A new approach to rare cancers

Over four million people in the European Union are living with a rare cancer. These patients face particular challenges. A Rare Cancers Europe consensus document is putting their needs on the European policy agenda.

Jackie Partarrieu, Rare Cancers Europe

Difficulties faced by rare cancer patients include late or incorrect diagnosis, inappropriate or unavailable treatment, lack of information, scarcity of registries and limited quality of clinical trials, due to the small number of patients involved and the lack of expertise in rare cancers in the community.[1] Despite the rarity of each of the 198 rare cancers known to date,[2] taken together, they represent about 20% of all cancer cases, including all cancers in children.

Rare Cancers Europe,[3] a multi stakeholder initiative dedicated to putting rare cancers firmly on the European policy agenda, has been busy trying to create awareness of the plight facing rare cancer patients.

Developing new methodologies

One of the areas where Rare Cancers Europe is advocating for change is for a greater sense of urgency about developing treatments and bringing them as soon as possible to patients with rare cancers. To accomplish this, new methodologies need to be applied to clinical studies in rare cancers. Current methodologies and regulations[4] for clinical trials require the benefit of new treatments to be proven in a large number of patients. Given the inherently low numbers of rare cancer patients, this is not possible. The risk of not building enough evidence to gain approval of new agents and the high cost of small trials may discourage industry from developing drugs for most rare cancers.

An important consensus paper[5] is now calling on both the community of researchers and European authorities to address research methodologies and regulatory criteria that limit rare cancer patients' access to new therapies. This paper was also presented at a meeting with the European Medicines Agency (EMA).

Rare Cancers Europe members pose by the RCE banner (patients, doctors, epidemiologist)

"Rare cancer patients should not have to wait for their diagnosis or for possible treatment," says Anita Margulies, oncology nurse in Zurich and co-chair of the EONS Education Working Group. "A cancer diagnosis is already distressing. Being diagnosed with a rare cancer and then being told there is no approved treatment for their condition is even worse. The Rare Cancers Europe consensus paper calls, among other things, for rare cancer patients to be allowed earlier access to promising experimental drugs. Of course, access to these drugs should be harmonised across Europe and supervised by specialised healthcare professionals."

Roadmap for a new approach

The Rare Cancers Europe consensus document states that new approaches to collect evidence are required for rare cancer studies.

"Regulatory decisions about rare cancer treatments try to avoid risk for many reasons, but patients with a

rare cancer will often agree to these risks, in order to receive some new treatment which may be their only hope. Even if not all wishes can be granted, we must listen more carefully to what patients and their families want and need," explains Margulies.

The consensus paper addresses four major issues:

- **Clinical decision-making in rare cancers:** Whilst decision-making in rare cancers should be rational, as for other conditions, patients' attitudes towards "risk" should be taken into consideration. Regulatory agencies and local health systems should avoid discriminating against patients with rare cancers by allowing a higher degree of uncertainty. Innovative approaches should be encouraged, making use of all available knowledge (not only randomised clinical trials), in order to collect the best evidence.
- **Study design in rare cancers:** Large trials are not feasible in rare cancers. Low power randomised clinical trials, "adaptive" trials, and the like, should be considered. Research on biomarkers should be inherent to research on new drugs. Bayesian approaches[6] allow gathering of information from a number of sources and can consider all available evidence. The availability of electronic patient records, which allow measuring the effectiveness of treatments via patient reported outcomes in real world conditions, is a great opportunity, though again their use must take place in a methodologically innovative fashion.
- **Surrogate endpoints in rare cancers (**such as PFS and TR) could replace clinical endpoints especially when available evidence needs to be brought to the patient's bedside, to compensate for its possible limitations. New treatments could be used temporarily, under the assumption that the surrogate endpoint is valid, while waiting for final results.
- **Critical organisational aspects of clinical research in rare cancers:** Reference Networks are needed in Europe, involving Centres of Expertise, to improve the quality of care for rare cancers. Patients should be able to easily access information about ongoing trials and be encouraged to participate in them. While data protection is important, patients should have the right to donate their clinical data and tissues for research by giving a "one-time" (withdrawable) enduring consent for their use. More cancer registries are needed. Multidisciplinary, national, international and even global collaboration is vital to assess the value of new treatment strategies. Regulatory obstacles to global investigator-driven collaborations and sharing of databases should be overcome.

"Rare cancer patients who participate in clinical trials will need additional support from healthcare professionals," says Margulies. "Because of the large amount of information, the informed consent process and the uncertainties, the decision to participate (or not) in a trial may be overwhelming for both patients and their caregivers. Nurses are in a prime position to help by providing correct information and psychosocial support. This, in turn, means oncology nurses should be empowered to help with the follow-up and gathering of information from new treatments. In my experience, rare cancer patients are often willing to tolerate a higher uncertainty and take risks in the hope that effective new therapies will be discovered."

Sharing information and experience

Multidisciplinary collaboration is essential in oncology and even more so in the treatment of rare cancers. "As the rare cancer community is looking to organise research and care through European Reference Networks, it is important for nurses to become involved in suggesting the best pathways of care for rare cancer patients. If such patients are frequently treated at a clinic, the nurses involved in patient care should be offered solid background information about rare cancers and about clinical trials, through continuing education courses, as better education definitely affects outcomes.[7] Also, more funded nursing research projects and more nurse involvement in multidisciplinary research is very necessary and long overdue. Seeing the numbers of rare cancers, a special platform for sharing information and experiences on the specific needs of specific rare cancer patients would certainly help consolidate dissemination of knowledge about the care issues for these patients,"concludes Margulies.

Rare Cancers Europe have also published an advocacy tool kit http://www.rarecancerseurope.org/Patient-Advocacy-Toolkit

Details of the references cited in this article can be accessed at www.cancernurse.eu/magazine

'Rare Cancers: Exploiting the potential of European Reference Networks', March 2015, Brussels. Left, Alojz Peterle MEP (EPP, Slovenia). Right, Dr Paolo G. Casali, Chair of Rare Cancers Europe.