ANNUAL REPORT 2025

The European Paediatric Soft tissue sarcoma Study Group

INDEX

THE EpSSG ASSOCIATION

The European Paediatric Soft Tissue Sarcoma Study Group (EpSSG) is an international organization of professionals dedicated to the care and treatment of children and young people with soft tissue sarcomas (STS). This includes the most common STS, rhabdomyosarcoma (RMS), as well as a diverse group of other tumors collectively referred to as Non-Rhabdomyosarcoma or Adult-type Soft Tissue Sarcomas (NRSTS).

The official legal body representing EpSSG's activities is the EpSSG Association. Its mission is to promote and manage clinical trials, support both clinical and basic research, foster the highest standards of care, organize educational events for members and healthcare professionals, and advocate for children and young people affected by STS.

EpSSG is legally and administratively based in Padua, Italy since 2009.

In 2024, it became recognized as an ETS (Third Sector Entity) Association—granting it greater visibility within Italy and enabling access to funding opportunities such as the "5 per mille" donation scheme and public sponsorships.

EpSSG actively collaborates with similar organizations across Europe, North America, and beyond. In particular, it has worked closely with the Cooperative Weichteilsarkom Studiengruppe (CWS) in Europe, and as of December, the two groups have merged into a single unified association.

Notably, since 2016, EpSSG has welcomed the involvement of parents of sarcoma patients, who have made valuable contributions in supporting and shaping the group's initiatives.

This report provides a summary of EpSSG's key activities in 2025.

For more information, please visit the EpSSG website: www.epssgassociation.it.

One united European pedatric Soft Tissue Sarcoma Study Group:

Countries of Cooperative Weichteilsarkom Studiengruppe (CWS) are part of EpSSG since two years

Monika Sparber-Sauer and Martin Ebinger

Times are passing quickly…since almost two years, the EpSSG board officially invited CWS to become part of EpSSG and at 6th December 2024, EpSSG members officially elected Monika and Martin as full members of the EpSSG board. From that moment on, a united EpSSG exists in Europe — dedicated to optimising the treatment and prognosis of all our patients with soft tissue sarcomas. What happened in these two years? Looking back, this integration has developed in a very positive and constructive way. New colleagues from Austria, Sweden, Finland, Switzerland, Poland and Germany have applied for EpSSG membership. Many of them were already well connected to the group and are now actively contributing to the surgery, radiotherapy, phase I, RMS and NRSTS working groups. The integration has developed gradually and has strengthened EpSSG's European network and has added expertise, data and motivation to our common work.

Many suggestions have been realized yet. E.g. the soft tissue sarcoma registry SoTiSaR 2.0-NIS is a non-interventional study, funded by the german childrens cancer foundation and open for all European countries.

So far, the german-speaking countries are involved; all European countries are welcome to join as a common European registry. Of note, data transfer of SoTiSaR 2.0-NIS to any other registry is possible and warranted and common analyses according to EpSSG publication rules are the aim. As another example we are very happy to announce that we were able to contribute with data of the former CWS studies and the SoTiSaR registry to the rare tumor registry PARTNER. Publications of rare tumors need all international available data and we are very happy to be able to enlarge this dataset and to join common publications.
We are also grateful for the opportunity to contribute ideas to the next generation of RMS and NRSTS studies, which are currently under discussion and in planning. This is exactly where a united European group can make a real difference: by combining clinical experience, trial expertise, registry data and translational research across countries.

Finally, we are proud and very much looking forward to hosting the EpSSG meeting in Germany in winter 2027. See you soon in Stuttgart!

EpSSG BOARD 2025

Hans Merks	EpSSG Chair, Utrecht, The Neterlands
Timothy Rogers	Treasurer, Bristol, UK
Andrea Ferrari	Chair elect, Milano, Italy
Gabriela Guillen Burrieza	Barcelona, Spain
Nadege Corradini	Lyon, France
Lisa Hjalgrim	Copenhagen, Denmark
Julia Chisholm	Sutton, UK
Gianni Bisogno	Padova, Italy
Daniel Orbach	Paris, France
Monika Sparber-Sauer	Stuttgart, Germany
Martin Ebinger	Tuebingen, Germany

Board meetings were held remotely in 2025 each first Tuesday of the month: January 7th, February 4th, March 4th, April 1st, May 6th, June 3rd, July 1st, September 2nd, October 7th and November 4th. The board met in Budapest in May and Athens in December the day before the official meetings. In Athens, we took the opportunity to thank Gabriela Guillen, Nadege Corradini and Timothy Rogers at the end of their term, expressing our gratitude, especially to Tim for his excellent collaboration as a treasurer. We also warmly welcomed the new Board members: Janet Shipley, Federica De Corti, Max van Noesel and Sheila Terwisscha van Scheltinga. Andrea Ferrari became the EpSSG Chair.

New Board member elected Dec 2025

Dr. Andrea Ferrari is pediatric oncologist at the Istituto Nazionale Tumori of Milan and professor of Medical Oncology at the University of Milan. He tackled research projects dedicated to soft tissue sarcomas, pediatric rare tumors and adolescents/young adults projects. He worked as chair of various international cooperative groups, developing a large experience in leading and coordinating multidisciplinary working team. In particular, he currently chair the European Network of Expertise on AYA developed within the JANE project.
Regarding soft tissue sarcoma in particular, he was founding member of the EpSSG and chairman of the NRSTS Scientific Committee. He was appointed chair of EpSSG in December 2025. He is author or co-author of more than 600 papers published on international scientific journals.

Federica De Corti is a pediatric surgeon at the University Hospital of Padua, Italy, with a longstanding focus on solid tumor surgery, particularly pediatric soft tissue sarcomas. She trained with Professor Giovanni Cecchetto and gained further expertise during an international fellowship with Professor Hélène Martelli in Paris. She is an active member of several national and international surgical oncology groups, including SICP, IPSO, SIOP-RTSG, SIOPEL, GICOP, and the EpSSG Surgical Committee, where she has contributed since its inception. She has authored more than 50 scientific publications. She will be the Association's Treasurer.

Janet Shipley is Group Leader in Sarcoma Molecular Pathology and Head of the Sarcoma Research Centre at the Institute of Cancer Research, London. Her research focuses on the biology and translational research of rhabdomyosarcoma and other pediatric soft tissue sarcomas. A member of the EpSSG Biological Committee since 2008 and its Chair from 2013 to 2020, she has played a key role in integrating biological research into EpSSG clinical trials, strengthening collaboration between laboratory and clinical researchers, and supporting the development of new investigators within the group.

Max M. van Noesel, MD, PhD, is Professor of Pediatric Solid Tumors and Clinical Director of the Solid Tumor Department at the Princess Máxima Center for Pediatric Oncology, Utrecht, the Netherlands. An EpSSG member since 1999, he has played a leading role in developing international clinical studies, including the landmark EpSSG-NRSTS-2005 trial, now considered the standard of care for non-rhabdomyosarcoma soft tissue sarcomas. He also co-founded the EpSSG Phase I/II Committee and currently serves as a principal investigator of the MyKids study.

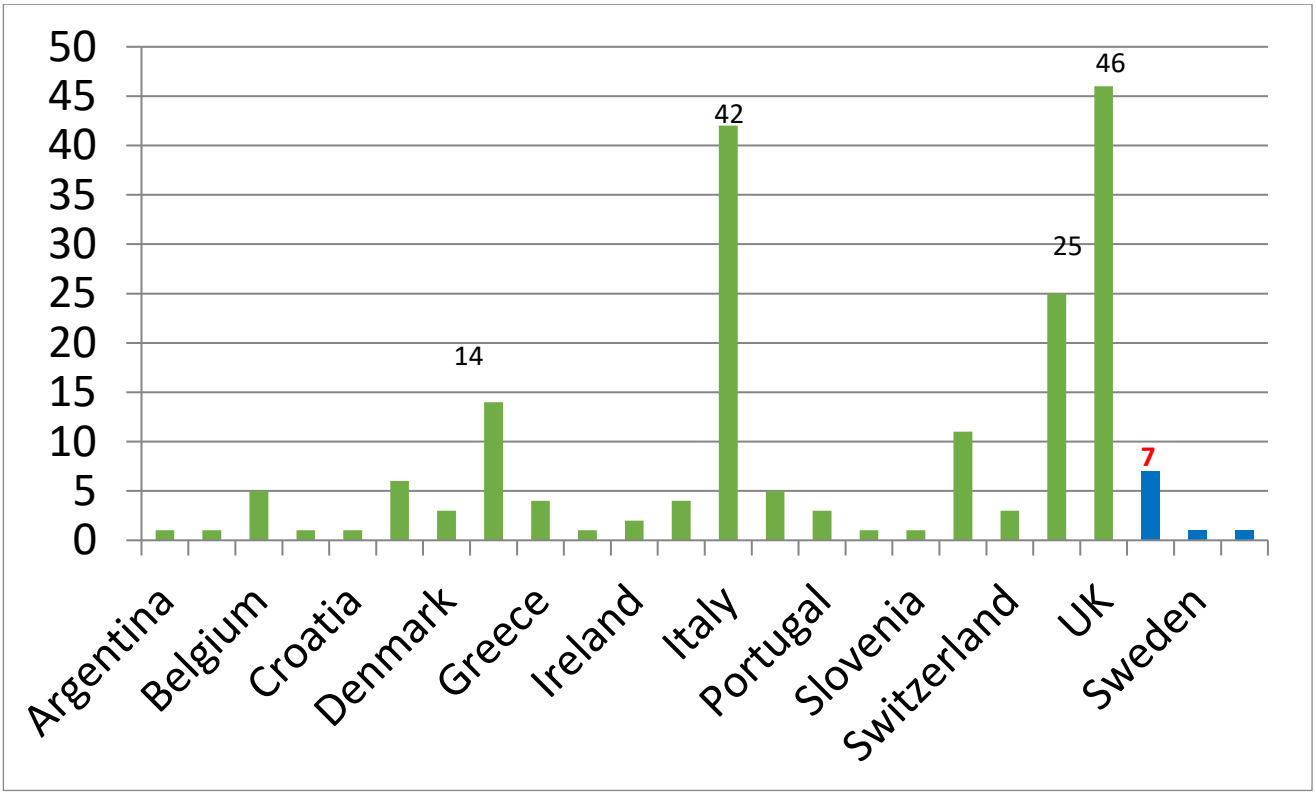
Sheila Terwisscha van Scheltinga is a pediatric surgical oncologist at the Princess Máxima Center for Pediatric Oncology, Utrecht, the Netherlands. From 2019 to 2025, she served as Chair of the EpSSG Surgical Committee, working to strengthen the role of surgery within multidisciplinary sarcoma care. Her clinical and research interests focus on pediatric soft tissue sarcomas and rare tumors. She is committed to advancing collaborative research, enhancing the role of surgeons within EpSSG, and improving the quality and consistency of care through studies such as the current FaR-RMS protocol.

EpSSG BOARD since December 2025

Andrea Ferrari	EpSSG Chair Milano, Italy
Hans Merks	EpSSG Past Chair, Utrecht, The Neterlands
Federica De Corti	Treasurer, Padova, Italy
Lisa Hjalgrim	Copenhagen, Denmark
Julia Chisholm	Sutton, UK
Gianni Bisogno	Padova, Italy
Daniel Orbach	Paris, France
Monika Sparber-Sauer	Stuttgart, Germany
Martin Ebinger	Tuebingen, Germany
Janet Shipley	London, UK
Sheila Terwisscha van Scheltinga	Utrecht, UK
Max van Noesel	Utrecht, UK

EpSSG Members

EpSSG members represent mostly: UK, Italy, The Netherlands, France, Spain, Portugal, Belgium, Ireland, Denmark, Norway, Czech Republic, Croatia, Slovenia, Israel, Argentina, Brazil, Greece and Australia. In 2025, new members from the CWS group and others joined EpSSG: Germany, Sweden, Finland and Turkey. There were 195 individual members of the EpSSG from 24 different countries compared to 174 members in 2024.



EpSSG Discipline panel COMMITTEES

Chair

Biology	Dr. Michael Meister
Pathology	Dr. Edmund Cheesman
Imaging	Dr. Lise Borgwardt & Nina Jehanno
Surgery	Dr. Florent Guerin
Radiotherapy	Dr. Raquel Davila Fajardo
Phase I/II trials	Dr. Susanne Gatz & Dr. Willemijn Breunis

BRIEF SUMMARY of DP Committees in 2025

EpSSG Biology Committee

In 2025, the EpSSG Biology Committee continued to develop as an active and highly engaged scientific platform for translational research in paediatric soft tissue sarcomas. Regular online committee meetings were held on 27 January, 31 March and 26 May, followed by a hybrid meeting on 3 December in Athens. These meetings combined high-quality scientific presentations with discussion of organisational matters and ongoing collaborative initiatives, with consistently strong participation from committee members.

A major highlight of the year was the second live Biology Committee meeting in Nutfield. The central theme of the meeting was the tumour microenvironment of paediatric soft tissue sarcomas. As an integral part of this Nutfield meeting, a dedicated workshop was organised to develop a preclinical framework for evaluating new therapeutic avenues and supporting their rational translation towards clinical trials. The meeting benefited from excellent support from charities and valuable contributions from patient advocates, further strengthening the translational and patient-centred focus of the committee.

Several deliverables from the previous Nutfield meeting in 2024 were advanced during 2025. These included the submission of the COST Action proposal SPARK and continued work on the concept of an online database linking preclinical data to clinical data. Individual committee members also contributed substantially to the field through multiple high-quality publications and successful grant applications.

The committee network expanded further in 2025, with particularly strong engagement from former CWS colleagues, many of whom joined the regular meetings as well as the Nutfield 2025 meeting. This broader participation has strengthened the committee's role as an inclusive European platform for biological and translational research in paediatric soft tissue sarcoma.

Key priorities for 2026 include the outcome of the COST Action application, publication of the preclinical framework developed as a deliverable from the Nutfield 2025 workshop, organisation of the Nutfield 2026 meeting with a focus on translating immuno-oncology approaches into the clinic, and the upcoming committee chair election.

EpSSG Pathology Committee

The EpSSG Pathology Committee continues to meet monthly via virtual Teams meetings. These serve a dual purpose: review of discrepant pathology cases arising from the FaR-RMS trial, aimed at ensuring consistent diagnostic standards across participating centres, and a general meeting to discuss non-FaR-RMS matters relevant to the committee. The committee plans to hold a face-to-face meeting at the EpSSG Winter Meeting in Padua.

The primary activity of the committee remains the central pathology review of cases entered into the FaR-RMS trial. To date, 635 individual cases with a diagnostic surgery have been reviewed (representing 716 surgeries in total), and 166 individual cases with a second surgery have been reviewed (195 surgeries in total).

The committee is also contributing to the FDG/BMT study, which involves central review of bone marrow trephine biopsies. One hundred cases with a completed international review have been included in dedicated trephine review batches, of which 72 had both right and left trephines reviewed, representing 172 surgical procedures in total.

The Pathology Committee continues to work with the Biology Committee with regards to prognostic markers for patient stratification in future trials.

Members of the Pathology Committee have contributed to a number of EpSSG publications and conference abstracts over this period, reflecting the breadth of ongoing collaborative work across the group. This work is carried out alongside clinical and academic commitments, without dedicated funding for pathology committee activities.

EpSSG Phase I/II committee

In 2025, the EpSSG Phase I/II Committee has welcomed several new members including former CWS colleagues and continued to have monthly online meetings to discuss new therapeutic targets and drugs that are promising for both RMS and NRSTS.

One of the main activities of the committee in 2025 was bringing MEK inhibitors into frontline RMS therapy. The MIRDAMAINT study proposal is in development introducing the MEKi Mirdametinib to the maintenance treatment with Vinorelbine/cyclophosphamide. The phase I/II committee applied for investigator initiated research application at Sprinworks and is awaiting an answer. Endorsement from the ITCC solid Tumor committee was requested and funding applications are outstanding.

There were several joint meetings with the Biology committee including active participation of the Phase I/II Committee during the Nutfield meeting, organized by the Biology Committee. On December 3th a workshop on cellular therapies was held in Greece involving experts in the field of CAR-T therapies in solid tumours.

In 2025 members of the Phase I/II Committee have published several EpSSG related papers including the guideline for relapsed patients in the Britisch Journal Of Cancer. Several of the Phase I/II Committee members have actively participated during the Third Paediatric Besproke Therapeutic Development Workshop on rhabdomyosarcoma that was held online and resulted in a published manuscript.

The results of Phase Ib IrIVA substudy where presented on ASCO by Prof. Hans Merks.

For 2026 the intention is to increase the focus on NRSTS and support the OCTOPUS platform, to open the MIRDAMAINT study arm within the Far-RMS trial and to further work on the development of future RMS treatment arms, more biology driven, and possible including ADC and /or cellular therapies.

EpSSG Radiotherapy committee

The EpSSG Radiotherapy discipline panel welcomed several new members during 2025, including colleagues from the former CWS (Cooperative Weichteilsarkom Studiengruppe). Regular meetings took place, including monthly reviewers' workshops, QUARTET research council meetings, and INSTRuCT Radiation Oncology working group meetings. Great efforts were made to keep the ongoing Frontline and Relapsed Rhabdomyosarcoma (FaR-RMS) clinical trial individual case reviews up to date, despite the challenges experienced by the EORTC/QUARTET platform.
The Radiotherapy Committee lead different research projects, and developed reference atlases and radiotherapy planning guidelines for various anatomical sites (e.g. pelvis, head and neck, whole-abdomen), reporting as well on advances in radiotherapy, imaging practice, and re-planning. These papers can currently be found in the literature. Reflecting a broad scope of collaborative initiatives, members of the Radiotherapy Committee co-authored multiple EpSSG publications and conference abstracts throughout this period.

EpSSG Imaging Committee

The EpSSG radiology committee would like to thank Lise Borgwardt and Nina Jehanno for their dedication to the EpSSG as co-chairs of our committee. The chair position currently is vacant, but we expect to fill it in the coming months.
The primary activity of the committee is focused on the FaR-RMS trial, currently PET-CT scans are double reviewed by a team of dedicated team (L. Adriaansen, K. Andersen, L. Borgwardt, A. Braat, N. Jehanno, B. de Keizer, L. Michaud, S. Wan).

At the 2025 International Pediatric Radiology meeting in Boston, Isabelle de Vries presented preliminary data on bone marrow trephines versus PET-CT. The full data analysis is underway and we expect to submit a manuscript in 2026. Members of the committee published two publications using EpSSG data, first a review on the impact of acquisition parameters on apparent diffusion coefficient estimates, showing the importance of homogenous data acquisition (Chatziantoniou C, et al. Acquisition matters - how do scan parameters affect apparent diffusion coefficient estimates in pediatric rhabdomyosarcoma. Pediatr Radiol. 2025 Jul;55(8):1598-1610). A second publication evaluated the prognostic value of early tumour volume response (de Vries ISA, et al.
Early radiologic tumour volume response in non-metastatic rhabdomyosarcoma is not predictive for survival. Pediatr 5 Radiol. 2025 Sep;55(10):2160-2170). This study highlights the need for new early response imaging biomarkers.

EpSSG Surgery Committee

EpSSG MEETINGS 2025

The EpSSG Spring meeting has been organised within the 6th Annual Meeting of the European Society for Paediatric Oncology in Budapest May 12-16, 2025. A full dedicated EpSSG Scientific day was held on Thursday May 15. The programme included the Assembly for the members and 3 open sessions. There were more than 150 attendants for each of the scientific EpSSG sessions.

During the FaR-RMS session, Sara Wakeling, EpSSG parent provided advice on the key messaging, tone, style, information provision and language requirements in the creation of a video designed to explain the radiotherapy arm of the trial with a view to enhancing recruitment. The audience watched the final video which had a great success underlining once more the importance of the voice of parents and patients becoming increasingly recognised in the formation of patient-centric research questions.

The EpSSG Winter Meeting was held in Athens, Greece, from December 3–5. The local organization was led by Dr. Apostolos Pourtsidis. The discipline-specific panel groups met on Wednesday, prior to the main Winter Meeting, at Elpida Hospital and at the meeting room of the Floga Parents' Association of Children with Cancer. The main meeting took place at the Royal Olympic Hotel and was attended by 133 international delegates. The meeting venue and social event were located at a historic site close to the Acropolis, overlooking the Temple of Zeus and the National Garden.

Highly productive sessions were held on refractory and relapsed rhabdomyosarcoma, genetic predisposition in soft tissue sarcomas, and a NRSTS session focused on the management of ultra-rare sarcomas in childhood, drawing on adult experience. The Biology Young Investigator Session addressed rare entities. Updates on ongoing clinical trials were presented, including FaR-RMS (with both a dedicated TMG meeting and an open meeting), MyKIDS, and OCTOPUS. We are grateful to our COG colleague, Aaron Weiss, who provided an update on North American soft tissue sarcoma trials conducted by the Children's Oncology Group.
Prof. Georgios Nasioulas delivered an outstanding keynote lecture on the applications of liquid biopsy for the diagnosis and monitoring of pediatric sarcomas.

During the social event, held under dramatic thunderstorms over the Acropolis, we bid farewell to Meriel Jenney upon her retirement, as well as to former Board colleagues Michela Casanova, Henry Mandeville, Véronique Minard-Colin, Timothy Rogers, Gabriela Guillen, and Nadège Corradini, all of whom will undoubtedly continue to collaborate within the association. We warmly welcome the new Board members and wish our Chair, Andrea Ferrari, every success.


Picture 1. EpSSG Social gathering in Budapest during the SIOPe meeting 2025
Picture 2. EpSSG Winter meeting in Athens 2025

THE NEW FRONTLINE AND RELAPSE STUDY IN RHABDOMYOSARCOMA

(BY DR. JULIA CHISHOLM on behalf of the CRCTU team)

Trial Update December 2025

An overarching study for children and adults with Frontline and Relapsed RhabdoMyoSarcoma

The FaR-RMS trial is an overarching trial for all patients with newly diagnosed and relapsed paediatric-type rhabdomyosarcoma and is open to patients of all ages. The trial has an innovative multi-arm, multi-stage design that allows the testing of new combinations of therapy in upfront and relapsed settings in phase Ib, phase II and phase III.

The trial has now been open for over five years and is recruiting well, with 1,087 patients registered so far. The CT3 relapse research question opened in March 2022, funded by Bayer, and closed to recruitment in August 2025. The phase 1b question completed recruitment in November 2023, and the CT1a and CT1b induction chemotherapy randomisations subsequently opened in April 2024.

We are delighted that there is widespread international interest, and we continue to work with new countries to open the trial. The current recruiting countries are:

Country		Number of open sites
	Australia	11
	Austria	5
	Belgium	7
	Czech Republic	2
	Denmark	2
	France	38
	Germany	8
	Greece	7
	Ireland	1
	Israel	6
	Italy	1
	Netherlands	2
	New Zealand	2
	Norway	5
	Portugal	0
	Slovenia	1
	Spain	13
	Sweden	8
	Switzerland	9
	United Kingdom	28

Countries still in set-up since last update:
Croatia, Finland, Slovakia, Singapore.

Open and Set-up Countries

Green = Countries Open
Orange = Countries in Set-up

Phase 1b Dose Escalation Study – Recruitment Complete

The purpose of the Phase 1b question was to establish the dose of irinotecan in combination with ifosfamide, vincristine and actinomycin D. This question was open at ITCC and early phase approved centres. It completed recruitment in December 2023, following recruitment of 22 patients.

An abstract "Determining the recommended phase 2 dose (RP2D) of dose intense Irinotecan combined with IVA chemotherapy (IRIVA) in newly diagnosed very high risk rhabdomyosarcoma: a phase Ib study within the EpSSG Frontline and Relapsed Rhabdomyosarcoma Study (FaR-RMS)" was presented at the American Society of Clinical Oncology 2025 Annual Meeting, and a full manuscript of the Phase 1b data is in preparation.

Induction Chemotherapy (CT1a/b) - Following the completion of Phase 1b, the CT1 randomisations opened on 10-Apr-2024 via a non-substantial protocol amendment. These questions compare the determined dose of irinotecan (50mg/m^2) in combination with ifosfamide, vincristine and actinomycin D, against the current standard of care for patients with High Risk and Very High Risk disease.

So far, 144 patients have been recruited to the CT1 induction questions.

Radiotherapy (RT1a/b/c, RT2) -The planned radiotherapy questions in FaR-RMS were: pre vs post-operative radiotherapy (RT1a), dose-escalation in patients at higher risk of local failure (RT1b for patients with resectable disease, RT1c for non-resectable disease) and comparing limited vs extensive radiotherapy for patients with extensive metastatic disease (RT2). An important aspect of the study focusses on the Quality of Life (QoL) of patients when receiving radiotherapy.

So far, 261 patients have been recruited to the Radiotherapy questions.

The RT1a and RT2 randomisations closed to recruitment on 21-Jul-2025. This decision follows consultation with the FaR-RMS Data Monitoring Committee (DMC), prompted by persistently low recruitment rates into RT1a and RT2. RT1a did not meet the feasibility endpoint specified in the protocol. No safety concerns have been identified in relation to these treatment arms. The QoL endpoints are being updated so that QoL questionnaires may still be collected.

Recruitment to the RT1b and RT1c radiotherapy randomisations was temporarily suspended on 11-Feb-2026. This is due to QUARTET being unable to provide Radiotherapy Quality Assurance (RTQA) at this time. We are currently working to resolve this issue and investigate other options to allow RT1b and RT1c to be re-opened as soon as possible.

Maintenance Chemotherapy (CT2a/b) - The purpose of the CT2 questions is to extend the number of maintenance chemotherapy cycles for patients with HR and VHR disease compared to the current standard of care i.e. 6 vs 12 cycles and 12 vs 24 cycles respectively. Please note that some younger patients may not be able to swallow cyclophosphamide capsules. Where sites need access to oral liquid formulations, this should be discussed with the National Coordinating Centres.

So far, 236 patients have been recruited to the Maintenance questions.

Relapsed RMS (CT3) -The CT3 relapse randomisation was closed to recruitment on 01-Aug-2025. Following a scheduled interim analysis, the DMC recommended discontinuation of the CT3 randomisation. This recommendation was based on the trial crossing the futility boundary, indicating a very low likelihood of demonstrating the protocol-defined 15% superiority of VIrR over VIrT. The Trial Steering Committee (TSC) endorsed the DMC's recommendation. No safety concerns were identified in the interim data. At the point of closure, 116 sites across 14 countries had been activated to CT3 in total, and 106 patients were recruited.

Pathology - Risk group assignment and fusion status are integral parts of the trial, and molecular diagnostics for all cases of RMS should be carried out at the local centre. All samples will be centrally reviewed in each country by the National Pathology Coordinator. An international review of scanned slides is ongoing with over 612 cases having undergone international review for diagnostic surgery so far.

FDG-PET Sub-Study - If FDG PET-CT or FDG PET-MRI scanning is available at diagnosis & facilities allow, there is the option to take part in this sub study where an additional scan after 3 courses of induction chemotherapy is undertaken to determine the prognostic value of FDG-PET imaging response for EFS and local failure free survival. The collection of scans started in 2024 and is ongoing.

DW-MRI Sub-Study: The aim of this sub-study is to investigate the prognostic value of DW-MRI imaging response by comparing DW-MRI at diagnosis and at reassessment (after 3 cycles of chemotherapy for patients with localised disease). Centres are encouraged to include diffusion-weighted series in their standard soft tissue sarcoma MRI protocols. Prinses Maxima and the EpSSG imaging group are leading this sub-study. The collection of scans started in 2024 and is ongoing.

Quality of Life (QoL)

A new set of sarcoma specific QoL questionnaires will be added to the next version of the Protocol. The Sarcoma Assessment Measure (SAM) is a QoL measure that was developed for teenage and adult patients. SAM-Paeds has more recently been developed using the same methodology. SAM-Paeds (self-report for patients age ≥8 to <18 years) and SAM-Paeds Parent Report (age ≥2 to <18 years) will be collected, in addition to the SAM for adults (≥18 years).

The aim is to extend the QoL study within FaR-RMS to correlate with a focus on the impact of local therapy (short- and longer-term outcomes). This will allow a more detailed understanding of the impact of local therapy for RMS for patients in the medium and long term. QoL questionnaires, including EORTC QLQ-C30, Peds-QL, SAM and SAM-Paeds will be collected from IRS III and IRS IV patients.

Surgery

This substudy will analyse the impact of surgery (as part of local control) on short term and late toxicity and Quality of Life. A surgical review of the data entry is ongoing.

Biology

This substudy will establish a virtual biobank for samples, including liquid biopsies, to evaluate prognostic factors at diagnosis, response to treatment and disease recurrence. The preferred storage of samples in is the VIVO biobank, Newcastle, UK, but some countries will use national biobanks. An upcoming protocol amendment will introduce specific biology questions into FaR-RMS.

Patient Videos

In collaboration with Alice's Arc, patient and parent representatives and Enfuse, videos are being developed to help prospective patients understand the study. Initially a video on the radiotherapy randomisations has been developed, with a FaR-RMS overview video additionally planned. The format of the videos will allow translation into other languages.

The patient video can be viewed on the FaR-RMS Website: Far-RMS - University of Birmingham. It is planned to develop further patient videos in future.

EU-CTR Transition

The European Union Clinical Trials Regulation (EU-CTR) was implemented on 31st January 2022, and the FaR-RMS trial was required to transition to the Clinical Trials Information System (CTIS) by 31st January 2025 for EU regulatory approvals to remain valid. The FaR-RMS trial successfully completed transition of 17 countries' ethical and competent authority approvals to the CTIS system on 15th November 2024. In order to fully comply with the updated regulations, a 1st amendment is in preparation for submission in 2026.

Planned Protocol Amendment 2026

The FaR-RMS Protocol is being amended with the following updates:

- Changes to inclusion criteria including:
  - MYOD1 L122R mutations will allow risk group to be upstaged to Very High Risk
  - Radiotherapy: Patients with tumours >5cm and IRS III / MYOD1 L122R mutations to be considered Higher Local Failure Risk
- Removal of specific requirement to have RTQA performed by QUARTET
- Quality of Life questionnaires SAM and SAM-Paeds will be implemented for consenting patients having radiotherapy and surgery
- Biology updates including:
  - Addition of biology endpoints
  - Collection of viably frozen tumour tissue where possible
  - Additional liquid biopsy sampling timepoints at maintenance and relapse
- Compliance with EU-CTR

Sponsor

The Study Sponsor is the University of Birmingham Cancer Research UK Clinical Trials Unit, EudraCT Number: 2018-000515-24, EU CT number 2024-510579-40-00.

FaR-RMS
Frontline and Relapse
RhabdoMyoSarcoma study

NRSTS PROJECTS

by Prof. Andrea Ferrari & Dr. Daniel Orbach, May 2026

The EpSSG NRSTS Committee continues its biological European study dedicated to NRSTS, called **MYKIDS** - Molecular Identification and Characterization of non-Rhabdomyosarcoma. Soft Tissue Sarcoma in Kids, Adolescents and Young Adults: an EpSSG NRSTS study. The MYKIDS study is designed to better understand the molecular diagnosis of pediatric NRSTS in view of optimal treatment. In particular, to a) understand the role of molecular profiling in pediatric NRSTS, b) enable a comprehensive decision on the treatment for individual patients, c) compare molecular profiles to histological grading for prognostification, and d) use molecular diagnostics to study non-invasive diagnosis (liquid biopsies). The international sponsor is The Princess Maxima center. Contact: mykids@prinsesmaximacentrum.nl. First patient has been enrolled in The Netherland 31 May 2024. Three National coordinating centers (NCCs) are already open for enrolment (Czech Republic, Greece and the Netherlands). In June 2026, Italy will open for enrollment. Others will open soon.

While the REACH project (REgorafenib in young adults, Adolescents and Children with High-risk NRSTS) was abandoned, the NRSTS group is ready to finalize the OCTOPUS project, which will open very shortly.

The master protocol OCTOPUS - 'Optimising Combination Therapy fOr Paediatric, adolescent and yoUng adult patients with non-rhabdomyosarcoma soft tissue Sarcomas' - is built as an adaptive platform trial comprising different sub-trials, a real-world data registry (Sarc Registry), translational studies, and overarching study questions assessing local therapy issues and patient reported outcomes (PROs). PIs of the study are Reienke Schoot and Michela Casanova. The International sponsor is the Princess Máxima Center. The platform trial provides an operational framework including a legal consortium structure, a network of national coordination centres (NCCs) and sites within the EpSSG and ITCC (Innovative Therapies for Children and adolescents with Cancer) community, dedicated study teams, a database with eCRFs that are fit for purpose, sample collection pipeline, a network of academic central labs, an online platform with PROs, and a registry with real world data collection of patients not included in sub-trials (SARC registry).
OCTOPUS will be strongly linked to the diagnostic MYKIDS study.
Main goal of the platform is the development of sub-trials identifying promising strategies ('go' vs 'no-go' approach) and data will be collected for registration and reimbursement purposes. Every sub-trial will have a unique design, tailored to the needs of the patients, the characteristics of the disease, and the stage of development of the experimental compound(s). Depending on the medical need in a specific patient population and the expected activity of a compound (or a combination), the innovative treatment(s) will be offered to patients with relapsed/refractory disease or placed in frontline treatment when appropriate.
The first three histotypes proposed within OCTOPUS to which the steering committee has decided to give priority for trial development are **Desmoid Fibromatosis, Extracranial Malignat Rhabdoid Tumors, and** Desmoplastic Small Round Cell Tumours**.**

- The BRAVE study, testing the efficacy and the tolerance of a new Gamma secretase inhibitor in pediatric patients with desmoid fibromatosis
- The WORTH study (WindOw therapy with iRinotecan and Trabectedin in patients witH DSRCT), exploring the role of the combination of trabectedin and irinotecan in widow therapy (single-arm, open-label, phase I-II dose-escalation and expansion study)
- the SMARTY study (Treatment for children, adolescents and young adults with any **SMARCB1** and **SMARCA4** al**T**ered tumour entit**Y**), to test the role of the Gemcitabine addition for young patients with rhabdoid and SMARCB1 deficient tumors.

While working on the opening of Octopus, the members of the NRSTS committee have also been working on other projects.

The development of a dedicated European Standard Clinical Practice (ESCP) for paediatric and adolescent NRSTS.

The collaboration within the INSTRuCT project (INternational Soft Tissue SaRcoma ConsorTium). Various publications have been produced within the framework of Instruct, while others are ongoing.

Orbach D et Al. Regional lymph node invasion in pediatric non-rhabdomyosarcoma soft tissue sarcoma: an international cohort study from the International Soft Tissue Sarcoma Consortium. EClinicalMedicine. 2025 Aug 7;87:103409.

Sparber-Sauer M, et al. Risk factors and outcome for children, adolescents and young adults with grossly resected (IRS group I/II) non-rhabdomyosarcoma soft tissue sarcomas In press, ESMO rare cancer Journal, 2026.

Weiss A et al. Risk factors and outcome of children and young adults with initially unresected non-rhabdomyosarcoma soft tissue sarcoma: An analysis from the INternational Soft Tissue SaRcoma ConsorTium (INSTRuCT). In press, Cancer

RMS future PROJECTS

by Prof. Gianni Bisogno and RMS-WG

EpSSG RMS Working Group – 2025 Update

While the FaR-RMS protocol continues successfully (see dedicated section above), the RMS Working Group has actively started discussing the next EpSSG RMS study. During 2025, the group initiated several strategic discussions and collaborative projects aimed at defining future study priorities. In particular, a dedicated project focusing on recently described rare molecular entities in rhabdomyosarcoma was launched, including the analyses of available information on tumor characterized by GLL-NCOA2 or EWSR1/FUS::TFCP2 fusion, and TP53 mutation. Several analyses are currently ongoing and manuscripts are already in preparation or submission. These analysis are important both for the current FaR-RMS protocol and for understanding how these rare entities should be considered in future studies.

The Working Group also organized multiple dedicated meetings throughout the year to discuss key aspects of the future protocol, including chemotherapy strategies, biology-driven questions, local treatment approaches, and integration of early phase studies. In person discussions on the next RMS protocol were held during the SIOP meeting in Amsterdam (October 2025), the EpSSG meeting in Athens (December 2025), and another is planned in Glasgow during the SIOPE meeting in May 2026. These meetings involved close collaboration between clinicians, surgeons, radiation oncologists, biologists, imaging specialists, and national coordinators.

Particular attention was given to engaging young investigators. A new initiative encouraging junior colleagues to lead focused analyses on specific primary tumor sites was launched successfully.

International working groups have already been established to analyze RMS arising in the nasal ala and nasolabial fold, airway sites, thoracic/trunk locations, pelvic sites, and abdominal/abdominal wall primaries.

Preliminary datasets have already been distributed and several projects are actively progressing.

Scientific productivity within the RMS Working Group remained strong in 2025. Several studies were published, others accepted for publication, and multiple manuscripts are currently under preparation or circulating among co-authors. New project proposals have also been submitted and approved, confirming the high level of activity and the continuing collaborative spirit within the group. Additional proposals are expected in the coming months.

New Study Proposals are welcome

The International Data Center (IDC) together with different PI's are working on many analyses in parallel to translate all the knowledge we gathered through our clinical trials into publications in peer reviewed journal to share this with professionals across the globe.

PAPERS IN 2025

1. **Maintenance therapy for pediatric patients with high-risk Rhabdomyosarcoma: A report of dose reductions and dose omissions on outcome.** By Daniela Di Carlo et al.
   EJC Paediatric Oncology. Volume 5, June 2025, 100221

A clinical trial called RMS2005 studied whether adding a lower-dose, long-term chemotherapy treatment (maintenance chemotherapy) could help patients with high-risk Rhabdomyosarcoma (RMS). The trial found that this extra treatment improved survival, leading to its adoption as a standard part of care. However, researchers wanted to understand if variations in how patients received the treatment—such as differences in drug doses—affected survival outcomes.

The study analyzed data from 171 patients who received maintenance chemotherapy. It found that about 60% of patients received at least 80% of the planned drug doses. However, when researchers examined whether receiving lower or higher doses influenced survival, they found no significant impact. This suggests that small adjustments to drug doses in this treatment phase do not change overall survival chances.

2. **Implications of Implementing Children's Oncology Group Risk Stratification to Patients With Rhabdomyosarcoma Treated on European Paediatric Soft Tissue Sarcoma Study Group Clinical Trial.** By Gianni Bisogno et al.
   Pediatric Blood Cancer. 2025 Feb;72(2):e31436. doi: 10.1002/pbc.31436.

Rhabdomyosarcoma (RMS) is a type of cancer that primarily affects children, and determining the right treatment depends on assessing how aggressive the disease is. Two major groups, the European paediatric Soft Tissue Sarcoma Study Group (EpSSG) and the Children's Oncology Group (COG), use different methods to assess this risk, leading to different treatment plans for similar..patients.

This study reanalyzed data from nearly 2,000 RMS patients to see how they would be classified under each system and how this affects treatment recommendations, particularly chemotherapy. The researchers found that a large portion of patients were placed in different risk groups depending on

the system used. For example, about one-third of patients classified as standard-risk by EpSSG were split into multiple risk groups by COG. Furthermore, two-thirds of all patients considered standard, high, or very high risk by EpSSG were classified as intermediate risk by COG. As a result, patients would receive different levels of chemotherapy intensity under the two systems, with some receiving more intense treatment. This mismatch highlights the challenges in treating RMS and the importance of agreeing on a single global system to ensure patients with similar conditions receive comparable care and to make it easier to compare the results of clinical trials worldwide

3. **Childhood, Adolescent and Young Adult Poor-Prognosis Rhabdomyosarcoma.**
   By Ajla Wasti et al.
   Cancers (Basel) 2025 Sep 23;17(19):3100. doi: 10.3390/cancers17193100.

Over the past few decades, treatments such as chemotherapy, surgery, and radiotherapy have improved survival of RMS patients, especially for children whose cancer is found early and has not spread.

However, children with more aggressive forms of RMS or cancer that has spread still have poorer outcomes.

Doctors use several factors to estimate how likely the cancer is to respond to treatment. These include specific genetic changes in the tumour, where the cancer started, whether it has spread to nearby lymph nodes or other parts of the body, the size of the tumour, and the patient's age.

These factors help doctors decide how intensive treatment should be.

As researchers learn more about the genetics of RMS, they are improving the way patients are grouped according to risk. This review focuses on children and young people with the highest-risk forms of RMS. These include patients with certain high-risk genetic changes, teenagers and young adults, patients whose cancer has already spread when diagnosed, and those whose cancer has come back or stopped responding to treatment. The review explains the characteristics of these high-risk patients, describes current standard treatments based on international clinical trials, and discusses promising new methods for diagnosing and treating RMS that may improve outcomes in the future.

4. **Maintenance Chemotherapy in Patients With High-Risk Rhabdomyosarcoma: Long-Term Survival Analysis of the European Paediatric Soft Tissue Sarcoma Study Group RMS 2005 Trial.** By Gianni Bisogno
   J Clin Oncol. 2025 Mar 7:JCO2402850. doi: 10.1200/JCO-24-02850. Online ahead of print.PMID: 40053891

The RMS2005 trial, conducted by the European Paediatric Soft Tissue Sarcoma Study Group (EpSSG), tested whether adding a long-term, low-dose chemotherapy treatment (maintenance chemotherapy) could help children with high-risk rhabdomyosarcoma (RMS), a rare and aggressive cancer. Patients were randomly assigned to either stop treatment after initial therapy (standard group) or continue with six additional months of maintenance chemotherapy (experimental group). Earlier results showed that maintenance chemotherapy improved overall survival, but its effect on preventing cancer recurrence was unclear. Now, after more than 10 years of follow-up, researchers have confirmed that patients who received maintenance chemotherapy had better long-term survival. After 10 years, 83% of patients in the experimental group were still alive compared to 71% in the standard group. The findings confirm that maintenance chemotherapy with vinorelbine and low-dose cyclophosphamide provides a lasting survival benefit for high-risk RMS patients.

5. **Early radiologic tumour volume response in non-metastatic rhabdomyosarcoma is not predictive for survival. By Isabel de Vries**
   Pediatr Radiol. 2025 Sep;55(10):2160-2170. doi: 10.1007/s00247-025-06359-3. Epub 2025 Aug 14.PMID: 40810863

Children with rhabdomyosarcoma usually have imaging scans during chemotherapy to see whether their tumour is shrinking. It is often

assumed that tumours that shrink quickly are linked to better long-term outcomes, but this has not been clearly proven.
This study investigated whether changes in tumour size seen on scans after the first three cycles of chemotherapy could predict how well children with rhabdomyosarcoma would do in the future. The study included 613 children with non-metastatic rhabdomyosarcoma who had measurable tumours at diagnosis and imaging available before and during treatment.
Most children showed some degree of tumour shrinkage after three cycles of chemotherapy. However, for children whose cancer did not worsen during this early treatment period, the amount of tumour shrinkage did not predict how long they lived or how likely their cancer was to return.
These findings suggest that early changes in tumour size on imaging alone should not be used to decide whether treatment should be changed for children with non-metastatic rhabdomyosarcoma. Other clinical and biological factors remain important for predicting outcomes and guiding treatment decisions.

6. **Surgical Lymph Node Staging in Extremity Rhabdomyosarcoma: The EpSSG RMS 2005 Trial Experience.** By Sheila Terwisscha van Scheltinga
   Ann Surg Oncol. 2025 Jul 24. doi: 10.1245/s10434-025-17908-3. Online ahead of print. PMID: 40705262

Rhabdomyosarcoma (RMS) is a rare childhood cancer that can spread to nearby lymph nodes. This study examined how different lymph node biopsy techniques helped determine whether the cancer had spread in children with RMS of the arms or legs. Biopsies revealed hidden cancer in some patients whose scans appeared normal and showed no cancer in others whose lymph nodes looked suspicious on imaging. This allowed doctors to more accurately determine the stage of the disease and guide treatment decisions.
These findings highlight the importance of lymph node biopsy for accurate staging, helping ensure that children receive the most appropriate treatment.

7. **Local therapy for rhabdomyosarcoma of the bladder and/or prostate without nodal or metastatic spread during the European paediatric Soft tissue sarcoma Study Group (EpSSG) RMS2005 study.** By Naima Smeulders
   JC Paediatric Oncology 6 (2025) 100313 https://doi.org/10.1016/j.ejcped.2025.100313

This study looked at children and young people with a rare cancer called bladder-prostate rhabdomyosarcoma that had not spread to lymph nodes or other parts of the body. Researchers compared different ways of treating the tumour locally after chemotherapy. One approach aimed to preserve the bladder and nearby organs using organ-sparing surgery combined with internal radiotherapy (brachytherapy). Other patients received more extensive surgery that removed organs, external radiotherapy, or combinations of these treatments.
A total of 176 patients were followed for about 6.5 years.
Overall outcomes were good: about 80% of patients remained free from disease progression after 5 years, and about 91% were alive at 5 years. Although patients receiving different treatments had different tumour features, the risk of tumour progression was similar across treatment types. However, survival differed: the best survival was seen in patients treated with surgery alone or with brachytherapy (with or without organ-sparing surgery). Patients treated with external radiotherapy had poorer outcomes if the tumour later returned, as rescue treatment was less successful.
Delaying local treatment until later in chemotherapy did not worsen outcomes.
In summary, when feasible, brachytherapy combined with organ-sparing surgery offers excellent chances of cure while preserving bladder function and avoiding external radiotherapy.

FINANCIAL STATEMENT 2025

(by T. Rogers, H. Merks)

An accountancy and treasurer's Report of the final year's account was presented and approved during the EpSSG Spring meeting Assembly held in May 7, 2026 during the 6th SIOPE Annual Meeting in Glasgow.
The 2025 Financial Report has closed with a result of €13,405.17 and is composed of the balance sheet, management report, and mission statement, as required by Article 13 of Legislative Decree 117/2017. The report was prepared according to the accrual accounting principle and reconciled with the ordinary cash flows of the financial year. The Treasurer reminded those present of the consistency of the data compared to the previous year and highlights the ongoing and coherent trend related to to general interest activities.
For 2026 we expect income from EpSSG membership fees and meeting fees from our Winter meeting; we aim to negotiate with Pharma whenever we substantially invest our expertise and network into Paediatric Investigation.

Plans or other work. As our association is vital to maintain both expertise and the clinical network this justifies financial support from parties that need substantial input from EpSSG members.

Funding Sources for 2025: EpSSG will receive financial support from Alice's Arc Foundation to support our EpSSG scientific project manager and statistician for the year 2025 and 2026.

We are grateful to Sara Wakeling and the trustees of Alice's Arc for the support so crucial for our scientific network organization.

Grateful to those who help implementing work resources in research!

Alice's ARC
CHILDREN'S CANCER CHARITY

WORK PLAN IN 2026

Continue to open the FaR-RMS study in countries and centers not open yet. Promote patient and parent participation in the randomized trial questions; this includes support from our parent organization to optimize explanation of these questions to patients and parents.
Implement and optimize participation in substudies to FaR-RMS including Imaging and Biology Biomarker studies and studies on Quality of Life

To extend Mykids to more and more EpSSG member countries, and to formally open the Octopus study, thereby starting patient enrollment in the three initial substudies, while working on the study and development of further substudies for other histotypes.

Efficient preparation of reports by the International Data Center (IDC) in close collaboration with PI of each project leading to timely delivery of manuscripts to be published in peer reviewed journals.
Consolidate funding for EpSSG IDC and secretariat activities essential for our network organization of professionals to optimally function and create scientific reports. Optimize collaboration with parents through involvement at meetings and in projects.
Continue the good work of the EpSSG Discipline Panels to deliver and update practice guidelines, initiate important analyses and new research.
Have our twice yearly EpSSG live meetings.

CALENDAR 2026-2027

DATE	MEETING	LOCATION	NOTES
2026			
May 4-8 (Mon-Fri)	EpSSG Spring Meeting & Association Assembly	SIOP Europe 2025 6th Annual Meeting Glasgow	Confirmed
December 2-4 (Thurs-Fri)	EpSSG Winter Meeting & Association Assembly	Padova	Confirmed
2027			
May 20-21 (Thurs-Fri)	EpSSG Spring meeting & Association Assembly	Utrecht	Confirmed
December 1-3 (Wed-Fri)	EpSSG Winter Meeting & Association Assembly	Stuttgart	Confirmed

WE HAVE A DONATION BUTTON ON OUR WEBSITE! HELP US SPREAD THE WORD!

Your donation will help to support the team of clinicians, scientists, statisticians and data managers in developing and running new clinical trials in paediatric STS in order to help future generations of children with STS.

The EpSSG coordinates European international clinical trials aimed at improving the treatment of soft tissue sarcoma (STS). Through research our goal is to improve the quality of care offered to children, teenagers and young adults. with STS and to improve the outcomes of treatment.

We invite italian EpSSG-ETS members to donate their 5 pro mille

Anche se non sei tenuto a presentare la dichiarazione dei redditi o presenti un documento diverso dal 730, puoi comunque donare il tuo 5×1000:

1. compila la scheda fornita insieme al CUD dal tuo datore di lavoro o dall'ente erogatore della pensione, firmando nel riquadro "Sostegno del volontariato…" e indicando il codice fiscale: 92240870284
2. inserisci la scheda in una busta chiusa;
3. scrivi sulla busta "Scelta per la destinazione del cinque per mille IRPEF" e indica il tuo cognome, nome e codice fiscale;
4. consegnala a un ufficio postale, a uno sportello bancario o a un intermediario abilitato alla trasmissione telematica (CAF, commercialisti…).

Firma…*Andrea Ferrari*……..

CF… 92240870284

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Sostegno degli enti del terzo settore iscritti nel runts di cui all'art. 46 C. 1 del D. lgs. 3 luglio 2017, n.117, comprese le cooperative sociali ed escluse le imprese sociali costituite in forma di società, nonché sostegno delle onlus iscritte all'anagrafe.

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and with the great
collaboration of all
EpSSG Members