RCE Patient Advocates Training Course for Rare Cancers

Milan, 2-4 December 2017

From the 2nd to the 4th of December 2017, RCE organised a specific training course for rare cancers patient advocates. The event brought together patient advocates from across Europe, including Turkey and Russia, who could exchange views and ideas with clinicians and researchers, who were attending the ESO-ESMO-RCE Clinical Update on Rare Cancers event in the same building and to learn about crucial points of rare cancers advocacy. This section provides an overview of the key sessions in this meeting.

Testimonials

"A programme where an experienced doctor is invited to talk openly with patient advocates about his (or her) area of expertise is always worth doing. It brings out questions they have never faced before, they need to think on their feet like never before. Thank you, we get so much from it: I think they love doing it too." – *Roger Wilson, Sarcoma Patients EuroNet (SPAEN)*

"In the world of rare cancers, collaboration is key. If we are to improve outcomes, all of us – rare cancer patient advocates, patient experts, researchers and clinicians – have to work together in every aspect of clinical trials, treatment, support, education and information. The recent ESMO-ESO-RCE course for patient advocates in Milan illustrated this principle perfectly by providing a course and atmosphere in which all of these stakeholders could freely mingle, exchange information and ideas and debate some of the pressing challenges facing rare cancer patients in Europe today". – *Kathy Oliver, International Brain Tumour Alliance (IBTA)*

2nd December Introductory Session

Jean-Yves Blay, Fedro Peccatori, Rolf Stahel and Paolo Casali chaired the introduction to the ESO-ESMO-RCE Clinical Update noting that the key aim of the course was to learn and that it was particularly crucial that patient advocates could join in a parallel track in order to better network amongst the rare cancers community. Paolo Casali highlighted the major challenge of rare cancers which was the theme of the weekend course – the lack of expertise available in the community and the quality of care that suffers as a result. The lack of data in rare cancers is a fundamental problem in achieving good clinical decision making but networking is our prime tool to fight this challenge. With the advent of the European Reference Networks (ERNs) we have a major tool to deal with rare cancers. This last theme was also highlighted by Annalisa Trama who spoke on the epidemiology of rare cancers and the importance of volume of patients in developing expertise – with recent studies showing enormous heterogeneity between incidence and survival rates, more needs to be done to bring all patients up to the same quality of life. The intrinsic difficulty of rare cancers diagnosis was raised by Angelo Paolo Dei Tos, noting that pathology is image recognition and there is simply no cure for the rarity of these images apart from training pathologists and sending them to expert centres. Finally, Jean-Yves Blay presented the ERNs and the progress made so far including the development of strategic governance and the initiation of developing scorecards, quality procedures and piloting tools. Noting that the first patient has been involved in the EURACAN CPMS, he highlighted we can say it is formally 'alive'.

The second plenary session focused specifically on patient empowerment with presentations from Francesco de Lorenzo, Kathy Oliver and Ketty Mazzocco. These presentations included an overview of the policy framework in rare cancers, highlighting best practices in Italian rare cancer policy which has been driven by successful patient empowerment at local level. The importance of the local level was stressed in the context of national rare cancer networks which are the key to fully benefitting from the ERNs. Platforms to empower patients to manage their own condition were also presented, including many e-solutions to manage a chronic illness. Clearly in rare cancers it is crucial to empower patients to manage their disease through novel health apps and secure eHealth services. Finally, the role of patient advocates in developing a better quality of life for all rare cancer patients was highlighted, particularly through the ERNs. It was a core theme of this session that patients can, and must get involved with their disease and community in order to improve their outcomes, the outcomes of the community and the wider policy framework governing rare cancers.

Understanding Important Rare Cancers Initiatives in Europe

The first session of the patient advocacy track gave an overview of the situation of rare cancers in Europe, from a policy, clinical and patient engagement point of view. Paolo Casali highlighted the great work that EU rare cancer advocacy has made in allowing a framework like the ERNs to exist but highlighted that now work also needs to happen at national level. With European clinical guidelines on rare cancers emerging and exciting Rare Cancers Europe initiatives such as the Access App and the fellowship on Rare Cancers, there are plenty of efforts to continue the strong advocacy work in

Europe. Annalisa Trama highlighted the promise that the Joint Action on Rare Cancers (JARC) to tackle major rare cancer issues like the methodological implications of tackling the big data generated by the ERNs. She highlighted that this course was a great example of how to effectively discuss data generation and include patients in this discussion. Excitingly, it emerged that the JARC are building relationships between population based oncology databases to ensure long term studies on cancer to look at long term quality of life in a different way. Finally, Kathy Oliver noted the need to disassociate rare cancers from themes such as misdiagnosis, fear, uncertainty, fragmentation, stigma and loneliness. She highlighted that patients have a key role to play in the ePAGs within the ERNs to represent the patient voice, communicate and connect with clinicians and to review the effectiveness of networks amongst several other roles. With the ERN motto of "share,care,cure", this sessions demonstrated that thousands of patients can expect to benefit from the ERNs.

Clinical, Regulatory and Commercial Challenges in Rare Cancers Drug Development

During this session, patient advocates were familiarised with main barriers clinicians perceive in their day-to-day work and the challenges with regards to medicines where a benefit in a particular rare disease has been shown but are not licensed for this specific disease. These topics were specifically addressed by Silvia Stacchiotti, while the broad regulatory perspective was presented by Kyriaki Tzogani from the EMA. The industry representative, Jens Tuischer, highlighted the importance of collaborating with regulators, clinicians, patients and patient advocates when it comes to rare diseases and rare cancers. With patient populations being significantly lower for rare cancers, patient advocates play a key role in bringing together all of the above-mentioned stakeholders. Mr. Tuischer concluded by encouraging Rare Cancers Europe to make the patient advocates training course a regular initiative.

Patient Organisations Tackling Rare Cancers Challenges

This third session on Saturday offered inspiration from several rare disease groups on what patients can do to impact policy, their own lives, and their community. EURORDIS, presented by Arianne Weinman, has conducted a number of initiatives towards empowering patients through community building, developing online resources, developing surveys and offering training and capacity building. Several educational tools were also promoted for people to get involved with. The following presentation was a heart-warming testimonial from Victoria Bassett about their work to ensure access to 3rd line treatment for GIST in the UK. Following their goals to promote health, support research and advance education of health professionals and general public, they were able to launch a country-wide campaign ensuring continued access to this product for patients. This presentation tangibly showed how patient power can make a significant impact on policy, and patients' lives. Finally, Teodora Kolarova presented the INCA, the European NETwork, who have also used tools such as surveys to produce key data from patients and healthcare professionals. The audience was captured by the INCA campaign video which reflected the

ability for patients to be active across all mediums. Creating a NET awareness day was another great effort by this group that was proposed as a building block for any other patient organisation looking to raise the profile of their disease.

3rd of December Diagnosis, Treatment & Rare Cancers Care -

This first session of Sunday morning was a highly technical medical discussion looking into the medical progression of cancer, molecular diagnostics in rare cancers and targeted therapies. The level of these presentations reflected the expertise of the patient advocates in the room. Anna Maria Frezza initiated the meeting with a presentation on cancer development which highlighted how cells exist in the body and the resistance of cancer cells, based around 'replicative immortality'. This presentation explained how new therapies are attempting to kill cancer cells or retrain the body to do so which was crucial for patients advocating in fields with new therapies so that they are a part of the discussion about what progress new therapies may offer. Angelo Paolo Dei Tos took on the challenging topic of morphologic and molecular diagnostics in rare cancers, highlighting that sub-specialisation is crucial for rare cancers, not just in pathology but also in medical oncology. Amongst a wide discussion on the limitations of foundational medicine, he also highlighted that pathology is morphologic observation based on simple observational skills from pathologists which means that you can only get 'good' through significant exposure. This highlighted a fundamental role of networking in pathology such as central pathology boards in France. Finally, Nicola Fazio looked into targeted therapies which, falling under the umbrella of personalised medicine, have been an ESMO focus and a patient guide has also been developed on this topic. Personalised treatment was described as 'the best treatment according to their personal medical history and their physiological status over the patients' lifetime'. Several trial designs were discussed to make sure that all diagnoses have a real therapeutic implication for a patient including basket trials and umbrella trials. Once more this session concluded with the idea that ERNs have as their objective to answer many of the questions raised in this session.

Rare Cancer Treatment: The Challenges

The challenges for rare cancer patients are early and correct diagnosis, limited clinical expertise, research and access to new therapies and a paucity of available guidelines. During this session, several crucial points were raised from a surgical, radio-therapy and oncology perspective. From a surgeon's perspective, Sergio Sandrucci noted that it is crucial to assess correctly every situation and be able to refer rare cancer patients to the right specialists, where they can obtain. From the radio-therapist's perspective, Vincent Gregoire noted the particular challenges faced in Belgium with 120 hospitals treating 120 head and neck cancer, some of them having potentially only 1 patient

For this reason, he advocated for a centralisation of expertise and the need for a fundamental change in oncology management in Belgium. Isabelle Ray-Coquart further elaborated on the rare cancer networks and sub-networks, which allows expertise to be able to travel across borders. She noted the case study of France with a well-developed national network for rare cancers. Beyond the treatment, Iain Galloway stated, from a patient's perspective that early diagnosis is perhaps one of the main issues of rare cancer patients. Furthermore, a structured coordination in clinical trials is imperative.

Clinical Research in Rare Cancers

Speakers and participants during this session emphasised the importance of data and data analysis for an expert opinion for rare cancer patients. Saskia Litiere familiarised patient advocates with how clinical trials have been done in the past decade. She further presented retrospective/prospective data collection and what are their advantages and disadvantages. For retrospective research, the information is already available and only needs to be collected. However, the research is limited to the data recorded. On the other side, prospective data collection has the advantage of controlling the collected information. The disadvantage is that researchers need to wait for the results. Furthermore, Silvia Stacchiotti presented the objective response vs survival with the difference between activity and efficacy. She examined the quality of life according to standard approaches and provided a larger perspective on patient reported outcomes. Finally, Paolo Bruzzi made a presentation on statistical facts for non-statisticians, which served as an introduction to the next session how to improve clinical research in rare cancers.

Clinical Research in Rare Cancers – Can it be Improved?

The final session of Sunday looked into the complex issue of improving clinical research, taking as a primary focus the role of statistics in developing clinical trial design. The role of Bayesian statistics in rare cancers clinical trial design is highlighted in the Rare Cancers Europe recommendations and was elaborated on in this discussion. The need to take into account observations and prior knowledge is fundamental when assessing such rare conditions and has brought about several breakthroughs in immunotherapies. . In a double act between Paolo Bruzzi and Paolo Casali, the patient advocates were informed about the differences between frequentist and Bayesian statistics.

The conclusions were that physicians should try to be more Bayesian and to take into account more clinical history of the patient. Looking into clinical ethics they highlighted that a good clinical decision is “a patient-physician shared decision in conditions of uncertainty”. The notion of uncertainty was taken up in the following presentation from Eric Low on Real World Evidence (RWE). The troubles with integrating RWE into clinical trials was highlighted and the corresponding issues with defining value in new therapies was clear. RWE has a large role to play in aligning patient preference with clinical endpoints and incentives for industry. Natural history studies were underlined as a great means to build blueprints for diseases and the call to action to patients was to ensure that they had a ‘blueprint’ for the way forward in their disease to be sure they were the ones calling for what trials were needed in their disease areas.

4 December Advocacy & Lobbying: Speaking Up for Rare Cancers

Monday morning started with an inspiring guide to improving advocacy and lobbying practices for patient advocates. The following are the 10 rules of advocacy and lobbying by Roger Wilson:

1. Use coffee breaks effectively
2. Get the doctors on your side
3. Use the data, get help interpreting it, draw the lessons, promote the lessons
4. When you do things, do them well, use your skills, be flexible
5. There are good ways to be right and bad ways to be right – know the difference and use the good ones,
6. A good way to be right is to be polite, be reasonable, quote evidence, let it speak for itself
7. Always prepare – have three simple important things to get across
8. Partnerships are powerful
9. Don’t think short term
10. Always learn from others

In addition, very engaging presentations were made by Rachel Giles on the World Kidney Cancer Day, Estelle Lecointe on SPAEN and Isabelle Manneh-Vangramberen on the ECPC. To add to this, Roger Wilson led a session on social media in rare cancers, which was an interactive session bringing all participants into the discussion. The results were particularly interesting:

- Despite between 75-100% of participants having either a Facebook group, Twitter account or other social media profiles, and posting regularly, less than 10% were engaging with policy makers through this means and just 10% were connected with the other patient advocates in the room

- Almost everyone was posting several times per week and community engagement ranged from several hundreds to several thousands

There was a wide consensus that a social media training course woudl be very useful for patient advocates.

Round Table Discussion

The final session of this training course took the form of roundtable discussions on several topics aimed at proposing potential new projects or priorities in these areas for the rare cancers community.

Round Table 1 and **Roundtable 2** merged to work on the topics of overcoming misdiagnosis and improving quality of life for rare cancer patients. Participants discussed the 2 topics and came up with the following main points:

- Only 15% of patients have support groups and to this end patient advocates should concentrate their efforts in ensuring all rare cancer patients are able to receive the proper support.
- Education is still one of the main challenges in the area of rare cancers. To this end, participants discussed fellowships/courses/online platforms for exchange of information at all levels.
- Having a key worker (or case manager) is crucial for rare cancer patients in order to get back to work and overcome the discrimination on access to employment
- There is a lack of expertise from pathologists and primary carers leading to big issues with misdiagnosis and improving the expertise of physicians should be one of the key focuses.

Round Table 3 focused on clinical trials in rare cancers and discussed the following:

- Endpoint analysis for rare diseases, where in many cases patients try a number of treatments or a combination of treatments, permit key secondary measures such as PFS or graded PFS (e.g. PFS1, PFS2, PFS3 measured at intervals to smooth out pseudo-progression in ITs) over OS
- Clinical trial eligibility criteria for rare diseases should be made more inclusive. This might include such initiatives as permitting some rare disease patients on broader trials for related diseases (e.g. uveal melanoma patients on cutaneous melanoma trials) — this will allow efficacy signals to be picked up for treatments which might otherwise not be spotted and help pave the way for further investigation. Broader inclusion will also allow for the analysis of rare subtypes
- Natural history of rare disease areas is better reflected as an outcome of research efforts. Specifically, this will provide a more robust footing for adaptive trial designs where the *a priori*

knowledge gained from research (and remembering that a lower level of evidence is required for rare diseases anyway) can inform the Bayesian model and help guide more realistic and efficient trial designs

- The recent recognition of Patient Advocates as Healthcare Professionals must translate into effective representation either via EMA or other bodies influential in CT design

Round Table 4 focused on RC patients in minority populations

- There are a number of minorities to consider in Europe ranging from refugees, people with poor literacy or low income to people with geographic isolation.
- The internet is a cultural mediator but the training of local communities is crucial. Patient organisations need to identify how to enrol members who are members of minorities and doctors in these minorities could be effective mediators.