



## TIME TO ACCELERATE: ACTION ON RARE CANCERS

### EXECUTIVE SUMMARY

In Europe, 1 in 5 cancers is rare. This paper underscores the urgent need to prioritise rare cancers, in the framework of the European Union's health agenda. Though individually uncommon, rare cancers collectively affect a significant population, requiring dedicated policies due to the unique challenges they pose, including late diagnosis, limited expertise and insufficient research and treatment options.

Key recommendations emphasise the integration of rare cancer priorities into Europe's Beating Cancer Plan (EBCP) and legislative mechanisms.

Efforts should focus on increasing awareness among healthcare professionals and advancing diagnostic technologies. Comprehensive cancer care must also ensure equitable access to multidisciplinary expertise, leveraging European reference Networks (ERNs) and fostering collaborations across national borders.

Innovation in drug development and treatment access are critical. Patients should be better and further integrated into regulatory processes to address unmet medical needs and combat treatment disparities.

Quality of life initiatives should tailor survivorship care to rare cancer patients' specific needs, providing psychological support and rehabilitation services.

Lastly, robust research and data collection efforts are essential. This includes supporting multicentric clinical trials, establishing rare cancer registries, and exploring adaptive licensing approaches to innovative therapies.

In essence, this Manifesto calls to decisive action, ensuring that each and every patient receives timely diagnosis, comprehensive care, and equitable access to what often are life-saving treatments.



## INTRODUCTION

### **The challenges of rare cancers**

In Europe, rare cancers amount to about 24% of new cancer cases per year occurring from birth up to elderly age groups<sup>1</sup>. Hereditary cancers (genetic predisposition to cancer), which are also rare, amount to about 5 to 10% of cancers<sup>2</sup>.

Rare cancers are defined as those malignancies whose incidence is less than 6 per 100,000 people a year<sup>3</sup>.

Each patient and caregiver, irrespective of age and type of rare cancer, shares the challenges linked to the rarity of the disease: late or incorrect diagnosis, lack of/ difficult access to adequate expertise and treatment, lack of understanding of the underlying science, insufficient registries/databases, difficulties in conducting well-powered clinical studies adding a layer of complexity in developing and then accessing innovative therapies, feelings of isolation and greatly reduced quality of life.

There are an estimated 5.1 million people living with a rare cancer across Europe. Though each rare cancer is rare, or even ultra-rare, altogether this population of patients represents a significant number of people affected by a rare form of cancer, across all ages, and as such constitutes a public health challenge which must be addressed.

If we focus on childhood cancer, every year in Europe, 35,000 children are diagnosed with cancer. The burden of childhood cancers in Europe constitutes the leading cause of children's death by disease over the age of one, with 6,000 lives lost annually. Although survival rates are now up to 80%, there are prevailing issues in the pace of development of treatments for paediatric cancers<sup>4</sup>. It is worth noting that childhood cancers, which are all rare, require specific approaches beyond those shared with rare adult cancers, in line with their distinct age-related biological, clinical and organisational needs and characteristics.

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<sup>1</sup> **Burden and centralised treatment in Europe of rare tumours: results of RARECAREnet - a population-based study**, Gemma Gatta et al., the Lancet Oncology, 2017; 18: 1022–39

<sup>2</sup> **Overview of the clinical challenges in hereditary cancer, from identification to treatment and prevention: the role of ERN GENTURIS in the EU**, Prof. Nicoline Hoogerbrugge, MD, PhD, ESMO Preceptorship on Hereditary Cancer Genetics, 29-30 September 2023

<sup>3</sup> **Rare cancers are not so rare: The rare cancer burden in Europe**, Gemma Gatta et al., European Journal of Cancer, 2011, 2493-2511

<sup>4</sup> **European Elections 2024, Manifesto for the Paediatric Oncology & Haematology Community: Beating Childhood Cancer: Cure more, cure better and tackle inequalities**, CCI Europe & SIOPE, February 2024



## Fill in the gaps

Europe's Beating Cancer Plan (EBCP) constitutes a major initiative and step forward to provide innovative and comprehensive approaches to reduce the impact of cancer as well as address health inequalities in Europe, with the objective to significantly improve cancer patients' health outcomes and their quality of life by 2030.

The rare cancers community greatly appreciates that several much-needed initiatives and projects are dedicated to improving holistic care for paediatric cancer patients and survivors.

However, the rare cancers community is worried about the lack of attention to rare adult cancers and the consequences this could have in the short, medium and long term on a potential lack of improvement to fair and timely access to specialised healthcare providers within and across European countries, as well as insufficient support to fundamental, clinical and social research dedicated to rare adult cancers despite crucial unmet needs in this adult population.

The entire rare cancers community calls on the European Commission, the European Parliament and Member States to ensure that recommendations set out in the Rare Cancer Agenda 2030<sup>5</sup> and in the European Parliament's resolution 2020/2267(INI)<sup>6</sup> (see below) be integrated in the work of the next legislative mandate to address rare cancers' challenges throughout the patient's journey, and across all ages including adults and the elderly.

## PREVENTION

Public health recommendations for behavioural strategies may not have a major impact on the prevention of these rare cancers as compared to, for instance, the increased risk of lung cancer from tobacco consumption. Some identified risk factors for certain rare tumours are exposure to ionising radiation or chemicals such as pesticides and asbestos. However, in many cases, the underlying causes of developing a rare tumour still need to be further investigated. Investment in patient-centred research with the inclusion of patient generated data is crucial in this area.

Concerning people potentially affected by a genetic tumour risk syndrome, a genetic predisposition to cancer, the implementation of adapted screening programmes facilitating

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<sup>5</sup> **RARE CANCER AGENDA 2030: Ten Recommendations from the EU Joint Action on Rare Cancers**, September 2019

<sup>6</sup> **European Parliament resolution of 16 February 2022 on strengthening Europe in the fight against cancer – towards a comprehensive and coordinated strategy (2020/2267(INI))**:

- Section V: *Challenges in cancer among children, adolescents and young adults*
- Section VI: *Challenges of rare adult cancers*



access to existing and adequate genetic testing should be further developed and harmonised across Europe.

Genetic tumour risk syndromes are disorders in which inherited genetic mutations strongly predispose individuals to the development of tumours. The carriers are at a very high lifetime risk of developing an early-onset cancer, sometimes reaching 100 %. At present, only 20-30 % of people with genetic tumour risk syndromes have been diagnosed<sup>7</sup>. Facilitating access to existing and appropriate genetic testing can help detect if someone has a genetic tumour risk syndrome before the onset of an early cancer. Identified carriers can thus receive adequate monitoring leading to improved survival and quality of life.

As highlighted in this Manifesto, “hereditary cancer risk counselling remains a severely under met need in Europe”. Hence, we welcome the “Genomic for Public Health” project and the establishment of a “roadmap to personalised prevention” set out in the EBCP.

As soon as people are diagnosed with a genetic tumour risk syndrome, they must be directed to specialised centres including a multidisciplinary team of experts well acquainted with their genetic cancer to be well monitored and receive personalised care.

Existing and arising digital tools should be taken into account to facilitate this kind of support such as, for instance, the recently launched [EVITA Platform](#)<sup>8</sup>.

## EARLIER DETECTION CAN SAVE LIVES

### **Fighting against late diagnosis/misdiagnosis: Implementing adequate referrals**

Rare cancer patients are often misdiagnosed, leading to late or inadequate treatment. Sometimes, patients receive an accurate diagnosis at a late stage in their disease, when treating options to save a life are unfortunately exhausted.

Given the uncommon nature of some tumours, specialised pathologists or relevant medical experts are needed to perform relevant tests on tissue and/or bodily fluids.

Another layer of challenge may stem from a difficult access to specialised healthcare professionals, whose centres may be located far away from where the patient lives, or even based in another country. Patients have reported that accessing cross-border care is costly and administratively burdensome in the EU since each Member State has its own policies.

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<sup>7</sup> [ERN-GENTURIS-flyer-Version2437.pdf](#)

<sup>8</sup> <https://evitaplatform.org/>



The rare cancer community has stressed the importance of increasing awareness of rare cancers (including genetic tumour risk syndromes) amongst primary and secondary healthcare professionals. National authorities must support the implementation of adequate referrals to specialised multidisciplinary expert centres at both national and European level (European Reference Networks) for paediatric cancers, rare adult solid cancers, rare adult blood cancers and patients with genetic tumour risk syndromes. The development of decision-making aides, training for GPs and specialised clinicians, and public health campaigns can increase awareness of rare cancers among health professionals. Such initiatives would surely dramatically increase rare cancer patients' life expectancy and quality of life.

### **Facilitating equal access to diagnosis techniques/tools**

Research on innovative diagnostic techniques/tools brings significant hope for rare cancer patients. Patients are notably calling for easier and timely access to existing molecular testing and even access relevant clinical trials where appropriate. Research on biomarkers is critical in this area and needs to be fully supported.

Furthermore, the potential of liquid biopsy is an additional tool for early detection that can be further developed.

As already mentioned above, patients' access to safe genetic testing where relevant must be facilitated and harmonised across countries.

Targeted screening approaches could be implemented using novel or established diagnostic tools to detect cancers in early stages before becoming symptomatic and thus improving overall prognosis.

Rare cancer registries to monitor variations in diagnosis times and access to tests can be powerful tools to support evidence-based recommendations for improving diagnosis (see the section "research").

In addition, the development of artificial intelligence in healthcare will bring new levels of precision and speed for the diagnosis of rare cancers. Specific algorithms could improve the accuracy of early diagnoses and predictive risk algorithms could help estimate the risk of a patient developing a rare cancer.

## **COMPREHENSIVE QUALITY CANCER CARE FOR ALL**

### **Facilitating equal access to specialised multidisciplinary teams of experts**

One of the main EBCP flagship initiatives is to foster access to comprehensive quality cancer care for all. It is crucial and fair that this initiative also applies to patients with a rare cancer.

5 / 10



The various EU projects and Joint Actions in the field<sup>9</sup> have demonstrated that people affected by a *rare disease (rare cancer included)* need to be directed and *have equal access in a timely fashion* to multidisciplinary teams of experts specialised in a specific rare disease or group of rare diseases, rare cancers included, to increase patients' health outcomes and survival.

In March 2017, the European Commission launched 24 European Reference Networks (ERNs) for rare diseases bringing together highly specialised centres across the EU, UK and Norway, selected against stringent quality criteria following an EU call for expressions of interest. The ERNs are virtual networks that connect specialised multidisciplinary healthcare providers to discuss rare and/or complex cases requiring a high degree of knowledge and resources. Within ERNs, the expertise travels rather than the patient. The patients' data are shared via a secured web-based platform, ensuring that these data are well protected. The ERNs' legal framework is provided by the EU Directive on patients' rights in cross-border healthcare (2011/24/EU).

Each ERN covers a broad range of rare diseases, grouped under a main clinical domain. There are four ERNs relevant to rare cancers: ERN PaedCan for paediatric cancers, ERN EURACAN for rare adult solid cancers, ERN EuroBloodNet for rare haematological diseases, including rare adult blood cancers, and ERN GENTURIS for genetic tumour risk syndromes. Some rare tumours are also covered in a few other ERNs (e.g. a range of rare endocrine tumours in ENDO-ERN, mesothelioma in ERN-LUNG). The ERN experts have established partnerships within each clinical domain.

Nonetheless, challenges remain to ensure that these ERNs fulfil their ambitious mission. The rare cancers community has put forward several recommendations – set out in the 'Rare Cancer Agenda 2030'<sup>10</sup> – to address these challenges:

- competent authorities at both national and European level must ensure the continuous financial sustainability of ERNs and support their expansion to cover more rare tumours as well as additional geographical areas. The European Commission is responsible for allocating adequate financial resources to ERNs for them to achieve their mission, and national health authorities must support their national centres of expertise which look after rare cancer and genetic tumour risk patients and provide the best state of the art care;
- awareness of ERNs, and their member centres, must be raised amongst healthcare professionals, patients and caregivers. Likewise, increasing awareness and knowledge of rare cancers amongst healthcare professionals will increase the chances of rare cancer patients to be directed to the relevant specialists; \*
- Member States are encouraged to establish *national networks for rare adult cancers*, with a view to optimise the referral of patients to specialised centres in a timely fashion

<sup>9</sup> **EUCERD EU Joint Action** (2012-2015), **RD-ACTION EU Joint Action** (2015-2018), **JARC EU Joint Action on Rare Cancers** (2016-2019)

<sup>10</sup> **RARE CANCER AGENDA 2030 - Ten Recommendations from the EU Joint Action on Rare Cancers;** September 2019



and facilitate interaction with ERNs to maximise the exchanges of multidisciplinary knowledge and high-quality care.\*

\* The new EU Joint Action “JARDIN” on the integration of (all) ERNs into national healthcare systems will support the provision of recommendations to optimise healthcare pathways and referrals from primary and secondary care to specialised multidisciplinary teams in ERNs.

EBCP has also launched a key initiative to establish an ‘EU Network of Comprehensive Cancer Centres’ to facilitate the uptake of quality-assured diagnosis and treatment, increase knowledge sharing and training and foster research. The Plan has set an ambitious goal: “**ensure that 90% of eligible patients have access to such centres by 2030**”. The establishment of this EU Network is supported by the EU Joint Action [CraNE](#) (Joint Action on network of Comprehensive Cancer Centres).

In addition, EBCP is supporting the creation of ‘EU Networks of Expertise’ that will leverage and harmonise quality standards of care in the following areas: complex and poor-prognosis cancer(s); personalised primary prevention; survivorship; palliative care; omics technologies; hi-tech medical resources; cancer in adolescents and young adults. The creation of these EU Networks of Expertise is supported by the EU Joint Action [JANE](#) (Joint Action on European Networks of Expertise).

To help patients with a rare form of cancer, and also to assist practitioners in navigating the health care system to access specialised multidisciplinary teams of experts in an easy and timely fashion, the connection and interaction between ERNs, the EU Network of Comprehensive Cancer Centres and Networks of Expertise must be clear, transparent and well defined.

In the field of childhood cancers, enhancing the sustainability of existing cross-border collaborations, in particular the ERN PaedCan, and greater clarity on access to cross-border clinical trials is of paramount importance. All oncology paediatric units should also be integrated into the EU Network of Comprehensive Cancer Centres, whether there are situated in paediatric or adult hospitals.

### **Facilitating equal access to available treatments and involvement of patients in defining unmet medical needs**

The rare cancers community welcomes the proposal for a new EU General Pharmaceutical Legislation, merging several existing EU Regulations to streamline drug development processes. This is described further in the main Time to Accelerate: Together Against Cancer manifesto.

The rare cancer patient community (patients, caregivers, families and patient advocates) particularly commend the attention given to foster research in areas of unmet needs, to address health inequalities and combat shortages of medicines. However, the rare cancer patient community asks to be fully integrated in the consultation processes to be established by the European Medicines Agency, aiming at establishing scientific guidelines for unmet medical



needs and the design of clinical trials. Given the rarity of the cancers, the patient advocates bring in an invaluable knowledge on the various challenges to live and cope with a rare form of cancer.

In the field of childhood cancer, inequalities in access to treatment, care and research protocols across Europe contributes to an estimated 20% gap in childhood cancer survival rates, with Eastern European countries facing challenges. Action is needed to reduce inequalities in access to high quality care and research for all children and adolescents with cancer across Europe, incorporating a patient-centred approach throughout<sup>11</sup>.

The rare cancer patient community also welcomes the implementation of the EU Regulation on Health Technology Assessment (HTA) and calls for the establishment of strong support for patient involvement throughout the implementation acts, including clear timelines and detailed involvement provisions.

The EU funded training projects (EUPATI, EUCAPA) targeting patient advocates are particularly useful to better understand medicines development and HTA processes as well as meaningfully involve the patient community in joint clinical assessment of a medicine. We believe this will help reduce current, significant disparities in terms of accessing treatments, including innovative therapies, in Europe.

## QUALITY OF LIFE DURING AND AFTER TREATMENT

One of the underlying objectives of the Time to Accelerate Manifesto is to enhance survivorship and quality of life to all cancer patients and survivors – including rare cancers.

The rare cancer patient community not only faces disease-specific challenges affecting their quality of life, but also obstacles directly stemming from the lack of specialised knowledge of many healthcare professionals.

Rare cancer patients indeed need to receive adequate psychological support, rehabilitation and monitoring of long-term side effects of treatments. To that end, several recommendations can be put forward, including, but not limited to:

- Establishing specific age-related rare cancer programmes dedicated to improving the quality of life of rare cancer patients and survivors,
- Adjusting survivorship care planning to the age and type of rare cancer of the patient,

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<sup>11</sup> **European Elections 2024, Manifesto for the Paediatric Oncology & Haematology Community: Beating Childhood Cancer: Cure more, cure better and tackle inequalities**, CCI Europe & SIOPE, February 2024





- Creating specialised training for healthcare professionals including nurses, psycho-oncologists, and physiotherapists, and caregivers.

## RESEARCH

Due to the rarity of each disease, the vast majority of rare cancers, some of which are ultra-rare, do not attract sufficient research interest and thus financial investment.

The rare cancer community is calling for public financial support as well as public-private investment to fund basic, translational, and clinical research on these rare and ultra-rare cancers that currently are very difficult to treat, and for which the underlying causes often remain unknown.

It is necessary to use or establish clinical registries for rare cancers to increase research on these cancers to better understand the natural history, predictive and prognostic factors and improve the quality of care. Registries are a powerful tool to help improve the quality of care and reduce inequalities. The European Reference Networks for Rare Cancers (paediatric, rare adult solid tumours, rare adult haematological malignancies, genetic tumour syndromes) play a crucial role in bringing together existing registries and supporting the development of new ones to ultimately cover all rare cancers and make data interoperable. It is an immense task that needs to be acknowledged by decision makers and adequately funded in a sustainable manner to ensure these networks will achieve their goals with a view to enhance research and ultimately improve patients' healthcare.

Given the small number of patients affected by the same rare cancer, it is difficult to conduct well-powered clinical trials. Multicentric clinical trials are needed and access to cross-border clinical trials must be facilitated in order to provide patients affected by a rare cancer with the same chance to access a clinical trial. The same fair principle applies to compassionate use programmes.

The Call to Action from Rare Cancers Europe, 'Rare Cancers in All Policies' encourages the adoption of novel regulatory approaches to enable rare cancer patients access to new innovative therapies under safe monitoring, while facilitating the collection of real-world data in addition to data collected in clinical trials. In this context, flexible licensing approaches such as the European Medicines Agency's pilot on adaptive licensing leading to pan-European new evidence generation, would be a solution to explore for rare cancers: "this could ensure the collection of robust data about new agents along with their availability within networks with medical expertise, e.g. ERNs, and the ability to generate new knowledge under a degree of control by national health systems"<sup>12</sup>.

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<sup>12</sup> **Rare Cancers in All Policies** – A Call to Action from Rare Cancers Europe, 2021



## ACKNOWLEDGEMENTS

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