



# Ending the isolation

*A guide to developing national rare cancer networks*

European Reference Networks can only work if member states designate and develop their own accredited specialist centres that can network across borders.

**Simon Crompton** talks to some of the policy makers, clinicians and patient advocates who are making it happen.

**“D**on’t speak about things you know nothing about.” Medical oncologist Lisa Licitra remembers the message being constantly driven home to her by teachers at school. Yet throughout her career she, like other cancer clinicians, has been faced with having to do exactly that.

“Patients with rare cancers want precise answers to their questions after diagnosis,” she says. “But what do you do if you’re uncertain of the data on a cancer, and you’re not sure of the best way forward? Maybe you shouldn’t even convey your uncertainty to the patient. Sometimes the uncertainty is so high that it’s best to just treat in the most appropriate way you can. But in your heart you know there is nothing there supporting your decision.”

Licitra today is one of Italy’s foremost authorities on head and neck cancers, Director of head and neck medical oncology at the Istituto Nazionale Tumori, Milan, and Associate professor of medical oncology at the University of Milan. But she freely acknowledges that even she has been left uncertain by untypical tumours. It’s hard, she says, for doctors who are supposed to be experts to say that they don’t know. Yet patients deserve answers.

This is not an uncommon experience. There are more than 300 rare cancers which – as rare cancer campaigning organisations continually point out – adds up to them not being very rare at all. Together, rare cancers account for 22% of all cancer cases diagnosed.

Diligent clinicians respond with a frenzy of activity: squeezing more information from pathologists, entering into long discussions at multi-disciplinary meetings and scouring PubMed, reports, books and the World

Health Organization classification for clues and information. “This is all very time-consuming,” says Licitra. “And then, at the end, you still don’t know if what you’re doing is the best course. And the uncertainty for patients remains.”

Text books and diligence are not the answer. Building knowledge and expertise requires opportunities to pool the experiences of similar patients with rare cancers, compare thoughts on best practice, develop research projects together. This can’t happen in one centre, or often even in one country.

## **“The value of networking at European level depends on strong national networks that are still largely non-existent”**

EU policy makers have recognised that this is an area where cross-border collaboration can play an important role. In March this year they launched their flagship European Reference Networks (ERNs) – with one specifically covering rare solid adult tumours, called EURACAN. In addition, there are ERNs for paediatric cancers, genetic tumour risk syndromes and haematological diseases including cancers.

The move has been welcomed by the rare cancer community. But as the policy rolls out, it is becoming increasingly clear that the value of networking at European level depends on strong national networks

that are still largely non-existent.

This is a concern of the Joint Action on Rare Cancers (JARC) – a collaboration for EU stakeholders and policy makers to set a European agenda to improve diagnostics and care for people with rare cancers.

“We have to make sure that the ERNs are a network of networks,” argues Paolo Casali, co-ordinator of JARC, whose partners include ministries of health, cancer control programmes, universities, public health institutions, cancer registries, oncological institutes, patients’ associations and other professional societies.

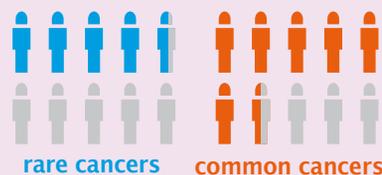
“Things can’t happen on a European level unless they’re happening at a national level. The European Commission is very much in agreement with this. And then the issue is that to have national networks, you need national governments and regions to be very much involved and motivated across the EU. This is a difficulty.”

Rare cancers patient advocate Kathy Oliver agrees that if people with rare cancers across Europe are to receive timely diagnosis and appropriate treatment, then pan-European aspirations in themselves are not enough. Infrastructure also needs to grow within each individual country.

“Certainly the arrival of the European Reference Networks demonstrates that there is a will throughout Europe, which is very heartening from the patient perspective,” says Oliver, who is Chair of the International Brain Tumour Alliance and a founding member of Rare Cancers Europe. “But it’s not just a matter of deciding something, and then it will be done.

“You need the resources to create proper durable links between existing centres of expertise. You need good solid cancer plans that include guidelines on treatment, care and support of people with rare cancers. You

### Improving services to improve survival



Five-year survival for rare cancers is 47% compared with 65% for more common cancers, reflecting deficiencies in early and correct diagnosis and effective treatment. This burden looks set to grow as the increasing fragmentation of 'common' cancers into molecular subgroups will effectively increase the numbers of rare cancers.

need multidisciplinary teams and you need quality research and standards. These things have to be achieved on a national level with solid and sustainable foundations.”

So how do you build standards of diagnosis and care nationally? JARC representatives are now looking at what lessons can be learnt from the progress some countries are making in defining expert centres, ensuring access to expertise for all patients with rare cancers, and establishing clinician buy-in to a system of referral.

### Establishing national consensus on expertise

Josep Maria Borrás, professor of public health at the University of Barcelona and a JARC advisor, believes that progress in establishing networks of expert reference centres for rare cancers in Spain provides hope that other countries can do the

same. Spain has a regionally organised health system but, after an initiative to identify reference centres of expertise in several regions, the country has now established national networks for sarcoma and childhood cancers.

It wasn't always a simple process. “The problem is that sometimes hospitals self-declare as reference centres without any kind of evidence,” he says. “What you need to establish are requirements for the minimum number of patients receiving treatment for a particular cancer annually, a demonstration that outcomes are good, a research commitment.”

## “You need solid cancer plans with guidelines on treatment, care and support of people with rare cancers”

With rare cancers, these requirements pose special problems. “How do you demonstrate that results are good, when typically the number of rare cancers receiving treatment in one hospital is very low? That makes evaluation, and finding differences in outcome, very difficult.” The solution in Spain, says Borrás, has been to make the big hospitals the reference centres, and encourage smaller hospitals to refer to them.

But this in turn can present human challenges. “How do you convince hospitals with smaller numbers of patients to send to bigger hospitals? There is a level of recognition that others can do the job better than you, but at the same time, there is an issue of... let's say self-esteem. There

are human emotions involved.”

The solution, he says, is establishing a clear national consensus on the criteria for what constitutes a centre of expertise for particular rare cancers. And this won't work unless it is agreed by all parties: clinical experts, representatives of scientific societies, patient representatives, health service managers, politicians.

Borrás acknowledges that the criteria established will – at least at first – be to some extent arbitrary. The required number of sarcoma cases treated annually, for example, was set at 60 – but current evidence provides very little consensus about the correct thresholds. Nonetheless, a national accreditation and audit process is now underway in Spain, co-ordinated by the Ministry of Health.

Any reference system for rare cancers, says Borrás, is bound to have shortcomings. The important thing is to have a national will, driven by policy, and then put into practice by achieving consensus between regions and all the parties involved.

### Achieving universal access to expertise

If Spain demonstrates the importance of a top down approach to improving access to expert rare cancer services, France has moved the concept considerably further. A national cancer control plan for 2009–13 required the certification of adult rare cancer reference centres, and has resulted in the establishment of 15 national clinical networks, recognised by the Institut National du Cancer (INCa). Each national network is comprised of national reference centres and regional or interregional centres of competence.

These networks were initially

approved through a process of self-assessment and independent external assessment, using quantitative and quality indicators to assess whether stated missions had been achieved.

## “The important thing is a national will, driven by policy and put into practice by achieving consensus ”

The result is not simply a network of national expert centres. The aim is to ensure that every single rare cancer patient has access to optimum care. So within each network, every new case is discussed at a virtual national expert multidisciplinary tumour board, held using Webex online meeting tools. And each network has a national database that is providing new clues to the best treatment, which can be tested in trials.

The French network for thymic (thymus gland) tumours, for example, consists of two co-ordinating centres – Hospices Civils de Lyon and Institut Gustave Roussy, Paris – and 12 regional centres. Representatives from all the centres gather at a web-based tumour board twice a monthly, bringing together national expertise in surgery, medical oncology, radiation oncology, radiology and pathology, to discuss each new diagnosis, and each patient who requires a new treatment strategy. It works to French guidelines adapted from the 2015 ESMO clinical guidelines for thymic cancers.

“We have a systematic pathological review of all cases,” says Nicolas Girard, senior attending physician in

### A network for rare adult cancers



The European Reference Network for rare adult solid cancers, EURACAN, aims to pool the expertise of 67 accredited rare cancer centres across 18 countries, using them as the basis of an integrated network of information, services and expertise covering the EU area.

It classifies rare adult cancers into 10 domains:

- Sarcoma of the soft tissue, bone and viscerae (Sarcoma)
- Rare neoplasm of the female genital organs and placentas (Rare GYN)
- Rare neoplasm of the male genital organs, and of the urinary tract (Rare GU)
- Neuroendocrine tumours (NET)
- Rare neoplasm of the digestive tract (Rare GI)
- Rare neoplasm of endocrine organs (Endocrine)
- Rare neoplasm of the head and neck: salivary gland tumours, nasopharyngeal cancer, nasal and sinonasal cancers, middle ear (Rare H&N)
- Rare neoplasm of the thorax: thymoma, mediastinum and pleura (Rare Thoracic)
- Rare neoplasm of the skin and eye melanoma (Rare Skin/Eye melanoma)
- Rare neoplasm of the brain, spinal cords (Rare Brain)

The European Commission wants European Reference Networks to reach all EU countries within five years, providing a referral system to ensure at least 75% of patients are treated in an accredited centre. It is seeking to improve patient survival, produce communication tools in all languages for patients and physicians, and develop multinational databases and tumour banks.

*For more information see [bit.ly/EURACAN](http://bit.ly/EURACAN)*

the thoracic oncology service of the Hospices Civils de Lyon. “We have found a 7% rate of major discrepancies between the initial diagnosis and the final diagnosis after pathological review. This will be an error in the stage or tumour type that modifies management for the patient.”

The benefit goes beyond accurate diagnosis. “Because we use the guidelines, and because of the way we analyse patient history and situation, we now have management that is more

consistent from patient to patient. Surgeons from the network have clearly progressed – there’s a lot of discussion at the boards about surgical technique and optimal approach.”

And because the networks provide access to larger numbers of patients, oncologists can finally target rare cancer patients for trials. Each network has an associated database – there are 2,000 patients in the new thymic tumour database.

“It’s a tool for sending patients for



### Clinician-driven network development: the ENET experience

Action taken by expert groups putting together criteria for reference centres, treatment guidelines and some basic quality indicators for networks can drive national and international development.

This is what happened in neuroendocrine tumours. Martyn Caplin, professor of gastroenterology and neuroendocrine tumours at the Royal Free Hospital in London, was involved in a European neuroendocrine tumour group instigated in the mid-1990s by Kjell Oberg from Sweden, Michelle Mignon from France and Bertram Widenmann from Germany. In 2000, when he realised there was “nothing in the UK for neuroendocrine tumours,” he started a UK neuroendocrine specialist group and a linked patient support group.

This led to the identification of expert specialists and centres in the UK, and the publication of UK guidelines

for the management of neuroendocrine tumours in 2004. The interest generated within such ‘enthusiast’ specialist groupings provided momentum to found a European Neuroendocrine Tumor Society (ENETS) in 2004. In turn ENETS developed a system of auditing centres of excellence throughout Europe. Today, there are 37 centres of excellence in Europe, eight of them in the UK ([www.enets.org/coe\\_map.html](http://www.enets.org/coe_map.html)).

“It’s a robust system of approval,” says Caplin, “looking at standard operating procedures, care pathways, pathology procedures, and adherence to ENET standards of care and guidelines.” Centralised frameworks are needed, he adds, if only to ensure that rare cancers move up the priority list throughout a health service. “Otherwise you are relying on the goodwill of one or two people to take it on.”

clinical trials in Paris or Lyon,” says Girard. “We are in the process of publishing many data from this prospective database, on radiotherapy, chemotherapy, pathological review and so on. The database is really useful for long-term follow-up. We started in 2012, so now we have a five-year follow-up for the first patients. It will be an incredible tool for better understanding of recurrences.”

The benefits are not just for thymic cancers. Bertrand Baujat, a head and neck cancer surgeon at Hôpital Tenon, Paris, says that it is now unusual for any French doctor not to refer head and neck cancers to the national network, at least for advice or pathology review. There are 5,000 head and neck cancer patients on their database, so more information on which to assess treatments and prognosis.

“For example, in salivary gland cancer there’s been no consensus on whether we should remove the nodes or not. Now we can provide recommendations based on our database. We know that in this kind of cancer we had ten people with node metastasis, and now we recommend doing the node dissection in the neck section systematically. This makes a difference to the patient.”

For Isabelle Ray-Coquard, gynaecological cancer specialist at the Centre Léon Bérard, Lyon, the beauty of the French networks has been that patients don’t always have to be physically referred to an expert centre, sometimes hundreds of miles away. “If they can be managed at regional level it’s clearly helpful for the patient and the physician in charge,” she says.

### Is France a template?

Is the French system replicable in other countries? Certainly, say those involved, but it needs top-down commitment, manifested in a national cancer plan backed by law and funding.

“None of this would have been possible without a national initiative to start it,” says Bertrand Baujat. “We needed the money so that we could set up the infrastructure.” Around €1 million was allocated over four years to establish a national network for head and neck cancers. It paid for setting up co-ordination systems, a database, clinical research technicians and other set-up costs. It receives annual government funding of €190,000.

Isabelle Ray-Coquard says that setting up the infrastructure required for

## Patient-driven policy and guidelines development: the sarcoma experience



European patient organisations for rare cancers can play a significant role in setting quality standards and templates for policy development. Last year, Sarcoma Patients EuroNet (SPAEN) – an international network of sarcoma, GIST and desmoid patient advocacy groups – launched a set of recommendations for service development, providing a clear statement on what sarcoma treatment and services should look like.

It includes pathways and recommendations for diagnosis, primary treatment and advanced disease, and is available at [bit.ly/SPAENpathway](http://bit.ly/SPAENpathway)

According to Markus Wartenberg, co-author of the paper and SPAEN Chair, the paper is already informing the certification of sarcoma centres in Germany – and will help guide their practice once established. SPAEN will be collecting information from its members on the extent to which it is influencing service development in other countries too.

“I think this is our way forward,” he says. “To produce service recommendations, guidelines and also position

papers with recommendations on certain issues in treatment. This could be part of a collaboration process on a national level between patient organisations and experts.”

This February, SPAEN also launched a Sarcoma Policy Checklist, drafted by an expert group to help policymakers close the gap in access to high-quality information and care for sarcoma patients across Europe. It describes five key areas where policy makers should focus their efforts to have the most impact on care for sarcoma patients:

- designated and accredited centres
- greater professional training
- a multidisciplinary approach
- incentives for research and innovation
- rapid access to effective treatment.

The document also provides examples from six countries to show the extent to which these recommendations have been implemented. The document is available in English, Spanish, Italian, French and German at [bit.ly/SPAENpolicychecklist](http://bit.ly/SPAENpolicychecklist)

these kinds of rare cancer networks is not as expensive as people imagine. “I think it is feasible,” she says. “We work with around €200,000 a year for gynaecological cancers, so that we can organise at national level. If you look at what misdiagnosis and unnecessary treatments cost, it is clearly more than organising a national network.”

But Baujat, who is involved with JARC and represents the French head and neck cancer network in EURACAN, is concerned that lack of funds will hold back the creation of a Europe-wide rare cancer network. And if other countries cannot replicate the kinds of national networks of expertise seen in France, then “har-

monising standards” across Europe will actually mean an extra burden placed on one or two expert centres.

“It’s true that, in France, we are

**“It is unusual for any French doctor not to refer head and neck cancers to the national network at least for advice or pathology review”**

a few years ahead of other countries because of our national plan,” he says. “And there are other countries, like Italy and the Netherlands, which are being quite active on a regional level. But there are countries where there is nothing for rare cancers. So harmonising quality of care across Europe is such a big project. I’m worried that for countries like France, EURACAN will mean double work. Developing things at a national level is a good place to start. But there’s no money in EURACAN to support this.”

This is a worry too for Martyn Caplin, founder and Vice Chair of the European Neuroendocrine Tumor Society, ENETS, which has set up a

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system of auditing centres of excellence throughout Europe (see box p 8).

“There’s no ERN funding that comes to individual hospitals, so no-one is sure what the next stages are. We have to take things forward in terms of meeting the ERN criteria for standards of care, teaching, access to multidisciplinary teams and so on.”

He worries particularly about patients in countries with less sophisticated and more fragmented health services. “First of all, a lot of patients will still be getting a delayed or wrong diagnosis. Then, they will be referred to their local oncologist, who may not be aware of where to refer for specialist treatment – or may not even want to refer them on. Part of the process needs to be for governments to state that it’s in the best interest of patients that they are sent to identified centres. But there are geographic issues related to that – patients separated from their families, travel costs. There are a lot of practical issues to be sorted.”

### A bottom-up approach

A way forward for some countries might be that forged in the field of sarcoma in Germany where, despite a fragmented health system, patients have linked with clinicians to provide a national momentum for change (see box p 9). Faced with problems of incorrect diagnosis, lack of authoritative information about experts in sarcoma, and centres self-declaring themselves as “expert”, the patient organisation Das Lebenshaus e.V. linked with the German Cancer Society and medical experts to establish a certification system for sarcoma centres.

The system is currently built on meeting organisational criteria such as number of patients treated and use of multidisciplinary teams. As with other

new certification systems for rare cancer units, independently monitored quality indicators are, as yet, a pipe dream. “But this is the aim,” says Markus Wartenberg, Senior Manager of Das Lebenshaus e.V, which supports patients with GIST, sarcomas and kidney cancer.

“The certification system is the first step to identifying 20–25 centres in Germany that are able and willing to move forward in the field of sarcoma.” The next step, he says, will be to create a real force for change by formally bringing sarcoma patients and expert clinicians together in a single German Sarcoma Foundation. “This is a very valuable development to raise awareness. Building common power between patients and experts is the way to build an infrastructure and move forward.”

Service improvements in rare cancers can be achieved from the bottom up, rather than the top down, he says. “It’s a question of whether or not you want to put your energy into a national battlefield to convince politicians that they need to do more for rare cancers. We decided to build from the bottom up, and try and make sarcomas something like a lighthouse for the rest of the rare cancer community to follow.”

### National responses to the EU lead

Despite the lack of funding to help countries develop their own reference centres and networks, Paolo Casali points out that European Reference Networks are having a positive effect on services in individual countries, by the mere fact of their existence.

“What I’ve come to realise is that the main meaning of these European mechanisms is national, rather than international,” he says. “The ERNs are

already forcing national governments to do something in their countries. For example, the process of selecting centres to join the ERNs was the first time some governments took political responsibility for explicitly endorsing centres for rare cancers.”

## “It was the first time some governments took responsibility for endorsing centres for rare cancers”

This was the case in Italy where, as a result of government and regions selecting rare cancer centres for the ERN, they are now discussing the possibility of establishing a formal rare cancer network. This follows many years of efforts by Casali and his colleagues in the clinician-led Italian Rare Cancer Network to connect centres, but without a formal accreditation system.

“We hope the selection process for our national network will mimic to some extent what is happening for the ERNs,” says Casali, “so it is as if the European action is giving rise to a virtual cycle of improvement nationally.”

Finally, he says, he sees the prospect of services for rare cancers improving at national and European level. “I didn’t expect it, because I saw some countries slowing down the process through bureaucracy and so on. But once you’ve started a process at European level, involving all the rare diseases communities on finding a framework, then the process is very difficult to slow down.”

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