Rare cancers: the landscape is changing

Kathy Oliver

International Brain Tumour Alliance, Tadworth, UK

ARTICLE HISTORY
Received 1 June 2018; Accepted 23 July 2018

KEYWORDS Brain tumor; European Reference Networks (ERNs); patient advocates; rare cancers

Fourteen years ago, when I was first thrust as a new patient advocate into the world of rare cancers – following my son’s diagnosis of a brain tumor – I found it to be as lonely and terrifying a landscape as you could ever stumble into.

At that time, I felt that rare cancers occupied a place on the cancer map which was cloaked in half light and shadows and which was an isolated and arid region, desperately crying out for the rain of more research and the sunshine of hope.

Today, however, that landscape is changing and rare cancers are now the focus of an improved level of attention.

One example of this encouraging trend has been the establishment of European Reference Networks (ERNs) [1]. To ensure that no one with a rare cancer (or indeed with any rare disease) faces inequities in diagnosis, treatment, and support, the ERNs were established under the 2011 EU Directive on Patients’ Rights in Cross-Border Healthcare [2]. ERNs are virtual networks of centers of expertise across the European Union which are specifically relevant to a particular rare disease.

The ERNs aim to be game-changers for people with rare cancers by facilitating access to information and care across these virtual networks, thus optimizing diagnosis and treatment options, and addressing significant unmet needs.

Rare cancer patient advocates are well aware of just what these unmet needs are. For example, there is inequity in accessing promising new therapies; a paucity of specialists to treat rare cancers; incomplete and inconsistent registries; not enough clinical trials; and a lack of sufficient research funding, to name just a few of the challenges. Additionally, people with rare cancers can be misdiagnosed or diagnosed very late, and they face huge uncertainties about treatment decisions. They can also struggle with a lack of information and support due to the uncommon nature of their disease.

It is anticipated that ERNs will:

- make economies of scale;
- develop international databases and tumor banks; and crucially,
- improve patient outcomes.

But there are yet other challenges.
Therapies for rare cancers do not easily fit into the regulatory system, and they certainly do not come cheap, causing reimbursement problems in national health systems.

We also know that even in the richest and most powerful countries on this planet, people with rare cancers can be lost in a maze of uneven and inequitable care. In some countries, there are no national guidelines to ensure consistent quality of treatment and service delivery. And heaven help those rare cancer patients in the less-developed countries where access to even the most basic therapies and palliative care is lacking.

Concerned by these situations and inspired by the patients who are struggling with them, people who work in the rare cancer landscape – including patient advocates, researchers, health-care providers, industry, regulators, and others worldwide – are putting their heads and resources together to improve outcomes for people with rare tumors.

The crucial keys to success in this tough arena are collaboration and innovation.

Collaboration because no one clinic, health-care system or country, in my opinion, can tackle rare cancers successfully on their own. It will take a global effort, not least because patients with these diseases are uncommon and spread far and wide, but also because – given the limited financial resources we have for health care today – we must avoid duplication and waste in research, treatment, and support.

Innovation because we must be creative in our approaches to the design of clinical trials for rare cancers. For example, endpoints should reflect the challenges and limitations thrown up by rare cancers. Furthermore research studies should embrace new structural approaches such as adaptive, basket, umbrella, and other innovative trial designs.

Thankfully, there are a rising number of laudable collaborative initiatives in the rare cancer landscape today – so many more than when I first set foot here 14 years ago, shipwrecked with fear for my son.
There is the multi-stakeholder Rare Cancers Europe (RCE) which this year celebrates its tenth anniversary of working with great determination to put rare cancers firmly on the European policy agenda. Over 4 million people in Europe are affected by a rare cancer, says RCE, so taken together, rare cancers make up significant numbers that must not go unnoticed [3]. There is EURORDIS, a non-governmental alliance representing over 800 rare disease patient organizations, including those for rare cancers, in more than 70 countries [4]. In the United Kingdom, there is Cancer52 which represents nearly 100 organizations united in improving the future for everyone affected by rare and less common (RLC) cancers [5].

Further afield there is Rare Cancers Australia, whose mission is to improve awareness, support and treatment of Australians with RLC cancers. In Australia in 2017, an estimated 52,000 people were diagnosed with an RLC cancer [6]. In the United States, there is the new Rare Tumor Patient Engagement Network (RT PEN), an initiative supported by the US National Cancer Moonshot, which ‘aims to advance research and discover new treatments for rare tumors through a collaborative network of national and international institutions that will provide expertise, personalized health care, and education to patients with rare tumors.’ Of particular note for those working in the field of neuro-oncology is the fact that within RT PEN is the NCI-Connect (Comprehensive Oncology Network Evaluating Rare CNS Tumors) initiative whose goal is to ‘advance the understanding of rare adult central nervous system (CNS) cancers by establishing and fostering patient-advocacy-provider partnerships and networks to improve approaches to care and treatment.’ [7]

Innovative, collaborative initiatives in rare cancers also extend to ‘repurposing’ (or ‘repositioning’) of already-licensed, non-oncological drugs with the potential to fill some of the substantial unmet treatment requirements of the rare cancer patient community. The attractions of this approach are numerous, for example: relatively low development costs, rapid access for patients, and already-existing evidence (including pre-clinical, pharmacokinetic, and safety data).

A major report – Facilitating adoption of off-patent, repurposed medicines into NHS Clinical Practice – was published in December 2017 by the UK’s Association of Medical Research Charities (AMRC) [8]. The report arose from the AMRC’s Drug Repurposing Group which includes, amongst other patient organizations, two key stakeholder not-for-profits (Brain Tumour Research and The Brain Tumour Charity) representing patients and families with these rare cancers. Brain Tumour Research highlighted that ‘Drug repurposing is an area of real promise for the development of new therapies for the treatment of brain tumours and ... this should be seen as a key research priority.’ [9]

Another initiative is the ReDO project (‘Repurposing Drugs in Oncology’) which is an international, collaborative group of researchers, clinicians, and patient advocates from non-profit organizations [10]. ReDO focusses on areas of high unmet needs including rare adult cancers and pediatric cancers, all of which are rare.

Undoubtedly, we still have far to travel before rare cancers are eradicated. But the changing rare tumor landscape around the world is bringing long-awaited hope not only to people whose lives have been upended by these devastating and intransigent diseases, but also to the dedicated and determined researchers and health-care professionals who strive so hard to improve survival.

Finally, it is important to remember that, with our increasing knowledge of rare molecular subsets in some of the more common cancers – such as lung, melanoma, and breast – new rare cancer entities will emerge in these patient populations too. Perhaps progress made today in the rare cancer world will help people with these common, but also rare, diseases in the future.

Indeed, the famous English physician William Harvey (1578–1657) wrote:

Nature is nowhere accustomed more openly to display her secret mysteries than in cases where she shows traces of her workings apart from the beaten path; nor is there any better way to advance the proper practice of medicine than to give our minds to the discovery of the usual law of nature, by the careful investigation of rarer forms of the disease. [11]

Although my son’s brain tumor journey ended in 2011 when he passed away, I decided to remain a rare cancer patient advocate. And thanks to some of the developments I have described, I am no longer struggling as much as I used to when I voyaged through the rare cancer landscape of 14 years ago. Today there is more determination and more hope here – as long as we keep traveling in this forward direction, strongly supporting innovation and global collaboration.

Funding

This paper was not funded.

Declaration of interest

With regard to the specific subject matter of this editorial, K Oliver serves as a patient representative on the steering committee for EURACAN, the European Reference Network (ERN) for rare adult solid tumours; is a founding member and current committee member of Rare Cancers Europe; serves as a EURORDIS ePAG (Patient Advocacy Group member – the IBTA is a member of EURORDIS); is a founding member and former board member of Cancer52 and serves as a member of NCI-Connect. On a broader scale, the author’s organisation, the International Brain Tumour Alliance (IBTA) publishes a sponsorship policy on its website at www.theibta.org. During 2005-2018, the IBTA accepted financial support and/or support in kind either directly or as part of a wider grouping of patient organisations, from the following companies and trusts: AbbVie, Accuray, Antisense Pharma, Apogenix, Archimedes, Ark Therapeutics, Astra Zeneca, Boehringer Ingelheim, Brain Tumor Network (USA), Brain Tumor Resource and Information Network (USA), Bristol-Myers Squibb (BMS) Celldex Therapeutics, Crusade, Dijon Designs (UK), Elekta, Eli Lilly, Gerry & Nancy Pencer Brain Trust (Canada), Gosling Foundation (UK), GlaxoSmithKline (GSK), Ivy Foundation (USA), Lilly, Link Pharmaceuticals, MagForce, Medac, Merck Serono, Merck, MGI Pharma, MSD Oncology, NeoPharm, Neuroendoscopy (Australia), Northwest Biotherapeutics, Novartis, Novocure, Pediatric Brain Tumor Foundation (USA), Pfizer, Photonicum, Roche, Schering-Plough (Global), Sontag Foundation (USA), Spink (UK), to-BBB, Vane Percy (UK), VBL Therapeutics and the Wallerstein Foundation (USA). The author has no other 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 apart from those disclosed.

**Reviewer Disclosures**

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

**References**

1. European Commission. European Reference Networks. [cited 2018 May 15]. Available from: [https://ec.europa.eu/health/ern_en](https://ec.europa.eu/health/ern_en)
2. Official Journal of the European Union. Directive 2011/24/EU of the European Parliament and of the Council of 9th March 2011 on the application of patients’ rights in cross-border healthcare. [cited 2018 May 15]. Available from: [http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32011L0024&from=EN](http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32011L0024&from=EN)
3. Rare Cancers Europe website. [cited 2018 May 15]. Available from: [http://www.rarecancerseurope.org/](http://www.rarecancerseurope.org/)
4. EURORDIS website. Rare Diseases Europe. [cited 2018 May 15]. Available from: [https://www.eurordis.org/](https://www.eurordis.org/)
5. Cancer 52 website. [cited 2018 May 14]. Available from: [https://www.cancer52.org.uk/](https://www.cancer52.org.uk/)
6. Rare Cancers Australia website. [cited 2018 May 16]. Available from: [https://www.rarecancers.org.au/page/1091/advocacy](https://www.rarecancers.org.au/page/1091/advocacy)
7. National Institutes of Health. National Cancer Institute (NCI) NCI-CONNECT website. [cited 2018 May 16]. Available from: [https://ccr.cancer.gov/nci-connect](https://ccr.cancer.gov/nci-connect)
8. Association of Medical Research Charities (AMRC). Facilitating adoption of off-patent, re-purposed medicines into NHS clinical practice, December 2017. [cited 2018 July 11]. Available from: [https://www.amrc.org.uk/Handlers/Download.ashx?IDMF=c1a3904c-78de-47ed-813c-b34b57ca587c](https://www.amrc.org.uk/Handlers/Download.ashx?IDMF=c1a3904c-78de-47ed-813c-b34b57ca587c)
9. Brain Tumour Research (BTR) website, Drug repurposing report published (online news report), 11 December 2017. [cited 2018 July 11]. Available from: [https://www.brain tumourresearch.org/media/news/news-item/2017/12/11/drug-repurposing-report-published](https://www.brain tumourresearch.org/media/news/news-item/2017/12/11/drug-repurposing-report-published)
10. Pantziarka, P. Repurposing drugs in rare cancers, PowerPoint presentation: [https://pdfs.semanticscholar.org/presentation/4a5e/863a64c1e3f0fb188409bb7c30ccce26b39d.pdf](https://pdfs.semanticscholar.org/presentation/4a5e/863a64c1e3f0fb188409bb7c30ccce26b39d.pdf) and ReDO website, MD, 1847:616–617, [cited 2018 July 17]. Available from: [http://www.redo-project.org/](http://www.redo-project.org/)
11. Willis R, The Works of William Harvey, MD, 1847:616–617, [cited 2018 May 19]. Available from: [https://www.biodiversitylibrary.org/item/56320#page/716/mode/1up](https://www.biodiversitylibrary.org/item/56320#page/716/mode/1up)