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UEMS 2020/11

Description of "Rare adult solid cancers" as a Medical Competency in EU: Aims and objectives for competency training

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This competency concerns the medical elements of diagnostic and care services provided to individuals and families, and sometimes populations with, or at risk of, conditions which have, or may have, a rare adult solid cancer basis. This includes the provision of diagnostic, counselling, and treatment services, information about the condition(s) and its implications, including management, prognosis, screening, prevention and reproductive options, and therapeutic possibilities. Provision of services is based on thorough clinical assessment, family medical information, conventional laboratory investigations and imaging, and specialized pathology tests. Other components of services include laboratory genetics (cytogenetics, molecular genetics, biochemical genetics, and genomics, including next generation techniques), specialized genetic counselling, and new techniques that are, or will, emerge from academic research. The core activities of the competency can be defined as an integrated clinical and laboratory service, provided for those with, or who are concerned about, a disorder that may be a rare oncology disease. Sometimes, due to the sharing of genetic alleles among family members, the whole family, not only the individual, represents the core patient in this disease cohort. The current sketch uses the conditions, descriptions, terms, and recommendations summarized by the Joint Action on Rare Cancer (JARC) project that are found in the booklet entitled "Rare cancer Agenda 2030: 10 recommendations from the EU Joint Action on Rare Cancers; ISBN 978-88-31637-28-2."

Rare cancers can be defined as those malignancies whose incidence is <6/100,000/year. This definition is somewhat arbitrary, since there is no absolute frequency threshold that

separates cancers, and diseases, into rare and common categories. Essentially, the definition was the product of a consensus process within the European oncology community, funded by the EU RARECARE project, that took into account problems posed by rare cancers in terms of health care organization, clinical research, clinical decision-making (Gatta et al., EJC 2011). It is based on incidence, because unlike prevalence, incidence does not change depending on a factor different from frequency, such as expected survival time. As many diagnostic and therapeutic steps take place only once in the course of cancer development, incidence, unlike prevalence, is more fit to measure cancer burden. Using this threshold, one can draw up a list of rare cancers, that is useful for healthcare organizations, clinical research, and new therapy assessment and financing.

Any list of rare cancers needs to be derived from an established list of all cancers. The most obvious of these is the International Classification of Diseases for Oncology (ICD-O), which incorporates topographical and histological labels. The morphologic entities enlisted in the ICD-O need to be grouped into clinically distinct entities, which in turn may be gathered into families of neoplastic diseases, such as rare adult solid cancers. In 2007 within the RARECARE project, a panel of experts, including clinicians, pathologists and epidemiologists, agreed to build the first list of clinically relevant rare cancer entities on the basis of all the combinations of topography and morphologies coded in the ICD-O3. In 2017, the EU launched the JARC and a consensus effort to re-examine the list of rare cancers as developed by the RARECARE project took place within it, with a view also to rare cancers. In essence, the new list comprises three tiers. Tier 3 corresponds to the morphological entities of the ICD-O. Then, the experts were asked to group the ICD-O3 morphological entities, to give rise to a second tier of clinically distinct entitie by using morphologies and topographies (e.g., “squamous cell carcinoma of nasal cavity and sinuses”, “soft tissue sarcoma of limb”, etc.). These entities had to be viewed as clinically relevant by clinicians. In general, these entities had to correspond to consistent diagnostic and therapeutic approaches, so that, for example, they could be used as eligibility criteria in a clinical trial). Then, the Tier-2 entities were assembled into a smaller number of Tier-1 entities. These were intended to be major cancer entities in a clinical sense (e.g., “epithelial tumours of nasal cavity and sinuses”, “soft tissue sarcoma”) and to have an organizational importance: for example, they could underlie patient referral policies. Focusing on referral of patients, Tier-1 entities can be grouped into gross partitions, which give rise to what were called “families” of rare cancers, identifying major groups of rare cancers (e.g., “rare cancers of head & neck”, “sarcomas”, etc.). By and large, these are dealt with by the same

disease-based communities of physicians and clinical researchers. Tier-1 entities with an incidence rate <6/100,000/year define the major families of rare cancers (Table 1).

With regard to cancers in children and adolescents, the RARECARE list includes some of them under the family of "paediatric cancers", but several were included along with adult cancers in specific families, including haematological tumours, sarcomas, central nervous system tumours, head and neck cancers, digestive cancers, thoracic cancers, and endocrine tumours. All childhood cancers are rare, and should be considered as distinct from adult cancers affecting the same organs because their etiology is usually different. Furthermore, the risk of some cancers has a hereditary component. Some heritable cancers are rare cancers as such (e.g., sarcomas in Li Fraumeni syndrome), while others belong to common entities (e.g., colon adenocarcinoma in a familial adenomatous polyposis). Currently, there is no specific code for registration of heritable cancers as such, and some are considered among rare diseases.

An important challenge in medical education in rare diseases, including rare cancers, that makes it essentially different from common diseases is the lack of reinforcement of information. For example, when a physician attends an educational event on a common cancer, they will be likely to encounter patients with that cancer very soon and very often throughout their practice. The same does not apply when the cancer or disease is rare. Thus, the educational frame of any educational initiative in rare cancers must take this challenge into account. As to the current state of affairs, a survey was made on training programmes currently available for under- and postgraduates related to adult and paediatric cancers and is available on the website of JARC.

Ten recommendations from the EU Joint Action on Rare Cancers

The recommendations listed below were originally provided to all stakeholders involved in the rare adult solid cancer care, but they appear to be very useful when we depict the rare adult solid cancer general characteristics (from JARC booklet):

1. **Rare cancers are the rare diseases of oncology**
   and need specific approaches by the cancer community and by national health systems.

2. **Rare cancers should be strictly monitored**

epidemiologically and clinically, properly valuing population-based cancer registry data and real-world clinical data, favouring all efforts to merge data from all available data bases.

3. **Health systems should exploit networking**
around multidisciplinary centres of reference, to improve quality of care in rare cancers while diminishing/rationalizing health migration.

4. **Medical education should exploit and serve healthcare networking**
by proper integration of the university system, continuous medical education providers and all educational players, serving dedicated career mechanisms and opportunities for rare cancers.

5. **Research should be fostered by networking**
exploiting clinically annotated bio banking, clinical registering, patient referral to ongoing clinical studies.

6. **Patient-physician shared clinical decision-making should be especially valued**
being crucial to the appropriate approach to the possibly high degree of uncertainty posed by rare cancers.

7. **Appropriate state-of-the-art instruments should be developed in rare cancers**
fit to serve clinical decision-making in conditions of uncertainty.

8. **Regulatory mechanisms on rare cancers should properly face the challenge of a possibly higher degree of uncertainty**
being disease-adapted, opening up to innovative research methodologies, assuring certainty of rules to developers of innovation, recognizing enough flexibility as to allow a personalized clinical decision-making in conditions of uncertainty.

9. **Sustainability should be addressed by exploiting networking**
also providing evidence of its economies, and by pursuing a value-based medicine aware of the many difficulties of rare cancers.

10. Rare cancer patient advocates should be always involved

in all crucial areas, such as disease awareness and education, healthcare organization, state-of-the-art instruments, regulatory mechanisms, clinical and translational research, while having access to continuous education.

Special features: medical education and healthcare networking

In general, the medical education should be done by appropriate integration of the university system, continuous medical education providers, and all educational players, serving dedicated career mechanisms and opportunities for rare cancers. It also must be responsive to feedback from patient advocacy groups. In the rare adult solid cancer area patients very often remain without a specific doctor who takes charge of their treatment, which is an unsatisfactory situation.

Clearly, medical personnel of reference centres are a natural target of medical education on rare cancers, for reasons that do not differ substantially from the rationale for medical education on common cancers. However, by definition, rare cancers are scarce and there may be fewer opportunities for private sponsorships for events that focus on them, which means they will require more institutional support.

Medical personnel belonging to spokes of hub-and-spoke networks should be provided opportunities for medical education on rare cancers, since such personnel represent a target to develop, as long as hub-and-spoke networks spread. It is instrumental to the virtuous circle of quality improvement of spokes that such an education reaches out to their personnel. In fact, it is vital that clinicians within the spokes are able to collaborate effectively with hubs, in such a way as to virtually create the same kind of environment that exists within physically contiguous centres of reference. In other words, clinicians in spokes should be well aware of the diseases they are dealing with, even though their institutions do not see a number of cases comparable to hubs. For example, a medical oncologist in a spoke must be able to interact effectively with an experienced surgeon in a reference centre, in order to make medical therapy match all the needs of a planned highly specialized surgery. Of course, clinicians in spokes will not specialize only in one cancer amongst rare adult solid cancers, and these do not constitute a single set of cancers, unlike paediatric cancers, that are grouped together in the paediatric oncology area, and haematological cancers, that are grouped within the domain of haemato-oncology. Thus, it

is logical to conceive educational events that focus on several related rare adult solid cancers, (e.g., sarcomas and mesothelioma, etc.).

Undergraduates and general practitioners are a particularly challenging target, since the lack of information reinforcement is a major problem. However these providers are extremely important because the initial clinical diagnosis of a new suspect case will often rely on their degree of intuition and proper referral often depends on them. In general, it is important that non-oncologists perceive and importance of rare cancers and are aware of the main organizational challenges, of the importance of proper referral, of the meaning and the organization of clinical networking, of the difficulties of clinical research, and of the methodology of shared decision-making in conditions of uncertainty.

Given the crucial importance of these professional figures for networks, training opportunities should be arranged for case managers, patient navigators and other health professionals specializing in supporting networking functioning and the rare cancer patient journey.

The development of professional figures of nurses specializing in single rare cancers, within centres of reference, or some rare cancers, within rare cancer networks, should be encouraged and training facilities should be properly provided.

Medical education should be done through networking, as this approach will help shape and extend the contents of education on offer, while, obviously, it also allows IT facilities to convey tools for distance learning, distance mentorships, and the like. Distance learning may have the drawback of a lack of interaction between the mentor and the learner, but over a network this may be easily overcome by complementing distance tools with privileged connections between one teacher and one learner. Teleconsultation, within clinical networks, is obviously a healthcare resource that can improve quality of care in single cases, but it is also a powerful educational tool. After being teleconsulted, several clinical cases can then be grouped and offered as background educational material to the other members of the network, with a special view to young oncologists and other specialists.

Fellowships within networks are especially important. A clinical network is also based on personal relationships among clinicians, and even a relatively short fellowship at a centre of reference may not only mean a big opportunity for a young oncologist, but also a way to make sure that in the future two institutions may continue to work together. In other words, a fellowship at another institution of the network will mean much more. This is the reason why funding fellowships, even short fellowships, can be a powerful tool. Proper funding thereof

should be guaranteed. It is important to realize that these fellowships may primarily have an educational aim, even before a research one. Thus, EU funding should be arranged accordingly.

Long term, or even lifetime medical careers in rare adult solid cancers should be foreseen and should correspond to training pathways. Training on rare cancers should always be viewed as connected with available medical careers. An effort should be made to implement new medical careers focusing on rare cancers. Otherwise, rare cancer patients will be inevitably discriminated against. In that case young clinicians will not be attracted to work on these diseases, while professionals specializing in specific rare cancers at a given time of their career face the choice of keeping focused on them or losing their specialization to improve their positions. In other words, it is vital that medical careers are fully developed on rare cancers, to make sure that professionals can spend their entire professional lives being dedicated to rare cancers. At the same time, these medical careers need relevant training pathways. Clearly, reference centres have developed careers on rare cancers, though with difficulties to avoid escapes of professionals to more attractive positions elsewhere. Centres belonging to ERNs should be the first to guarantee medical careers on rare cancers. Now, it would be important to develop careers also in the spokes of the hub-and-spoke networks on rare cancers.

Dedicated institutions do exist in the paediatric oncology area, and also in the haemato-oncology area, therefore with dedicated full medical careers. However, these areas do not belong to the current competency. Contrary, institutions and units dedicated exclusively to rare adult solid cancers are scarce or lacking, while there may exist institutions or units dedicated to one or few rare adult solid cancers. Medical oncology units dedicated to rare adult solid cancers should be created within spokes of hub-and-spoke networks on rare cancers, with full careers. Any specific training is lacking. A clinical oncologist specializing in rare adult solid cancers (or some of them) is likely already a medical oncologist, a radiation oncologist, or a surgical oncologist. Thus, there is the need to provide educational pathways for clinical oncologists willing to specialize on rare adult solid cancers. These educational pathways should provide education on such diseases under a multidisciplinary perspective. They should be flexible enough to accommodate educational needs that may cover all or only some of the 10 families or rare adult solid cancers. These educational pathways could be provided in collaboration with the universities linked to EURACAN, during or after the conventional board certification pathway (i.e., in medical oncology, radiation oncology, surgical oncology). These pathways should include: a) courses on each of the rare adult solid cancers, based on a syllabus; b) clinical fellowships on selected rare adult solid cancers. There should be an examination, with a certification of competence. All this could give rise to an integrated system leading to the

creation of experts on rare adult solid cancers, hopefully finding dedicated careers for them at the centres of hub-and-spoke networks.

Taken together, at the moment exclusively a new UEMS examination and qualification system may serve as the provider of the certification and the European training requirements. This may serve later a base for the ERNs private and dedicated systems, and for future national qualification systems as well.

Table 1.
Rare cancers: RARECARE "families" and "Tier-1" entities with an incidence <6/100,000

HEAD & NECK
Epithelial tumours of the larynx
Epithelial tumours of the hypopharynx
Epithelial tumours of the nasal cavity and sinuses
Epithelial tumours of the nasopharynx
Epithelial tumours of major salivary glands and salivary-gland type tumours
Epithelial tumours of the oropharynx
Epithelial tumours of the oral cavity and lip
Epithelial tumours of the eye and adnexa
Epithelial tumours of the middle ear

DIGESTIVE
Epithelial tumours of the small intestine
Epithelial tumours of the anal canal
Epithelial tumours of the gallbladder and extrahepatic biliary duct

THORACIC
Epithelial tumours of the trachea
Thymomas and thymic carcinomas
Malignant mesothelioma

MALE GENITAL
Tumours of the testis and paratestis
Epithelial tumours of penis
Extragonadal germ cell tumours

FEMALE GENITAL
Non-epithelial tumours of the ovary
Epithelial tumours of the vulva and vagina
Trophoblastic tumours of the placenta

UROLOGICAL/UROGENITAL
Epithelial tumours of renal pelvis, ureter and urethra

SKIN CANCERS - Rare & **NON CUTANEOUS MELANOMA**
Mucosal melanoma
Uveal melanoma
Adnexal skin carcinomas
Kaposi sarcoma
Merkel Cell carcinomas

SARCOMAS
Soft tissue sarcoma
Bone sarcoma
Gastrointestinal stromal tumours

NEUROENDOCRINE (NET)
NET GEP
NET lung
NET other sites

ENDOCRINE ORGAN cancers
Thyroid cancers
Parathyroid cancer
Adrenal cortex cancer
Pituitary gland cancer

CENTRAL NERVOUS SYSTEM (CNS) tumors
Glial tumours and others**
Malignant meningioma
Embryonal tumours of CNS

#PEDIATRIC CANCERS*
Hepatoblastoma
Neuroblastoma & ganglioneuroblastoma
Nephroblastoma
Odontogenic malignant tumours
Olfactory neuroblastoma
Pancreatoblastoma
Pleuropulmonary blastoma
Retinoblastoma

#HEMATOLOGICAL
Lymphoid malignancies**
Myelodysplastic syndromes
Myeloproliferative neoplasms (including mastocytosis)
Myelodysplastic/myeloproliferative neoplasms
Myeloid/ lymphoid neoplasms with eosinophilia and abnormalities of PDGFRA, PDGFRB, or FGFR1, or with PCM1-JAK2
Acute myeloid leukaemia and related neoplasms

#Neither the Paediatric, nor the hematological rare diseases belong to this competency; here we did not delete them from the original classification to help the reader to be able to understand the full classification as it was described in the JARC.
* Other neoplasms which mainly, or also, occur in childhood are included under other labels (e.g., Ewing's sarcoma and osteosarcoma under bone sarcomas; rhabdomyosarcoma under soft tissue sarcoma; medulloblastoma under embryonal tumor of CNS)
** All subgroups (Tier-2 entities) within are rare