Taylor & Francis
Taylor & Francis Group

Expert Review of Pharmacoeconomics & Outcomes Research

ISSN: 1473-7167 (Print) 1744-8379 (Online) Journal homepage: http://www.tandfonline.com/loi/ierp20

The evolving role of patient advocates in rare cancers: opportunities and challenges

Ornella Gonzato & Alessandro Gronchi

To cite this article: Ornella Gonzato & Alessandro Gronchi (2018): The evolving role of patient advocates in rare cancers: opportunities and challenges, Expert Review of Pharmacoeconomics & Outcomes Research, DOI: 10.1080/14737167.2019.1526083

To link to this article: https://doi.org/10.1080/14737167.2019.1526083

Accepted author version posted online: 19 Sep 2018.
Published online: 27 Sep 2018.

EXPERT REVIEW OF PHARMACOECONOMICS & OUTCOMES RESEARCH
https://doi.org/10.1080/14737167.2019.1526083

Taylor & Francis
Taylor & Francis Group

EDITORIAL

The evolving role of patient advocates in rare cancers: opportunities and challenges

Ornella Gonzato[a] and Alessandro Gronchi [b]

[a]Associazione Paola for Muskulo-Skeletal Tumors – Onlus, Udine, Italy; [b]Department of Surgery, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy

ARTICLE HISTORY Received 27 January 2018; Accepted 17 September 2018

KEYWORDS Rare cancers; sarcoma; patients advocacy group; reference centers; orphan drugs

The role of Patient Advocates (PAs) has evolved over time. In general, it has expanded ranging from direct support to patients and families to research and public influence. In this evolving scenario, the main activities are summarized in Table 1.

Rare cancers are one of the areas in which PAs are assuming an increasingly more active role as partners with all others stakeholders including healthcare professionals, academics, companies, regulators, and politicians. Because of the rarity, patients face additional difficulties, as summarized in Table 2 [1–3].

Research challenges, access to new drugs and referral of patients to expert centers are the main intervention areas in order to address rare cancer patients' needs and improve quality of care [4].This is the 'field' where PAs' role is carried out bringing the patients' unique perspective on their conditions and the challenges they face in the rarity. In the past, many felt that rarity led scientists and policymakers to paying too little attention to their diseases. This is the basis on which the legislation on orphan medicinal products developed and entered in force in Europe (in 2000), establishing that patients affected by rare diseases have a right to the same quality of treatments of all other patients [5].

Research challenges are several and comprise all basic, translational and clinical research without neglecting social/economic research. There has traditionally been a lack of public funding in rare cancers for basic research that is the prerequisite of any therapeutic advance. In rare cancers, PAs' role is not and can't be only that of fundraising for supporting basic research but also that of driving research efforts [6,7]. Disease models, including cell lines and xenografts, are critical resources to understand biology and identify new treatment strategies in particular for very rare cancers still without care. Non-profit patient organizations – especially in the United States – are both funding and investing in these activities to overcome barriers in order to allow researchers to enter in the field. Biobanking, which means pooling tumor specimens and making them easily accessible to qualified researchers, is another activity performed by these organizations for accelerating search for cure. Adenoid Cystic Carcinoma Foundation and Chordoma Foundation are some of the most renowned among these realities [8,9].

Taking into consideration that the development of new drugs is a primary objective, translational research, which accelerates the transfer of knowledge from 'bench to bedside' is consequently one of the most urgent priorities for the upcoming years [10,11]. *In vivo*/*in vitro* proofs of concept of new drugs, where already existing, could be transformed into translational research if motivation and funding become available. Bridging the gap between promising laboratory observations and the development of effective therapies remains risky and expensive. Patient advocates can and should call on public authorities to invest more in translational research or develop new models of patient–private partnerships for drug development, such as the venture philanthropy model which consists of partnerships among patient organizations, industry, and regulatory agencies to share the financial risk of therapeutic development, shorten the early translational pipeline, and advance research with 'a focus on human, not financial, return.'[12–14]

The involvement of PAs in steering committees/advisory boards of both basic and translational research projects is critical to accelerate progress in rare cancer research. Advocacy representation is also often required by the funding organization; researchers and advocates (the latter also in the role of coinvestigators) are increasingly working together around key research issues. Mutual education on both sides is required, that means respectively high training on both scientific and clinical issues and understanding of appropriate involvement of patient perspective in the research process.

Involving patients and patient advocates in establishing research priorities, in all areas of research, ensures the relevance of the research produced. Incorporating their voice amid the research continuum, which ranges from contributing to conceptualize the research to designing the study, conducting the research and reporting the results, has the potential to help research progress faster and further [15].

PAs' role in clinical research encompasses more and more closer partnerships and working relationships with investigators, ethics committees, industry, regulatory bodies, and HTA bodies.

Generally, their activities in clinical research can be summarized as shown in Table 3:

The use of patient reported outcomes (PROs) data, in addition to conventional and safety data, are increasingly providing value in the clinical trial setting also from a regulatory viewpoint even if there are several methodological obstacles still to be addressed [16,17].

In rare cancers then, considering the difficulty to collect clinical evidence by conventional trials due to the paucity of

CONTACT Alessandro Gronchi alessandro.gronchi@istitutotumori.mi.it Sarcoma Service, Department of Surgery, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy

Table 1. PAs' main activities.

- *Patient support by providing psycho/social support to patients and families*
- *Education and information dissemination by informing/educating about diseases, treatment options, quality of life*
- *Fund raising and engagement for research activities*
- *Participation in the drug development process*
- *Lobbying government for increasing research funding, improving legislation, regionalizing care, directing patients to referral centers*
- *Advocacy in order to give voice to patients' needs*

Table 2. Patient difficulties in rare cancers.

- *Misdiagnosis and/or late diagnosis and consequent lack or late treatment*
- *Variability of quality of care, due to lack of expertise and no adherence to clinical practice guidelines, if any*
- *Limited access to appropriate treatments, including compassionate use of drugs*
- *Reduced number of referral centers, with specialized experience and expertise*
- *Difficulties to carry out clinical trials, due to the small number of patients with each a specific rare cancer*
- *Lack of information on the disease, available treatments, care pathways, and on-going clinical trials.*

Table 3. PAs' main activities in clinical research.

- *Involvement in trial designs, eligibility criteria, and study procedures*
- *Ensuring that information about trials and consent forms are written in understandable language*
- *Educating patients and facilitating their recruitment*
- *Identifying and addressing potential ethical issues in clinical trials*
- *Promoting patient safety*

numbers, early involvement of patients and PAs is crucial for pharma companies in order to adequately investigate the unmet medical needs from the patients' perspective.

Therefore, patient advocates are having more influence across the entire drug development continuum, from discovery and approval to market. The European Medical Agency (EMA) encourages patients and PAs' participation in the Scientific Advice (or Protocol Assistance in the case of orphan drug designation), which consists in giving advice to companies regarding the appropriate tests and studies to be conducted in order to facilitate drug development [17]. Patient real-life perspective and experience is relevant in decision-making both for regulators and companies. PA's representatives sit at the EMA Committee for Orphan Medicinal Product (COMP) which is responsible for evaluating applications for orphan drug designation that allows companies to gain benefit from incentives in developing medicines for rare diseases in a not too attractive market for profit-players [18].

Nevertheless, timely patient access to drugs encounters methodological and regulatory barriers which delay drug approval, both in the United States and in Europe. In the United States, the recent signing of the 21st Century Cures Act into law (in December 2016) marks a pivotal point in the history of drug approval, emphasizing on patient-focused drug development and including mechanisms aimed to 'accelerate the discovery, development, and delivery' of new drugs to assure patient timely access to them [19]. This law demonstrates patients' will to speed up the drug approval process accepting a higher degree of risk. This is all the more true when patients suffer from diseases, such as rare cancers, where few or none therapeutic options exist [20].

In Europe, in these recent years regulators have introduced early access tools for conditions in which 'the benefits of immediate availability outweigh the risks inherent in the fact that additional data are still required' in addition to the orphan drug designation for rare diseases. These tools include accelerated assessment, compassionate use, conditional marketing authorization/approval which allow flexible licensing pathways [21,22].

Despite this, even when regulatory approval is obtained, health technology assessment (HTA) and decisions on drug pricing and reimbursement often delay access to medicines at national level. The generally high costs for innovative drugs together with the 'intrinsic lack of or defect in evidence' in rare cancers are the new challenges in a context characterized by limited resources and health systems under pressure. An early interaction of all stakeholders involved in drug development together with a greater degree of risk-sharing among all of them are crucial factors to seek to overcome these constraints and assure timely patient access to drugs. The new approach launched by EMA, named 'adaptive pathways/licensing', aims to conjugate timely patient access and sustainability of innovative drugs, involving patients and HTA bodies early in the discussion of the product development program [23]. PAs' inputs can range from the evaluation of the acceptability of the surrogate points to the PROs and gathering of evidence through real-world data to supplement clinical trial data.

However, for a better access to drugs in rare cancers, many challenges still have to be faced and some of them regard the legislative framework itself. This is the case of the new European Resolution, just adopted by the European Parliament (15th December, 2016), on the Paediatric Medicines Regulation, called by the pan-European childhood cancer community on the European Institutions to modernize the legislation in order to better address the needs of children and adolescents with life-threatening-diseases, including cancers which are all rare cancers [24].

Organization of care is another area in which PAs' role is becoming more relevant in order to give advice/provide recommendations on both healthcare policymakers and organizations for the development of high-quality services to patients affected by rare cancers. In Europe, the Sarcoma Patients Euronet (SPAEN) has recently developed a policy paper on recommendations for health service development, specific for sarcoma patients [25].

Specialized/reference centers, multidisciplinarity, and patient-centered pathways from diagnosis to treatment along with quality monitoring are fundamental to improve survival and quality of life for patients. PAs involvement both in the definition of the essential requirements for quality cancer care and the services' compliance to them is of great value both for patients and healthcare systems [26].In addition, ePAs (European Patient Advocacy Groups) are involved in the governance of the European Reference Networks (ERNs) – such as EURACAN, the network dedicated to adult rare solid cancers; their presence is included in the Board, the Steering Committees and different subgroups working on the 10 domains of EURACAN [25]. Moreover, they participate in the Task Forces on Clinical guidelines, fund research, educate/train and communicate and disseminate information and results achieved. Therefore, their principal roles can be summarized in the contribution to the following activities:

- the definition of the scientific strategies for research
- the elaboration of communication strategies not only for patients but also for general practitioners and primary care physicians

- the elaboration of funding strategies
- the interactions with the health authorities.

In conclusion, new roles for PAs are emerging and taking place, defining a new scenario in which the rarity is the cause and at the same time the opportunity to find new ways of acting and interacting among all the stakeholders. Working in partnership is the right direction in order to assure that risks and benefits in achieving timely and better patient treatments will be shared by all the stakeholders.

Raising money to provide patient support and educational materials are certainly valuable activities. But, in particular in rare cancers, more needs to be addressed. Drawing health policies attention and making rare cancer needs a priority in their agenda; lobbying institutions to fund research as well as changing legislation; playing a larger role in driving research; developing new models of drug development and timely patient access; being involved in health-care services organization for high quality services, including regionalization of care: all of these activities are reshaping the role of PAs in this field, between opportunities and challenges.

Funding

This paper was not funded.

Declaration of interest

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

Reviewer disclosures

Peer reviewers on this manuscript have no relevant financial or other relationships to disclose.

Web based information resources

http://euracan.ern-net.eu
https://www.eurobloodnet.eu
http://paedcan.ern-net.eu
http://jointactionrarecancers.eu
http://www.rarecancers.eu
http://www.rarecarenet.eu
https://www.orpha.net
https://www.eurordis.org
http://www.ecpc.org
https://www.cancer.gov/about-cancer/treatment/clinical-trials
https://www.clinicaltrialsregister.eu
http://www.isrctn.com

ORCID

Alessandro Gronchi http://orcid.org/0000-0002-4703-3534

References

1. Gatta G, Capocaccia R, Trama A, et al. The burden of rare cancers in Europe. Adv Exp Med Biol. 2010;686:285–303.
• **A review on the epidemiology of rare cancers, which shows how rare cancers are not so rare.**
2. Gatta G, Trama A, Capocaccia R. RARECARENet Working Group Epidemiology of rare cancers and inequalities in oncologic outcomes. Eur J Surg Oncol. 2017 Sep 19. pii: S0748-7983(17)30685-6. doi: 10.1016/j.ejso.2017.08.018. [Epub ahead of print].
3. [Cited 2018 Sep 22]. Available from: www.rarecancerseurope.org/
4. Working to improve the management of sarcoma patients across Europe: a policy checklist. BMC Cancer. 2018 Apr 16;18(1):424.
•• **A manuscript by physicians and patients advocates to identify priorities for improving care and reearch in sarcoma as a model for rare cancers.**
5. The European Parliament and the Council of the European Union. Regulation (EC) No. 141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products. Off J Eur Commun. 2000;43:1–5. OJ L 18(22.1.2000).
6. Dockser Marcus A. To make progress in rare cancers, patients must lead the way. J Of Clin Oncol. 2009;27(16):2575-2577
7. Pushparajah DS. Making patient engagement a reality. DOI:10.1007/s40271-017-0264-6
8. [Cited 2018 Sep 22]. Available from: https://www.accrf.org
9. [Cited 2018 Sep 22]. Available from: https://www.chordomafoundation.org
10. Aymé S, Kole A, Groft S. Empowerment of patients: lessons from the rare diseases community. Lancet. 2008;371:2048–2051.
11. EURORDIS, Rare Diseases Europe. Patients' Priorities and Needs for Rare Disease Research 2014–2020.
12. Ramsey BW, Nepom GT, Lonial S. Academic, foundation, and industry collaboration in finding new therapies. N Engl J Med. 2017 May 4;376: 1762–1769. .
13. P Kanavos, R Sullivan, Lewison G, et al. The role of funding and policies on innovation in cancer drug development. Ecancermedicalscience. 2010;4:164.
14. Wagstaff A. A breakthrough business model for drug development Cancerworld March/April 2017, 56–63
15. [Cited 2018 Sep 22]. Available from: http://www.eupati.eu
16. EMA/CHMP/292464/2014. Appendix 2 to the guideline on the evaluation of anticancer medicinal products in man. The use of patient-reported outcome (PRO) measures in oncology studies. April 2016
17. Involvement of patient representatives in scientific advice procedures at EMA, 10 January 2017, EMA/736615/2013 Rev 2
18. The Committee for Orphan Medicinal Products and the European Medicines Agency Scientific Secretariat. European regulation on orphan medicinal products. 10 years of experience and future perspectives. Nat Rev Drug Discov. 2011;10:341.
19. 21st Century Cures Act PUBLIC LAW 114–255—DEC. 13, 2016
20. Mattingly JT, Simoni-Wastila L. Patient-centered drug approval: the role of patient advocacy in the drug approval process. J Manag Care Specialty Pharm JMCP. 2017;23(10):1078-1082
21. Liberti L, Stolk P, McAuslane N et al. Adaptive Licensing and Facilitated Regulatory Pathways: A Survey of Stakeholder Perceptions Clinical Pharmacology & Therapeutics, Vol. 98 5 November 2015
22. EMA Adaptive Pathways. [Cited 2018 Sep 22]. Available from: http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general/content/000601.jsp&mid=WC0b01ac05807d58ce.
23. Gonzato O. The new risk-sharing paradigm in rare cancers: patient perspective. J Cancer Policy. 2017;12:36–42.
24. Regulation 1901/2006/EC of the European Parliament and of the Council of 12 December 2006 on Medicinal Products for Paediatric Use. [Cited 2018 Sep 22]. Available from: http://ec.europa.eu/health//sites/health/files/files/eudralex/vol1/reg/2006/1901en.pdf.
25. Sarcoma patient pathway analysis and recommendations for service development, SPAEN Sarcoma Policy Paper, 2016
26. Andritscha E, Beishonb M, Bielackc S, et al. ECCO Essential Requirements for Quality Cancer Care: Soft Tissue Sarcoma in Adults and Bone Sarcoma. A critical review. In: Critical Reviews in Oncology/Hematology, 2017;110:94–105.
•• **The first manuscript to address the requirements foridentifying referral centers and regionalize cancer care**