
| 1    | <b>EPITHELIAL TUMOURS OF NASAL CAVITY AND SINUSES</b>                    | C30.0, C31              | 8000, 8001, 8003,8004, 8010, 8011, 8012, 8020-8022, 8030,8031, 8032, 8033-8034, 8046, 8050-8076, 8078, 8082-8084, 8120, 8121,8122, 8123, 8130, 8140, 8144, 8560, 8980 |
| 2    | <b>Squamous cell carcinoma with variants of nasal cavity and sinuses</b> | C30.0, C31              | 8004, 8120, 8121,8122, 8130, 8032, 8050-8076, 8078, 8083-8084, 8123, 8560, 8980   |
| 3    | Squamous carcinoma   | C30.0, C31              | 8070  |
| 3    | Verrucous carcinoma  | C30.0, C31              | 8051  |
| 3    | Squamous cell carcinoma spindle cell                                     | C30.0, C31              | 8004, 8032, 8074, 8980  |
| 3    | Papillary squamous cell carcinoma  | C30.0, C31              | 8052  |
| 3    | Adenosquamous carcinoma  | C30.0, C31              | 8560  |
| 3    | Squamous cell carcinoma, adenoid   | C30.0, C31              | 8075  |
| 3    | Basaloid squamous cell carcinoma   | C30.0, C31              | 8083  |
| 2    | <b>Lymphoepithelial carcinoma of nasal cavity and sinuses</b>            | C30.0, C31              | 8082  |
| 2    | <b>Undifferentiated carcinoma of nasal cavity and sinuses</b>            | C30.0, C31              | 8020-8022   |
| 2    | <b>Intestinal type adenocarcinoma of nasal cavity and sinuses</b>        | C30.0, C31              | 8144, 8140  |

Rare cancers are the tier 2 entities with incidence rate <6/100,000. In the list there are 198 rare tier 2 cancer entities. Orphanet and RARECAREnet teams reviewed all these tier 2 cancer entities. The results of the comparison between the RARECAREnet list of rare cancers with the list of rare cancers included in Orphanet are summarized in Table 1. Annex 1 reports the details of the comparison between Orphanet and RARECAREnet.

Table 1. List of comments about the list of RARECAREnet rare cancers

| Orphanet                                       | RARECAREnet   |
|--|---|
| <b>Missing entities</b>                        |   |
| Gastric linitis plastica                       | Not missing. ICD-O3 8142 it is included in the group of adenocarcinoma of stomach   |
| Tumour of appendix                             | Not missing. Appendix is part of the colon. ICD-O3 topography code C18.1 appendix   |
| Mucinous adenocarcinoma of the appendix        | Not missing. RARECAREnet list include mucinous adenocarcinoma of colon (colon includes appendix)  |
| Carcinoma of the ampulla of Vater              | Not missing. The ICD-O3 topography code C24 means all C24 thus also C24.1 which is in the ICD_O3 for Ampulla di Vater   |
| Undifferentiated carcinoma of the corpus uteri | Not missing. RARECAREnet list includes both Undifferentiated tumours (ICD-O3 codes 8020; 8021; 8022) and Papillary carcinoma (ICD-O3 8050: 8051; 8052. Tier 1 of the revised list includes 8000, 8001,8003-8005, 8010, 8011, 8012, 8014, 8015, 8020-8022, 8030-8033, 8050-8052, 8070-8078, 8082-8084, 8120, 8122, 8123, 8130, 8313, 8140-8141, 8143, 8144, 8147, 8190, 8200, 8201, 8210-8211, 8221, 8230, 8231, 8255, 8260-8263, 8290, 8310, 8315, 8320, 8323, 8333, 8380-8384, 8401, 8430, 8460, 8440-8441, 8470-8471, 8480-8482, 8490, 8503, 8504, 8510, 8512, 8514, 8525, 8542, 8550-8551, 8560, 8562-8576, 8950-8951, 8980, 8981, 9000, 9110). The 8050/3 Papillary carcinoma, NOS and 8051/3 Verrucous carcinoma, NOS are included in the tier 2 "adenocarcinoma "includes The 8052/3 Papillary squamous cell carcinoma is included in the "tier 2 squamous" The undifferentiated because are undifferentiated cannot be included in any tier 2. |
| Papillary carcinoma of the corpus uteri        |   |
| Adenoid cystic carcinoma of the cervix uteri   | Not missing. The adenoid cystic carcinoma corresponds to the ICD-O3 morphology 8200 and it is included in both, the tier 1 and the tier 2 adenocarcinoma of cervix uteri  |
| Adenoid basal carcinoma of the cervix uteri    | Not missing. In the RARECAREnet list the 8098 is included in the tier 1 and in the tier 2 adk of cervix uteri.  |
| Glassy cell carcinoma of the cervix uteri      | Not missing. We can add a row for this tier 3 because those listed are just some (the most relevant) and not all those included in tier 2. This was done to avoid to have a too long list.  |
| Carcinofibroma of the corpus uteri             | Not missing. It is a sarcoma thus, it is in the sarcoma. Please refer to tier 1 and tier 2 of soft tissue sarcoma.  |
| Carcinosarcoma of the corpus uteri             | Not missing. The carcinosarcoma is the ICD-O3 morphology 8980 and the RARECAREnet list includes this morphology. The topographies include C53 cervix uteri; C54 corpus uteri; C 55.9 utero nos. In the RARECAREnet list there is a tier 2 Mullerian mixed tumour in C54   |
| Carcinosarcoma of the cervix uteri             | Not missing. Please refer to my previous comment on carcinosaroma of corpus uteri. It was included among the sites of our tier 1. In the RARECAREnet list there is a tier 2 Mullerian mixed tumour of cervix uteri  |
| Small cell carcinoma of the ovary              | Not missing. Small cell carcinomas: ICD-O3 codes 8041-8045 are neuroendocrine tumours. Thus, they are included among the neuroendocrine tumours Tier 1 and in the tier 2: neuroendocrine tumours of other sites.  |
| Primary peritoneal serous/papillary carcinoma  | Not missing. In the RARECAREnet list there is a tier 2 named Primary peritoneal serous/papillary carcinoma. It is within the Tier 1 epithelial tumour of ovary but the specific topography is C48   |

|  |  |
|--|--|
| Epithelioid trophoblastic tumour                             | Not missing. Trophoblastic tumour, epithelioid (ICD-O3 9105/3) is included in tier 1. We can add it as tier 3 to make it more evident  |
| Dermatofibrosarcoma protuberans                              | Not missing. This is a sarcoma. Thus, it is included in the soft tissue sarcoma. You can see it also specifically in the tier 3 DFSP (8832-8833)   |
| Neuroblastoma and ganglioneuroblastoma                       | Not missing. In the RARECAREnet there is a tier 1 per each of the major embryonal tumours. Discussing with the experts of the CNS they asked us to differentiate tumours of the CNS and embryonal tumours of the CNS. Thus the revised list follow a different grouping with embryonal tumours of CNS being a tier 1 |
| Pleuropulmonary blastoma                                     | Not missing. The RARECAREnet list includes pleuropulmonary blastoma (ICD-O3 8973) as a separated tier 1  |
| Malignant perineurioma                                       | Not missing. ICD-O3 code 9571. It is a sarcoma and it is included in the group of sarcomas   |
| Solitary fibrous tumour                                      | Not missing. ICD-O3 8815. It is included among the sarcomas  |
| Alveolar soft part sarcoma                                   | Not missing. ICD-O3 9581. It is included in the sarcomas. Please refer to tier 1 soft tissue sarcoma or to any tier 2  |
| Undifferentiated pleomorphic sarcoma (Bone site)             | Not missing. Undifferentiated sarcoma are included in tier 1 of bone sarcomas. Because are undifferentiated we cannot include them in any tier 2.  |
| Bronchial neuroendocrine tumour                              | Not missing. In the RARECAREnet list, there is a tier 2 for neuroendocrine tumours of other sites, which includes all the sites not listed in the other tiers 2.   |
| Laryngeal neuroendocrine tumour                              |  |
| Middle ear neuroendocrine tumour                             |  |
| Primary hepatic neuroendocrine carcinoma                     |  |
| Gallbladder neuroendocrine tumour                            |  |
| Anaplastic oligoastrocytoma                                  | Not missing. This is included in the tier 2. Tiers 3 listed include only some of the histotype to reduce the length of the list. We can include another tier 3 to make it easier to find.  |
| Primary germ cell tumour of central nervous system           | Not missing. In the RARECAREnet list there is a tier 1 (extra gonadal germ cell) including these entities in all the sites different from the gonadal ones.  |
| Embryonal carcinoma of the central nervous system            |  |
| Germinoma of the central nervous system                      |  |
| Yolk sac tumour of central nervous system                    |  |
| Choriocarcinoma of the central nervous system                |  |
| Teratoma of the central nervous system                       |  |
| Mixed germ cell tumour of central nervous system             |  |
| Precursor B/T lymphoblastic leukaemia/lymphoblastic lymphoma | Not missing. In the RARECAREnet list, there are 2 tiers 3: Precursor B/T lymphoblastic leukaemia/lymphoblastic lymphoma and Burkitt leukaemia/lymphoma. It is not relevant whether there is a tier 3 because, as explained earlier on, we included only some   |

|   |  |
|---|--|
| Precursor B-cell acute lymphoblastic leukemia   | tiers 3.   |
| Precursor T-cell acute lymphoblastic leukemia   |  |
| Non Hodgkin Mature T cell and NK-cell neoplasms                                       | Not missing. The RARECAREnet list has different tiers 2: T cutaneous lymphoma (Sezary syn, Mycosis fung); Other T cell lymphomas and NK cell neoplasms   |
| Non Hodgkin, Mature B cell lymphoma   | Not missing. The RARECAREnet list includes several tiers 2: Diffuse B lymphoma; Follicular B lymphoma; Hairy cell leukaemia; Plasmacytoma/Multiple Myeloma (and Heavy chain diseases); Other non Hodgkin, Mature B cell lymphoma, Mantle cell lymphoma; Prolymphocytic leukaemia, B cell |
| Lymphoplasmacytic lymphoma without IgM production                                     | Not missing. In the WHO 2008 and the recent 2017 we have only Lymphoma lymphoplasmacitic/macroglobulinemia Waldstrom 9671 and 9761. they are both in our list  |
| Primary effusion lymphoma   | Not missing. It is in the tier 1 lymphoma but not in tier 2  |
| Chronic eosinophilic leukemia   | Not missing. ICD-O3 code 9964. Chronic eosinophilic leukemia, NOS or Hypereosinophilic syndrome  |
| Myelodysplastic/myeloproliferative diseases nos                                       | Updates of the RARECAREnet list ongoing  |
| Myelodysplastic/myeloproliferative neoplasm with ring sideroblasts and thrombocytosis | Updates of the RARECAREnet list ongoing  |
| Myelodysplastic/myeloproliferative diseases nos                                       | Updates of the RARECAREnet list ongoing  |
| Myelodysplastic/myeloproliferative neoplasm with ring sideroblasts and thrombocytosis | Updates of the RARECAREnet list ongoing  |
| Myeloid/lymphoid neoplasm associated with PDGFRA rearrangement                        | Updates of the RARECAREnet list ongoing  |
| Myeloid/lymphoid neoplasm associated with PDGFRB rearrangement                        | Updates of the RARECAREnet list ongoing  |
| Myeloid/lymphoid neoplasm associated with FGFR1 rearrangement                         | Updates of the RARECAREnet list ongoing  |
| Myeloid/lymphoid neoplasm associated with PCM1-JAK2                                   | Updates of the RARECAREnet list ongoing  |
| Tubulocystic renal cell carcinoma   | Updates of the RARECAREnet list ongoing  |
| Acquired cystic disease-associated renal cell carcinoma                               | Updates of the RARECAREnet list ongoing  |
| Composite hemangioendothelioma  | Updates of the RARECAREnet list ongoing  |
| Retiform hemangioendothelioma   | Updates of the RARECAREnet list ongoing  |
| Plasmablastic lymphoma  | Updates of the RARECAREnet list ongoing  |
| High grade B-cell lymphoma with MYC and/ or BCL2 and/or BCL6 rearrangement            | Updates of the RARECAREnet list ongoing  |

|  |   |
|--|---|
| Acute myeloid leukaemia with CEBPA somatic mutations                           | Updates of the RARECAREnet list ongoing   |
| Acute myeloid leukaemia with t(8;16)(p11;p13) translocation                    | Updates of the RARECAREnet list ongoing   |
| Acute myeloid leukaemia with t(6;9)(p23;q34)                                   | Updates of the RARECAREnet list ongoing   |
| Acute myeloid leukaemia with t(9;11)(p22;q23)                                  | Updates of the RARECAREnet list ongoing   |
| Acute myeloid leukaemia with inv3(p21;q26.2) or t(3;3)(p21;q26.2)              | Updates of the RARECAREnet list ongoing   |
| Megakaryoblastic acute myeloid leukaemia with t(1;22)(p13;q13)                 | Updates of the RARECAREnet list ongoing   |
| Acute myeloid leukaemia with NPM1 somatic mutations +865:870J870864:870864:870 | Updates of the RARECAREnet list ongoing   |
| Acute leukaemia with ambiguous lineage   | Updates of the RARECAREnet list ongoing   |
| Acute erythroid leukaemia  | Updates of the RARECAREnet list ongoing   |
| <b>Rationale for including/excluding cancer entities</b>                       |   |
| Epstein-Barr virus-associated gastric carcinoma                                | The RARECAREnet list do not differentiate the cancer based on the aetiology. Anyway it is a gastric carcinoma that will be treated by oncologist knowing whether there are differences. For oropharynx cancers, the WHO has created codes for HPV+ and HPV- oropharynx cancers and we are including them in the list. In the WHO blue book, we do not see a code for this entity. |
| Renal cell carcinoma with variants   | The most important carcinoma of the kidney is the renal cell carcinoma as shown by the incidence rate. This carcinoma is within the big group of adenocarcinoma but, for the kidney it is standardised recognised to talk about renal cell thus we said renal cell + variants which includes other type of adk  |
| Pleomorphic rhabdomyosarcoma   | Pleomorphinc sarcoma is typical of adult and has a completely different treatment from the childhood rabdomiosarcoma. Thus, it is included among the sarcomas.  |
| Embryonal rhabdomyosarcoma of soft tissue                                      | Because these are typical of children and therefore are treated differently from those of the adults  |
| Alveolar rhabdomyosarcoma of soft tissue                                       |   |
| Kaposiform hemangioendothelioma  | 9130/1. Only malignant cancers are included thus this is not included in the RARECAREnet list.  |
| Subependymal giant cell astrocytoma  | Upon request of the experts, some relevant borderline entities have been included. Thus, this is included in the RARECAREnet list.  |
| Subependymoma  | It is borderline. Some borderline entities have been included upon request of the experts. Thus, this is included in the RARECAREnet list.  |
| Myxopapillary ependymoma   |   |

|   |   |
|---|---|
| Atypical papilloma of choroid plexus        | ICD-O 9390/1 it is in the ICD-O updates of the 2011. anyway it is a border line and I am afraid we will not include it in our list which includes malignant cancer only with few expectations requested by consensus  |
| Borderline epithelial tumor of ovary        | During the discussion, we had with the consensus group, there were 2 entities not malignant that were considered relevant to include: granulosa cell tumour malignant, adult type and granulosa cell tumour malignant, juvenile type. We added them with the following clarification: 8620/1 and 8622/1 included in the list however will not be included in the analyses because border line |
| Gynandroblastoma                            | this is a borderline morphology thus it is not included in the RARECAREnet list (8632/1)  |
| Invasive mole                               | this is a borderline morphology thus it is not included in the RARECAREnet list (9100/1)  |
| Placental site trophoblastic tumor          | this is a borderline morphology thus it is not included in the RARECAREnet list (9104/1)  |
| SMARCA4-deficient sarcoma of thorax         | This is a cancer predisposing syndrome and not a cancer itself (no code available in WHO blue book). Thus, we do not have it in the RARECAREnet list  |
| <b>Differences between tiers 2 and 3</b>    |   |
| Clear cell adenocarcinoma, NOS              | Tier 2 combine different tier 3 (which are WHO blue book code) based on the way they are treated. Thus, if all these morphologies are combined together it means that experts will treat them in the same way thus they are not clinical distinct entities. Thus, they are included as tier 3. We listed them so that people can have an idea of the different incidence of these histotypes. |
| Papillary adenocarcinoma, NOS               |   |
| Renal cell carcinoma chromophobe type       |   |
| Collecting duct carcinoma                   |   |
| Xp translocation carcinoma                  |   |
| Carcinoma associated with neuroblastoma     |   |
| Renal medullary carcinoma                   |   |
| Mucinous tubular and spindle cell carcinoma |   |
| Basaloid carcinoma of rectum                | Tier 2 includes all tiers 3. If it is a tier 2 the reason is that the consensus group has recognised it relevant from the clinical point of view because it is treated differently from the others epithelial tumours of rectum   |
| Endometrioid adenofibroma malignant         | It was discussed with the consensus group who did not consider this entity to be a tier 2. This means that it is not a clinically distinct entity per se. We can anyway confirm that it is rare and it is a tier 3.   |

Based on this comparison we agree that there are no major differences in the list of rare cancers considered by RARECAREnet and by Orphanet. The main comments raised because:

- The RARECAREnet list includes only malignant tumours. Exceptions were included based on experts request and consensus.
- Tier 3 do not include all morphologies of tiers 2. Thus, it is important to consider all the morphologies included in tiers 2 to understand which cancers are included.
- We are currently updates the RARECAREnet list with the latest WHO blue book. Thus, some entities were missing when Orphanet did the review.

#### Consensus meeting to review the rationale of the list and the definition of rare cancers

On January 17<sup>th</sup> 2018, a meeting was organized to review and enlarge the consensus on the rationale of the rare cancer definition and on the list of rare cancers.

All major stakeholders were invited:

- European reference networks (ERNs) coordinators
  - o EURACAN (ERN on rare adult solid cancers)
  - o EuroBloodNet (ERN on haematological diseases)
  - o PaedCan (ERN on pediatric cancers)
  - o GENTURIS (ERN on rare genetic tumour risk syndromes)
- Scientific societies
  - o The European Society of Medical Oncology (ESMO)
  - o The European Society of Surgical Oncology (ESSO)
  - o The European Society for Pediatric Oncology (SIOPE)
  - o The European Society of Pathology (ESP)
- Patients organisations
  - o European Cancer Patients Coalition (ECPC)
  - o Rare Diseases Europe (EURORDIS)
- Member States involved in the JARC
- Orphanet
- The European Cooperative Study Group for Pediatric Rare Tumors (EXPeRT)
- Epidemiologists, oncologists, cancer registries staff with previous experience on rare cancers

A preliminary document about the rationale for the definition and the list of rare cancers was circulated to all the stakeholders involved. The comments were included in a second version discussed during the consensus meeting.



A consensus was reached about:

- The definition of rare diseases based on indicators of frequency since they are problematic because of their low frequency
- The list of rare cancer which includes rare cancers identified on the basis of the European incidence rate  $<6/100,000$ . Thus, rare cancers are the same in each country regardless of the country-specific incidence rate.
- The classification used for rare cancers which is the International Classification of Diseases for Oncology (ICD-O), which translates the WHO blue book. Thus, the list of rare cancers will be revised on the basis of the WHO blue book and ICD-O updates.
- cancer presentation that may be rare, even within a common cancer denomination, as much as it gives rise to a distinct clinical pattern, as long as it is worth studying in clinical research and treating in clinical practice unlike other presentations within the same label.
- The families of rare cancers including the rationale for their definition.
- The importance to recognize that all pediatric cancers are rare and to acknowledge the existence of very rare pediatric cancers.

After the consensus meeting a document was drafted and circulated among the stakeholders involved (please refer to Annex 2 consensus document on the definition and list of rare cancers for detail). The consensus document will be published in a relevant scientific journal and will be promoted among the JARC recommendations.

## Comparison between cancer and rare diseases registration

Rare cancers belong to the world of cancer and therefore the registration of rare cancers do not differ from that of common cancers. The cancer registration has a long history with the first population-based cancer registry established in Europe at the beginning of the 1900s (1926: first cancer registry in Hamburg).

Rare diseases are a highly variegated group of chronic diseases most of which of genetic origins. The definition of rare diseases is pretty new as well as their registration history.

To compare cancer and rare diseases registration we focus on population-based registries. We identified the relevant characteristics of population-based registry, we summarized these characteristics for cancer registries (based on our experience and based on the ENCR and IARC guidelines) in a table and we asked to rare diseases expert with experience in rare disease registration to fill in the same table for rare diseases.

The characteristics considered were:

- Definition of cancer/rare disease registration
- Objectives of the registration
- How the registry operates (data sources, methods of data collection, Items of patient information which may be collected by the registry)
- Classification and coding used by the registry
- Cancers/ rare diseases registered
- Quality control procedures
- Epidemiological indicator provided

We involved rare diseases representative from Spain and Italy since these 2 countries have formally established rare diseases registries. We tried to involve also a representative from France but he will never come back to us.

Table 3 reports the comparison between cancer and rare diseases registration.

Table 3. Comparison of cancer and rare diseases registration.

| Cancer registries   | Rare diseases (RD) registries   |  |
|---|---|--|
|   | National RD registry in Italy   | Population and clinical registry in Spain  |
| <p><b>Definition</b><br/>Cancer registration may be defined as the process of continuing, systematic collection of data on the occurrence and characteristics of neoplasms with the purpose to assess and control the impact of malignancies on the community. The cancer registry (CR) is the office or institutions who collect, store, analyse and interpret data on persons with cancer with the purpose to assess and control the impact of malignancies on the community.</p>   | <p><b>Definition</b><br/>The National Registry of Rare Diseases (NRRD) established by Article 3 of DM 279/2001 is, together with the Centers of Regional Rare Diseases (RD) and Regional / Interregional Registries, one of the main nodes of the National Rare Disease Network. It is an important scientific and institutional tool that can provide useful information on health planning, epidemiological surveillance and the improvement of the governance of the Network, both at national and regional level. Data collected by NRRD is one of the criteria for identifying Expertise Centers for the establishment of European reference networks (ERNs)</p> | <p><b>Definition</b><br/>Population-based RD registries are not different from cancer registries. The definition could be the same just changing cancer for rare diseases. For congenital anomalies registries follow the EUROCAT methodology.<br/><br/>Patients RD registries are different but not in terms of definition. They are addressed to collect cases in a systematic way but without a reference population.</p>   |
| <p><b>Objectives</b><br/>Epidemiological surveillance with the estimation of incidence, mortality, survival and prevalence, etiological studies, health care service evaluation.</p>  | <p><b>Objectives</b><br/>Epidemiological surveillance, tool for the identification and evaluation of ERNs.</p>  | <p><b>Objectives</b><br/>For population-based RD: epidemiological surveillance, etiological studies, health care service evaluation, natural history study.<br/>For patients RD registries: etiological studies, health technology assessment, drugs assessment with real world data, and several clinical purposes. Research in general.</p>  |
| <p><b>How the registry operates</b><br/>The population-based CR must collect information on every case of cancer identified within a specified population over a given period of time. This implies that the registry will operate within a defined geographical area, will be able to distinguish between residents of the area and those who have come from outside, register cases of cancer in residents treated outside the area, have sufficient information on each case to avoid registering the same case twice, and have access to an adequate number of sources within the area.<br/>The way in which a CR operates depends, inevitably, on local conditions</p> | <p><b>How the registry operates</b><br/>The flow of data collected by the National Register of Rare Diseases: the accredited centers send data to regional/ interregional registries; these are responsible for submitting to the Rare Diseases National Registry the shared minimum set of data established by the May 2007 Agreement. In view of the fact that the Regions have activated the registers in different ways and times (indeed the last regional register was activated in 2012), the National Registry received data from the entire country only in 2014.</p>  | <p><b>How the registry operates</b><br/>The population-based RD registries collects data on every case of rare diseases identified within a specified population over a given period of time. They distinguish between residents of the area and those who have come from outside. The difference with cancer registries is the object: there are many RD and sometimes it is difficult to recognize an entity as a rare disease (problem between genotypes and phenotypes). Population-based registries have access to medical facilities and they have also access to reliable</p> |

|   |   |  |
|---|---|--|
| <p>and on the material resources available. There must also be a system for reporting clinical and pathological data, and reliable population data should be available.</p> <p>Population figures by sex and five-year age group are required for the registration area and for any subdivisions which the registry might wish to examine. In countries where it is not possible to monitor internal and external migration, estimates of population for intercensal years may be imprecise.</p> <p><b>Data sources</b></p> <ul style="list-style-type: none"> <li>- Medical records department</li> <li>- Outpatient clinics</li> <li>- Private clinics and hospitals</li> <li>- Pathology laboratories</li> <li>- Autopsy services</li> <li>- Haematology laboratories</li> <li>- Radiotherapy department</li> <li>- Other laboratories. A variety of biochemical and immunological tests which are of value in the diagnosis of cancer may be carried out by other laboratory services. They include, for example, serum alphafetoprotein (hepatocellular carcinoma), pattern of plasma proteins (multiple myeloma).</li> <li>- Death certificates</li> <li>- General practitioners</li> <li>- Health insurance (workers' compensation funds, etc.)</li> <li>- Screening program</li> <li>- Administrative data</li> </ul> <p><b>Methods of data collection</b></p> <ul style="list-style-type: none"> <li>- Active. Involves registry personnel actually visiting the sources of data and abstracting the required information</li> <li>- Passive. Relies upon other health care workers to complete notification forms and forward them to the registry, or to send copies of discharge abstracts etc. from which the necessary data can be obtained, and using existing data flows generated for administrative purposes</li> </ul> | <p>According to the DM279 / 2001 the NRRD monitors an updateable list of 283 individual and 47 groups of RD. The new Essential levels of assistance (March 2017), Attached 7, provides for the update of rare diseases of the national health system.</p> <p><b>Data sources</b></p> <p>The regional / interregional registers receive data from the accredited centers and feed the NRRD</p> <p><b>Methods of data collection</b></p> <p>Passive. The regional / interregional registers receive data from the accredited centers and feed the NRRD</p> <p>The methods of collecting and transmitting data by Regions to the NRRD are essentially two :</p> <ul style="list-style-type: none"> <li>- Regions using the ISS software for rare diseases data collection</li> </ul> | <p>population data (for the whole registration area and for subdivisions).</p> <p>The patients RD registries collect data about RD cases but there is not a reference population. But they try don't collect duplicates. This is a problem for international registries without a good personal patient identifier. Usually, they have not data about population.</p> <p><b>Data sources</b></p> <p>Population-based RD registries: medical records, outpatients clinics (primary health care also), private clinics and public hospitals (usually private hospitals have less cases), genetic diagnosis services, hospital pharmacy services (for orphan drugs), other registries (for example renal diseases registries), mortality data (from death certificates), screening programs (metabolic diseases).</p> <p>Patients RD registries: usually direct notification (from the physicians) and, sometimes, also directly from patients. But they can use also data from clinical sources.</p> <p><b>Methods of data collection</b></p> <p>Population-based RD registries<br/>Active and Passive</p> <p>Patients RD registries<br/>Only active: They usually use a standardize report form – SCRF -using a limited list of common data elements plus specialized data elements, which depends on the</p> |
|---|---|--|

|   |   |   |
|---|---|---|
| <ul style="list-style-type: none"> <li>- Mixture of these systems</li> </ul>  | <ul style="list-style-type: none"> <li>- Regions that have their own regional software to collect regional rare diseases data</li> </ul>  | <p>disease. They are focused on details of the clinical features and their evolution and they do not pay attention in getting all cases included, although clinicians think they have all cases</p> <p>General practitioner are not usually engaged in this types of registries and lethal cases are usually lost by the researchers because they do not have access to find this information.</p>  |
| <p><b>Items of patient information which may be collected by CR</b></p> <ul style="list-style-type: none"> <li>- systematic collection of basic variable (Person identification and demographic; Tumor: Incidence date, Most valid basis of diagnosis, Topography (site) Primary tumor, Morphology (histology), Behavior, Source of information)</li> <li>- additional variables (stage, treatment, hospital of diagnosis and treatment)</li> <li>- systematic follow-up to know vital status</li> </ul> <p>Additional clinical variable can be collected ad hoc (high resolution studies)</p>  | <p><b>Items of patient information which may be collected by registries</b></p> <ul style="list-style-type: none"> <li>- systematic collection of basic variable (Person identification and demographic; vital status, rare disease, date of diagnosis, date of certification, date of onset, diagnosis center, taking charge center, orphan drugs.</li> </ul> <p>The data at national level are still not homogeneous, in relation to the collection of diseases, dates, diagnosis centers.</p>  | <p><b>Items of patient information which may be collected by registries</b></p> <p>Population-based RD registries: basic patient information (personal identification and demographic data), data about RD (diagnosis, source of information), additional variables (treatment, centre of diagnosis, affected gene and type), follow-up, vital status, cause of death, additional clinical variable (depending on the diseases).</p> <p>The patients RD registries are more rich on clinical, diagnosis, and treatment variables.</p>   |
| <p><b>Classification and coding</b></p> <p>International classification of diseases for oncology (ICD-O) Quite good classification in agreement with pathologists and used by the expert groups involved in the WHO blue book.</p> <p><b>Cancer registered</b></p> <ul style="list-style-type: none"> <li>- All primary malignant tumours (behaviour=3), including basal cell and squamous cell carcinomas of skin.</li> <li>- Benign tumours of the central nervous system (CNS).</li> <li>- Uncertain behaviour tumours of CNS and urinary bladder.</li> <li>- In situ tumours: breast, cervix, colon, rectum, urinary bladder and melanoma of the skin.</li> </ul> | <p><b>Classification and coding</b></p> <p>Exemption code (external classification), ICD-9(internal classification), Orphacode (internal classification).</p> <p><b>Diseases registered (are rare cancers registered too? If yes, please list which cancers are included in the registry)</b></p> <p>Into the new LEA (March 2017), there is an entire chapter dedicated to tumors, among which :</p> <p>Wilms tumor, retinoblastoma, Cronkhite-Canada syndrome Gardner-Diamond syndrome, Familial polyposis, Lymphangioliomyomatosis, Gorlin syndrome, Neurofibromatosis, Carney complex, Familial melanoma, Lynch syndrome.</p> | <p><b>Classification and coding</b></p> <p>The RD registries uses: ICD (9 or 10), ORPHA numbers, SNOMEDT- CT codes, or specifics classifications like ICD-BPA (for congenital anomalies), ERA-EDTA codes (for renal diseases), OMIM (for genetics)</p> <p><b>Diseases registered (are rare cancers registered too? If yes, please list which cancers are included in the registry)</b></p> <p>This is the clue point. There are many RD. RD registries have difficulties to collect data for all RD. Usually they are working with lists of RD based on classifications (ICD or ORPHA). Spanish RD registries are not working with rare cancers because it exists cancer registries working on them. But several Spanish regions without cancer registry are collecting rare cancer data.</p> |

|  |  |   |
|--|--|---|
| <p><b>Quality and quality control</b><br/> Long history of coordination and standardization, WHO (IARC)<br/> Rules and documentation defined internationally and continuously updated by the IARC and in Europe by the ENCR + national association</p> <p><b>ENCR: proposal on cancer data quality checks: one common procedure for European cancer registries</b></p> <ul style="list-style-type: none"> <li>- Consistency within variables</li> <li>- Consistency between variables</li> <li>- Unlikely and rare combinations of age and tumour type</li> <li>- Invalid sex and topography combinations</li> <li>- Unlikely sex and morphology combinations</li> <li>- Valid combinations for behaviour and topography/morphology</li> <li>- Valid combinations for morphology and grade</li> <li>- Morphology code and description, and correct associated grade for ICD-O-3 terms with implied statement of grade</li> <li>- Morphology codes and allowed/refused topography codes</li> <li>- Specific checks for survival analysis</li> <li>- Additional checks on the extent of the disease</li> <li>- Valid values for T, N, M and stage by cancer topography and TNM edition</li> <li>-</li> </ul> | <p><b>Quality and quality control</b><br/> Once the data are received by the regions, a quality control procedure is started, managed directly by the NRRD operators.</p> <p>Data control is performed for all data on:</p> <ol style="list-style-type: none"> <li>2. National univocal identification of the patient</li> <li>3. Date of birth</li> <li>4. Municipality / province / region of birth</li> <li>5. Municipality / province / region of residence of the patient</li> <li>6. Living-dead status and date of death</li> <li>7. Diagnosis of the disease (defined on the basis of the exemption code of Ministerial Decree 279/2001</li> <li>8. Region, institution, structure (standard national codes) that take charge and that have made the diagnosis</li> <li>9. Municipality / province / region of accredited centers</li> <li>10. Municipality / province / region of the diagnosis body</li> <li>11. Date of diagnosis</li> <li>12. Date of certification</li> <li>13. Date of onset</li> <li>14. Orphaned drug</li> </ol> | <p><b>Quality and quality control</b><br/> RD registries are relatively young. It doesn't exist any institution similar to IARC. And they are not rules about quality control accepted in a general way. They are some important projects working on that (EpiRare or EUCERD for example) and some indications about data elements or personal identifiers have been done. The Joint Research Centre (JRC) have the European RD platform but nowadays they are working just on cerebral palsy and congenital anomalies. For the last case, EUROCAT have quality controls and the registries affiliated follow them (in Spain they are two regional registries full members of EUROCAT and two others are associated members).</p> <p>RD registries follow similar rules for consistency between variables as cancer registries.</p> |
| <p><b>Epidemiological indicator provided by registries</b></p> <ul style="list-style-type: none"> <li>- Incidence</li> <li>- Prevalence (observed and complete)</li> <li>- Mortality</li> <li>- Survival</li> <li>- Time trends of all the above indicators</li> <li>- Proportion of cured</li> <li>- Standardized Incidence Ratios (SIR)</li> <li>- International comparative studies (CI5C, CONCORD, EUROCARE, RARECARE)</li> </ul>  | <p><b>Epidemiological indicator provided by registries</b></p> <ul style="list-style-type: none"> <li>- Incidence</li> <li>- Prevalence</li> <li>- Health migration</li> <li>- Analysis of age at onset, diagnosis, and diagnostic delay of rare diseases</li> </ul>   | <p><b>Epidemiological indicator provided by registries</b><br/> Population-based registries included: incidence, prevalence, mortality, standardized incidence or mortality ratios. Survival is also possible but it is not usual nowadays to work on it.</p> <p>Patients registries provides data on clinical features.</p>  |

## Population based registries

In general population-based registries are more common for cancers than for RD because of the different history, long-lasting experience in cancers vs rare diseases. Standardization is assured by the IARC and comparative cancers survival studies.

### Similarities between population based RD and cancer registries

- Definition based on a geographical area
- Objectives
- Basic variables collected
- Data sources (with different related to the characteristic of the disease (e.g. pathological lab for cancers, genetic lab for rare diseases, cancer screening for cancers, metabolic screening for rare diseases, etc)
- Methods of data collection
- Indicators provided

### Differences between population based RD and cancer registries

- Classification and coding  
(ICD, ICD-O3 and WHO blue book for cancers vs ICD, ORPHA numbers, SNOMED-CT codes, or specific classifications like ICD-BPA (for congenital anomalies), ERA-EDTA codes (for renal diseases), OMIM (for genetics)). Thus RD registries have a higher heterogeneity in the codes used
- Diseases registered  
RD registries have difficulties to collect data for all RD. Usually they are working with lists of RD based on classifications (ICD or ORPHA) whereas cancer registries collect data on all cancers recognised by the WHO blue book). In different countries the RD registries might register only some RD whereas cancer registries collect always all cancers. In countries/areas without cancer registries, RD registries could collect information also on cancers. The definition of rare cancer is different from that of rare disease, so rare cancers included in rare diseases list may be different.
- Quality control  
Much more standardised and internationally agreed on for cancers vs RD. For cancers there is a large experience in international comparison studies for incidence and survival. Ascertainment of completeness of incidence data assessed for cancer registries (definition of indicators of completeness. like the % of the deaths certificate only, etc)
- Rare diseases are defined by prevalence, while rare cancers are defined by incidence
- Centralization of the data for comparative studies is frequently organised for cancers, while is less developed for rare diseases, apart EUROCAT for congenital anomalies.

### The way forward

In the framework of the JARC a meeting will be organised in collaboration with the Joint Research Centre. At the meeting will be invited the representatives of the European Network of Cancer Registries, Orphanet, rare diseases population-based representatives, epidemiologists and pathologists. The objectives will be to discuss the classification of cancers and rare diseases, the updates of the list of rare cancers and the updates of the Orphanet list of rare cancers, the epidemiological indicators produced by cancer registries vs those produced by the rare diseases registries and those provided by Orphanet.

Rare cancers are those with incidence < 6/100,000

Orpha  
number/comments

| C = common R = rare | Tier | Tumour   | Rate            | Patients      | Topography code                   | Morphology code  |
|---------------------|------|--|-----------------|---------------|-----------------------------------|--|
|                     | 1    | <b>EPITHELIAL TUMOURS OF NASAL CAVITY AND SINUSES</b>                              | <b>0.44</b>     | <b>3,555</b>  | C30.0, C31                        | 8000, 8001, 8004, 8010, 8011, 8020-8078  |
| R                   | 2    | <b>Squamous cell carcinoma with variants of nasal cavity and sinuses</b>           | <b>0.31</b>     | <b>2,498</b>  | C30.0, C31                        | 8004, 8032, 8050-8076, 8078, 8083-8092   |
|                     | 3    | Squamous carcinoma   | 0.24            | 1,913         | C30.0, C31                        | 8070   |
|                     | 3    | Verrucous carcinoma  | <0.01           | 38            | C30.0, C31                        | 8051   |
|                     | 3    | Squamous cell carcinoma spindle cell   | <0.01           | 31            | C30.0, C31                        | 8004, 8032, 8074, 8980   |
|                     | 3    | Papillary squamous cell carcinoma  | <0.01           | 10            | C30.0, C31                        | 8052   |
|                     | 3    | Adenosquamous carcinoma  | <0.01           | 18            | C30.0, C31                        | 8560   |
|                     | 3    | Squamous cell carcinoma, adenoid   | <0.01           | 3             | C30.0, C31                        | 8075   |
|                     | 3    | Basaloid squamous cell carcinoma   | <0.01           | 5             | C30.0, C31                        | 8083   |
| R                   | 2    | <b>Lymphoepithelial carcinoma of nasal cavity and sinuses</b>                      | <b>&lt;0.01</b> | <b>19</b>     | C30.0, C31                        | 8082   |
| R                   | 2    | <b>Undifferentiated carcinoma of nasal cavity and sinuses</b>                      | <b>0.02</b>     | <b>139</b>    | C30.0, C31                        | 8020-8022  |
| R                   | 2    | <b>Intestinal type adenocarcinoma of nasal cavity and sinuses</b>                  | <b>&lt;0.01</b> | <b>20</b>     | C30.0, C31                        | 8144   |
|                     | 1    | <b>EPITHELIAL TUMOURS OF NASOPHARYNX</b>   | <b>0.44</b>     | <b>3,566</b>  | C11                               | 8000-8001, 8004, 8010-8011, 8020-8076  |
| R                   | 2    | <b>Squamous cell carcinoma with variants of nasopharynx</b>                        | <b>0.33</b>     | <b>2,630</b>  | C11                               | 8004, 8020-8022, 8032, 8051-8076   |
|                     | 3    | Squamous carcinoma   | 0.16            | 1,294         | C11                               | 8070   |
|                     | 3    | Squamous cell carcinoma nonkeratinizing, NOS                                       | 0.02            | 173           | C11                               | 8072   |
|                     | 3    | Squamous cell carcinoma keratinizing, NOS  | 0.02            | 139           | C11                               | 8071   |
|                     | 3    | Papillary squamous cell carcinoma  | <0.01           | 7             | C11                               | 8052   |
|                     | 3    | Basaloid squamous cell carcinoma   | NE              | 0             | C11                               | 8083   |
|                     | 3    | Squamous cell carcinoma, adenoid   | <0.01           | 1             | C11                               | 8075   |
|                     | 3    | Lymphoepithelial carcinoma   | 0.06            | 494           | C11                               | 8082   |
|                     | 3    | Undifferentiated carcinoma   | 0.06            | 497           | C11                               | 8020-8022  |
| R                   | 2    | <b>Papillary adenocarcinoma of nasopharynx</b>                                     | <b>&lt;0.01</b> | <b>7</b>      | C11                               | 8050, 8260   |
|                     | 1    | <b>EPITHELIAL TUMOURS OF MAJOR SALIVARY GLANDS AND SALIVARY-GLAND TYPE TUMOURS</b> | <b>1.31</b>     | <b>10,514</b> | C00-C14, C30.0, C31, C32          | (For C00-C14, C30.0, C31, C32)<br>8140, 8147, 8200, 8290, 8310, 8430, 8440, 8450, 8480, 8500, 8525, 8550, 8562, 8941, 8982 |
| R                   | 2    | <b>Epithelial tumours of major salivary glands</b>                                 | <b>0.73</b>     | <b>5,861</b>  | C7, C8                            | 8004, 8012, 8020-8022, 8032, 8050-8078   |
|                     | 3    | Squamous carcinoma   | 0.12            | 965           | C7, C8                            | 8070   |
|                     | 3    | Large cell carcinoma   | 0.01            | 38            | C7, C8                            | 8012   |
|                     | 3    | Lymphoepithelial carcinoma   | <0.01           | 21            | C7, C8                            | 8082   |
|                     | 3    | Carcinosarcoma, NOS  | <0.01           | 30            | C7, C8                            | 8004, 8032, 8074, 8980   |
|                     | 3    | Adenocarcinoma NOS   | 0.14            | 1,128         | C7, C8                            | 8140   |
|                     | 3    | Clear cell adenocarcinoma, NOS   | <0.01           | 21            | C7, C8                            | 8310   |
|                     | 3    | Mucinous adenocarcinoma  | <0.01           | 27            | C7, C8                            | 8480   |
|                     | 3    | Ductal carcinoma   | 0.01            | 92            | C7, C8                            | 8500   |
|                     | 3    | Oxyphilic adenocarcinoma   | <0.01           | 28            | C7, C8                            | 8290   |
|                     | 3    | Papillary cystadenocarcinoma, NOS  | <0.01           | 4             | C7, C8                            | 8450   |
|                     | 3    | Adenoid cystic carcinoma   | 0.12            | 956           | C7, C8                            | 8200   |
|                     | 3    | Mucoepidermoid carcinoma   | 0.12            | 927           | C7, C8                            | 8430   |
|                     | 3    | Acinic cell adenocarcinoma   | 0.09            | 701           | C7, C8                            | 8550   |
|                     | 3    | Malignant myoepithelioma   | <0.01           | 15            | C7, C8                            | 8982   |
|                     | 3    | Carcinoma in pleomorphic adenoma   | 0.02            | 159           | C7, C8                            | 8941   |
|                     | 3    | Polymorphous low grade adenocarcinoma  | <0.01           | 2             | C7, C8                            | 8525   |
|                     | 3    | Basal cell adenocarcinoma  | 0.01            | 55            | C7, C8                            | 8147   |
|                     | 3    | Epithelial-myoepithelial carcinoma   | 0.02            | 140           | C7, C8                            | 8562   |
|                     | 3    | Sebaceous adenocarcinoma   | NE              | 0             | C7, C8                            | 8410   |
|                     | 3    | Cystadenocarcinoma, NOS  | <0.01           | 35            | C7, C8                            | 8440   |
|                     | 3    | Low grade cribriform cystadenocarcinoma  | NE              | 0             | C7, C8                            | malignancy without ICD-O   |
| R                   | 2    | <b>Salivary gland type tumours of head and neck</b>                                | <b>0.43</b>     | <b>3,451</b>  | C00-C06, C09-C14, C30.0, C31, C32 | 8140, 8147, 8200, 8290, 8310, 8430, 8440, 8450, 8480, 8500, 8525, 8550, 8562, 8941, 8982                                   |
|                     | 3    | Mucoepidermoid carcinoma   | 0.09            | 706           | C00-C06, C09-C14, C30.0, C31, C32 | 8430   |
|                     | 3    | Adenocarcinoma NOS   | 0.18            | 1,436         | C00-C06, C09-C14, C30.0, C31, C32 | 8140   |
|                     | 3    | Adenoid cystic carcinoma   | 0.12            | 962           | C00-C06, C09-C14, C30.0, C31, C32 | 8200   |
|                     | 3    | Acinic cell adenocarcinoma   | 0.01            | 87            | C00-C06, C09-C14, C30.0, C31, C32 | 8550   |

RARECAREnet replies to Orphanet



|          |   |   |             |               |  |  |
|----------|---|---|-------------|---------------|--|--|
|          | 3 | Ductal carcinoma  | <0.01       | 4             | C00-C06,<br>C09-C14,<br>C30.0,<br>C31, C32 | 8500   |
|          | 3 | Mucinous adenocarcinoma                                     | 0.01        | 114           | C00-C06,<br>C09-C14,<br>C30.0,<br>C31, C32 | 8480   |
|          | 3 | Basal cell adenocarcinoma                                   | <0.01       | 26            | C00-C06,<br>C09-C14,<br>C30.0,<br>C31, C32 | 8147   |
|          | 3 | Clear cell adenocarcinoma, NOS                              | 0.01        | 44            | C00-C06,<br>C09-C14,<br>C30.0,<br>C31, C32 | 8310   |
|          | 3 | Epithelial-myoepithelial carcinoma                          | <0.01       | 15            | C00-C06,<br>C09-C14,<br>C30.0,<br>C31, C32 | 8562   |
|          | 3 | Polymorphous low grade adenocarcinoma                       | <0.01       | 7             | C00-C06,<br>C09-C14,<br>C30.0,<br>C31, C32 | 8525   |
|          | 3 | Carcinoma in pleomorphic adenoma                            | <0.01       | 17            | C00-C06,<br>C09-C14,<br>C30.0,<br>C31, C32 | 8941   |
|          | 3 | Malignant myoepithelioma                                    | <0.01       | 6             | C00-C06,<br>C09-C14,<br>C30.0,<br>C31, C32 | 8982   |
|          | 3 | Cystadenocarcinoma, NOS                                     | <0.01       | 22            | C00-C06,<br>C09-C14,<br>C30.0,<br>C31, C32 | 8440   |
|          | 3 | Oncocytic carcinoma   | <0.01       | 5             | C00-C06,<br>C09-C14,<br>C30.0,<br>C31, C32 | 8290   |
|          | 3 | Papillary cystadenocarcinoma, NOS                           | NE          | 0             | C00-C06,<br>C09-C14,<br>C30.0,<br>C31, C32 | 8450   |
|          | 1 | <b>EPITHELIAL TUMOURS OF HYPOPHARYNX AND LARYNX</b>         | <b>6.26</b> | <b>50,360</b> | C12, C13,<br>C32                           | 8000-8001, 8004, 8010-8011, 8020-8022, 8031-8032, 8050-8076, 8078. |
| <b>R</b> | 2 | <b>Squamous cell carcinoma with variants of hypopharynx</b> | <b>1.19</b> | <b>9,550</b>  | C12, C13                                   | 8004, 8020-8022, 8031-8032, 8050-                                  |
|          | 3 | Squamous carcinoma  | 0.88        | 7,104         | C12, C13                                   | 8070   |
|          | 3 | Lymphoepithelial carcinoma                                  | <0.01       | 29            | C12, C13                                   | 8082   |
|          | 3 | Verrucous carcinoma   | <0.01       | 10            | C12, C13                                   | 8051   |
|          | 3 | Squamous cell carcinoma spindle cell                        | <0.01       | 23            | C12, C13                                   | 8004, 8032, 8074, 8980   |
|          | 3 | Giant cell carcinoma  | NE          | 0             | C12, C13                                   | 8031   |
|          | 3 | Adenosquamous carcinoma                                     | <0.01       | 14            | C12, C13                                   | 8560   |
|          | 3 | Squamous cell carcinoma, adenoid                            | <0.01       | 3             | C12, C13                                   | 8075   |
|          | 3 | Undifferentiated carcinoma                                  | 0.01        | 82            | C12, C13                                   | 8020-8022  |
|          | 3 | Papillary squamous cell carcinoma                           | <0.01       | 11            | C12, C13                                   | 8052   |
|          | 3 | Basaloid squamous cell carcinoma                            | <0.01       | 5             | C12, C13                                   | 8083   |
| <b>R</b> | 2 | <b>Squamous cell carcinoma with variants of larynx</b>      | <b>4.64</b> | <b>37,330</b> | C32  | 8004, 8020-8022, 8031-8032, 8050-                                  |
|          | 3 | Squamous carcinoma  | 3.56        | 28,621        | C32  | 8070   |
|          | 3 | Verrucous carcinoma   | 0.05        | 388           | C32  | 8051   |
|          | 3 | Squamous cell carcinoma spindle cell                        | 0.02        | 188           | C32  | 8004, 8074, 8032, 8980   |
|          | 3 | Papillary squamous cell carcinoma                           | 0.01        | 50            | C32  | 8052   |
|          | 3 | Adenosquamous carcinoma                                     | 0.01        | 41            | C32  | 8560   |
|          | 3 | Squamous cell carcinoma, adenoid                            | <0.01       | 10            | C32  | 8075   |
|          | 3 | Undifferentiated carcinoma                                  | 0.01        | 104           | C32  | 8020-8022  |
|          | 3 | Lymphoepithelial carcinoma                                  | <0.01       | 10            | C32  | 8082   |
|          | 3 | Giant cell carcinoma  | NE          | 0             | C32  | 8031   |
|          | 3 | Basaloid squamous cell carcinoma                            | <0.01       | 5             | C32  | 8083   |

|   |   |   |       |        |  |   |
|---|---|---|-------|--------|--|---|
|   | 1 | <b>EPITHELIAL TUMOURS OF OROPHARYNX</b>             | 2.75  | 22,104 | C01.9,<br>C02.4,<br>C02.8,<br>C05.1-<br>C05.2,<br>C05.9,<br>C09.0-<br>C10.3,<br>C10.8-10.9,<br>C14.2 | 8000-8001, 8004, 8010-8011, 8020-8022, 8032, 8050-8076, 8078, 8082-8084, 8123, 8560, 8980 |
| R | 2 | Squamous cell carcinoma with variants of oropharynx | 2.58  | 20,795 | C01.9,<br>C02.4,<br>C02.8,<br>C05.1-<br>C05.2,<br>C05.9,<br>C09.0-<br>C10.3,<br>C10.8-10.9,<br>C14.2 | 8004, 8020-8022, 8032, 8050-8076, 8078, 8082-8084, 8123, 8560, 8980                       |
|   | 3 | Squamous carcinoma                                  | 1.91  | 15,351 | C01.9,<br>C02.4,<br>C02.8,<br>C05.1-<br>C05.2,<br>C05.9,<br>C09.0-<br>C10.3,<br>C10.8-10.9,<br>C14.2 | 8070  |
|   | 3 | Lymphoepithelial carcinoma                          | 0.01  | 85     | C01.9,<br>C02.4,<br>C02.8,<br>C05.1-<br>C05.2,<br>C05.9,<br>C09.0-<br>C10.3,<br>C10.8-10.9,<br>C14.2 | 8082  |
|   | 3 | Verrucous carcinoma                                 | 0.01  | 54     | C01.9,<br>C02.4,<br>C02.8,<br>C05.1-<br>C05.2,<br>C05.9,<br>C09.0-<br>C10.3,<br>C10.8-10.9,<br>C14.2 | 8051  |
|   | 3 | Squamous cell carcinoma spindle cell                | <0.01 | 37     | C01.9,<br>C02.4,<br>C02.8,<br>C05.1-<br>C05.2,<br>C05.9,<br>C09.0-<br>C10.3,<br>C10.8-10.9,<br>C14.2 | 8004, 8032, 8074, 8980  |

|          |   |   |             |               |  |   |
|----------|---|---|-------------|---------------|--|---|
|          | 3 | Papillary squamous cell carcinoma                           | <0.01       | 29            | C01.9,<br>C02.4,<br>C02.8,<br>C05.1-<br>C05.2,<br>C05.9,<br>C09.0-<br>C10.3,<br>C10.8-10.9,<br>C14.2 | 8052  |
|          | 3 | Squamous cell carcinoma, adenoid                            | <0.01       | 8             | C01.9,<br>C02.4,<br>C02.8,<br>C05.1-<br>C05.2,<br>C05.9,<br>C09.0-<br>C10.3,<br>C10.8-10.9,<br>C14.2 | 8075  |
|          | 3 | Basaloid squamous cell carcinoma                            | <0.01       | 8             | C01.9,<br>C02.4,<br>C02.8,<br>C05.1-<br>C05.2,<br>C05.9,<br>C09.0-<br>C10.3,<br>C10.8-10.9,<br>C14.2 | 8083  |
|          | 3 | Adenosquamous carcinoma                                     | <0.01       | 37            | C01.9,<br>C02.4,<br>C02.8,<br>C05.1-<br>C05.2,<br>C05.9,<br>C09.0-<br>C10.3,<br>C10.8-10.9,<br>C14.2 | 8560  |
|          | 3 | Undifferentiated carcinoma                                  | 0.02        | 166           | C01.9,<br>C02.4,<br>C02.8,<br>C05.1-<br>C05.2,<br>C05.9,<br>C09.0-<br>C10.3,<br>C10.8-10.9,<br>C14.2 | 8020-8022   |
|          | 1 | <b>EPITHELIAL TUMOURS OF ORAL CAVITY AND LIP</b>            | <b>4.79</b> | <b>38,537</b> | C00.0-<br>C00.9<br>C02.0-<br>C02.3,<br>C02.9,<br>C03.0-<br>C05.0,<br>C06.0-<br>C06.9                 | 8000-8001, 8004, 8010-8011, 8020-<br>8022, 8032, 8050-8076, 8078, 8082-<br>8084, 8123, 8560, 8980 |
| <b>R</b> | 2 | <b>Squamous cell carcinoma with variants of oral cavity</b> | <b>3.28</b> | <b>26,422</b> | C02.0-<br>C02.3,<br>C02.9,<br>C03.0-<br>C05.0,<br>C06.0-<br>C06.9                                    | 8004, 8020-8022, 8032, 8050-8076,<br>8078, 8082-8084, 8123, 8560, 8980                            |

|             |   |   |       |        |   |  |
|-------------|---|---|-------|--------|---|--|
|             | 3 | Squamous carcinoma                                    | 2.42  | 19,496 | C02.0-<br>C02.3,<br>C02.9,<br>C03.0-<br>C05.0,<br>C06.0-<br>C06.9 | 8070   |
|             | 3 | Verrucous carcinoma                                   | 0.06  | 445    | C02.0-<br>C02.3,<br>C02.9,<br>C03.0-<br>C05.0,<br>C06.0-<br>C06.9 | 8051   |
|             | 3 | Squamous cell carcinoma spindle cell                  | 0.01  | 69     | C02.0-<br>C02.3,<br>C02.9,<br>C03.0-<br>C05.0,<br>C06.0-<br>C06.9 | 8004, 8032, 8074, 8980                             |
|             | 3 | Adenosquamous carcinoma                               | <0.01 | 39     | C02.0-<br>C02.3,<br>C02.9,<br>C03.0-<br>C05.0,<br>C06.0-<br>C06.9 | 8560   |
|             | 3 | Papillary squamous cell carcinoma                     | <0.01 | 25     | C02.0-<br>C02.3,<br>C02.9,<br>C03.0-<br>C05.0,<br>C06.0-<br>C06.9 | 8052   |
|             | 3 | Squamous cell carcinoma, adenoid                      | <0.01 | 4      | C02.0-<br>C02.3,<br>C02.9,<br>C03.0-<br>C05.0,<br>C06.0-<br>C06.9 | 8075   |
|             | 3 | Basaloid squamous cell carcinoma                      | <0.01 | 6      | C02.0-<br>C02.3,<br>C02.9,<br>C03.0-<br>C05.0,<br>C06.0-<br>C06.9 | 8083   |
|             | 3 | Lymphoepithelial carcinoma                            | <0.01 | 9      | C02.0-<br>C02.3,<br>C02.9,<br>C03.0-<br>C05.0,<br>C06.0-<br>C06.9 | 8082   |
|             | 3 | Undifferentiated carcinoma                            | 0.01  | 96     | C02.0-<br>C02.3,<br>C02.9,<br>C03.0-<br>C05.0,<br>C06.0-<br>C06.9 | 8020-8022  |
| R           | 2 | Squamous cell carcinoma with variants of lip          | 1.22  | 9,854  | C00.0-<br>C00.9   | 8004, 8032, 8050-8076, 8078, 8082-8084, 8560, 8980 |
|             | 3 | Squamous carcinoma                                    | 0.98  | 7,946  | C00.0-<br>C00.9   | 8070   |
| ORPHA314425 |   | Odontogenic and maxillofacial bone tumor to be added? |       |        |   |  |
| ORPHA314422 |   | Ameloblastic carcinoma                                |       |        |   |  |
|             | 1 | EPITHELIAL TUMOURS OF OESOPHAGUS                      | 7.51  | 60,454 | C15   | 8000-8001, 8004, 8010-8011, 8020-                  |
| R           | 2 | Squamous cell carcinoma with variants of oesophagus   | 3.40  | 27,376 | C15   | 8004, 8032, 8050-8076, 8078, 8082-                 |

It is already in our list please refer to odontogenic tumors row 632 in the new list included in the e-mail. I am sorry but you worked on the old list of rare cancers. It includes also the ameloblastic ICD-O3 9270. Please refer to row 632 of the RARECAREnet list

|   |    |   |              |                |          |                                    |
|---|----|---|--------------|----------------|----------|------------------------------------|
|   | 3  | Squamous carcinoma  | 2.85         | 22,947         | C15      | 8070                               |
|   | 3  | Adenosquamous carcinoma   | 0.04         | 319            | C15      | 8560                               |
|   | 3  | Squamous cell carcinoma spindle cell                            | 0.01         | 90             | C15      | 8004, 8032, 8074, 8980             |
|   | 3  | Verrucous carcinoma   | <0.01        | 15             | C15      | 8051                               |
|   | 3  | Papillary squamous cell carcinoma                               | <0.01        | 6              | C15      | 8052                               |
|   | 3  | Basaloid squamous cell carcinoma                                | <0.01        | 6              | C15      | 8083                               |
|   | 3  | Squamous cell carcinoma, adenoid                                | <0.01        | 5              | C15      | 8075                               |
| R   | 2  | <b>Adenocarcinoma with variants of oesophagus</b>               | <b>2.85</b>  | <b>22,936</b>  | C15      | 8140-8141, 8143, 8147, 8190, 8201, |
| R   | 2  | <b>Salivary gland type tumours of oesophagus</b>                | <b>0.01</b>  | <b>47</b>      | C15      | 8200, 8430, 8550, 8562             |
|   | 3  | Mucoepidermoid carcinoma  | <0.01        | 24             | C15      | 8430                               |
|   | 3  | Adenoid cystic carcinoma  | <0.01        | 12             | C15      | 8200                               |
| R   | 2  | <b>Undifferentiated carcinoma of oesophagus</b>                 | <b>0.07</b>  | <b>593</b>     | C15      | 8020-8022                          |
|   | 1  | <b>EPITHELIAL TUMOURS OF STOMACH</b>                            | <b>18.62</b> | <b>149,842</b> | C16      | 8000-8001, 8004, 8010-8011, 8020-  |
| C   | 2  | <b>Adenocarcinoma with variants of stomach</b>                  | <b>15.23</b> | <b>122,547</b> | C16      | 8050, 8140-8145, 8147, 8190, 8201, |
|   | 3  | Adenocarcinoma NOS  | 9.78         | 78,649         | C16      | 8140                               |
|   | 3  | Adenocarcinoma intestinal type                                  | 1.75         | 14,113         | C16      | 8144                               |
|   | 3  | Signet ring cell carcinoma                                      | 1.62         | 13,047         | C16      | 8490                               |
|   | 3  | Carcinoma diffuse type  | 0.66         | 5,311          | C16      | 8145                               |
|   | 3  | Mucinous adenocarcinoma   | 0.38         | 3,088          | C16      | 8480                               |
|   | 3  | Tubular adenocarcinoma  | 0.39         | 3,140          | C16      | 8211                               |
|   | 3  | Papillary adenocarcinoma, NOS                                   | 0.06         | 506            | C16      | 8050, 8260                         |
|   | 3  | Adenosquamous carcinoma   | 0.03         | 205            | C16      | 8560                               |
| R   | 2  | <b>Squamous cell carcinoma with variants of stomach</b>         | <b>0.13</b>  | <b>1,044</b>   | C16      | 8004, 8032, 8051-8076, 8078, 8082- |
|   | 3  | Squamous carcinoma  | 0.10         | 833            | C16      | 8070                               |
|   | 3  | Squamous cell carcinoma spindle cell                            | 0.01         | 72             | C16      | 8004, 8032, 8074, 8980             |
|   | 3  | Basaloid carcinoma  | <0.01        | 1              | C16      | 8083                               |
|   | 3  | Verrucous carcinoma   | <0.01        | 1              | C16      | 8051                               |
|   | 3  | Squamous cell carcinoma, adenoid                                | <0.01        | 1              | C16      | 8075                               |
|   | 3  | Papillary squamous cell carcinoma                               | NE           | 0              | C16      | 8052                               |
| R   | 2  | <b>Salivary gland-type tumours of stomach</b>                   | <b>0.01</b>  | <b>41</b>      | C16      | 8200, 8430                         |
|   | 3  | Mucoepidermoid carcinoma  | <0.01        | 13             | C16      | 8430                               |
|   | 3  | Adenoid cystic carcinoma  | <0.01        | 28             | C16      | 8200                               |
| R   | 2  | <b>Undifferentiated carcinoma of stomach</b>                    | <b>0.17</b>  | <b>1,355</b>   | C16      | 8020-8022                          |
| ORPHA36273;<br>Missing? Specific<br>presentation of diffuse<br>carcinoma.<br>ORPHA313920;<br>Missing? PMID:<br>22392024 | 2? | Gastric linitis plastica  |              |                |          |                                    |
|   |    | Epstein-Barr virus-associated gastric carcinoma                 |              |                |          |                                    |
|   | 2? |   |              |                |          |                                    |
|   | 1  | <b>EPITHELIAL TUMOURS OF SMALL INTESTINE</b>                    | <b>0.72</b>  | <b>5,815</b>   | C17      | 8000-8001, 8004, 8010-8011, 8020-  |
|   | 1  | <b>EPITHELIAL TUMOURS OF SMALL INTESTINE</b>                    |              |                |          |                                    |
| R   | 2  | <b>Adenocarcinoma with variants of small intestine</b>          | <b>0.57</b>  | <b>4,566</b>   | C17      | 8020-8022, 8140-8141, 8143, 8147,  |
|   | 3  | Adenocarcinoma NOS  | 0.47         | 3,756          | C17      | 8140                               |
|   | 3  | Mucinous adenocarcinoma   | 0.02         | 197            | C17      | 8480                               |
|   | 3  | Signet ring cell carcinoma                                      | 0.01         | 82             | C17      | 8490                               |
|   | 3  | Adenosquamous carcinoma   | <0.01        | 6              | C17      | 8560                               |
|   | 3  | Medullary carcinoma, NOS  | NE           | 0              | C17      | 8510                               |
|   | 3  | Undifferentiated carcinoma                                      | 0.01         | 89             | C17      | 8020-8022                          |
| R   | 2  | <b>Squamous cell carcinoma with variants of small intestine</b> | <b>0.01</b>  | <b>49</b>      | C17      | 8004, 8032, 8050-8076, 8078, 8082- |
|   | 3  | Squamous carcinoma  | <0.01        | 11             | C17      | 8070                               |
|   | 1  | <b>EPITHELIAL TUMOURS OF COLON</b>                              | <b>42.64</b> | <b>343,019</b> | C18, C19 | 8000- 8001, 8004, 8010-8011, 8020- |
| C   | 2  | <b>Adenocarcinoma with variants of colon</b>                    | <b>37.21</b> | <b>299,351</b> | C18, C19 | 8020-8022, 8140-8141, 8143, 8147,  |
|   | 3  | Adenocarcinoma NOS  | 29.96        | 241,044        | C18, C19 | 8140                               |
|   | 3  | Mucinous adenocarcinoma   | 2.23         | 17,949         | C18, C19 | 8480                               |
|   | 3  | Signet ring cell carcinoma                                      | 0.21         | 1,711          | C18, C19 | 8490                               |
|   | 3  | Adenosquamous carcinoma   | 0.02         | 136            | C18, C19 | 8560                               |
|   | 3  | Undifferentiated carcinoma                                      | 0.07         | 541            | C18, C19 | 8020-8022                          |
|   | 3  | Medullary carcinoma, NOS  | <0.01        | 7              | C18, C19 | 8510                               |
| R   | 2  | <b>Squamous cell carcinoma with variants of colon</b>           | <b>0.02</b>  | <b>169</b>     | C18, C19 | 8004, 8032, 8050-8076, 8078, 8082- |
|   | 1  | <b>EPITHELIAL TUMOURS OF RECTUM</b>                             | <b>17.11</b> | <b>137,686</b> | C20      | 8000-8001, 8004, 8010-8011, 8020-  |
| C   | 2  | <b>Adenocarcinoma with variants of rectum</b>                   | <b>15.52</b> | <b>124,864</b> | C20      | 8020-8022, 8140-8141, 8143, 8147,  |
|   | 3  | Adenocarcinoma NOS  | 12.81        | 103,023        | C20      | 8140                               |
|   | 3  | Mucinous adenocarcinoma   | 0.55         | 4,429          | C20      | 8480                               |
|   | 3  | Signet ring cell carcinoma                                      | 0.06         | 444            | C20      | 8490                               |
|   | 3  | Adenosquamous carcinoma   | 0.01         | 68             | C20      | 8560                               |
|   | 3  | Undifferentiated carcinoma                                      | 0.02         | 158            | C20      | 8020-8022                          |
|   | 3  | Medullary carcinoma, NOS  | <0.01        | 2              | C20      | 8510                               |
| R   | 2  | <b>Squamous cell carcinoma with variants of rectum</b>          | <b>0.07</b>  | <b>595</b>     | C20      | 8004, 8032, 8050-8076, 8078, 8082- |
|   | 3  | Verrucous carcinoma   | <0.01        | 5              | C20      | 8051                               |

ICD-O3 8142 it is included in the group of adk that clarifies from 8140 to 8145 thus also 8142. if you wish we can add a tier 3 under the tier 2 to show Iso the linitis plastica. However, it is not missing

we do not differentiate the cancer on the basis of the etiology. It is anyway a gastric carcinoma that will be treated by oncologist knowing whether there are differences. For oropharinx cancers the WHO has created codes for HPV+ and HPV- oropharinx cancers and we are including them in the list. in the WHO blu book we do not see a code for this entry. doyou? in case would you please let us noe the code?

|  |   |   |   |          |   |                                    |  |
|--|---|---|---|----------|---|------------------------------------|--|
| Comment: is it really tier 2 or should it be tier 3? See PMID: 26157950, <a href="https://www.google.fr/url?sa=t&amp;rct=j&amp;q=&amp;esrc=s&amp;source=web&amp;cd=1&amp;cad=rja&amp;uact=8&amp;ved=0ahUKEwj-9s-85OPWAhVG0hoKHSZMBpsQFggsMAA&amp;url=http%3A%2F%2Fwww.journalmc.org%2Findex.php%2FJMC%2Farticle%2Fdownload%2F1456%2F771&amp;usq=AOvVaw1vQOK2Fv4v3uNeWokZVBHa">https://www.google.fr/url?sa=t&amp;rct=j&amp;q=&amp;esrc=s&amp;source=web&amp;cd=1&amp;cad=rja&amp;uact=8&amp;ved=0ahUKEwj-9s-85OPWAhVG0hoKHSZMBpsQFggsMAA&amp;url=http%3A%2F%2Fwww.journalmc.org%2Findex.php%2FJMC%2Farticle%2Fdownload%2F1456%2F771&amp;usq=AOvVaw1vQOK2Fv4v3uNeWokZVBHa</a> | 2   | Basaloid carcinoma of rectum                                  | 0.01                                    | 119      | C20   | 8123-8124                          | Tier 2 includes all tiers 3. If it is a tier 2 the reason is that the consensus group has recognised it relevant from the clinical point of view because it is treated differently from the others epithelial tumors of rectum   |
|  | 1   | EPITHELIAL TUMOURS OF ANAL CANAL                              | 1.09                                    | 8,777    | C21   | 8000-8001, 8004, 8010-8011, 8020-  |  |
| R  | 2   | Squamous cell carcinoma with variants of anal canal           | 0.73                                    | 5,879    | C21   | 8004, 8020-8022, 8032, 8050-8076,  |  |
|  | 3   | Verrucous carcinoma   | 0.01                                    | 63       | C21   | 8051                               |  |
|  | 3   | Undifferentiated carcinoma                                    | <0.01                                   | 35       | C21   | 8020-8022                          |  |
|  | 3   | Basaloid carcinoma of anal canal                              | 0.12                                    | 964      | C21   | 8123-8124                          |  |
|  | 2   | Adenocarcinoma with variants of anal canal                    | 0.26                                    | 2,063    | C21   | 8140-8141, 8143, 8147, 8190, 8201, |  |
|  | 3   | Mucinous adenocarcinoma                                       | 0.02                                    | 123      | C21   | 8480                               |  |
|  | 2   | Paget's disease of anal canal                                 | <0.01                                   | 32       | C21   | 8542                               | It is an example of extramammary Paget disease. Our list combine the morphology by site because the site is still the main referral pathway. Thus we listed all possible type of cancers arising in anal canal and Paget's diseases is one of it. Extramammary Paget's disease is considered an adenocarcinoma originating from the skin or skin appendages in areas with apocrine glands. In the ICD-O3 there is only one code the 8542 for the Paget disease, extramammary |
|  | 1?  | Tumor of appendix   |   |          |   |                                    | appendix is part of the colon. ICD-O3 topography code C18.1 appendix   |
|  |   |   | Mucinous adenocarcinoma of the appendix |          |   |                                    | It is not missing, please refer to row 166. we have mucinous adk of colon including appendix   |
|  | Comment: does it correspond to the more general terminology extamamary paget disease or is it really only specific of the ORPHA423982; Missing? <a href="http://www.iarc.fr/en/publications/pdfs-online/patgen/bb2/bb2-chap5.pdf">http://www.iarc.fr/en/publications/pdfs-online/patgen/bb2/bb2-chap5.pdf</a> ORPHA391723; Missing? | 1   | EPITHELIAL TUMOURS OF PANCREAS          | 11.79    | 94,837  | C25                                | 8000-8001, 8004, 8010-8011, 8020-  |
| 2  |   | Adenocarcinoma with variants of pancreas                      | 7.59                                    | 61,066   | C25   | 8010, 8020-8022, 8140-8141, 8143,  |  |
| C  | 3   | Adenocarcinoma NOS  | 3.99                                    | 32,079   | C25   | 8140                               |  |
|  | 3   | Mucinous adenocarcinoma                                       | 0.01                                    | 65       | C25   | 8480                               |  |
|  | 3   | Undifferentiated carcinoma                                    | 0.08                                    | 631      | C25   | 8020-8022                          |  |
|  | 3   | Signet ring cell carcinoma                                    | 0.02                                    | 179      | C25   | 8490                               |  |
|  | 3   | Adenosquamous carcinoma                                       | 0.02                                    | 176      | C25   | 8560                               |  |
|  | 2   | Squamous cell carcinoma with variants of pancreas             | 0.03                                    | 209      | C25   | 8004, 8032, 8050-8076, 8078, 8082- |  |
|  | 2   | Acinar cell carcinoma of pancreas                             | 0.02                                    | 175      | C25   | 8550                               |  |
|  | 2   | Mucinous cystadenocarcinoma of pancreas                       | 0.01                                    | 65       | C25   | 8470                               |  |
|  | 2   | Intraductal papillary mucinous carcinoma invasive of pancreas | <0.01                                   | 5        | C25   | 8453                               |  |
|  | 2   | Solid pseudopapillary carcinoma of pancreas                   | <0.01                                   | 6        | C25   | 8452                               |  |
|  | 2   | Serous cystadenocarcinoma of pancreas                         | <0.01                                   | 1        | C25   | 8441                               |  |
|  | 2   | Carcinoma with osteoclast-like giant cells of pancreas        | NE                                      | 0        | C25   | 8035                               |  |
|  | 1   | EPITHELIAL TUMOURS OF LIVER AND INTRAEPATIC BILE TRACT (IBT)  | 6.19                                    | 49,816   | C22   | 8000-8001, 8004, 8010-8011, 8020-  |  |
|  | 2   | Hepatocellular carcinoma of Liver and IBT                     | 3.09                                    | 24,829   | C22   | 8170-8175, 8180                    |  |
|  | 3   | Combined hepatocellular carcinoma and cholangiocarcinoma      | 0.04                                    | 357      | C22   | 8180                               |  |
|  | 3   | Hepatocellular carcinoma, fibrolamellar                       | 0.01                                    | 76       | C22   | 8171                               |  |
|  | 2   | Cholangiocarcinoma of IBT                                     | 0.84                                    | 6,740    | C22   | 8160                               |  |
|  | 2   | Adenocarcinoma with variants of liver and IBT                 | 0.21                                    | 1,661    | C22   | 8140-8141, 8143, 8147, 8162, 8190, |  |
|  | 2   | Undifferentiated carcinoma of liver and IBT                   | 0.02                                    | 131      | C22   | 8020-8022                          |  |
|  | 2   | Squamous cell carcinoma with variants of liver and IBT        | 0.01                                    | 92       | C22   | 8004, 8032, 8051-8076, 8078, 8082- |  |
| 2  | Bile duct cystadenocarcinoma of IBT   | <0.01   | 14                                      | C22      | 8161  |                                    |  |
| 3  | Hepatocellular carcinoma, fibrolamellar   |   |   |          |   |                                    |  |
| 1  | EPITHELIAL TUMOURS OF GALLBLADDER AND EXTRAHEPATIC BILIARY TRACT (EBT)  | 4.37  | 35,198                                  | C23, C24 | 8000-8001, 8004, 8010-8011, 8020-8022, 8032, 8050-8076, 8078, 8082- |                                    |  |
| R  | 2   | Adenocarcinoma with variants of gallbladder and EBT           | 2.62                                    | 21,086   | C23, C24  | 8020-8022, 8050, 8140-8141, 8143,  |  |
|  | 3   | Cholangiocarcinoma  | 0.18                                    | 1,466    | C23, C24  | 8160                               |  |
|  | 3   | Papillary adenocarcinoma, NOS                                 | 0.08                                    | 608      | C23, C24  | 8050, 8260                         |  |
|  | 3   | Adenocarcinoma intestinal type                                | <0.01                                   | 24       | C23, C24  | 8144                               |  |

ORPHA300557

|          |   |  |              |                |          |                                    |
|----------|---|--|--------------|----------------|----------|------------------------------------|
|          | 3 | Mucinous adenocarcinoma  | 0.05         | 440            | C23, C24 | 8480                               |
|          | 3 | Clear cell adenocarcinoma, NOS                                 | <0.01        | 27             | C23, C24 | 8310                               |
|          | 3 | Signet ring cell carcinoma                                     | 0.02         | 173            | C23, C24 | 8490                               |
|          | 3 | Adenosquamous carcinoma  | 0.03         | 259            | C23, C24 | 8560                               |
|          | 3 | Undifferentiated carcinoma                                     | 0.05         | 367            | C23, C24 | 8020-8022                          |
|          | 3 | Bile duct cystadenocarcinoma                                   | <0.01        | 1              | C23, C24 | 8161                               |
| R        | 2 | <b>Squamous cell carcinoma of gallbladder and EBT</b>          | <b>0.04</b>  | <b>291</b>     | C23, C24 | 8004, 8032, 8051-8076, 8078, 8082- |
| Missing? |   | <b>Carcinoma of the ampulla of Vater</b>                       |              |                |          |                                    |
|          | 1 | <b>EPITHELIAL TUMOUR OF TRACHEA</b>                            | <b>0.13</b>  | <b>1,084</b>   | C33      | 8000-8001, 8004, 8010-8011, 8044,  |
| R        | 2 | <b>Squamous cell carcinoma with variants of trachea</b>        | <b>0.08</b>  | <b>660</b>     | C33      | 8004, 8020-8022, 8031-8032, 8050-  |
|          | 3 | Squamous carcinoma   | 0.07         | 540            | C33      | 8070                               |
|          | 3 | Papillary squamous cell carcinoma                              | <0.01        | 1              | C33      | 8052                               |
|          | 3 | Basaloid squamous cell carcinoma                               | NE           | 0              | C33      | 8083                               |
|          | 3 | Squamous cell carcinoma clear cell type                        | NE           | 0              | C33      | 8084                               |
|          | 3 | Verrucous carcinoma  | NE           | 0              | C33      | 8051                               |
|          | 3 | Squamous cell carcinoma, adenoid                               | NE           | 0              | C33      | 8075                               |
|          | 3 | Spindle cell carcinoma   | <0.01        | 8              | C33      | 8004, 8032, 8074, 8980             |
|          | 3 | Adenosquamous carcinoma  | <0.01        | 8              | C33      | 8560                               |
|          | 3 | Lymphoepithelial carcinoma                                     | NE           | 0              | C33      | 8082                               |
|          | 3 | Giant cell carcinoma   | NE           | 0              | C33      | 8031                               |
|          | 3 | Undifferentiated carcinoma                                     | <0.01        | 20             | C33      | 8020-8022                          |
| R        | 2 | <b>Adenocarcinoma with variants of trachea</b>                 | <b>0.01</b>  | <b>108</b>     | C33      | 8140-8141, 8143, 8144, 8147, 8190, |
|          | 3 | Adenocarcinoma NOS   | 0.01         | 94             | C33      | 8140                               |
|          | 3 | Mucinous adenocarcinoma  | NE           | 0              | C33      | 8480                               |
|          | 3 | Papillary adenocarcinoma, NOS                                  | <0.01        | 1              | C33      | 8260                               |
|          | 3 | Solid carcinoma, NOS   | <0.01        | 5              | C33      | 8230                               |
|          | 3 | Clear cell adenocarcinoma, NOS                                 | <0.01        | 1              | C33      | 8310                               |
|          | 3 | Acinic cell adenocarcinoma                                     | NE           | 0              | C33      | 8550                               |
|          | 3 | Signet ring cell carcinoma                                     | NE           | 0              | C33      | 8490                               |
|          | 3 | Mucinous cystadenocarcinoma, NOS                               | NE           | 0              | C33      | 8470                               |
| R        | 2 | <b>Salivary gland type tumours of trachea</b>                  | <b>0.01</b>  | <b>78</b>      | C33      | 8200, 8430, 8982                   |
|          | 3 | Adenoid cystic carcinoma                                       | 0.01         | 72             | C33      | 8200                               |
|          | 3 | Mucoepidermoid carcinoma                                       | <0.01        | 6              | C33      | 8430                               |
|          | 3 | Myoepithelial carcinoma  | NE           | 0              | C33      | 8982                               |
|          | 1 | <b>EPITHELIAL TUMOUR OF LUNG</b>                               | <b>55.93</b> | <b>449,977</b> | C34      | 8000-8001, 8004, 8010-8014, 8020-  |
| C        | 2 | <b>Squamous cell carcinoma with variants of lung</b>           | <b>13.49</b> | <b>108,562</b> | C34      | 8050-8070, 8073, 8075-8084         |
|          | 3 | Squamous carcinoma   | 13.36        | 107,521        | C34      | 8070                               |
|          | 3 | Papillary squamous cell carcinoma                              | 0.01         | 56             | C34      | 8052                               |
|          | 3 | Basaloid squamous cell carcinoma                               | <0.01        | 10             | C34      | 8083                               |
|          | 3 | Squamous cell carcinoma small cell nonkeratinizing             | 0.10         | 826            | C34      | 8073                               |
|          | 3 | Squamous cell carcinoma clear cell type                        | <0.01        | 1              | C34      | 8084                               |
| C        | 2 | <b>Adenocarcinoma with variants of lung</b>                    | <b>10.29</b> | <b>82,794</b>  | C34      | 8140-8141, 8143, 8144, 8147, 8190, |
|          | 3 | Adenocarcinoma NOS   | 9.28         | 74,640         | C34      | 8140                               |
|          | 3 | Mucinous adenocarcinoma  | 0.11         | 923            | C34      | 8480                               |
|          | 3 | Papillary adenocarcinoma, NOS                                  | 0.15         | 1,181          | C34      | 8260                               |
|          | 3 | Solid carcinoma, NOS   | 0.05         | 371            | C34      | 8230                               |
|          | 3 | Clear cell adenocarcinoma, NOS                                 | 0.05         | 436            | C34      | 8310                               |
|          | 3 | Acinic cell adenocarcinoma                                     | 0.04         | 343            | C34      | 8550                               |
|          | 3 | Signet ring cell carcinoma                                     | 0.02         | 154            | C34      | 8490                               |
|          | 3 | Adenosquamous carcinoma  | 0.31         | 2,515          | C34      | 8560                               |
|          | 3 | Mucinous cystadenocarcinoma, NOS                               | <0.01        | 2              | C34      | 8470                               |
|          | 3 | Adenocarcinoma with mixed subtypes                             | <0.01        | 1              | C34      | 8255                               |
|          | 3 | Fetal adenocarcinoma   | NE           | 0              | C34      | 8333                               |
| R        | 2 | <b>Large cell carcinoma of lung</b>                            | <b>4.01</b>  | <b>32,242</b>  | C34      | 8012, 8034, 8071-72, 8123          |
| R        | 2 | <b>Well differentiated endocrine carcinoma of lung</b>         | <b>0.63</b>  | <b>5,091</b>   | C34      | 8240-8246, 8249                    |
| C        | 2 | <b>Poorly differentiated endocrine carcinoma of lung</b>       | <b>7.68</b>  | <b>61,815</b>  | C34      | 8013, 8041-8046                    |
|          | 3 | Small cell endocrine carcinoma of the lung                     | 7.68         | 61,761         | C34      | 8041-8045                          |
|          | 3 | Large cell endocrine carcinoma of the lung                     | 0.01         | 54             | C34      | 8013                               |
| R        | 2 | <b>Bronchiolo-alveolar carcinoma of lung</b>                   | <b>0.68</b>  | <b>5,472</b>   | C34      | 8250-8254                          |
|          | 3 | Bronchiolo-alveolar carcinoma, mucinous                        | <0.01        | 12             | C34      | 8253                               |
|          | 3 | Bronchiolo-alveolar carcinoma, non mucinous                    | <0.01        | 9              | C34      | 8252                               |
|          | 3 | Bronchiolo-alveolar carcinoma, mixed mucinous and non-mucinous | <0.01        | 4              | C34      | 8254                               |
| R        | 2 | <b>Salivary gland type tumours of lung</b>                     | <b>0.04</b>  | <b>355</b>     | C34      | 8200, 8430, 8982                   |
|          | 3 | Adenoid cystic carcinoma                                       | 0.02         | 135            | C34      | 8200                               |
|          | 3 | Mucoepidermoid carcinoma                                       | 0.03         | 220            | C34      | 8430                               |
|          | 3 | Myoepithelial carcinoma  | NE           | 0              | C34      | 8982                               |
| R        | 2 | <b>Sarcomatoid carcinoma of lung</b>                           | <b>0.14</b>  | <b>1,128</b>   | C34      | 8004, 8022, 8030-8033, 8074, 8980  |
|          | 3 | Sarcomatoid carcinoma  | 0.01         | 48             | C34      | 8033                               |
|          | 3 | Pleomorphic carcinoma  | 0.03         | 260            | C34      | 8022                               |
|          | 3 | Giant cell carcinoma   | 0.04         | 301            | C34      | 8031                               |
|          | 3 | Carcinosarcoma, NOS  | 0.02         | 198            | C34      | 8980                               |
|          | 3 | Spindle cell carcinoma   | 0.04         | 300            | C34      | 8004, 8032, 8074                   |
| R        | 2 | <b>Undifferentiated carcinoma of lung</b>                      | <b>0.98</b>  | <b>7,904</b>   | C34      | 8020-8021                          |

C24 means all C24 thus also C24.1 which is in the ICD\_O3 Ampulla di Vater

|             |          |  |   |         |     |   |
|-------------|----------|--|---|---------|-----|---|
|             | 1        | <b>EPITHELIAL TUMOURS OF THYMUS</b>                          | 0.17  | 1,341   | C37 | 8000-8001, 8010-8011, 8020-8022.  |
| R           | 2        | <b>Malignant thymoma</b>                                     | 0.13  | 1,030   | C37 | 8580-8586   |
|             | 3        | Thymoma, malignant, NOS                                      | 0.12  | 991     | C37 | 8580  |
|             | 3        | Malignant thymoma, type AB                                   | <0.01   | 9       | C37 | 8582  |
|             | 3        | Malignant thymoma, type A                                    | <0.01   | 1       | C37 | 8581  |
|             | 3        | Malignant thymoma, type B                                    | <0.01   | 17      | C37 | 8583, 8584, 8585  |
|             | 3        | Malignant thymoma, type C                                    | <0.01   | 12      | C37 | 8586  |
| R           | 2        | <b>Squamous cell carcinoma of thymus</b>                     | <0.01   | 38      | C37 | 8051-8076, 8078, 8083-8084  |
| R           | 2        | <b>Undifferentiated carcinoma of thymus</b>                  | <0.01   | 20      | C37 | 8020-8022   |
| R           | 2        | <b>Lymphoepithelial carcinoma of thymus</b>                  | <0.01   | 6       | C37 | 8082  |
| R           | 2        | <b>Adenocarcinoma with variants of thymus</b>                | <0.01   | 16      | C37 | 8050, 8140-8141, 8143, 8144, 8147.  |
|             | 3        | Adenocarcinoma NOS   | <0.01   | 6       | C37 | 8140  |
|             | 3        | Papillary adenocarcinoma, NOS                                | <0.01   | 2       | C37 | 8050, 8260  |
|             | 1        | <b>EPITHELIAL TUMOURS OF BREAST</b>                          | 63.85   | 513,690 | C50 | 8000-8001, 8010-8011, 8022, 8070.   |
| C           | 2        | <b>Invasive ductal carcinoma of breast</b>                   | 40.32   | 324,366 | C50 | 8201, 8500, 8501, 8503, 8514, 8521.   |
| C           | 2        | <b>Invasive lobular carcinoma of breast</b>                  | 7.18  | 57,805  | C50 | 8022,8520, 8524   |
|             | 3        | Classic type   | 7.14  | 57,479  | C50 | 8520  |
|             | 3        | Pleomorphic carcinoma  | 0.02  | 141     | C50 | 8022  |
| R           | 2        | <b>Mammary Paget's disease of breast</b>                     | 0.51  | 4,115   | C50 | 8540, 8541, 8543  |
| R           | 2        | <b>Special types of adenocarcinoma of breast</b>             | 3.55  | 28,597  | C50 | 8050, 8201, 8211, 8260, 8290, 8314-   |
|             | 3        | Tubular adenocarcinoma                                       | 1.40  | 11,297  | C50 | 8211  |
|             | 3        | Mucinous carcinoma   | 1.16  | 9,360   | C50 | 8480  |
|             | 3        | Medullary carcinoma, NOS                                     | 0.46  | 3,681   | C50 | 8510  |
|             | 3        | Papillary adenocarcinoma, NOS                                | 0.28  | 2,261   | C50 | 8050, 8260  |
|             | 3        | Cribriform carcinoma   | 0.18  | 1,426   | C50 | 8201  |
|             | 3        | Apocrine adenocarcinoma                                      | 0.06  | 498     | C50 | 8401  |
|             | 3        | Secretory carcinoma  | 0.01  | 50      | C50 | 8502  |
|             | 3        | Glycogen-rich clear cell carcinoma                           | <0.01   | 16      | C50 | 8315  |
|             | 3        | Lipid-rich carcinoma   | <0.01   | 7       | C50 | 8314  |
|             | 3        | Oncocytic carcinoma  | <0.01   | 1       | C50 | 8290  |
| R           | 2        | <b>Metaplastic carcinoma of breast</b>                       | 0.06  | 490     | C50 | 8070, 8560, 8571, 8572, 8575  |
|             | 3        | Squamous carcinoma   | 0.04  | 291     | C50 | 8070  |
|             | 3        | Adenosquamous carcinoma                                      | 0.01  | 79      | C50 | 8560  |
|             | 3        | Adenocarcinoma with cartilaginous and osseous metaplasia     | 0.01  | 45      | C50 | 8571  |
|             | 3        | Adenocarcinoma with spindle cell metaplasia                  | <0.01   | 35      | C50 | 8572  |
| R           | 2        | <b>Salivary gland type tumours of breast</b>                 | 0.05  | 423     | C50 | 8200, 8430, 8550, 8982  |
|             | 3        | Mucoepidermoid carcinoma                                     | <0.01   | 18      | C50 | 8430  |
|             | 3        | Adenoid cystic carcinoma                                     | 0.03  | 277     | C50 | 8200  |
|             | 3        | Myoepithelial carcinoma                                      | <0.01   | 16      | C50 | 8982  |
|             | 3        | Acinic cell adenocarcinoma                                   | 0.01  | 112     | C50 | 8550  |
| R           | 2        | <b>Epithelial tumour of male breast</b>                      | 0.47  | 3,782   | C50 | 8000-8001, 8010-8011, 8022, 8070.   |
|             | 1        | <b>EPITHELIAL TUMOURS OF CORPUS UTERI</b>                    | 10.40   | 83,684  | C54 | 8000, 8001, 8010, 8011, 8070-8078.  |
| C           | 2        | <b>Adenocarcinoma with variants of corpus uteri</b>          | 9.53  | 76,649  | C54 | 8140-8141, 8143, 8144, 8147, 8190.  |
|             | 3        | Adenocarcinoma, NOS  | 5.54  | 44,578  | C54 | 8140  |
|             | 3        | Endometrioid adenocarcinoma, NOS                             | 2.80  | 22,497  | C54 | 8380  |
|             | 3        | Adenosquamous carcinoma                                      | 0.21  | 1,654   | C54 | 8560  |
|             | 3        | Clear cell adenocarcinoma, NOS                               | 0.14  | 1,096   | C54 | 8310  |
|             | 3        | Serous cystadenocarcinoma, NOS                               | 0.02  | 151     | C54 | 8441  |
|             | 3        | Mucinous adenocarcinoma                                      | 0.07  | 530     | C54 | 8480  |
|             | 3        | Mixed cell adenocarcinoma                                    | <0.01   | 38      | C54 | 8323  |
|             | 3        | Endometrioid adenocarcinoma secretory variant                | <0.01   | 14      | C54 | 8382  |
|             | 3        | Villous adenocarcinoma                                       | <0.01   | 19      | C54 | 8262  |
|             | 3        | Endometrioid adenocarcinoma ciliated cell variant            | <0.01   | 1       | C54 | 8383  |
| R           | 2        | <b>Squamous cell carcinoma with variants of corpus uteri</b> | 0.12  | 940     | C54 | 8070-8078, 8082-8084  |
| R           | 2        | <b>Adenoid cystic carcinoma of corpus uteri</b>              | <0.01   | 11      | C54 | 8200  |
| R           | 2        | <b>Transitional cell carcinoma of corpus uteri</b>           | <0.01   | 1       | C54 | 8120, 8122, 8123  |
| ORPHA213721 | Missing? | 2?   | <b>Undifferentiated carcinoma of the corpus uteri</b> |         |     |   |
| ORPHA213726 | Missing? | 2?   | <b>Papillary carcinoma of the corpus uteri</b>        |         |     |   |
|             | 1        | <b>EPITHELIAL TUMOURS OF CERVIX UTERI</b>                    | 6.08  | 48,886  | C53 | 8000, 8001, 8010, 8011, 8015, 8020-8022, 8032, 8050-8084, 8120, 8123, 8140-8141, 8143, 8144, 8147, 8190, 8200-8201, 8210-8211, 8221, 8230, 8231, 8255, 8260, 8262, 8290, 8310 |
| R           | 2        | <b>Squamous cell carcinoma with variants of cervix uteri</b> | 4.28  | 34,441  | C53 | 8015, 8120, 8123, 8050-8084   |

I am sorry, you worked on the old list. the RARECAREnet list includes Undifferentiated tumors are ICD O3 codes 8020; 8021; 8022. Papillary are ICD-O3 8050; 8051; 8052. Tier 1 of the revised list includes 8000, 8001,8003-8005, 8010, 8011, 8012, 8014, 8015, 8020-8022, 8030-8033, 8050-8052, 8070-8078, 8082-8084, 8120, 8122, 8123, 8130, 8313, 8140-8141, 8143, 8144, 8147, 8190, 8200, 8201, 8210-8211, 8221, 8230, 8231, 8255, 8260-8263, 8290, 8310, 8315, 8320, 8323, 8333, 8380-8384, 8401, 8430, 8460, 8440-8441, 8470-8471, 8480-8482, 8490, 8503, 8504, 8510, 8512, 8514, 8525, 8542, 855, 8551, 8560, 8562-8576, 8950-8951, 8980, 8981, 9000, 9110. The papillary are included in 2 tiers 2: the adk includes 8050/3 Papillary carcinoma, NOS and 8051/3 Verrucous carcinoma, NOS. Tier 2 squamous includes 8052/3 Papillary squamous cell carcinoma. The undifferentiated because are underdifferentiated cannot be included in any tier 2.



|             |                            |    |   |             |               |                    |  |  |
|-------------|----------------------------|----|---|-------------|---------------|--------------------|--|--|
|             |                            | 3  | Squamous carcinoma  | 2.92        | 23,473        | C53                | 8070   |  |
|             |                            | 3  | Squamous cell carcinoma nonkeratinizing, NOS              | 0.40        | 3,258         | C53                | 8072   |  |
|             |                            | 3  | Squamous cell carcinoma keratinizing, NOS                 | 0.42        | 3,401         | C53                | 8071   |  |
|             |                            | 3  | Papillary squamous cell carcinoma                         | 0.01        | 77            | C53                | 8052   |  |
|             |                            | 3  | Papillary carcinoma, NOS                                  | <0.01       | 26            | C53                | 8050   |  |
|             |                            | 3  | Verrucous/Warty carcinoma                                 | <0.01       | 24            | C53                | 8051   |  |
|             |                            | 3  | Basaloid carcinoma  | <0.01       | 22            | C53                | 8123   |  |
|             |                            | 3  | Squamous cell carcinoma spindle cell                      | <0.01       | 20            | C53                | 8074   |  |
|             |                            | 3  | Lymphoepithelial carcinoma                                | <0.01       | 12            | C53                | 8082   |  |
|             |                            | 3  | Transitional cell carcinoma, NOS                          | <0.01       | 13            | C53                | 8120   |  |
|             |                            | 3  | Glassy cell carcinoma                                     | <0.01       | 1             | C53                | 8015   |  |
| R           |                            | 2  | <b>Adenocarcinoma with variants of cervix uteri</b>       | <b>1.01</b> | <b>8,123</b>  | C53                | 8140-8141, 8143, 8144, 8147, 8190, 8200-8201, 8210-8211, 8221, 8230, 8231, 8255, 8260-8263, 8290, 8310,  |  |
|             |                            | 3  | Adenocarcinoma, NOS                                       | 0.67        | 5,352         | C53                | 8140   |  |
|             |                            | 3  | Adenocarcinoma with squamous metaplasia                   | <0.01       | 35            | C53                | 8570   |  |
|             |                            | 3  | Mucinous adenocarcinoma                                   | 0.03        | 213           | C53                | 8480   |  |
|             |                            | 3  | Clear cell adenocarcinoma, NOS                            | 0.03        | 247           | C53                | 8310   |  |
|             |                            | 3  | Endometrioid adenocarcinoma, NOS                          | 0.02        | 188           | C53                | 8380   |  |
|             |                            | 3  | Serous cystadenocarcinoma, NOS                            | <0.01       | 6             | C53                | 8441   |  |
|             |                            | 3  | Signet ring cell carcinoma                                | <0.01       | 11            | C53                | 8490   |  |
|             |                            | 3  | Mesonephroma malignant                                    | <0.01       | 17            | C53                | 9110   |  |
|             |                            | 3  | Villous adenocarcinoma                                    | <0.01       | 9             | C53                | 8262   |  |
|             |                            | 3  | Mucinous adenocarcinoma, endocervical type                | <0.01       | 2             | C53                | 8482   |  |
|             |                            | 3  | Adenocarcinoma intestinal type                            | <0.01       | 2             | C53                | 8144   |  |
|             |                            | 3  | Mixed cell adenocarcinoma                                 | <0.01       | 4             | C53                | 8323   |  |
| R           |                            | 2  | <b>Undifferentiated carcinoma of cervix uteri</b>         | <b>0.03</b> | <b>202</b>    | C53                | 8020-8022  |  |
| ORPHA213823 | Missing?                   | 2? | Adenoid cystic carcinoma of the cervix uteri              |             |               |                    |  |  |
| ORPHA213828 | Missing?                   | 2? | Adenoid basal carcinoma of the cervix uteri               |             |               |                    |  |  |
| ORPHA213833 | Missing?                   | 2? | Glassy cell carcinoma of the cervix uteri                 |             |               |                    |  |  |
|             |                            | 1  | <b>MIXED EPITHELIAL AND MESENCHYMAL TUMOURS OF UTERUS</b> | <b>0.44</b> | <b>3,579</b>  | C53.0-C55.9        | 8933, 8950-8951, 8980  |  |
|             |                            | 3  | Mullerian mixed tumour                                    | 0.36        | 2,912         | C53.0-C55.9        | 8950, 8980   |  |
|             |                            | 3  | Adenosarcoma  | 0.02        | 198           | C53.0-C55.9        | 8933   |  |
| ORPHA213605 | Missing?                   |    | Carcinofibroma of the corpus uteri                        |             |               |                    |  | it is a sarcoma thus it is in the sarcoma. Please refer to tier 1 and tier 2 of soft tissue sarcoma.   |
| ORPHA213610 | Missing?                   |    | Carcinosarcoma of the corpus uteri                        |             |               |                    |  | the carcinosarcoma is the ICD-O3 8980 thus we have this morphology. The topographies include C53 cervix uteri; C54 corpus uteri; C 55.9 utero nos. In the RARECAREnet list there is a tier 2 Mullerian mixed tumour in C54 |
|             |                            | 1  | <b>MIXED EPITHELIAL AND MESENCHYMAL TUMOURS OF UTERUS</b> | <b>0.44</b> | <b>3,579</b>  | C53.0-C55.9        | 8933, 8950-8951, 8980  |  |
|             |                            | 3  | Mullerian mixed tumour                                    | 0.36        | 2,912         | C53.0-C55.9        | 8950, 8980   |  |
|             |                            | 3  | Adenosarcoma  | 0.02        | 198           | C53.0-C55.9        | 8933   |  |
| ORPHA213787 | Missing?                   |    | Carcinosarcoma of the cervix uteri                        |             |               |                    |  | please refer to my previous comment on carcinosarcoma of corpus uteri. It was included among the sites of our tier 1. In the RARECAREnet list there is a tier 2 Mullerian mixed tumour of cervix uteri                     |
|             |                            | 1  | <b>EPITHELIAL TUMOURS OF OVARY AND FALLOPIAN TUBE</b>     | <b>9.39</b> | <b>75,585</b> | C56.9, C57.0-C57.3 | 8000, 8001, 8010, 8011, 8050, 8140-8141, 8143, 8147, 8190, 8200-8201, 8210-8211, 8221, 8230, 8231, 8255, |  |
| R           |                            | 2  | <b>Adenocarcinoma with variants of ovary</b>              | <b>5.97</b> | <b>48,021</b> | C56.9              | 8050, 8140-8141, 8143, 8147, 8190,   |  |
|             |                            | 3  | Serous cystadenocarcinoma, NOS                            | 1.00        | 8,013         | C56.9              | 8441   |  |
|             |                            | 3  | Adenocarcinoma NOS  | 1.52        | 12,197        | C56.9              | 8140   |  |
|             |                            | 3  | Endometrioid adenocarcinoma, NOS                          | 0.82        | 6,595         | C56.9              | 8380   |  |
|             |                            | 3  | Papillary adenocarcinoma, NOS                             | 0.35        | 2,789         | C56.9              | 8050, 8260   |  |
|             |                            | 3  | Serous surface papillary carcinoma                        | 0.12        | 964           | C56.9              | 8461   |  |
|             |                            | 3  | Endometrioid adenofibroma malignant                       | 0.02        | 136           | C56.9              | 8381   | this was discussed with the consensus group who did not consider this entity to be a tier 2. This means that it is not a clinically distinct entity per se. We can anyway confirm that it is rare.                         |
|             | may be transfer on tier 2? | 3  | Clear cell adenocarcinofibroma                            | <0.01       | 7             | C56.9              | 8313   |  |
|             |                            | 3  | Serous adenocarcinofibroma                                | <0.01       | 8             | C56.9              | 9014   |  |
|             |                            | 3  | Mucinous adenocarcinofibroma                              | <0.01       | 1             | C56.9              | 9015   |  |
| R           |                            | 2  | <b>Mucinous adenocarcinoma of ovary</b>                   | <b>0.85</b> | <b>6,803</b>  | C56.9              | 8470- 8490   |  |
| R           |                            | 2  | <b>Clear cell adenocarcinoma of ovary</b>                 | <b>0.32</b> | <b>2,605</b>  | C56.9              | 8310   |  |
| R           |                            | 2  | <b>Adenocarcinoma with variants of fallopian tube</b>     | <b>0.26</b> | <b>2,129</b>  | C57.0-C57.3        | 8050, 8140-8141, 8143, 8147, 8190, 8200-8201, 8210-8211, 8221, 8230,                                     |  |

the adenoid cystic carcinoma corresponds to the ICD-O3 morphology 8200 and it is included in both, the tier 1 (please refer to row 355) and the tier 2 adk (please refer to row 368).  
in the RARECAREnet list the 8098 is included in the tier 1 and in the tier 2 adk: 8098, 8140-8141, 8143, 8144, 8147, 8190, 8200-8201, 8210-8211, 8221, 8230, 8231, 8255, 8260-8263, 8290, 8310, 8315, 8320, 8323, 8333, 8380-8384, 8410, 8430, 8440-8441, 8460, 8480-8482, 8490, 8504, 8510, 8512, 8514, 8525, 8542, 8550-8551, 8562-8576, 9110  
The Glassy cell carcinoma is already a tier 3. Please refer to row 368. If you want we can add a row for this tier 3 because those listed are just some not all those included in tier 2. This was done onl to avoid to have a list too long

it is a sarcoma thus it is in the sarcoma. Please refer to tier 1 and tier 2 of soft tissue sarcoma.  
the carcinosarcoma is the ICD-O3 8980 thus we have this morphology. The topographies include C53 cervix uteri; C54 corpus uteri; C 55.9 utero nos. In the RARECAREnet list there is a tier 2 Mullerian mixed tumour in C54

please refer to my previous comment on carcinosarcoma of corpus uteri. It was included among the sites of our tier 1. In the RARECAREnet list there is a tier 2 Mullerian mixed tumour of cervix uteri

this was discussed with the consensus group who did not consider this entity to be a tier 2. This means that it is not a clinically distinct entity per se. We can anyway confirm that it is rare.

|             |          |    |  |                 |                |                 |                                    |  |
|-------------|----------|----|--|-----------------|----------------|-----------------|------------------------------------|--|
|             |          | 3  | Adenocarcinoma NOS   | 0.07            | 591            | C57.0-<br>C57.3 | 8140                               |  |
|             |          | 3  | Papillary serous cystadenocarcinoma                              | 0.03            | 224            | C57.0-<br>C57.3 | 8460                               |  |
|             |          | 3  | Serous cystadenocarcinoma, NOS                                   | 0.02            | 130            | C57.0-<br>C57.3 | 8441                               |  |
|             |          | 3  | Papillary adenocarcinoma, NOS                                    | 0.02            | 166            | C57.0-<br>C57.3 | 8050, 8260                         |  |
| ORPHA370396 | Missing? |    | Small cell carcinoma of the ovary                                |                 |                |                 |                                    |  |
| ORPHA206473 | Missing? |    | Borderline epithelial tumor of ovary                             |                 |                |                 |                                    |  |
| ORPHA398980 | Missing? |    | Primary peritoneal serous/papillary carcinoma                    |                 |                |                 |                                    |  |
|             |          | 1  | <b>NON EPITHELIAL TUMOURS OF OVARY</b>                           | <b>0.43</b>     | <b>3,482</b>   | C56             | 8600, 8620, 8630-8631, 8634, 8640, |  |
| R           |          | 2  | <b>Mixed epithelial/mesenchymal tumours of ovary</b>             | <b>0.16</b>     | <b>1,253</b>   | C56             | 8933, 8950-8951, 8980              |  |
|             |          | 3  | Mullerian mixed tumour   | 0.12            | 976            | C56             | 8950, 8980                         |  |
|             |          | 3  | Adenosarcoma   | <0.01           | 7              | C56             | 8933                               |  |
| R           |          | 2  | <b>Sex cord tumours of ovary</b>                                 | <b>0.13</b>     | <b>1,084</b>   | C56             | 8600, 8620, 8630-8631, 8634, 8640, |  |
|             |          | 3  | Granulosa cell tumour malignant                                  | 0.12            | 982            | C56             | 8620                               |  |
|             |          | 3  | Sertoli-Leydig cell tumour poorly differentiated                 | <0.01           | 20             | C56             | 8631                               |  |
|             |          | 3  | Steroid cell tumour, malignant                                   | <0.01           | 3              | C56             | 8670                               |  |
| ORPHA99914  | Missing? | 3? | Gynandroblastoma   |                 |                |                 |                                    |  |
| R           |          | 2  | <b>Malignant/Immature teratomas of ovary</b>                     | <b>0.07</b>     | <b>545</b>     | C56             | 9080-9084, 9090, 9102, 9391, 9440, |  |
|             |          | 3  | Teratoma, malignant, NOS   | 0.05            | 420            | C56             | 9080                               |  |
|             |          | 3  | Struma ovarii, malignant   | <0.01           | 20             | C56             | 9090                               |  |
|             |          | 3  | Primitive neuroectodermal tumour, NOS                            | <0.01           | 1              | C56             | 9473                               |  |
|             |          | 3  | Ependymoma   | NE              | 0              | C56             | 9391                               |  |
|             |          | 3  | Medulloepithelioma, NOS  | NE              | 0              | C56             | 9501                               |  |
|             |          | 3  | Glioblastoma   | NE              | 0              | C56             | 9440                               |  |
| R           |          | 2  | <b>Germ cell tumour of ovary</b>                                 | <b>0.07</b>     | <b>600</b>     | C56             | 9060-9065, 9070-9072, 9085, 9100-  |  |
|             |          | 3  | Dysgerminoma/Seminoma  | 0.04            | 337            | C56             | 9060-9065                          |  |
|             |          | 3  | Yolk sac tumour  | 0.02            | 173            | C56             | 9071                               |  |
|             |          | 3  | Mixed germ cell tumour   | <0.01           | 38             | C56             | 9085                               |  |
|             |          | 3  | Embryonal adenocarcinoma   | <0.01           | 26             | C56             | 9070                               |  |
|             |          | 3  | Choriocarcinoma, NOS   | <0.01           | 17             | C56             | 9100                               |  |
|             |          | 3  | Polyembryoma   | <0.01           | 3              | C56             | 9072                               |  |
| R           |          | 1  | <b>EPITHELIAL TUMOURS OF VULVA AND VAGINA</b>                    | <b>1.91</b>     | <b>15,392</b>  | C51, C52        | 8000, 8001, 8010, 8011, 8020-8022, |  |
| R           |          | 2  | <b>Squamous cell carcinoma with variants of vulva and vagina</b> | <b>1.50</b>     | <b>12,097</b>  | C51, C52        | 8050-8084                          |  |
| R           |          | 2  | <b>Adenocarcinoma with variants of vulva and vagina</b>          | <b>0.08</b>     | <b>620</b>     | C51, C52        | 8140-8141, 8143, 8147, 8190-8211,  |  |
| R           |          | 2  | <b>Paget's disease of vulva and vagina</b>                       | <b>0.05</b>     | <b>403</b>     | C51, C52        | 8542                               |  |
| R           |          | 2  | <b>Undifferentiated carcinoma of vulva and vagina</b>            | <b>0.01</b>     | <b>65</b>      | C51, C52        | 8020-8022                          |  |
|             |          | 1  | <b>TROPHOBLASTIC TUMOUR OF PLACENTA</b>                          | <b>0.02</b>     | <b>192</b>     | C58.9           | 9100, 9105                         |  |
| R           |          | 2  | <b>Choriocarcinoma of placenta</b>                               | <b>0.02</b>     | <b>192</b>     | C58.9           | 9100                               |  |
| ORPHA99925  | Missing? |    | Invasive mole  |                 |                |                 |                                    |  |
| ORPHA99928  | Missing? |    | Placental site trophoblastic tumor                               |                 |                |                 |                                    |  |
| ORPHA254698 | Missing? |    | Epithelioid trophoblastic tumor                                  |                 |                |                 |                                    |  |
|             |          | 1  | <b>EPITHELIAL TUMOURS OF PROSTATE</b>                            | <b>47.89</b>    | <b>385,278</b> | C61, C637       | 8000-8001, 8020-8022, 8032, 8050,  |  |
| C           |          | 2  | <b>Adenocarcinoma with variants of prostate</b>                  | <b>40.51</b>    | <b>325,916</b> | C61             | 8032, 8074, 8082, 8140-8141, 8143, |  |
|             |          | 3  | Adenocarcinoma NOS   | 39.70           | 319,386        | C61             | 8140                               |  |
|             |          | 3  | Acinic cell adenocarcinoma                                       | 0.41            | 3,302          | C61             | 8550                               |  |
|             |          | 3  | Mucinous adenocarcinoma  | 0.03            | 208            | C61             | 8480                               |  |
|             |          | 3  | Signet ring cell carcinoma                                       | 0.01            | 82             | C61             | 8490                               |  |
|             |          | 3  | Adenocarcinoma with neuroendocrine differentiation               | <0.01           | 2              | C61             | 8574                               |  |
|             |          | 3  | Oxyphilic adenocarcinoma   | <0.01           | 1              | C61             | 8290                               |  |
|             |          | 3  | Spindle cell adenocarcinoma                                      | <0.01           | 2              | C61             | 8032, 8074, 8572                   |  |
|             |          | 3  | Lymphoepithelial carcinoma                                       | NE              | 0              | C61             | 8082                               |  |
| R           |          | 2  | <b>Squamous cell carcinoma with variants of prostate</b>         | <b>0.11</b>     | <b>909</b>     | C61             | 8070-8072, 8560                    |  |
|             |          | 3  | Squamous carcinoma   | 0.01            | 121            | C61             | 8070                               |  |
|             |          | 3  | Adenosquamous carcinoma  | <0.01           | 14             | C61             | 8560                               |  |
| R           |          | 2  | <b>Infiltrating duct carcinoma of prostate</b>                   | <b>0.47</b>     | <b>3,777</b>   | C61             | 8050, 8201, 8230, 8260, 8500, 8503 |  |
|             |          | 3  | Cribriform carcinoma   | 0.35            | 2,777          | C61             | 8201                               |  |
|             |          | 3  | Solid carcinoma, NOS   | 0.02            | 185            | C61             | 8230                               |  |
|             |          | 3  | Papillary adenocarcinoma, NOS                                    | 0.01            | 112            | C61             | 8050, 8260                         |  |
| R           |          | 2  | <b>Transitional cell carcinoma of prostate</b>                   | <b>0.06</b>     | <b>518</b>     | C61             | 8120, 8122, 8130-8131              |  |
| R           |          | 2  | <b>Salivary gland type tumours of prostate</b>                   | <b>&lt;0.01</b> | <b>13</b>      | C61             | 8123, 8147 and 8200                |  |
|             |          | 3  | Adenoid cystic carcinoma   | <0.01           | 12             | C61             | 8200                               |  |
|             |          | 3  | Basaloid carcinoma   | <0.01           | 1              | C61             | 8123                               |  |

small cell carcinomas: ICD-O3 codes 8041-8045 are neuroendocrine tumors. Thus, they are included among the neuroendocrine tumors Tier 1 and in the tier 2: neuroendocrine tumors of other sites (this tier 2 was added in the RARECAREnet list) during the discussion we had with the consensus group there were 2 entities not malignant that were considered relevant to include: granulosa cell tumour malignant, adult type and granulosa cell tumour malignant, juvenile type. We added them with the following clarification: 8620/1 and 8622/1 included in the list however will not be included in the analyses because border line you have the old list. In the RARECAREnet list we have a tier 2 named Primary peritoneal serous/papillary carcinoma. It is within the Tier 1 epithelial tumor of ovary but the specific topography is C48 (row 401 of the RARECAREnet list)

this is a borderline morphology thus it is not included in our list (8632/1)

this is a borderline morphology thus it is not included in our list (9100/1)  
this is a borderline morphology thus it is not included in our list (9104/1)  
trophoblastic tumor, epithelioid (ICD-O3 9105/3. It is included in tier 1. if you want we can add it as tier 3 to make it more evident

|  |                 |  |                 |               |                          |  |  |
|--|-----------------|--|-----------------|---------------|--------------------------|--|--|
|  | 3               | Basal cell adenocarcinoma                                  | NE              | 0             | C61                      | 8147   |  |
|  | 1               | <b>TUMOURS OF TESTIS AND PARATESTIS</b>                    | <b>3.15</b>     | <b>25,357</b> | C62, C63.0, C63.1, C63.8 | 8000, 8001, 8010, 8011, 8120, 8123, 8140-8141, 8147, 8190, 8210-8211, 8221, 8231, 8255, 8260, 8261-8263, 8290, 8310, 8320, 8323, 8333, 8380- |  |
| <b>R</b>   | 2               | <b>Adenocarcinoma with variants of paratestis</b>          | <b>&lt;0.01</b> | <b>12</b>     | C63.0, C63.1             | 8120, 8123, 8140-8141, 8147, 8190, 8200, 8210-8211, 8221, 8230, 8231,  |  |
|  | 3               | Endometrioid adenocarcinoma, NOS                           | <0.01           | 12            | C63.0, C63.1             | 8380   |  |
|  | 3               | Clear cell adenocarcinoma, NOS                             | NE              | 0             | C63.0, C63.1             | 8310   |  |
|  | 3               | Serous cystadenocarcinoma, NOS                             | NE              | 0             | C63.0, C63.1             | 8441   |  |
|  | 3               | Mucinous cystadenocarcinoma, NOS                           | NE              | 0             | C63.0, C63.1             | 8470   |  |
|  | 3               | Collecting duct and rete testis carcinoma                  | NE              | 0             | C63.0, C63.1             | malignancy without ICD-O morphology code   |  |
|  | 3               | Transitional cell carcinoma, NOS                           | NE              | 0             | C63.0, C63.1             | 8120   |  |
|  | 2               | <b>Germ cell non seminomatous tumours of testis</b>        | 1.21            | 9,754         | C62                      | 9080-9083, 9085, 9100-9102, 9065,  |  |
|  | 3               | Mixed germ cell tumour                                     | 0.22            | 1,791         | C62                      | 9085   |  |
|  | 3               | Teratocarcinoma  | 0.12            | 981           | C62                      | 9081   |  |
|  | 3               | Choriocarcinoma combined with other germ cell elements     | 0.04            | 316           | C62                      | 9101   |  |
|  | 3               | Embryonal adenocarcinoma, NOS                              | 0.29            | 2,371         | C62                      | 9070   |  |
|  | 3               | Yolk sac tumour  | 0.06            | 459           | C62                      | 9071   |  |
|  | 3               | Choriocarcinoma, NOS                                       | 0.02            | 139           | C62                      | 9100   |  |
|  | 2               | <b>Germ cell seminomatous tumours of testis</b>            | 1.71            | 13,777        | C62                      | 9060-9062  |  |
|  | 3               | Seminoma, NOS  | 1.66            | 13,391        | C62                      | 9061   |  |
|  | 2               | <b>Spermatocytic seminoma</b>                              | <b>0.03</b>     | <b>221</b>    | C62                      | 9063   |  |
|  | 2               | <b>Teratoma with malignant transformation</b>              | <b>&lt;0.01</b> | <b>11</b>     | C62                      | 9084   |  |
| <b>R</b>   | 2               | <b>Sex cord tumours of testis</b>                          | <b>0.02</b>     | <b>177</b>    | C62                      | 8630-8640, 8650, 8590-8592   |  |
|  | 3               | Leydig cell tumour malignant                               | 0.02            | 131           | C62                      | 8650   |  |
|  | 3               | Sertoli cell carcinoma                                     | <0.01           | 38            | C62                      | 8640   |  |
|  | 3               | Malignant sex cord/gonadal stromal tumours                 | <0.01           | 2             | C62                      | 8590-8592 borderline malignancy  |  |
|  | 1               | <b>EPITHELIAL TUMOURS OF PENIS</b>                         | <b>0.62</b>     | <b>5,016</b>  | C60                      | 8000-8001, 8010-8011, 8020-8022,   |  |
| <b>R</b>   | 2               | <b>Squamous cell carcinoma with variants of penis</b>      | <b>0.57</b>     | <b>4,611</b>  | C60                      | 8020-8022, 8050-8084, 8123   |  |
|  | 3               | Squamous carcinoma   | 0.42            | 3,418         | C60                      | 8070   |  |
|  | 3               | Verrucous carcinoma  | 0.04            | 288           | C60                      | 8051   |  |
|  | 3               | Squamous cell carcinoma, sarcomatoid                       | <0.01           | 8             | C60                      | 8074   |  |
|  | 3               | Adenosquamous carcinoma                                    | <0.01           | 2             | C60                      | 8560   |  |
|  | 3               | Basaloid carcinoma   | NE              | 0             | C60                      | 8123   |  |
| <b>R</b>   | 2               | <b>Adenocarcinoma with variants of penis</b>               | <b>&lt;0.01</b> | <b>40</b>     | C60                      | 8140-8141, 8147, 8190, 8200-8201,  |  |
|  | 3               | Extramammary Paget's disease                               | <0.01           | 20            | C60                      | 8542   |  |
|  | 3               | Sebaceous adenocarcinoma                                   | NE              | 0             | C60                      | 8410   |  |
|  | 3               | Papillary adenocarcinoma, NOS                              | NE              | 0             | C60                      | 8260   |  |
|  | 3               | Mixed tumour malignant, NOS                                | NE              | 0             | C60                      | 8940   |  |
|  | 3               | Clear cell adenocarcinoma, NOS                             | NE              | 0             | C60                      | 8310   |  |
|  | 3               | Basal cell adenocarcinoma                                  | NE              | 0             | C60                      | 8147   |  |
|  | 1               | <b>EPITHELIAL TUMOURS OF KIDNEY</b>                        | <b>10.55</b>    | <b>84,863</b> | C64                      | 8000-8001, 8010-8011, 8020, 8022,  |  |
| <b>C Comment: why in this case adenocarcinoma is tier 3, not tier 2?</b> | 2               | <b>Renal cell carcinoma with variants</b>                  | <b>8.35</b>     | <b>67,152</b> | C64                      | 8050, 8140-8141, 8143, 8147, 8190, 8200, 8201, 8211, 8221, 8230-8231, 8255-8263, 8290, 8310, 8312, 8315-8320, 8323, 8333, 8401, 8430, 8440,  | the most important carcinoma of the kidney is the renal cell carcinoma as you can see from the incidence rate. This carcinoma is within the big group of adk but, for the kidney it is standardised recognised to talk about renal cell thus we said renal cell + variants which includes other type of adk  |
|  | 3               | Adenocarcinoma NOS   | 0.51            | 4,071         | C64                      | 8140   |  |
|  | 3               | Renal cell adenocarcinoma                                  | 5.55            | 44,638        | C64                      | 8312   |  |
|  | 3               | Clear cell adenocarcinoma, NOS                             | 1.99            | 15,994        | C64                      | 8310   |  |
| <b>Comment: recognized as rare entity, to be included in de</b>          | 3               | Papillary adenocarcinoma, NOS                              | 0.14            | 1,135         | C64                      | 8050, 8260   | Tier 2 combine different tier 3 (which are WHO blu book code) based on the way they are treated. Thus, if all these morphologies are combined together it means that experts will treat them in the same way thus they are not clinical distinct entities. Thus they are included as tier 3. We listed them thus people can have an idea of the different incidence of these histotypes. |
| <b>Comment: recognized as rare entity, to be included in de</b>          | 3               | Renal cell carcinoma chromophobe type                      | 0.01            | 107           | C64                      | 8317   |  |
| <b>Comment: recognized as rare entity, to be included in de</b>          | 3               | Collecting duct carcinoma                                  | <0.01           | 15            | C64                      | 8319   |  |
| <b>Comment: recognized as rare entity, to be included in de</b>          | 3               | Xp translocation carcinoma                                 |                 |               | C64                      | malignancy without ICD-O   |  |
| <b>Comment: recognized as rare entity, to be included in de</b>          | 3               | Carcinoma associated with neuroblastoma                    |                 |               | C64                      | malignancy without ICD-O   |  |
| <b>Comment: recognized as rare entity, to be included in de</b>          | 3               | Renal medullary carcinoma                                  | <0.01           | 4             | C64                      | 8510   |  |
| <b>Comment: recognized as rare entity, to be included in de</b>          | 3               | Mucinous tubular and spindle cell carcinoma                |                 |               | C64                      | malignancy without ICD-O   |  |
| <b>R</b>   | 2               | <b>Squamous cell carcinoma spindle cell type of kidney</b> | <b>0.01</b>     | <b>56</b>     | C64                      | 8032, 8074, 8980   |  |
| <b>R</b>   | 2               | <b>Squamous cell carcinoma with variants of kidney</b>     | <b>0.04</b>     | <b>283</b>    | C64                      | 8020-8022, 8051-8073, 8075-8084,   |  |
| ORPHA319325  | <b>Missing?</b> | Tubulocystic renal cell carcinoma                          |                 |               |                          |  | 8316/3 this code comes from the new WHO blu book for kidney and it is approved for the ICD-O. we are including them in the RARECAREnet list. However we will see whether to include this entity among th squamous cell or the renal cell tier 2  |
| ORPHA404514  | <b>Missing?</b> | Acquired cystic disease-associated renal cell carcinoma    |                 |               |                          |  | 8316/3 this code comes from the new WHO blu book for kidney and it is approved for the ICD-O. we are including them in the RARECAREnet list. However we will see whether to include this entity among th squamous cell or the renal cell tier 3  |
|  | 1               | <b>EPITHELIAL TUMOURS OF PELVIS, URETER AND URETHRA</b>    | <b>1.58</b>     | <b>12,728</b> | C65.9,C66.9,C68.0        | 8000-8001, 8010-8011, 8020, 8022, 8031, 8050-8084, 8090, 8094, 8120,   |  |

|  |   |  |       |         |                   |   |
|--|---|--|-------|---------|-------------------|---|
| R  | 2 | <b>Transitional cell carcinoma of pelvis, ureter and urethra</b>           | 1.37  | 11,005  | C65.9,C66.9,C68.0 | 8020-8022, 8031,8082, 8120, 8122, 8130-8131                           |
|  | 3 | Undifferentiated carcinoma   | 0.01  | 44      | C65.9,C66.9,C68.0 | 8020-8022   |
|  | 3 | Transitional cell carcinoma spindle cell                                   | <0.01 | 9       | C65.9,C66.9,C68.0 | 8122  |
|  | 3 | Lymphoepithelioma-like carcinoma   | NE    | 0       | C65.9,C66.9,C68.0 | 8082  |
|  | 3 | Transitional cell carcinoma, giant cell                                    | NE    | 0       | C65.9,C66.9,C68.0 | 8031  |
|  | 3 | Transitional cell carcinoma, micropapillary                                | NE    | 0       | C65.9,C66.9,C68.0 | 8131  |
| R  | 2 | <b>Squamous cell carcinoma with variants of pelvis, ureter and urethra</b> | 0.05  | 411     | C65.9,C66.9,C68.0 | 8050-8076   |
|  | 3 | Verrucous carcinoma  | <0.01 | 2       | C65.9,C66.9,C68.0 | 8051  |
| R  | 2 | <b>Adenocarcinoma with variants of pelvis, ureter and urethra</b>          | 0.04  | 299     | C65.9,C66.9,C68.0 | 8140-8141, 8143, 8147, 8190, 8201, 8211, 8221, 8230-8231, 8255, 8260- |
|  | 3 | Mucinous adenocarcinoma  | <0.01 | 8       | C65.9,C66.9,C68.0 | 8480  |
|  | 3 | Clear cell adenocarcinoma, NOS   | 0.01  | 83      | C65.9,C66.9,C68.0 | 8310  |
|  | 3 | Signet ring cell carcinoma   | <0.01 | 3       | C65.9,C66.9,C68.0 | 8490  |
| R  | 2 | <b>Salivary gland-type tumours of pelvis, ureter and urethra</b>           | <0.01 | 2       | C65.9,C66.9,C68.0 | 8123, 8200, 8430  |
|  | 3 | Basaloid carcinoma   | <0.01 | 2       | C65.9,C66.9,C68.0 | 8123  |
|  | 3 | Adenoid cystic carcinoma   | NE    | 0       | C65.9,C66.9,C68.0 | 8200  |
|  | 3 | Mucoepidermoid carcinoma   | NE    | 0       | C65.9,C66.9,C68.0 | 8430  |
| Missing entities, probably both in rarecare and orphanet | 1 | <b>EPITHELIAL TUMOURS OF BLADDER</b>                                       | 20.11 | 161,780 | C67               | 8000-8001, 8010-8011, 8020, 8022,                                     |
| C  | 2 | <b>Transitional cell carcinoma of bladder</b>                              | 17.41 | 140,075 | C67               | 8020-8022, 8031,8082, 8120, 8122,                                     |
|  | 3 | Undifferentiated carcinoma   | 0.08  | 666     | C67               | 8020-8022   |
|  | 3 | Transitional cell carcinoma spindle cell                                   | 0.01  | 68      | C67               | 8122  |
|  | 3 | Transitional cell carcinoma with squamous differentiation                  |       |         | C67               | malignancy without ICD-O  |
|  | 3 | Lymphoepithelial carcinoma   | <0.01 | 7       | C67               | 8082  |
|  | 3 | Giant cell carcinoma   | <0.01 | 8       | C67               | 8031  |
|  | 3 | Transitional cell carcinoma micropapillary                                 | <0.01 | 3       | C67               | 8131  |
| R  | 2 | <b>Squamous cell carcinoma with variants of bladder</b>                    | 0.43  | 3,428   | C67               | 8050-8076   |
|  | 3 | Verrucous carcinoma  | <0.01 | 29      | C67               | 8051  |
| R  | 2 | <b>Adenocarcinoma with variants of bladder</b>                             | 0.29  | 2,305   | C67               | 8140-8141, 8143, 8147, 8190, 8201,                                    |
|  | 3 | Mucinous adenocarcinoma  | 0.01  | 121     | C67               | 8480  |
|  | 3 | Clear cell adenocarcinoma, NOS   | 0.01  | 117     | C67               | 8310  |
|  | 3 | Signet ring cell carcinoma   | 0.01  | 99      | C67               | 8490  |
| R  | 2 | <b>Salivary gland type tumours of bladder</b>                              | <0.01 | 9       | C67               | 8123, 8200, 8430  |
|  | 3 | Basaloid carcinoma   | <0.01 | 3       | C67               | 8123  |
|  | 3 | Adenoid cystic carcinoma   | <0.01 | 5       | C67               | 8200  |
|  | 3 | Mucoepidermoid carcinoma   | <0.01 | 1       | C67               | 8430  |
|  | 1 | <b>EPITHELIAL TUMOURS OF EYE AND ADNEXA</b>                                | 0.16  | 1,277   | C69               | 8000-8001, 8010-8011, 8020, 8050-                                     |
| R  | 2 | <b>Squamous cell carcinoma with variants of eye and adnexa</b>             | 0.04  | 303     | C69               | 8020, 8050-8082, 8090   |
|  | 3 | Squamous carcinoma   | 0.03  | 251     | C69               | 8070  |
|  | 3 | Basal cell carcinoma   | <0.01 | 4       | C69               | 8090  |
| R  | 2 | <b>Adenocarcinoma with variants of eye and adnexa</b>                      | 0.01  | 88      | C69               | 8140, 8147, 8190, 8200, 8221, 8230-                                   |
|  | 3 | Adenocarcinoma NOS   | <0.01 | 36      | C69               | 8140  |
|  | 3 | Adenoid cystic carcinoma   | <0.01 | 38      | C69               | 8200  |
|  | 3 | Mucoepidermoid carcinoma   | <0.01 | 7       | C69               | 8430  |
|  | 1 | <b>EPITHELIAL TUMOURS OF MIDDLE EAR</b>                                    | 0.03  | 244     | C30.1             | 8000-8001, 8010-8011, 8020, 8050-                                     |
| R  | 2 | <b>Squamous cell carcinoma with variants middle ear</b>                    | 0.02  | 180     | C30.1             | 8050-8084, 8090, 8094, 8120, 8121,                                    |
|  | 3 | Squamous carcinoma   | 0.02  | 134     | C30.1             | 8070  |
| R  | 2 | <b>Adenocarcinoma with variants of middle ear</b>                          | <0.01 | 29      | C30.1             | 8140, 8147, 8190, 8200, 8221, 8230-                                   |
|  | 3 | Adenocarcinoma NOS   | <0.01 | 13      | C30.1             | 8140  |
|  | 3 | Adenoid cystic carcinoma   | <0.01 | 8       | C30.1             | 8200  |
|  | 1 | <b>MALIGNANT MESOTHELIOMA</b>  | 1.90  | 15,263  | all cancer sites  | 9050-9053   |
| R  | 2 | <b>Mesothelioma of pleura and pericardium</b>                              | 1.60  | 12,881  | C38               | 9050-9053   |
|  | 3 | Epithelioid malignant mesothelioma   | 0.24  | 1,910   | C38               | 9052  |
|  | 3 | Sarcomatoid malignant mesothelioma   | 0.04  | 285     | C38               | 9051  |
| R  | 2 | <b>Mesothelioma of peritoneum and tunica vaginalis</b>                     | 0.12  | 998     | C48, C63.7        | 9050-9053   |
|  | 3 | Epithelioid malignant mesothelioma   | 0.02  | 134     | C48, C63.7        | 9052  |
|  | 3 | Sarcomatoid malignant mesothelioma   | <0.01 | 11      | C48, C63.7        | 9051  |

|            |                            |  |       |         |   |  |  |  |   |
|------------|----------------------------|--|-------|---------|---|--|--|--|---|
| ORPHA31112 | Missing? ccan be malignant | Dermatofibrosarcoma protuberans                      |       |         |   |  |  |  | this is a sarcoma. Thus, it is included in the soft tissue sarcoma. You can see it also specifically in the tier 3 DFSP (8832-8833)   |
| C          | 1                          | <b>MALIGNANT SKIN MELANOMA</b>                       | 12.41 | 99,872  | C44   | 8720-8780  |  |  |   |
|            | 3                          | Superficial spreading melanoma                       | 5.04  | 40,568  | C44   | 8743   |  |  |   |
|            | 3                          | Nodular melanoma                                     | 1.73  | 13,917  | C44   | 8721   |  |  |   |
|            | 3                          | Lentigo maligna melanoma                             | 0.64  | 5,153   | C44   | 8742   |  |  |   |
|            | 3                          | Acral lentiginous melanoma malignant                 | 0.15  | 1,197   | C44   | 8744   |  |  |   |
| R          | 1                          | <b>MALIGNANT MELANOMA OF MUCOSA</b>                  | 0.51  | 4,104   | all cancer sites except C7, C8, C69.3- C69.4                | 8720-8780  |  |  |   |
| R          | 1                          | <b>MALIGNANT MELANOMA OF UVEA</b>                    | 0.65  | 5,268   | C69.3- C69.4  | 8720-8780  |  |  |   |
|            | 1                          | <b>EPITHELIAL TUMOURS OF SKIN</b>                    | 48.58 | 390,861 | C44, C63.2  | 8011, 8032, 8050-8052, 8070-8078,                              |  |  |   |
| C          | 2                          | <b>Basal cell carcinoma of skin</b>                  | 32.05 | 257,815 | C44, C63.2  | 8090-8098  |  |  |   |
|            | 3                          | Basal cell carcinoma NOS                             | 29.52 | 237,497 | C44, C63.2  | 8090, 8092   |  |  |   |
|            | 3                          | Basosquamous carcinoma                               | 1.50  | 12,069  | C44, C63.2  | 8094   |  |  |   |
|            | 3                          | Multifocal superficial basal cell carcinoma          | 0.80  | 6,473   | C44, C63.2  | 8091   |  |  |   |
|            | 3                          | Basal cell carcinoma nodular                         | 0.10  | 827     | C44, C63.2  | 8097   |  |  |   |
|            | 3                          | Basal cell carcinoma fibroepithelial                 | 0.03  | 245     | C44, C63.2  | 8093   |  |  |   |
|            | 3                          | Adenoid basal carcinoma                              | 0.01  | 55      | C44, C63.2  | 8098   |  |  |   |
| C          | 2                          | <b>Squamous cell carcinoma with variants of skin</b> | 16.39 | 131,897 | C44, C63.2  | 8011, 8032, 8050-8052, 8070-8078,                              |  |  |   |
|            | 3                          | Squamous carcinoma                                   | 14.87 | 119,632 | C44, C63.2  | 8070   |  |  |   |
|            | 3                          | Verrucous carcinoma                                  | 0.07  | 528     | C44, C63.2  | 8051   |  |  |   |
|            | 3                          | Spindle cell carcinoma                               | 0.03  | 277     | C44, C63.2  | 8032, 8074   |  |  |   |
|            | 3                          | Pseudo vascular/ Squamous cell carcinoma adenoid     | 0.01  | 79      | C44, C63.2  | 8075   |  |  |   |
|            | 3                          | Adenosquamous carcinoma                              | <0.01 | 39      | C44, C63.2  | 8560   |  |  |   |
| R          | 1                          | <b>ADNEXAL CARCINOMA OF SKIN</b>                     | 0.28  | 2,228   | C44, C63.2  | 8100-8110, 8200, 8211, 8390-8420,                              |  |  |   |
|            | 3                          | Nodular hidradenoma, malignant                       | 0.02  | 138     | C44, C63.2  | 8402   |  |  |   |
|            | 3                          | Sebaceous adenocarcinoma                             | 0.06  | 506     | C44, C63.2  | 8410   |  |  |   |
|            | 3                          | Adenoid cystic carcinoma                             | 0.02  | 155     | C44, C63.2  | 8200   |  |  |   |
|            | 3                          | Paget's disease extramammary                         | 0.02  | 192     | C44, C63.2  | 8542   |  |  |   |
|            | 3                          | Apocrine adenocarcinoma                              | 0.01  | 59      | C44, C63.2  | 8401   |  |  |   |
|            | 3                          | Mucinous adenocarcinoma                              | <0.01 | 35      | C44, C63.2  | 8480   |  |  |   |
|            | 3                          | Pilomatrix carcinoma                                 | <0.01 | 32      | C44, C63.2  | 8110   |  |  |   |
|            | 3                          | Eccrine poroma, malignant                            | <0.01 | 27      | C44, C63.2  | 8409   |  |  |   |
|            | 3                          | Mixed tumour malignant, NOS                          | <0.01 | 15      | C44, C63.2  | 8940   |  |  |   |
|            | 3                          | Sclerosing sweat duct carcinoma                      | <0.01 | 16      | C44, C63.2  | 8407   |  |  |   |
|            | 3                          | Malignant eccrine spiradenoma                        | <0.01 | 7       | C44, C63.2  | 8403   |  |  |   |
|            | 3                          | Tubular adenocarcinoma                               | <0.01 | 3       | C44, C63.2  | 8211   |  |  |   |
|            | 3                          | Eccrine papillary adenocarcinoma                     | <0.01 | 2       | C44, C63.2  | 8408   |  |  |   |
|            | 1                          | <b>EMBRYONAL NEOPLASMS</b>                           | 0.34  | 2,771   | all cancers sites, except CNS and ANS and peripheral nerves | 8960, 8970-8973, 9490, 9500, 9510-9514                         |  |  |   |
| R          | 2                          | <b>Neuroblastoma and ganglioneuroblastoma</b>        | 0.12  | 975     | all cancers sites, except CNS and ANS and peripheral nerves | 9490, 9500   |  |  | the RARECAREnet list is completely different. In the RARECAREnet we do not have a group of embryonal tumors but we have a tier 1 per each of the major embryonal tumors. Discussing with the experts of the CNS they asked us to differentiate tumors of the CNS and embryonal tumors of the CNS. Thus the revised list follow a different grouping with embryonal tumors of CNS being a tier 1 (please refer to row 790 of the RARECAREnet list) |
| R          | 2                          | <b>Nephroblastoma</b>                                | 0.14  | 1,141   | C64.9   | 8960   |  |  |   |
| R          | 2                          | <b>Retinoblastoma</b>                                | 0.05  | 434     | C69.2   | 9510-9514  |  |  |   |
| R          | 2                          | <b>Hepatoblastoma</b>                                | 0.02  | 181     | C22.0   | 8970   |  |  |   |
| R          | 2                          | <b>Pulmonary blastoma</b>                            | <0.01 | 34      | C34   | 8972-8973  |  |  |   |
| R          | 2                          | <b>Pancreatoblastoma</b>                             | <0.01 | 6       | C25   | 8971   |  |  |   |
| ORPHA64742 | Missing?                   | Pleuropulmonary blastoma                             |       |         |   |  |  |  | the RARECAREnet list includes pleuropulmonary blastoma (ICD-O3 8973) as a separated tier 1 (please refer to row 626 of the RARECAREnet list)  |
|            | 1                          | <b>EXTRAGONADAL GERM CELL TUMOURS</b>                | 0.13  | 1,019   | all cancers sites except C56 and C62                        | 9060-9072, 9080-9085, 9101, and 9100 if not in placenta (C589) |  |  |   |
| R          | 2                          | <b>Extragenadal malignant/immature teratomas</b>     | 0.04  | 335     | all cancers sites except C56 and C62                        | 9080-9085, 9101  |  |  |   |
|            | 3                          | Teratoma malignant                                   | 0.03  | 230     | all cancers sites except C56 and C62                        | 9080   |  |  |   |
|            | 3                          | Mixed germ cell tumour                               | 0.01  | 44      | all cancers sites except C56 and C62                        | 9085   |  |  |   |

|             |  |  |   |             |                                      |  |   |
|-------------|--|--|---|-------------|--------------------------------------|--|---|
|             | 3                                      | Teratocarcinoma  | <0.01                                       | 29          | all cancers sites except C56 and C62 | 9081   |   |
|             | 3                                      | Choriocarcinoma combined with other germ cell elements | <0.01                                       | 7           | all cancers sites except C56 and C62 | 9101   |   |
| ORPHA314613 | Missing?                               | Growing teratoma syndrome                              |   |             |                                      |  |   |
| R           | Comment: same terminology as the tier1 | 2  | Extragenital germ cell tumours              | 0.09        | 684                                  | all cancers sites except C56 and C62 (C58.9)                       | 9060-9072; 9100 if not in placenta  |
|             |  | 3  | Dysgerminoma/Seminoma                       | 0.05        | 414                                  | all cancers sites except C56 and C62                               | 9060-9065   |
|             |  | 3  | Embryonal adenocarcinoma                    | 0.01        | 78                                   | all cancers sites except C56 and C62                               | 9070  |
|             |  | 3  | Yolk sac tumour                             | 0.01        | 93                                   | all cancers sites except C56 and C62                               | 9071  |
|             |  | 3  | Choriocarcinoma, NOS                        | 0.01        | 98                                   | all cancers sites except C56 and C62                               | 9100  |
|             |  | 3  | Polyembryoma                                | <0.01       | 1                                    | all cancers sites except C56 and C62                               | 9072  |
|             |  | 1  | <b>SOFT TISSUE SARCOMA</b>                  | <b>4.74</b> | <b>38,127</b>                        | all cancers sites except C40.0-C41.9                               | 8800-8935, 8940, 8950-8959, 8963-8964, 8990-8991, 9020-9044, 9120-9133, 9150, 9170, 9180, 9231, 9240, 9251, 9364-9372, 9540, 9560-9571, 9580-9581 (includes sarcoma of unknown primary sites) |
| R           |  | 2  | <b>Soft tissue sarcoma of head and neck</b> | <b>0.29</b> | <b>2,314</b>                         | C00.0-C14.8, C30.0-C32.9, C49.0, C73.9, C75.2, C75.4, C76.0        | 8800-8902, 8912, 8921, 8933-8935, 8940, 8963, 8990-8991, 9040-9044, 9120-9133, 9150, 9170, 9180, 9231, 9240, 9365-9372, 9540, 9560-9571, 9580-9581  |
|             |  | 3  | Sarcoma NOS                                 | 0.03        | 212                                  | C00.0-C14.8, C30.0, C31.0-C32.9, C47.0, C49.0, C73.9, C75.2, C75.4 | 8800  |
|             |  | 3  | Epithelioid sarcoma                         | <0.01       | 10                                   | C00.0-C14.8, C30.0, C31.0-C32.9, C47.0, C49.0, C73.9, C75.2, C75.4 | 8804  |

Growing teratoma syndrome (GTS) is a rare condition among patients with non-seminomatous germ cell tumors who present with enlarging metastatic masses during appropriate systemic chemotherapy and in the context of normalized serum markers. In the WHO blu book this entity has not been identified with a code thus we cannot include it in the list.

|  |   |                                       |       |     |   |                              |
|--|---|---------------------------------------|-------|-----|---|------------------------------|
|  | 3 | Desmoplastic small round cell tumour  | <0.01 | 1   | C00.0-<br>C14.8,<br>C30.0,<br>C31.0-<br>C32.9,<br>C47.0,<br>C49.0,<br>C73.9,<br>C75.2,<br>C75.4 | 8806                         |
|  | 3 | Fibrosarcoma                          | 0.01  | 85  | C00.0-<br>C14.8,<br>C30.0,<br>C31.0-<br>C32.9,<br>C47.0,<br>C49.0,<br>C73.9,<br>C75.2,<br>C75.4 | 8810                         |
|  | 3 | Fibromyxosarcoma                      | <0.01 | 21  | C00.0-<br>C14.8,<br>C30.0,<br>C31.0-<br>C32.9,<br>C47.0,<br>C49.0,<br>C73.9,<br>C75.2,<br>C75.4 | 8811                         |
| Comment: Why this infantile form has been specifically i | 3 | Infantile fibrosarcoma                | <0.01 | 2   | C00.0-<br>C14.8,<br>C30.0,<br>C31.0-<br>C32.9,<br>C47.0,<br>C49.0,<br>C73.9,<br>C75.2,<br>C75.4 | 8814                         |
|  | 3 | Myxoinflammatory fibroblastic sarcoma | NE    | 0   | C00.0-<br>C14.8,<br>C30.0,<br>C31.0-<br>C32.9,<br>C47.0,<br>C49.0,<br>C73.9,<br>C75.2,<br>C75.4 | 8825.1 borderline malignancy |
|  | 3 | Malignant fibrous histiocytoma        | 0.04  | 280 | C00.0-<br>C14.8,<br>C30.0,<br>C31.0-<br>C32.9,<br>C47.0,<br>C49.0,<br>C73.9,<br>C75.2,<br>C75.4 | 8830                         |
|  | 3 | DFSP                                  | NE    | 0   | C00.0-<br>C14.8,<br>C30.0,<br>C31.0-<br>C32.9,<br>C47.0,<br>C49.0,<br>C73.9,<br>C75.2,<br>C75.4 | 8832-8833                    |

the tiers 3 listed are some of the most relevant and not all the histotypes included in the tier 2 (from 8800 to 8902). Please let us know which histotype you are looking for and we can check whether it is in the tier 2.

|   |   |                                 |       |     |   |      |   |
|---|---|---------------------------------|-------|-----|---|------|---|
|   | 3 | Well differentiated liposarcoma | 0.01  | 33  | C00.0-<br>C14.8,<br>C30.0,<br>C31.0-<br>C32.9,<br>C47.0,<br>C49.0,<br>C73.9,<br>C75.2,<br>C75.4 | 8851 |   |
|   | 3 | Myxoid liposarcoma              | <0.01 | 16  | C00.0-<br>C14.8,<br>C30.0,<br>C31.0-<br>C32.9,<br>C47.0,<br>C49.0,<br>C73.9,<br>C75.2,<br>C75.4 | 8852 |   |
|   | 3 | Pleomorphic liposarcoma         | <0.01 | 4   | C00.0-<br>C14.8,<br>C30.0,<br>C31.0-<br>C32.9,<br>C47.0,<br>C49.0,<br>C73.9,<br>C75.2,<br>C75.4 | 8854 |   |
|   | 3 | Mixed type liposarcoma          | NE    | 0   | C00.0-<br>C14.8,<br>C30.0,<br>C31.0-<br>C32.9,<br>C47.0,<br>C49.0,<br>C73.9,<br>C75.2,<br>C75.4 | 8855 |   |
|   | 3 | Dedifferentiated liposarcoma    | <0.01 | 3   | C00.0-<br>C14.8,<br>C30.0,<br>C31.0-<br>C32.9,<br>C47.0,<br>C49.0,<br>C73.9,<br>C75.2,<br>C75.4 | 8858 |   |
|   | 3 | Leiomyosarcoma                  | 0.05  | 387 | C00.0-<br>C14.8,<br>C30.0,<br>C31.0-<br>C32.9,<br>C47.0,<br>C49.0,<br>C73.9,<br>C75.2,<br>C75.4 | 8890 |   |
| <b>R Comment: Why Pleomorphic rhabdomyosarcoma is considered as tier 3 and not tier 2 as the two other types of Rhabdomyosarcoma?</b> | 3 | Pleomorphic rhabdomyosarcoma    | <0.01 | 13  | C00.0-<br>C14.8,<br>C30.0,<br>C31.0-<br>C32.9,<br>C47.0,<br>C49.0,<br>C73.9,<br>C75.2,<br>C75.4 | 8901 | Pleomorphic sarcoma is typical of adult and has a completely different treatment from the childhood rhabdomyosarcoma. Thus it is included among the sarcomas. |



|             |   |                                      |       |     |   |      |  |  |
|-------------|---|--------------------------------------|-------|-----|---|------|--|--|
|             | 3   | Extrarenal rhabdoid tumour           | <0.01 | 2   | C00.0-<br>C14.8,<br>C30.0,<br>C31.0-<br>C32.9,<br>C47.0,<br>C49.0,<br>C73.9,<br>C75.2,<br>C75.4 | 8963 |  |  |
|             | 3   | Synovial sarcoma                     | 0.01  | 35  | C00.0-<br>C14.8,<br>C30.0,<br>C31.0-<br>C32.9,<br>C47.0,<br>C49.0,<br>C73.9,<br>C75.2,<br>C75.4 | 9040 |  |  |
|             | 3   | Clear cell sarcoma of soft tissue    | NE    | 0   | C00.0-<br>C14.8,<br>C30.0,<br>C31.0-<br>C32.9,<br>C47.0,<br>C49.0,<br>C73.9,<br>C75.2,<br>C75.4 | 9044 |  |  |
|             | 3   | Epithelioid angiosarcoma             | 0.03  | 180 | C00.0-<br>C14.8,<br>C30.0,<br>C31.0-<br>C32.9,<br>C47.0,<br>C49.0,<br>C73.9,<br>C75.2,<br>C75.4 | 9120 |  |  |
|             | 3   | Epithelioid hemangioendothelioma     | <0.01 | 2   | C00.0-<br>C14.8,<br>C30.0,<br>C31.0-<br>C32.9,<br>C47.0,<br>C49.0,<br>C73.9,<br>C75.2,<br>C75.4 | 9133 |  |  |
| ORPHA458758 | Missing? if Myxoinflammatory fibroblastic sarcoma included, why | Composite hemangioendothelioma       |       |     |   |      | thanks, we are updating the list to include the WHOupdates which includes also this morphology |  |
| ORPHA458763 | Missing? if Myxoinflammatory fibroblastic sarcoma included, why | Retiform hemangioendothelioma        |       |     |   |      |  | thanks, we are updating the list to include the WHOupdates which includes also this morphology |
| ORPHA2122   | Missing? if Myxoinflammatory fibroblastic sarcoma included, why | Kaposiform hemangioendothelioma      |       |     |   |      |  | 9130/1   |
|             | 3   | Extraskelletal osteosarcoma          | <0.01 | 2   | C00.0-<br>C14.8,<br>C30.0,<br>C31.0-<br>C32.9,<br>C47.0,<br>C49.0,<br>C73.9,<br>C75.2,<br>C75.4 | 9180 |  |  |
|             | 3   | Extraskelletal myxoid chondrosarcoma | <0.01 | 2   | C00.0-<br>C14.8,<br>C30.0,<br>C31.0-<br>C32.9,<br>C47.0,<br>C49.0,<br>C73.9,<br>C75.2,<br>C75.4 | 9231 |  |  |

|             |          |   |   |      |     |   |   |   |
|-------------|----------|---|---|------|-----|---|---|---|
|             |          | 3 | Malignant peripheral nerve sheath tumours | 0.02 | 135 | C00.0-<br>C14.8,<br>C30.0,<br>C31.0-<br>C32.9,<br>C47.0,<br>C49.0,<br>C73.9,<br>C75.2,<br>C75.4 | 9540, 9561, 9571                            |   |
| ORPHA252128 | Missing? |   | Malignant perineurioma                    |      |     |   |   | ICD-O3 code 9571. It is a sarcoma and it is included in the group of sarcomas |
|             |          | 3 | Intimal Sarcoma                           | NE   | 0   | C00.0-<br>C14.8,<br>C30.0,<br>C31.0-<br>C32.9,<br>C47.0,<br>C49.0,<br>C73.9,<br>C75.2,<br>C75.4 | malignancy without ICD-O<br>morphology code |   |
|             |          | 3 | Low grade fibromyxoid sarcoma             | NE   | 0   | C00.0-<br>C14.8,<br>C30.0,<br>C31.0-<br>C32.9,<br>C47.0,<br>C49.0,<br>C73.9,<br>C75.2,<br>C75.4 | malignancy without ICD-O<br>morphology code |   |
|             |          | 3 | Low grade myofibroblastic sarcoma         | NE   | 0   | C00.0-<br>C14.8,<br>C30.0,<br>C31.0-<br>C32.9,<br>C47.0,<br>C49.0,<br>C73.9,<br>C75.2,<br>C75.4 | malignancy without ICD-O<br>morphology code |   |
|             |          | 3 | PEComas                                   | NE   | 0   | C00.0-<br>C14.8,<br>C30.0,<br>C31.0-<br>C32.9,<br>C47.0,<br>C49.0,<br>C73.9,<br>C75.2,<br>C75.4 | malignancy without ICD-O<br>morphology code |   |
|             |          | 3 | Sclerosing epithelioid fibrosarcoma       | NE   | 0   | C00.0-<br>C14.8,<br>C30.0,<br>C31.0-<br>C32.9,<br>C47.0,<br>C49.0,<br>C73.9,<br>C75.2,<br>C75.4 | malignancy without ICD-O<br>morphology code |   |
|             |          | 3 | Undifferentiated pleomorphic sarcoma      | 0.04 | 247 | C00.0-<br>C14.8,<br>C30.0,<br>C31.0-<br>C32.9,<br>C47.0,<br>C49.0,<br>C73.9,<br>C75.2,<br>C75.4 | 8805, 8803                                  |   |
| ORPHA2126   | Missing? |   | Solitary fibrous tumor                    |      |     |   |   | ICD-O3 8815. it is included among the sarcomas                                |



|   |   |  |                 |               |   |  |
|---|---|--|-----------------|---------------|---|--|
|   | 3 | Paraosteal osteosarcoma  | 0.01            | 75            | C40.0-C41.9                               | 9192   |
|   | 3 | High grade surface osteosarcoma  | <0.01           | 4             | C40.0-C41.9                               | 9194   |
|   | 3 | Low grade central osteosarcoma   | NE              | 0             | C40.0-C41.9                               | 9187   |
|   | 3 | Periosteal osteosarcoma  | NE              | 0             | C40.0-C41.9                               | 9193   |
|   | 3 | Secondary osteosarcoma   | NE              | 0             | C40.0-C41.9                               | malignancy without ICD-O morphology code   |
| R   | 2 | <b>Chondrogenic sarcomas</b>   | <b>0.24</b>     | <b>1,965</b>  | C40.0-C41.9                               | 9220, 9240, 9242-9243  |
|   | 3 | Chondrosarcoma   | 0.24            | 1,919         | C40.0-C41.9                               | 9220   |
|   | 3 | Mesenchymal chondrosarcoma   | <0.01           | 35            | C40.0-C41.9                               | 9240   |
|   | 3 | Clear cell chondrosarcoma  | <0.01           | 2             | C40.0-C41.9                               | 9242   |
|   | 3 | Dedifferentiated chondrosarcoma  | <0.01           | 9             | C40.0-C41.9                               | 9243   |
| R   | 2 | <b>Notochordal sarcomas, chordoma</b>  | <b>0.04</b>     | <b>352</b>    | C40.0-C41.9                               | 9370   |
| R   | 2 | <b>Vascular sarcomas</b>   | <b>&lt;0.01</b> | <b>26</b>     | C40.0-C41.9                               | 9120-9133, 9150, 9170  |
|   | 3 | Angiosarcoma   | <0.01           | 26            | C40.0-C41.9                               | 9120   |
| R: Comment: Should Ewing sarcoma be listed as a separated entity? | 2 | <b>Ewing's family of tumours</b>   | <b>0.13</b>     | <b>1,046</b>  | C40.0-C41.9                               | 9260, 9364   |
|   |   | <b>Ewing's family of tumours</b>   |                 |               |   |  |
| R   | 2 | <b>Epithelial tumours, adamantinoma</b>  | <b>0.01</b>     | <b>69</b>     | C40.0-C41.9                               | 9261, 9310   |
| R   | 2 | <b>Other high grade sarcomas (fibrosarcoma, malignant fibrous histiocytoma)</b>                | <b>0.02</b>     | <b>146</b>    | C40.0-C41.9                               | 8810, 8830   |
|   | 3 | Fibrosarcoma   | 0.01            | 48            | C40.0-C41.9                               | 8810   |
|   | 3 | Malignant fibrous histiocytoma   | 0.01            | 98            | C40.0-C41.9                               | 8830   |
| ORPHA2023   |   | Undifferentiated pleomorphic sarcoma (Bone site)   |                 |               |   | undifferentiated sarcoma are included in tier 1 of bone sarcomas. Because are undifferentiated we cannot include them in any tier 2. |
|   |   | Missing?   |                 |               |   |  |
| R   | 1 | <b>GASTROINTESTINAL STROMAL SARCOMA</b>  | <b>0.07</b>     | <b>535</b>    | any sites                                 | 8936   |
| R   | 1 | <b>KAPOSIS SARCOMA</b>   | <b>0.34</b>     | <b>2,775</b>  | any sites                                 | 9140   |
|   |   | <b>NEUROENDOCRINE TUMOURS</b>  | <b>2.53</b>     | <b>20,357</b> | all cancer sites except C34               | 8013, 8041-8045, 8150-8157, 8240-8247, 8249, 8345-8347, 8510, C34  |
| R   | 2 | <b>Well differentiated endocrine tumours, carcinoid</b>  | <b>0.37</b>     | <b>2,956</b>  | All cancer sites except C15-C26, C34, C44 | 8240-8246  |
| R   | 2 | <b>Well differentiated endocrine tumours, atypical carcinoid</b>                               | <b>&lt;0.01</b> | <b>6</b>      | All cancer sites except C15-C26, C34, C44 | 8249   |
| R   | 2 | <b>Poorly differentiated endocrine carcinoma (lung small cell carcinoma and skin excluded)</b> | <b>0.52</b>     | <b>4,199</b>  | All cancer sites except C34, C44, C73     | 8013, 8041-8045  |
|   | 3 | Small cell endocrine carcinoma   | 0.52            | 4,181         | All cancer sites except C34, C44, C73     | 8041-8045  |
|   | 3 | Large cell endocrine carcinoma   | <0.01           | 18            | All cancer sites except C34, C44, C73     | 8013   |
| R   | 2 | <b>Mixed endocrine-exocrine carcinoma</b>  | <b>&lt;0.01</b> | <b>17</b>     | All cancer sites except C34, C44          | 8154   |
| R   | 2 | <b>Endocrine carcinoma of thyroid gland</b>  | <b>0.22</b>     | <b>1,753</b>  | C73                                       | 8041, 8510, 8345-8347  |
|   | 3 | Medullary carcinoma  | 0.22            | 1,747         | C73                                       | 8510, 8345   |

yes and thus it is a distinct tier 2

undifferentiated sarcoma are included in tier 1 of bone sarcomas. Because are undifferentiated we cannot include them in any tier 2.

|             |          |  |             |               |                                   |                                   |
|-------------|----------|--|-------------|---------------|-----------------------------------|-----------------------------------|
|             | 3        | Mixed medullary-follicular carcinoma   | <0.01       | 6             | C73                               | 8346                              |
| R           | 2        | <b>Well differentiated not functioning endocrine carcinoma of pancreas and digestive tract</b> | <b>1.26</b> | <b>10,099</b> | C15-26                            | 8240-8246, 8249, 8150             |
|             | 3        | Carcinoid tumour, NOS  | 1.22        | 9,841         | C15-26                            | 8240-8246                         |
|             | 3        | Islet cell carcinoma   | 0.03        | 253           | C15-26                            | 8150                              |
| R           | 2        | <b>Well differentiated functioning endocrine carcinoma of pancreas and digestive tract</b>     | <b>0.02</b> | <b>197</b>    | C15-26                            | 8151-8153, 8155-8157              |
|             | 3        | Insulinoma, malignant  | 0.01        | 108           | C15-26                            | 8151                              |
|             | 3        | Glucagonoma, malignant   | <0.01       | 23            | C15-26                            | 8152 and 8157                     |
|             | 3        | Somatostatinoma, malignant   | NE          | 0             | C15-26                            | 8156                              |
|             | 3        | Gastrinoma, malignant  | 0.01        | 57            | C15-26                            | 8153                              |
|             | 3        | VIP-oma  | <0.01       | 9             | C15-26                            | 8155                              |
|             | 3        | Other ectopic hormone producing tumours  | NE          | 0             | C15-26                            | malignancy without ICD-O          |
|             | 3        | Other ectopic hormone producing tumours  | NE          | 0             | C15-26                            | malignancy without ICD-O          |
| R           | 2        | <b>Endocrine carcinoma of skin</b>   | <b>0.13</b> | <b>1,079</b>  | C44                               | 8041-8044, 8240-8247              |
|             | 3        | Merkel cell carcinoma  | 0.12        | 972           | C44                               | 8247                              |
| ORPHA97287  | Missing? | Bronchial neuroendocrine tumor   |             |               |                                   |                                   |
| ORPHA100083 | Missing? | Laryngeal neuroendocrine tumor   |             |               |                                   |                                   |
| ORPHA100084 | Missing? | Middle ear neuroendocrine tumor  |             |               |                                   |                                   |
| ORPHA100085 | Missing? | Primary hepatic neuroendocrine carcinoma   |             |               |                                   |                                   |
| ORPHA100086 | Missing? | Gallbladder neuroendocrine tumor   |             |               |                                   |                                   |
|             | 1        | <b>CARCINOMA OF ENDOCRINE ORGANS</b>   | <b>4.13</b> | <b>33,257</b> | C73-C75.1                         | 8000-8001, 8003-8004, 8010-8012,  |
| R           | 2        | <b>Carcinomas of pituitary gland</b>   | <b>0.04</b> | <b>333</b>    | C75.1                             | 8000-8001, 8010, 8140-8381        |
|             | 3        | Pituitary carcinoma  | NE          | 0             | C75.1                             | 8272                              |
| R           | 2        | <b>Carcinomas of thyroid gland</b>   | <b>3.65</b> | <b>29,333</b> | C73.9                             | 8000-8001, 8003-8004, 8010, 8012, |
|             | 3        | Papillary adenocarcinoma, NOS  | 2.05        | 16,506        | C73.9                             | 8050, 8260                        |
|             | 3        | Follicular carcinoma, NOS  | 0.57        | 4,550         | C73.9                             | 8330                              |
|             | 3        | Pleomorphic carcinoma  | NE          | 0             | C73.9                             | 8022                              |
|             | 3        | Undifferentiated/anaplastic carcinoma  | 0.17        | 1,373         | C73.9                             | 8020-8021                         |
|             | 3        | Mucoepidermoid carcinoma   | <0.01       | 9             | C73.9                             | 8430                              |
|             | 3        | Mucinous carcinoma   | <0.01       | 4             | C73.9                             | 8480                              |
|             | 3        | Spindle cell tumour with thymus-like differentiation (SETTLE)                                  | <0.01       | 1             | C73.9                             | 8588                              |
|             | 3        | Carcinoma showing thymus-like differentiation (CASTLE)   | NE          | 0             | C73.9                             | 8589                              |
| R           | 2        | <b>Carcinomas of parathyroid gland</b>   | <b>0.02</b> | <b>176</b>    | C75.0.                            | 8000-8001, 8010-8012, 8014-8035,  |
| R           | 2        | <b>Carcinoma of adrenal gland</b>  | <b>0.18</b> | <b>1,459</b>  | C74                               | 8000-8001, 8010-8012, 8014-8035,  |
|             | 3        | Adrenal cortical carcinoma   | 0.07        | 598           | C74                               | 8370                              |
|             | 1        | <b>GLIAL TUMOURS OF CENTRAL NERVOUS SYSTEM (CNS)</b>   | <b>5.35</b> | <b>43,037</b> | C71,<br>C72.0,<br>C72.8-<br>C72.9 | 9380-9384, 9391-9460              |
| R           | 2        | <b>Astrocytic tumours of CNS</b>   | <b>4.80</b> | <b>38,588</b> | C71,<br>C72.0,<br>C72.8-72.9      | 9380-9382, 9384, 9400-9442        |
|             | 3        | Astrocytoma, NOS   |             |               | C71,<br>C72.0,<br>C72.8-<br>C72.9 | 9400                              |
|             | 3        | Astrocytoma, anaplastic  | 0.87        | 7,028         | C71,<br>C72.0,<br>C72.8-<br>C72.9 | 9401                              |
|             | 3        | Glioblastoma   | 0.40        | 3,253         | C71,<br>C72.0,<br>C72.8-<br>C72.9 | 9440                              |
|             | 3        | Gliosarcoma  | 2.52        | 20,292        | C71,<br>C72.0,<br>C72.8-<br>C72.9 | 9442                              |
|             | 3        | Giant cell glioblastoma  | 0.03        | 228           | C71,<br>C72.0,<br>C72.8-<br>C72.9 | 9441                              |
|             | 3        | Astroblastoma  | 0.02        | 182           | C71,<br>C72.0,<br>C72.8-<br>C72.9 | 9430                              |
|             | 3        | Protoplasmic astrocytoma   | 0.01        | 106           | C71,<br>C72.0,<br>C72.8-<br>C72.9 | 9410                              |

in the RARECAREnet list there is a tier 2 for neuroendocrine tumors of other sites which includes all the sites not listed in the other tiers 2. please refer to row 744-772 of the RARECAREnet list

|             |   |   |             |              |                         |  |   |
|-------------|---|---|-------------|--------------|-------------------------|--|---|
|             | 3 | Gliomatosis cerebri   | 0.01        | 73           | C71, C72.0, C72.8-C72.9 | 9381   |   |
|             | 3 | Pleomorphic xanthoastrocytoma   | 0.01        | 75           | C71, C72.0, C72.8-C72.9 | 9424   |   |
|             | 3 | Pilocytic and Pilocitoid astrocytoma  | <0.01       | 1            | C71, C72.0, C72.8-C72.9 | 9421.1 borderline tumour                     |   |
|             | 3 | Oligoastrocytoma  | 0.11        | 859          | C71, C72.0, C72.8-C72.9 | 9382   |   |
| ORPHA251663 |   | Anaplastic oligoastrocytoma   |             |              |                         |  | this is included in the tier 2. Tiers 3 listed include only some of the histotype to reduce the length of the list. If you wish we can include another tier 3 but the histotype is not missing                    |
|             |   | Missing?  |             |              |                         |  |   |
|             | 3 | Subependymal giant cell astrocytoma   |             |              | C71, C72.0, C72.8-C72.9 | 9384.1 borderline tumour                     | upon request of the experts, some relevant border line entities have been included.   |
|             |   | Comment: borderline malignancy  |             | NE           | 0                       |  |   |
|             | R | <b>Oligodendroglial tumours of CNS</b>  | <b>0.35</b> | <b>2,845</b> | C71, C72.0, C72.8-72.9  | 9450-9451,9460                               |   |
|             | 3 | Oligodendroglioma   | 0.25        | 2,046        | C71, C72.0, C72.8-72.9  | 9450   |   |
|             | 3 | Oligodendroglioma, anaplastic   | 0.09        | 740          | C71, C72.0, C72.8-72.9  | 9451   |   |
|             | R | <b>Ependymal tumours of CNS</b>   | <b>0.20</b> | <b>1,604</b> | C71, C72.0, C72.8-C72.9 | 9383, 9391-9394                              |   |
|             | 3 | Ependymoma, NOS   | 0.16        | 1,318        | C71, C72.0, C72.8-C72.9 | 9391   |   |
|             | 3 | Ependymoma, anaplastic  | 0.03        | 239          | C71, C72.0, C72.8-C72.9 | 9392   |   |
|             | 3 | Subependymoma   | <0.01       | 1            | C71, C72.0, C72.8-C72.9 | 9383.1 borderline malignancy                 | as specified, it is border line. Some border line entities have been included upon request of the experts.  |
|             |   | Comment: isn't a benign form?   |             |              |                         |  |   |
|             | 3 | Myxopapillary ependymoma  | <0.01       | 9            | C71, C72.0, C72.8-C72.9 | 9394.1 borderline malignancy                 |   |
|             |   | Comment: isn't a benign form?   |             |              |                         |  |   |
|             | R | <b>NON GLIAL TUMOURS OF CNS AND PINEAL GLAND</b>                                      | <b>0.22</b> | <b>1,805</b> | C71, C72.0, C75.3       | 9362, 9390, 9470-9474, 9490, 9500-9505, 9508 |   |
|             | R | <b>Embryonal tumours of CNS</b>   | <b>0.22</b> | <b>1,755</b> | C71, C72.0, C75.3       | 9362, 9470-9474, 9490, 9500-9505, 9508       |   |
|             | 3 | Medulloblastoma   | 0.11        | 886          | C71, C72.0              | 9470   |   |
|             | 3 | Desmoplastic nodular medulloblastoma  | 0.01        | 99           | C71, C72.0              | 9471   |   |
|             | 3 | PNET  | 0.07        | 566          | C71, C72.0              | 9473, 9490, 9500                             |   |
|             | 3 | Anaplastic ganglioglioma  | <0.01       | 25           | C71, C72.0              | 9505   |   |
|             | 3 | Atypical teratoid/rhabdoid tumour   | <0.01       | 6            | C71, C72.0              | 9508   |   |
|             | 3 | Medulloepithelioma, NOS   | <0.01       | 1            | C71, C72.0              | 9501   |   |
|             | 3 | Pineoblastoma   | 0.02        | 128          | C75.3                   | 9362   |   |
|             | R | <b>Choroid plexus carcinoma of CNS</b>  | <b>0.01</b> | <b>50</b>    | C71.5                   | 9390   |   |
| ORPHA251902 |   | Atypical papilloma of choroid plexus  |             |              |                         |  | ICD-O 9390/1 it is in the ICD-O updates of the 2011. anyway it is a border line and I am afraid we will not include it in our list which include malignant cancer only with few exceptions requested by consensus |
|             |   | Missing? borderline malignancy?   |             |              |                         |  |   |
|             | R | <b>MALIGNANT MENINGIOMAS</b>  | <b>0.15</b> | <b>1,223</b> | C70                     | 9530, 9538-9539                              |   |
| ORPHA251995 |   | Missing? Maybe interesting to include these entities as extragonadal germ cell tumor? |             |              |                         |  | there is a tier 1 (extra gonadal germ cell) including these entities in all the sites different from the gonadal ones. Please refer to row 634 of the RARECAREnet list  |
|             | 1 | Primary germ cell tumor of central nervous system                                     |             |              |                         |  |   |

|             |   |   |   |                 |            |  |  |  |
|-------------|---|---|---|-----------------|------------|--|--|--|
| ORPHA48736  | Missing? Maybe interesting to include these entities as extragonadal germ cell tumor? |   | Embryonal carcinoma of the central nervous system   |                 |            |  |  |  |
| ORPHA91352  | Missing? Maybe interesting to include these entities as extragonadal germ cell tumor? |   | Germinoma of the central nervous system   |                 |            |  |  |  |
| ORPHA252006 | Missing? Maybe interesting to include these entities as extragonadal germ cell tumor? |   | Yolk sac tumor of central nervous system  |                 |            |  |  |  |
| ORPHA252015 | Missing? Maybe interesting to include these entities as extragonadal germ cell tumor? |   | Choriocarcinoma of the central nervous system   |                 |            |  |  |  |
| ORPHA252018 | Missing? Maybe interesting to include these entities as extragonadal germ cell tumor? |   | Teratoma of the central nervous system  |                 |            |  |  |  |
| ORPHA252021 | Missing? Maybe interesting to include these entities as extragonadal germ cell tumor? |   | Mixed germ cell tumor of central nervous system   |                 |            |  |  |  |
|             |   | 1 | <b>GLIAL TUMOURS OF CRANIAL AND PERIPHERAL NERVES, AUTONOMIC NERVOUS SYSTEM</b>                     | <b>0.01</b>     | <b>82</b>  | C47.0-C47.9, C72.1-C72.5   | 9391-9393, 9400-9442,9505                          |  |
| R           |   | 2 | <b>Astrocytic tumours of cranial and peripheral nerves, autonomic nervous system</b>                | <b>&lt;0.01</b> | <b>40</b>  | C47.0-C47.9, C72.1-C72.5   | 9400-9442, 9505                                    |  |
|             |   | 3 | Astrocytoma, NOS  | <0.01           | 23         | C47.0-C47.9, C72.1-C72.5   | 9400   |  |
|             |   | 3 | Astrocytoma anaplastic  | <0.01           | 8          | C47.0-C47.9, C72.1-C72.5   | 9401   |  |
|             |   | 3 | Glioblastoma  | <0.01           | 6          | C47.0-C47.9, C72.1-C72.5   | 9440   |  |
|             |   | 3 | Gliosarcoma   | <0.01           | 1          | C47.0-C47.9, C72.1-C72.5   | 9442   |  |
|             |   | 3 | Ganglioglioma, anaplastic   | <0.01           | 1          | C47.0-C47.9, C72.1-C72.5   | 9505   |  |
| R           |   | 2 | <b>Ependymal tumours of cranial and peripheral nerves and autonomic nervous system</b>              | <b>0.01</b>     | <b>42</b>  | C47.0-C47.9, C72.1-C72.5   | 9391-9393  |  |
|             |   | 3 | Ependymoma  | 0.01            | 42         | C47.0-C47.9, C72.1-C72.5   | 9391-9393  |  |
|             |   | 1 | <b>NON-GLIAL TUMOURS OF CRANIAL AND PERIPHERAL NERVES, AUTONOMIC NERVOUS SYSTEM AND PARAGANGLIA</b> | <b>0.10</b>     | <b>790</b> | C47.0-C47.9, C72.1-C72.5 for 9473,9490, 9500, 9502-9503<br>C30.0-C31.9 only for 9520-9523 (olfactory tumours)<br>Any sites only for 8680, 8693 (paraganglioma) | 9473, 9490, 9500, 9502-9503, 9520-9523, 8680, 8693 |  |

|             |   |  |    |   |       |         |   |  |   |
|-------------|---|--|----|---|-------|---------|---|--|---|
|             | R   |  | 2  | <b>Embryonal tumours of cranial and peripheral nerves, autonomic nervous system</b> | 0.07  | 590     | C47.0-C47.9,C72.1-C72.5, C30.0-C31.9 only for 9520-9523 (olfactory tumours) | 9473,9490, 9500, 9502-9503, 9520-9523  |   |
|             |   |  | 3  | PNET  | 0.04  | 335     | C47.0-C47.9, C72.1-C72.5  | 9473, 9490, 9500   |   |
|             |   |  | 3  | Olfactory neuroblastoma   | 0.02  | 194     | C30.0-C31.9   | 9522   |   |
|             |   |  | 3  | Olfactory neuroepithelioma  | <0.01 | 18      | C30.0-C31.9   | 9523   |   |
|             |   |  | 3  | Olfactory neurogenic tumour   | <0.01 | 4       | C30.0-C31.9   | 9520   |   |
|             |   |  | 3  | Teratoid medulloepithelioma   | <0.01 | 1       | C47.0-C47.9,C72.1-C72.5   | 9502   |   |
|             |   |  | 3  | Neuroepithelioma, NOS   | <0.01 | 28      | C47.0-C47.9,C72.1-C72.5   | 9503   |   |
|             | R   |  | 2  | <b>Paraganglioma</b>  | 0.02  | 200     | any sites   | 8680, 8693,  |   |
|             |   |  | 1  | <b>LYMPHOID DISEASES</b>  | 29.09 | 234,036 |   | 9590, 9591, 9596, 9650-9655, 9659,   |   |
|             | R   |  | 2  | <b>Classical Hodgkin lymphoma</b>   | 2.38  | 19,131  |   | 9650-9655, 9661-9667   |   |
|             |   |  | 3  | Lymphocyte-rich   | 0.10  | 799     |   | 9651   |   |
|             |   |  | 3  | Mixed cellularity   | 0.42  | 3,366   |   | 9652   |   |
|             |   |  | 3  | Lymphocyte-depleted   | 0.04  | 333     |   | 9653-9655  |   |
|             |   |  | 3  | Nodular sclerosis   | 1.28  | 10,310  |   | 9663-9667  |   |
|             | R   |  | 2  | <b>Hodgkin lymphoma nodular lymphocyte predominance</b>                             | 0.06  | 466     |   | 9659   |   |
|             | R   |  | 2  | <b>Composite Hodgkin and Non Hodgkin lymphoma</b>                                   | 0.01  | 42      |   | 9596   |   |
| ORPHA99860  | R   |  | 2  | <b>Precursor B/T lymphoblastic leukaemia/lymphoblastic lymphoma</b>                 | 1.28  | 10,316  |   | 9727-9729, 9835-9837   | In the RARECAREnet list there are 2 tiers 3: Precursor B/T lymphoblastic leukaemia/lymphoblastic lymphoma and Burkitt leukaemia/lymphoma. It is not relevant whether there is a tier 3 because, as explained earlier on, we included only some tiers 3. To check whether an histotype is included you should look at the morphologies listed in Tier 1 and 2. |
| ORPHA99861  | Missing?  |  | 3? | Precursor B-cell acute lymphoblastic leukemia                                       |       |         |   |  |   |
|             | Missing?  |  | 3? | Precursor T-cell acute lymphoblastic leukemia                                       |       |         |   |  |   |
|             | Comment: does it make sense to have more detailed subtypes?   |  | 2  | <b>Non Hodgkin Mature T cell and NK-cell neoplasms</b>                              | 0.99  | 7,947   |   | 9700-9702, 9705, 9708-9709, 9714, 9716-9719, 9827, 9831, 9834, 9948                                    | the RARECAREnet list has different tiers 2: T cutaneous lymphoma (Sezary syn, Mycosis fung); Other T cell lymphomas and NK cell neoplasms   |
|             |   |  | 3  | T cutaneous lymphoma (Sezary syn, Mycosis fung)                                     | 0.52  | 4,144   |   | 9700-9701, 9709, 9718  |   |
|             |   |  | 3  | other T cell lymphomas  | 0.47  | 3,803   |   | 9702, 9705, 9708, 9714, 9716-9717,   |   |
|             | C Comment: Tier 2 is considered common but all tier 3 are really considered as rare entities.   |  | 2  | <b>Non Hodgkin, Mature B cell lymphoma</b>  | 17.45 | 140,361 |   | 9670-9671, 9673, 9675, 9678-9680, 9684, 9687, 9689-9691, 9695, 9698, 9699, 9731-9734, 9760-9762, 9764, | the RARECAREnet list includes several tiers 2: Diffuse B lymphoma; Follicular B lymphoma; Hairy cell leukaemia; Plasmacytoma/Multiple Myeloma (and Heavy chain diseases); Other non Hodgkin, Mature B cell lymphoma, Mantle cell lymphoma; Prolymphocytic leukaemia, B cell   |
|             |   |  | 3  | Small cell lymphocytic lymph/chronic lymphatic leukaemia                            | 4.7   | 37,844  |   | 9670, 9823   |   |
|             |   |  | 3  | Mantle cell/lymph centrocytic   | 0.36  | 2,912   |   | 9673   |   |
|             |   |  | 3  | Prolymphocytic leukaemia, B cell  | 0.05  | 414     |   | 9832-9833  |   |
|             |   |  | 3  | Lymphoma lymphoplasmacitic/macroglobulinemia Waldstrom                              | 0.81  | 6,510   |   | 9671, 9761   |   |
|             |   |  | 3  | Burkitt leukaemia/lymphoma  | 0.17  | 1,355   |   | 9687, 9826   |   |
|             | Comment: Should large be precised?  |  | 3  | Diffuse B lymphoma  | 2.79  | 22,429  |   | 9678-9680, 9684  | for one entities yes, we will ask ho it is better to refer to this. Thank you   |
|             |   |  | 3  | Splenic/nodal marginal zone/extra nodal MALT type                                   | 0.3   | 2,396   |   | 9689, 9699, 9764   |   |
|             |   |  | 3  | Follicular B lymphoma   | 2.12  | 17,055  |   | 9675, 9690-9691, 9695, 9698  |   |
|             |   |  | 3  | Hairy cell leukaemia  | 0.29  | 2,320   |   | 9940   |   |
|             |   |  | 3  | Hairy cell leukaemia  |       |         |   |  |   |
|             |   |  | 3  | Plasmocitoma/multiple mieloma   | 5.86  | 47,112  |   | 9731-9734  |   |
|             |   |  | 3  | Plasmocitoma/multiple mieloma   |       |         |   |  |   |
|             |   |  | 3  | Heavy chain disease   | <0.01 | 14      |   | 9762   |   |
| ORPHA443159 | Missing? PMID: 26421453, 23544948, 21300984   |  |    | Lymphoplasmacytic lymphoma without IgM production                                   |       |         |   |  | in the WHO 2008 and the recent 2017 we have only Lymphoma lymphoplasmacytic/macroglobulinemia Waldstrom 9671 and 9761. they are both in our list  |
| ORPHA48686  | Missing? large B-cell lymphoma  |  |    | Primary effusion lymphoma   |       |         |   |  | it is in the tier 1 lymphoma but not in tier 2  |
| ORPHA99860  | Missing?  |  |    | Precursor B-cell acute lymphoblastic leukemia                                       |       |         |   |  | please refer to my previous comment row 833   |
| ORPHA289666 | Missing?  |  |    | Plasmablastic lymphoma  |       |         |   |  | ICD-O3 codes 9735 of the updates. We are updating the RARECAREnet list  |
| ORPHA480541 | Missing? PMID: 28447410   |  |    | High grade B-cell lymphoma with MYC and/ or BCL2 and/or BCL6 rearrangement          |       |         |   |  | 9680 is the new code from WHO 2017. Updates of our list ongoing   |
|             |   |  | 1  | <b>ACUTE MYELOID LEUKEMIA AND RELATED PRECURSOR NEOPLASMS</b>                       | 3.69  | 29,719  |   | 9805, 9840, 9860-9861, 9866-9867,  |   |
|             | R Comment:All the AML with recurrent genetic abnormalities as defined by the last version of the WHO classification should be included as tier 3. |  | 2  | <b>AML with recurrent genetic abnormalities</b>                                     | 0.11  | 914     |   | 9866, 9871, 9896, 9897   | we are updating the list. Thank you   |
|             |   |  | 3  | AML with t(8;21)(q22;q22); AML 1/ETO  | <0.01 | 20      |   | 9896   |   |
|             |   |  | 3  | AML with inv(16)(p13.1q22)or t(16; 16)(p13.1q22),(CBFbeta/MYH)                      | <0.01 | 8       |   | 9871   |   |
|             |   |  | 3  | Acute promyelocytic leukemia (AML with t(15;17) with variants                       | 0.11  | 885     |   | 9866   |   |





|   |  |  |                 |              |                          |
|---|--|--|-----------------|--------------|--------------------------|
| Comment: Should be named 'Myelodysplastic syndrome' | 3  | Refractory anemia  | 0.21            | 1,695        | 9980                     |
|   | 3  | Refractory anemia with sideroblasts  | 0.09            | 767          | 9982                     |
|   | 3  | Refractory anemia with excess blasts   | 0.15            | 1,172        | 9983                     |
|   | 3  | Refractory cytopenia with multilineage dysplasia   | <0.01           | 2            | 9985                     |
|   | 3  | Myelodysplastic syndrome with 5q syndrome  | <0.01           | 3            | 9986                     |
|   | 3  | Myelodysplastic syndrome NOS   | 1.04            | 8,429        | 9989                     |
|   | 1  | <b>MYELODYSPLASTIC/MYELOPROLIFERATIVE DISEASES</b>   | <b>0.29</b>     | <b>2,322</b> | 9876, 9945-9946, 9975    |
| R   | 2  | <b>Chronic myelomonocytic leukemia NOS</b>   | <b>0.29</b>     | <b>2,313</b> | 9945                     |
| R   | 2  | <b>Juvenile myelomonocytic leukemia</b>  | <b>&lt;0.01</b> | <b>3</b>     | 9946                     |
| R   | 2  | <b>Atypical chronic myeloid leukemia BCR/ABL negative</b>                                    | <b>&lt;0.01</b> | <b>6</b>     | 9876                     |
| ORPHA98825  | Missing?   | <b>MYELODYSPLASTIC/MYELOPROLIFERATIVE DISEASES NOS</b>                                       |                 |              |                          |
|   | Missing? <a href="http://publications.iarc.fr/media/download/1478">http://publications.iarc.fr/media/download/1478</a> | <b>Myelodysplastic/myeloproliferative neoplasm with ring sideroblasts and thrombocytosis</b> |                 |              |                          |
|   | R  | <b>HISTIOCYTIC AND DENDRITIC CELL NEOPLASMS</b>  | <b>0.05</b>     | <b>393</b>   | 9750-9758                |
|   |  | Histiocytic sarcoma  | <0.01           | 31           | 9755                     |
|   |  | Langherans cell histiocytosis  | NE              | 0            | 9751/1                   |
|   |  | Langherans cell sarcoma  | NE              | 0            | 9756                     |
|   |  | Interdigitating dendritic cell sarcoma   | <0.01           | 4            | 9757                     |
|   |  | Follicular dendritic cell sarcoma  | <0.01           | 3            | 9758                     |
|   |  | Fibroblastic reticular cell tumour   | NE              | 0            | ICD-O code not available |

we are updating the RARECAREnet list based on the WHO , thanks  
we are updating the RARECAREnet list based on the WHO , thanks

-1

Missing? very rare, usually benign but some aggressive cases de: Indeterminate dendritic cell neoplasm

|             |          |    |  |  |   |
|-------------|----------|----|--|--|---|
| ORPHA168943 | Missing? | 2? | Myeloid/lymphoid neoplasms associated with eosinophilia and abnormality of PDGFRA, PDGFRB or FGFR1 |  |   |
| ORPHA168947 | Missing? | 3? | Myeloid/lymphoid neoplasm associated with PDGFRA rearrangement                                     |  | WHO blu book 2008 9965. Updates of our list ongoing |
| ORPHA168950 | Missing? | 3? | Myeloid/lymphoid neoplasm associated with PDGFRB rearrangement                                     |  | WHO blu book 2008 9966. Updates of our list ongoing |
| ORPHA168953 | Missing? | 3? | Myeloid/lymphoid neoplasm associated with FGFR1 rearrangement                                      |  | WHO blu book 2008 9967. Updates of our list ongoing |
| -1          | Missing? | 3? | Myeloid/lymphoid neoplasm associated with PCM1-JAK2  |  | WHO blu book 2017 9968. Updates of our list ongoing |

NOS = not otherwise specified