



## Twinning to reduce research and innovation inequalities in paediatric solid tumours across Europe

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### ARTICLE INFO

#### Keywords:

Twinning  
Research  
Inequalities  
Paediatric oncology  
Horizon 2020  
Survival

### ABSTRACT

Inequalities in research and innovations affect childhood cancer survival across Europe. Vilnius University Hospital Santaros Klinikos (VULSK, the coordinator) and eight research-intensive institutions from seven European countries implemented the TREL project (Twinning in Research and Education to improve survival in childhood solid tumours in Lithuania) supported by the Horizon 2020 Widening programme. TREL aimed to enhance translational, clinical, and survivorship research in paediatric CNS, neuroblastoma, and renal tumours to improve future treatment outcomes in Lithuania. From January 2021 to December 2023, 49 VULSK professionals and 55 peers from partner institutions collaborated in this twinning program. Achievements after three years were: nine educational events, the initiation of basic and clinical research on fertility preservation, ten VULSK researchers joining international research groups, six signed agreements to participate in international academic clinical trials and the implementation of the European Survivorship Passport. Thirty patients received individual treatment recommendations following multidisciplinary discussions with experts from partner institutions. Twenty-five rare genetic variants were classified by the twinning bioinformatician teams with direct consequences on patient management. In conclusion, coordination of the Horizon 2020 project enhanced VULSK's research capacities, networking channels and attractiveness for industry and academia-initiated innovative actions that will improve survival rates in the long run.

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## 1. Introduction

Childhood cancer has become curable for most children over the last decades – current overall 5-year survival rates reach 81 %, in some cancers surpassing 90 % [1]. The progress was achieved due to collaborative research efforts within multicentre observational studies and academic clinical trials [2,3]. However, the most recent EURO CARE-6 study highlighted persistent inequalities in Europe with five-year survival rates ranging from 71 % to 87 % across EU member states [1]. The least favourable outcomes were reported for countries defined as “widening”, i.e. underperforming in research and innovation as compared to the European average [4].

Lithuania – a small Eastern European country – is considered a widening country. The population-based EURO CARE-5 study reported a 10–18 % lower 5-year overall survival rates of children treated in 2000–2007 for CNS and solid tumours as compared to the European average [5,6]. Twinning is considered a powerful tool to bridge gaps in research and innovation between underperforming and research-intensive countries. The support includes networking, coordination, training, management, and increasing mobility [7].

Given existing challenges, we built a nine-partner consortium to initiate twinning activities within the TREL project (“Twinning in Research and Education to improve survival in Childhood Solid Tumours in Lithuania”) supported through Horizon 2020 (Grant agreement ID: 952438).

## 2. Methods

The project concept was developed in collaboration with members of the European Reference Network for Paediatric Oncology (ERN Paed-Can) and is depicted in Fig. 1. Eight objectives, addressing all aspects of childhood solid tumours from diagnosis and treatment to survivorship

were defined to achieve the strategic goal (Table 1). The work plan was divided into seven Work Packages (WP). The most frequent paediatric solid tumours – CNS tumours, neuroblastoma (NBL), and renal tumours (RT) – were selected for the twinning activities in translational research and modern diagnostics, innovative therapies, clinical trial preparedness and cross-disciplinary training, and quality of survival and late-effect research. As per the “WIDESPREAD-05-2020 – Twinning” call definition, a dedicated WP on Research Methodology and Management was developed to increase specific knowledge, capacities and skills of project managers and administrators in the management of large-scale European projects.

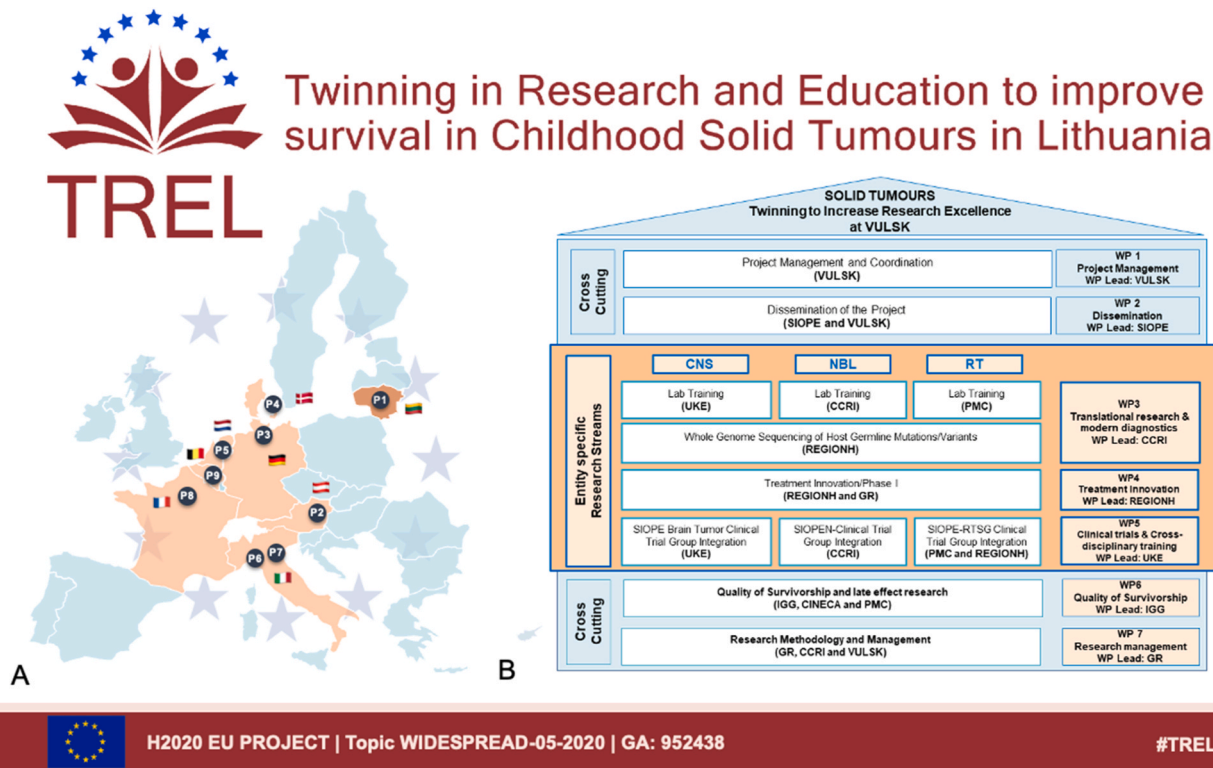
## 3. Consortium

**Vilnius University Hospital Santaros Klinikos (VULSK, the Coordinator)**, a leading paediatric oncology centre in Lithuania, stepped up as the project Coordinator to scale up its research excellence. VULSK was responsible for the WP1 (Project Management and Coordination).

The research-intensive counterparts included eight institutions leading research activities in Europe on childhood solid tumours. Each beneficiary contributed its specific expertise relevant to achieving the project objectives. The consortium included the following partners:

**Children’s Cancer Research Institute (CCRI, Austria)** is an acknowledged European leader in biology and clinical research on neuroblastoma as well as has solid experience in the management of large-scale research projects. Additionally, CCRI coordinates ERN-PaedCan. CCRI led WP3 (Translational research and modern diagnostics) and contributed to WP5 and WP7.

**University Medical Centre Hamburg-Eppendorf (UKE, Germany)** coordinates European clinical research projects on CNS tumours on behalf of the European Society for Paediatric Oncology Brain Tumour Group (SIOPE-BTG). UKE led WP5 (Clinical trial preparedness and



**Fig. 1.** The TREL consortium (a) and project concept (b). Abbreviations: CCRI (P2) – St. Anna Children’s Cancer Research Institute, Austria; CINECA (P7) – Consorzio Interuniversitario, Italy; CNS – Central Nervous System; GR (P8) – Institut Gustave Roussy, France; IGG (P6) – Istituto Giannina Gaslini, Italy; NBL – neuroblastoma; P – Partner; PMC (P5) – Princess Maxima Centrum, the Netherlands; REGIONH (P4) – Rigshospitalet, Denmark; RT – Renal Tumours; SIOPE (P9) – European Society for Paediatric Oncology, Belgium; UKE (P3) – University Medical Centre Hamburg, Germany; VULSK (P1) – Vilnius University Hospital Santaros Klinikos, Lithuania.

**Table 1**

The objectives and sustainable results, the corresponding Work Package (WP) and involved partners (WP leader indicated in bold).

<p><b>Objective 1.</b> Increase knowledge sharing in <b>basic-translational research</b> to standardize interpretation of tumour biomarkers for risk stratification and whole genome sequencing for elucidation of cancer driver mechanisms</p> <p>Results</p> <p>Novel diagnostic and biobanking techniques aligned with ongoing research protocols implemented and documented as institutional SOPs: i) <i>Illumina Infinium HumanCytoSNP-12</i> methylation arrays technique upgraded for correct stratification of CNS tumours; ii) sample collection, handling and storage workflow developed for patients with NBL and RT</p> <p>Standard operating procedure on the workflow of bioinformaticians developed</p>	<p>WP3 <b>CCRI</b> UKE PMC REGIONH</p>
<p><b>Objective 2.</b> Gain specific knowledge and skills necessary to <b>handle innovative therapies</b> in early-phase clinical trials including the implementation of educational and research activities in pharmacogenetics, clinical pharmacology, and drug metabolism</p> <p>Results</p> <p>A team of pharmacists, a paediatric oncologist, a pharmacologist, a geneticist and nurses received training on handling innovative therapies and drug monitoring</p> <p>Busulfan once-daily administration and drug-level monitoring procedure implemented at VULSK for patients with NBL and other indications exploitable for future use in clinical trials beyond the TREL project</p>	<p>WP4 <b>REGIONH</b> GR</p>
<p><b>Objective 3.</b> Fostering research and collaborative activities in clinical research (including pathology, radiology, radiotherapy, and patient care) to <b>increase preparedness to conduct prospective clinical trials and observational studies</b> based on modern biology-driven approaches to tumour classification and treatment</p> <p>Results</p> <p>Sustainable networking between VULSK and partner researchers (and beyond) through joining specialty-corresponding working groups (Table 2)</p> <p>Several international multicentre clinical trials and observational studies were initiated (Table 2)</p> <p>Perfusion, spectroscopy, and tractography protocols were implemented and the protocols in use were revised to ensure CNS tumour response assessment according to RAPNO criteria</p>	<p>WP5 <b>UKE</b> CCRI PMC</p>
<p><b>Objective 4.</b> Scale-up research on survivorship quality and late effects by implementation of <b>Survivorship Passport</b> and integration in the pan-European research activities for standardization of follow-up recommendations as well as enhancement of <b>fertility</b> research</p> <p>Results</p> <p>Survivorship Passport version 1.2 implemented and issued for five survivors who benefited from international follow-up recommendations</p> <p>VULSK researchers joined the International Guideline Harmonization Group in the development of long-term follow-up guidelines</p> <p>The quality of fertility counselling at VULSK was evaluated; an innovative TRIAGE tool to assess gonadal damage risk was implemented</p> <p>Ovarian tissue maturation in vitro protocol developed, systematic review on minimal infiltrative disease in ovarian cryopreserved tissue carried out and published</p>	<p>WP6 <b>IGG</b> CINECA PMC</p>
<p><b>Objective 5.</b> <b>Promotion of early-stage researchers*</b> by training research active and innovative young scientists, possessing sufficient knowledge and technical skills to collaborate within large-scale research groups as well as to initiate and accomplish their own research project</p> <p>Results</p> <p>Five early-stage researchers and two research-active medical students were involved in the training activities.</p> <p>A new PhD project on pediatric CNS tumours was initiated because of the project activities.</p>	<p>WP3-7 All</p>
<p><b>Objective 6.</b> <b>Dissemination and communication</b> (respecting intellectual property rights) of the impact of the twinning activities for the scientific community, widening country and ultimate benefit for patients as well as <b>exploitation</b> of the established research platform and development of the <b>sustainability plan</b></p> <p>Results</p> <p>TREL project website was launched under the umbrella of SIOPE website to maximize international visibility (<a href="https://siope.eu/TREL-project">https://siope.eu/TREL-project</a>). For the internal dissemination VULSK website was</p>	<p>WP1-2 <b>SIOPE</b> VULSK</p>

**Table 1 (continued)**

<p>exploited (<a href="https://www.santa.lt/horizontas-2020-programa/">https://www.santa.lt/horizontas-2020-programa/</a>)</p> <p>Project activities were disseminated in 16 conferences and meeting and awarded twice as the best presentation</p>	
<p><b>Objective 7.</b> Strengthening <b>capabilities</b> of the coordinating institution <b>in research management</b> and coordination of large-scale collaborative projects including proposal preparation, project management and administration and innovation transfer abilities.</p> <p>Results</p> <p>A team of project managers, a data protection officer, a lawyer, a statistician, a communication specialist, and clinical trial coordinators were trained.</p> <p>Informative leaflet for medical professionals on the principles of innovation management and intellectual property protection. Available at the VULSK website.</p> <p>Guidelines on research methodology for young researcher were produced. Available at the VULSK website</p> <p>A new proposal for Horizon Europe with VULSK acting as Coordinator was submitted</p>	<p>WP7 <b>GR</b> CCRI</p>
<p><b>Objective 8.</b> Preparation of joint <b>peer-reviewed publications</b> in collaboration with project partners</p> <p>Results</p> <p>Five publications were released. Early-stage researchers and medical students are the first authors in four publications.</p>	<p>WP3-7 All</p>

RAPNO – Response Assessment in Paediatric Neuro-Oncology

\* Early-stage researchers shall, at the time of recruitment, be in the first four years of their research careers and have not been awarded a doctoral degree.

Cross-disciplinary training) contributed to the CNS-focused Task within WP3.

**Rigshospitalet** (REGIONH, Denmark) contributed with expertise on childhood cancer aetiology, whole genome sequencing, pharmacology of anticancer agents and innovative therapies; This partner led WP4 (Treatment Innovations) and bioinformatician training within WP3 and contributed to WP5.

**Princess Maxima Centrum** (PMC, The Netherlands) is the international data centre for the SIOP-RTSG as well as leading UMBRELLA biology and clinical study on RT. PMC led specific Tasks within WP3 and WP5 focused on RT biology and clinical research. In addition, PMC has a strong institutional oncofertility programme that was exploited in late effect research focused on fertility (WP6).

**Istituto Giannina Gaslini** (IGG, Italy) leads European research initiatives in long-term follow-up studies. IGG developed the Survivorship Passport (SurPass) [8] and led its implementation at VULSK; Within WP6 (Quality of survival and late-effect research) IGG led the implementation of SurPass and monitored the participation of VULSK researchers in the development of follow-up recommendations in collaboration with the international Guidelines Harmonization Group (IGHG) ([www.ighg.org](http://www.ighg.org)).

**Consorzio Interuniversitario** (CINECA, Italy) developed an advanced pan-European web platform and interacted in parallel with IGG providing IT support for the implementation of SurPass within WP6.

**Institut Gustave Roussy** (GR, France) has unique expertise in conducting first-in-man studies and phase II trials in children. GR was responsible for the implementation of two Tasks in WP4. In addition, GR led learning and education activities within WP7 (Research methodology and management) targeting knowledge transfer, innovation and research management as well as intellectual property rights and protection.

**European Society for Paediatric Oncology** (SIOPE, Belgium) is the only Pan-European organisation representing all professionals working in childhood cancers. SIOPE was and is responsible for the dissemination of several EU-funded projects in paediatric oncology. Its expertise was exploited for disseminating the TREL project activities and leadership of WP2 (Dissemination of the Project).

### 3.1. Twinning methodology

The twinning methodology comprised a set of actions supported by

the Widening Programme and necessary to meet the defined objectives: i) learning and education of VULSK professionals at partner premises to upgrade knowledge; ii) expert visit to VULSK; iii) organization of educational events; iv) participation in international knowledge-transfer meetings; v) virtual tumour boards. In addition, the funding supported certain basic and translational research activities.

#### 4. Results

##### 4.1. Twinning efforts

The project was launched on January 1st, 2021 and ended on December 31st, 2023. The summary of key results corresponding to the pre-defined objectives is provided in Table 1.

Due to the COVID-19 lockdown, physical interaction between twinning peers started later than planned. Nevertheless, during the 3-year project period, 37 professionals (11 researchers and 26 non-researchers) from VULKS received training at the partner premises. Amongst them, five early-stage researchers (ESRs) benefited from additional knowledge to promote their ongoing PhD project or embark on a new one. Twenty-five researchers and 30 non-researchers from partner institutions were engaged in the twinning programme. The majority of staff involved in the twinning program, both from the Coordinator and the partner side, were women.

The TREL activities comprised nine educational workshops corresponding to each WP (Table 2). The outreach initiatives engaged participants from other Lithuanian institutions and neighbouring Baltic countries to maximise knowledge dissemination. The material delivered during the workshops on research methodology was summarized in the written recommendations available on the VULSK website.

TREL facilitated the regular participation of VULSK researchers in project-related knowledge transfer meetings and networking. Ten researchers joined speciality-related working groups. During the 3 years, three clinical studies and trial agreements were signed as planned (Table 2). For the SIOP-RTSG2016 UMBRELLA study, the whole initiation process was completed, including twinning arrangements for the international review of pathology and radiology, and the country is ready for recruitment. Additionally, three studies were initiated or are in the opening process due to the increased visibility of the Coordinator following TREL implementation. To increase clinical trial management skills, two clinical trial coordinators, a statistician and a paediatric oncologist received specific training at partner premises.

Within the WP6, the SurPass variables list as well as the corresponding vocabularies (e.g. cancer types and drug names) were translated into Lithuanian as well as the text of the organ-specific recommendations for follow-up.

TREL had a dedicated WP7 aiming to increase the specific knowledge, abilities, and skills of VULSK project managers and administrators. Five Coordinator employees directly involved in project preparation, management, and administration benefited from a dedicated workshop, visits to two partner premises and participation at the dedicated knowledge transfer meeting (Table 2). Moreover, VULSK staff were exposed to continuous training while implementing the TREL project through frequent interaction with partners, the European Commission, and all relevant stakeholders.

As mentioned above, TREL engaged five ESRs in different years of their PhD studies and two scientifically active medical students. The interaction with ESRs from partner institutions resulted in the expansion of the ongoing research on fertility preservation and three joint publications [9–11]. In addition, TREL facilitated the initiation of a new PhD project on CNS tumour biology at Vilnius University and the publication on genetic predisposition written by a medical student [12].

The twinning efforts were appreciated by patients and families who benefited from the partner's expertise. Over the 3 years, 23 virtual multidisciplinary tumour boards were held to discuss 30 patients, mostly with brain tumours. TREL exploited the Clinical Patient

**Table 2**  
Summary of twinning efforts and results.

Educational events			
Related WP	Topic		
WP3	Genome analysis for translational and clinical research		Virtual
WP4	Innovative therapies		Virtual
WP5	Clinical trials in paediatric oncology		Virtual
WP6	Survivorship care in paediatric oncology		Physical
WP7	Research management and administration		Virtual
	Research Methodology I		
	Research Methodology II		
	Early phase clinical trials in paediatrics		
	Response assessment in solid tumours		
Participation in knowledge-transfer meetings			
Annual meeting date and location			VULSK staff joined specialty WG
SIOP-BTG, ISPNO	11–15 June, Hamburg, 2022 4–6 September Berlin, 2023		Paediatric oncologist Radiotherapist Radiologist
SIOP-RTSG	27–28 June, Sevilla, 2022 22–23 June, Wroclaw, 2023		Paediatric oncologist Pathologist
SIOPEN AGM	6–8 October, Barcelona, 2021 12–14 October, Athens, 2022 3–6 October, Ljubljana, 2023		Two paediatric oncologists Biologist Paediatric surgeon
PanCare	12–14 October, Budapest, 2022 20–22 September, Ghent, 2023		Paediatric oncologist
SIOPE	8–12 May, Valencia, 2023		n.a.
NOPHO	5–8 May, Lund, 2023		n.a.
ASTP	24–26 May, Tallinn, 2023		n.a.
Initiation of clinical research			
Acronym	Study type	Focus	Initiation stage
UMBRELLA	Clinical Study	RT	Open for recruitment
AT-RT	Phase III	Atypical teratoid-Rhabdoid tumours	Agreement signed
MAPPYACTS2	Prospective precision medicine trial	R/R solid tumours	Agreement signed
LudoN*	Phase II	R/R NBL	Open for recruitment
HR-NBL-2*	Phase III	High-risk NBL, from-line treatment	Agreement signed
PRIMAGE*	Observational study	Radiomics biomarkers in CNS and NBL	Initiated and closed in 2021–2023

Abbreviations: ASTP – Annual Conference Joint Action for Global Impact; NOPHO – Nordic Society of Paediatric Haematology and Oncology; n.a. – not applicable; NBL – neuroblastoma, PanCare – Pan-European Network for Care of Survivors after Childhood and Adolescent Cancer; R/R – relapsed/refractory; RT – renal tumours; SIOPE-BTG – International Society of Paediatric Oncology Europe Brain Tumour Group; SIOPEN – International Society of Paediatric Oncology Europe Neuroblastoma; SIOP-RTSG – International Society of Paediatric Oncology Renal Tumour Study Group.

\* International multicentre research activities initiated due to increased visibility of the Coordinator as a result of the project implementation.

Management System (CPMS) – 11 panels were opened for virtual discussions. Additionally, 21 patients with identified genetic variants were discussed through regular meetings with bioinformaticians and geneticists. Finally, four survivors received personal follow-up recommendations outlined in the SurPass.

##### 4.2. Dissemination and communication

During the TREL project period, four publications and twelve conference proceedings were disseminated at various scientific meetings. Seven oral presentations, including one at the SIOPE annual meeting, communicated project results to the scientific community. TREL was presented twice at the ERN PaedCan General Assembly. Continuous

dissemination was ensured through the SIOPE and VULSK websites, where regular project Newsletters were uploaded. Finally, the TREL project was mentioned in the European Cancer Plan for Children and Adolescents 2021–2026 as one of the achievements in reducing inequalities across Europe [13].

#### 4.3. Exploitation of the results and sustainability plan

TREL achievements will be exploited beyond the project duration. Specifically, the knowledge gained in tumour biology will contribute to the correct tumour diagnosis and risk stratification that will be applied to future patients who will be diagnosed with CNS, NBL or RT and enrolled in international research projects. The network established through the TREL project will facilitate access to expertise, when necessary, in the upcoming years. Implemented innovations in sample collection, preparation and biobanking as well as drug administration were documented in the internal standard operation procedures and will thus become available for all VULSK staff. In addition, they will be exploited in the upcoming clinical trials. The studies and clinical trials initiated during the 3 years will be continued beyond the project, ensuring equal access for Lithuanian children. Mirroring partners' best practices, a long-term follow-up clinic was established at VULSK. It will ensure continuity of proper patient triage for gonadal damage risk as well as provide recommendations for childhood cancer survivors based on the SurPass.

## 5. Discussion

TREL was the first Horizon 2020 project in medicine coordinated by VULSK. Despite this, supported by all members of the consortium, we did not face major issues in management and coordination. The biggest challenge in implementation was related to the COVID-19 outbreak-related lockdown in 2021 that perturbed the secondment plan and forced all partners to reorient part of the twinning from face-to-face to virtual. Despite encountering obstacles in physical interaction, we managed to speed it up in the following years and complete the work plan. The second major obstacle to physical interaction was the outbreak of the war in Ukraine in early 2022. The worrisome geopolitical situation in Eastern Europe rendered travelling and face-to-face meetings in Lithuania unsafe. Therefore, mobility in general was somehow affected throughout the whole project period.

The TREL concept was developed in collaboration with ERN PaedCan members which VULSK joined in 2017. ERN PaedCan pursues reducing inequalities across Europe by enabling access to up-to-date diagnostics and treatments by facilitating the exchange of knowledge and expertise [14,15] and offers a platform for collaboration for all European centres within the network.

Despite the challenges, the TREL consortium achieved all objectives and was evaluated as a success story [16]. The achievements will have a sustainable impact at VULSK, in Lithuania and in the Baltic countries. TREL increased the research excellence of VULSK through the rise in research output and initiation of new international collaborative scientific initiatives. Coordination of the EU-funded project enhanced the Coordinator's reputation, attractiveness and networking channels and improved its visibility for industry and academia-initiated innovative actions. The twinning activities improved innovation management abilities including data that resulted in the submission of a related follow-up proposal for the EU finding.

The Horizon 2020 Twinning programme provided a powerful platform for expanding scientific collaboration in a less research-intensive country. The activities initiated within the TREL project in 2021–2023 will have a sustainable impact on the roadmap of paediatric oncology in Lithuania. Ultimately, our twinning efforts responded to the actions defined in Europe's Beating Cancer Plan – “Reducing cancer inequalities across the EU” and “Putting childhood cancer under the spotlight” [17].

## Funding

The TREL project has received funding from the European Union's Horizon 2020 Spreading Excellence and Widening Participation programme under Grant Agreement No 952438. There was no additional funding for the manuscript writing or its submission.

## CRediT authorship contribution statement

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## Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Acknowledgements

We are grateful to all researchers and professionals from the Coordinator and Partner institutions who participated in the twinning programme and contributed to the TREL project achievements.

We would like to thank Prof. Brigitte Bison, Department of Neuro-radiology, University Hospital, Augsburg, Germany, for providing her expertise in neuroradiology during the multidisciplinary tumours board using the CPMS platform.

## References

- [1] L. Botta, G. Gatta, R. Capocaccia, C. Stiller, A. Cañete, L. Dal Maso, et al., Long-term survival and cure fraction estimates for childhood cancer in Europe (EUROCORE)

- 6): results from a population-based study, *Lancet Oncol.* 23 (12) (2022) 1525–1536.
- [2] C. Rossig, H. Juergens, M. Schrappe, A. Moericke, G. Henze, A. Von Stackelberg, et al., Effective childhood cancer treatment: the impact of large scale clinical trials in Germany and Austria: childhood cancer treatment in Germany and Austria, *Pedia Blood Cancer* 60 (10) (2013) 1574–1581.
- [3] M. O’Leary, M. Krailo, J.R. Anderson, G.H. Reaman, Children’s Oncology Group, Progress in childhood cancer: 50 years of research collaboration, a report from the Children’s Oncology Group, *Semin Oncol.* 35 (5) (2008) 484–493.
- [4] European Commission. Directorate General for Research and Innovation. Innovation Union competitiveness report 2013: Commission staff working document. [Internet]. LU: Publications Office; 2014 [cited 2023 Oct 9]. Available from: (<https://data.europa.eu/doi/10.2777/44320>).
- [5] G. Gatta, L. Botta, S. Rossi, T. Aareleid, M. Bielska-Lasota, J. Clavel, et al., Childhood cancer survival in Europe 1999–2007: results of EURO CARE-5—a population-based study, *Lancet Oncol.* 15 (1) (2014) 35–47.
- [6] G. Gatta, R. Peris-Bonet, O. Visser, C. Stiller, R. Marcos-Gragera, M.J. Sánchez, et al., Geographical variability in survival of European children with central nervous system tumours, *Eur. J. Cancer* 82 (2017) 137–148.
- [7] (<https://wayback.archive-it.org/12090/20220124151629/https://ec.europa.eu/programmes/horizon2020/en/h2020-section/twinning>) M. Accessed 14 October 2023.
- [8] R. Haupt, S. Essiaf, C. Dellacasa, C.M. Ronckers, S. Caruso, E. Sugden, et al., The ‘Survivorship Passport’ for childhood cancer survivors, *Eur. J. Cancer* 102 (2018) 69–81.
- [9] M.E.M. van der Perk, E. Stukaitė-Ruibienė, Ž. Bumbulienė, G.E. Vaitkevicienė, A.M. E. Bos, M.M. van den Heuvel-Eibrink, et al., Development of a questionnaire to evaluate female fertility care in pediatric oncology, a TREL initiative, *BMC Cancer* 22 (1) (2022) 450.
- [10] M. Grubliauskaite, M.E.M. Van Der Perk, A.M.E. Bos, A.J.M. Meijer, Z. Gudleviciene, M.M. Van Den Heuvel-Eibrink, et al., Minimal infiltrative disease identification in cryopreserved ovarian tissue of girls with cancer for future use: a systematic review, *Cancers* 15 (17) (2023) 4199.
- [11] E. Stukaite-Ruibiene, M.E.M. Van Der Perk, G.E. Vaitkeviciene, A.M.E. Bos, Z. Bumbuliene, M.M. Van Den Heuvel-Eibrink, et al., Evaluation of oncofertility care in childhood cancer patients: the EU-Horizon 2020 twinning project TREL initiative, *Front Pediatr* 11 (2023) 1212711.
- [12] M. Mikalonyte, E. Preiksaitiene, R. Nemanienė, G. Vaitkeviciene, I. Adomaitienė, K. Wadt, et al., Familial Renal Tumor Associated with a Novel Loss-of-Function Germline Variant in DICER1, *J. Clin. Cases Rep.* S9 (2023) 1–6.
- [13] (<https://siope.eu/media/documents/siop-europes-strategic-plan-update-2021-2026.pdf>). Accessed 16 October 2023.
- [14] (<https://paedcan.ern-net.eu/>). Accessed 17 October 2023.
- [15] V. Héon-Klin, European Reference networks for rare diseases: what is the conceptual framework? *Orphanet J. Rare Dis.* 12 (1) (2017 Dec) 137.
- [16] (<https://ec.europa.eu/research-and-innovation/en/projects/success-stories/all/cross-border-skills-exchange-helps-children-lithuania-get-cancer-treatment-they-deserve>). Cross-border skills exchange helps children in Lithuania get the cancer treatment they deserve. Accessed 12 November 2023.
- [17] ([https://health.ec.europa.eu/system/files/2022-02/eu\\_cancer\\_plan\\_en\\_0.pdf](https://health.ec.europa.eu/system/files/2022-02/eu_cancer_plan_en_0.pdf)). Europe’s Beating Cancer Plan. Accessed 12 November 2023.