EPSSG ASSOCIATION

THE EUROPEAN PAEDIATRIC SOFT TISSUE SARCOMA STUDY GROUP

ANNUAL REPORT 2020

THE EPSSG ASSOCIATION

The European Paediatric Soft tissue sarcoma Study Group (EpSSG) is an international organisation for professionals devoted to the care and treatment of children and young people with cancers known as soft tissue sarcoma (STS). This includes the most common STS, rhabdomyosarcoma (RMS), and a wide range of other cancers known collectively, as Non Rhabdomyosarcoma Soft Tissue Sarcomas (NRSTS).

The legal entity for EpSSG activities is the EpSSG Association. This exists to promote and manage clinical trials, encourage and facilitate clinical and basic science research, foster optimal standards of care, organise educational meetings for its members and other professionals, and advocate for patients with STS.

It collaborates with other similar groups in Europe, North America and elsewhere.

EpSSG has its administrative and legal home in Padua, Italy. An elected board manages it, and its membership is open, by application, to professionals who have an interest in the research or treatment of these diseases when they occur in children, teenagers and young adults.

This report summarises the main EpSSG activities for 2020. Importantly, we have had the opportunity since 2016, to welcome parents of sarcoma patients to collaborate with us and support the development of our activities.

Further information is available on the EpSSG website: www.epssgassociation.it

EpSSG Board

Dr. Hans Merks	•Chairman - Utrecht, The Netherlands
Dr. Andrea Ferrari	•Treasurer, Milano, Italy
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Dr. Michela Casanova	•Milan, Italy
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Prof. Gianni Bisogno	•Board representative- Padua, Italy
Dr. Julia Daragjati	•Secretary, Padua, Italy

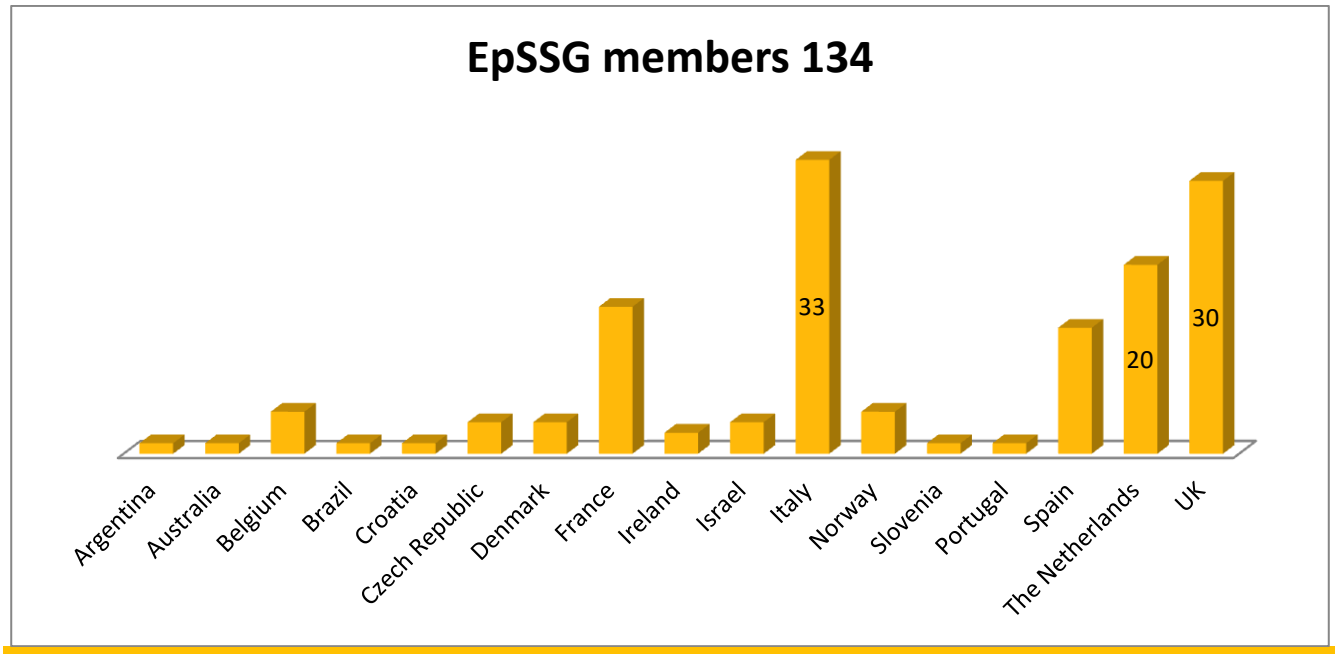
Board meetings were all held virtually on the following dates in 2020 due to the pandemic emergency: February 3rd, May 8th, June 22nd, September 17th, October 26th and November 23rd. Unfortunately the EpSSG 2020 Spring meeting had to be canceled, but the EpSSG 2020 Winter meeting was held virtually with support by the Princess Maxima Center.
Gianni Bisogno ended his term as past Chair but remains as Association representative for legal matters. Heidi Glosli, a valued and dedicated board member completed her term in December 2020. Lisa Hjalgrim, a pediatric oncologist and Head of the Department of Pediatric Hematology and Oncology at Rigshopitalet in Copenhagen, was appointed as a new board member. Her clinical interests include lymphoma and sarcoma with a special focus on the adolescent and young adult patient group. She will join the board for a first three-year term, bringing her expertise and perspectives to the work of our mission to deliver best treatment, cure and improvements in quality of life for patients with Sarcoma.

EpSSG MEMBERSHIP

EpSSG studies are undertaken in the following countries: Italy, France, UK, The Netherlands, Spain, Portugal, Belgium,

Ireland, Denmark, Norway, Czech Republic, Croatia, Slovenia, Israel, Argentina, Brazil, Greece, Australia and New Zealand. Each country has an EpSSG National Coordinator.

In 2020, there were 134 individual members of the EpSSG from 17 different countries. This year we welcomed new members from Portugal, Switzerland and Greece.



EpSSG Subcommittees

	Chair
Biology	Prof Beat Schaefer, Zürich, Switzerland
Pathology	Dr Rita Alaggio, Rome, Italy
Radiology	Prof Rick R. van Rijn, Amsterdam, The Netherlands
Surgery	Dr Sheila Terwisscha van Scheltinga, Utrecht, The Netherlands
Radiotherapy	Dr Raquel Davila Fajardo, Utrecht, The Netherlands
Phase I/II trials	Dr Michela Casanova, Milan, Italy
Biostatistics/Data management	Dr Gian Luca De Salvo, Padua, Italy

EpSSG Meetings 2020

The Spring meeting in 2020 did not take place because of the COVID Pandemic, however the group continued work via virtual meetings and has maintained momentum with research projects and analyses.

EpSSG 2020
Winter Virtual Meeting
December 3 & 4

Princess máxima center
pediatric oncology

We had a very successful EpSSG Winter meeting which took place on 3rd and 4th of December, supported by the Princess Maxima Center. It was hosted by Dr. Hans Merks and included presentations from key EpSSG members and young investigators. The discipline panel groups for biology, radiotherapy, NRSTS TMC, surgery, pathology, phase I/II, and radiology, met separately in the week leading to the main meeting.

The 'virtual' format was a new way of disseminating knowledge and maintaining close working-relationships within our association and delivered an interesting meeting that welcomed 118 participants.

THE NEW FRONTLINE AND RELAPSE STUDY IN RHABDOMYOSARCOMA

(BY PROF. MERIEL JENNEY AND DR. JULIA CHISHOLM)

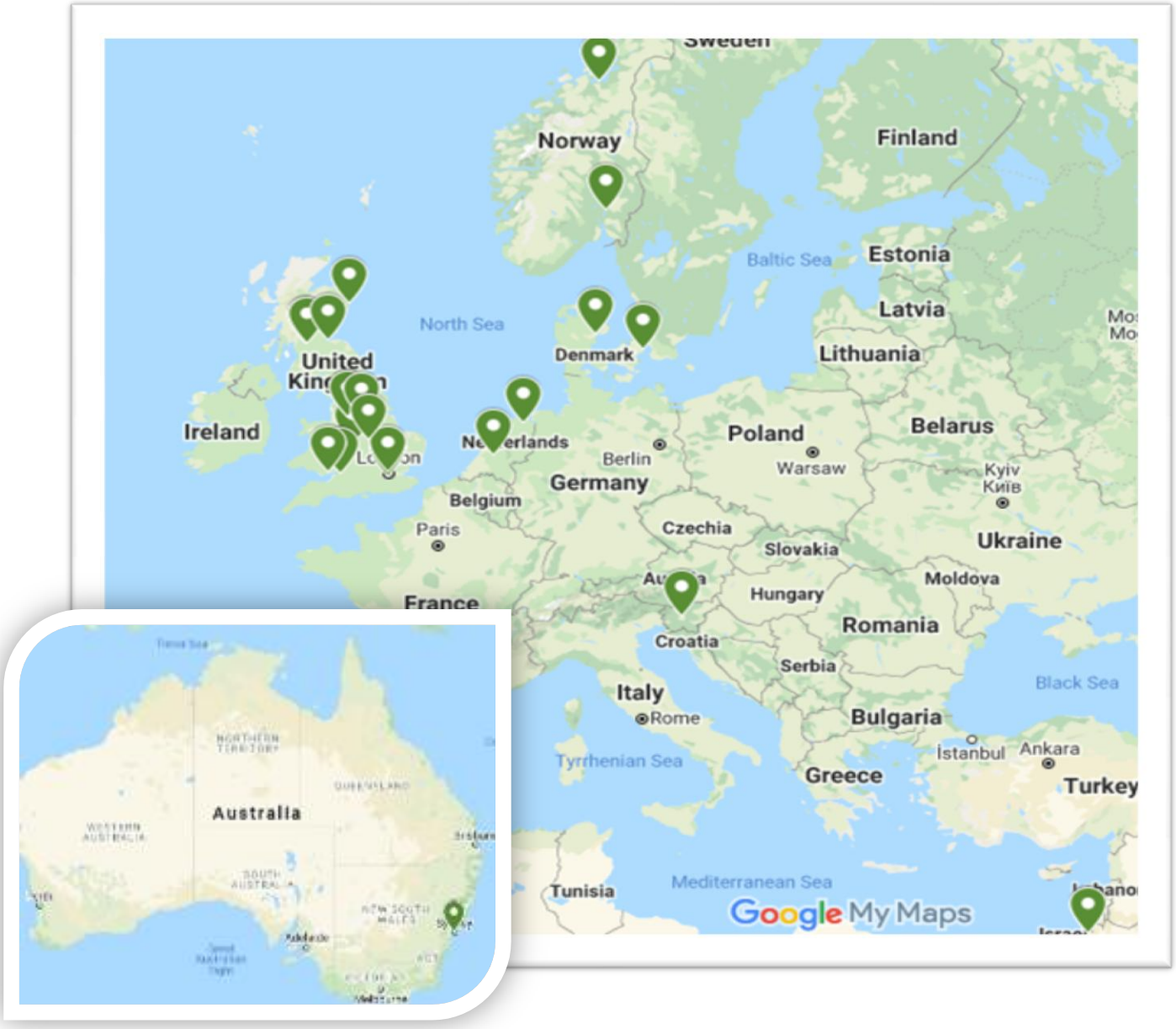
Trial Update March 2021

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 opened to recruitment on the 17th September 2020. There were some delays in the study opening and the finalisation of the trial database due to the COVID-19 pandemic, however the study is now actively recruiting. We are delighted that there is wide international interest and several countries are now open to recruitment. The current recruiting countries are: Australia (1 site open)

- Denmark (2 sites open)
- Greece (No sites open currently)
- Israel (1 site open)
- Netherlands (2 sites open)
- Norway (2 sites open)
- Slovenia (1 site open)
- UK (13 sites open)
- Australia



Several other participating National Coordinating Centres are forging ahead with country set-up and many have made regulatory submissions. Current participating countries that are still in set-up are:

- Belgium
- Croatia
- Czech Republic
- France
- Ireland
- Spain
- Italy
- Portugal
- Slovakia
- Switzerland
- Germany

We are strongly encouraging NCCs to open the study in as many adult sites as possible – this is a very important opportunity and the **first time randomised studies have been possible for adults with RMS.**
The number of actively recruiting sites is continuously increasing. So far, the FaR-RMS trial has **30 patients registered to study entry by 16th March 2021.**

The FaR-RMS trial has multiple research questions:

- **Phase 1b Dose Escalation Study** – To find the dose of irinotecan in combination with ifosfamide, vincristine and actinomycin-D. This is open at ITCC and early phase approved centres.
  - So far, **1 patient** has been recruited to this question.

- **Induction Chemotherapy (CT1a/b)** – The CT1 randomisations will be open at all participating centres, upon completion of the Phase 1b question. These questions will compare the determined dose of irinotecan in combination with ifosfamide, vincristine and actinomycin-D, against the current standard of care.
  - The CT1 questions will open upon completion of phase 1b.

- **Radiotherapy (RT1a/b/c, RT2)** – The Radiotherapy randomisations opened to recruitment in January 2021. These randomisations are delivered at all open sites, where QUARTET approval has been obtained. The radiotherapy questions involve pre vs post-operative radiotherapy (RT1a), dose-escalation in patients at higher risk of local failure (RT1b & 1c) and the role of radiotherapy to metastatic sites (RT2). An important aspect of the study focusses on the Quality of Life of patients when receiving radiotherapy in RT1a and RT2.
  - So far, **2 patients** have been recruited to the RT1c question.

- **Maintenance Chemotherapy (CT2a/b)** – All sites will open to the maintenance randomisations. The purpose of the CT2 questions is to look at doubling the number of maintenance chemotherapy cycles compared to the current standard of care. Please note that some younger patients may not be able to swallow cyclophosphamide capsules. Where possible oral liquid cyclophosphamide should be prepared at sites. The UK has amended its clinical trial authorisation to allow powder for solution for injection to be mixed with sodium chloride for oral administration. Where countries need access to oral liquid formulations, country- specific options are being sought.
    - So far, **7 patients** have entered CT2 research questions.

- **Relapse (CT3)** – The relapsed randomisation is due to open in Q2 of 2021. The first new combination to be tested in the relapse setting will be vincristine, irinotecan (VI) + regorafenib, a multityrosine kinase inhibitor, with VI + Temozolomide (VIT) as the control arm. The relapse study is an investigator-led collaboration between EpSSG and Bayer, the manufacturer of regorafenib.
    - The CT3 question is not yet open to recruitment.

Pathology

Risk group assignment and fusion status are integral part of the trial, molecular diagnostics on all cases of RMS should be carried out at the local centre. **All samples will be centrally reviewed by the national pathology coordinator.**

FDG-PET Sub-Study

If FDG PET-CT or FDG PET-MRI scanning is available at diagnosis & facilities allow, there will be the option for an additional scan after 3 courses of induction chemotherapy to determine retrospectively its prognostic value at centres that wish to participate. The prognostic value of response will be related to EFS and local failure free survival.

Parents and EpSSG 2020

BY DR. HEIDI GLOSLI AND ANGELIKA SANDAKLY

We welcomed five parents, to the EpSSG Virtual Winter meeting. To date 12 parents in total have attended EpSSG meetings and 7 EpSSG countries are now represented (France, Italy, Netherlands, Norway, Denmark, Belgium and UK). A main topic for the parent group is to define the best way for interaction between the parent group, the EpSSG and the board. After the winter meeting the parent group met with Julia Chisholm, Meriel Jenney, Nicola Fenwick and Heidi Glosli. It was discussed how to involve parents in the FaR-RMS study.

From a parents' point of view: 'On the administrative side we have overcome some funding issues by involving our local associations.' 'We do our best to progress on the gathering of relevant information for the website project.'

'We continue to be available for all review activity related to the FaR-RMS study. Priorities for 2020 were to enhance understanding and interest for the participation in clinical studies, and in in particular the FaR-RMS study .'

'We are looking forward to enlarging our activities to turn our experience into something beneficial for EpSSG and the public whom it serves. It's good to know that our contribution might be useful for your work, it's a very small give-back for the efforts you do for our children.'

REPORTS FROM TRIAL COMMITTEES

(BY PROF. GIANNI BISOGNO & IDC)

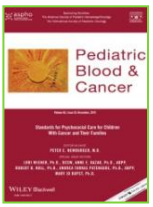
a) RMS 2005

This was the first International EpSSG trial for children and adolescents with localized rhabdomyosarcoma. Patients were included in 4 different risk groups according to 6 prognostic factors (result of initial surgery, histology subtype, tumour site and size, nodal involvement and patient age). Overall, 1733 patients were enrolled from 134 centres in 14 countries.

b) MTS 2008

EpSSG trial has been opened for children and adolescents with metastatic rhabdomyosarcoma.
Overall, 270 patients were enrolled across EpSSG European centers. Here below you can find the list of authors and studies which are ongoing on December 30, 2020.

The IDC together with different PI's is working on many analyses in parallel to translate all the knowledge we gathered through our clinical trial into publications in peer reviewed journal to share this with professionals across the globe.



PAPERS IN 2020

1. **A NEW STANDARD OF CARE FOR PATIENTS WITH HIGH-RISK RHABDOMYOSARCOMA? .** The Lancet Oncol, Correspondence letter, Vol 21 Jan 2020

Bisogno G, Ferrari F, Gallego Melcon S, De Salvo GL, Bergeron C, Jenney M

2. **PARATESTICULAR RHABDOMYOSARCOMA - IMPACT OF LOCO-REGIONAL APPROACH ON PATIENT OUTCOME. A REPORT FROM THE EUROPEAN PAEDIATRIC SOFT TISSUE SARCOMA STUDY GROUP** (EpSSG) Pediatr Blood Cancer. 2020 Jun 23;e28479. doi: 10.1002/pbc.28479.

Rogers T, De Corti F, Burrieza GG, Guérin F, van Scheltinga ST, Smeulders N, Craigie R, Jenney M, Kelsey A, Zanetti I, Coppadoro B,. De Salvo G.L,. Bisogno G, Martelli H.

The paper concluded that paratesticular rhabdomyosarcoma is rare compared to benign scrotal pathology and the surgeon not anticipating malignancy can result in inappropriate first surgery; however, with supplementary treatment, patients maintain excellent outcomes. Analysis of the data also showed that surgical staging of lymph nodes should be performed in older patients.

The data did not support the systematic use of hemi-scrotectomy for patients needing further surgery. Survival after relapse remains poor. The challenge for surgeons is to improve locoregional disease control by adequate surgical staging of lymph nodes, and to decrease the rate of inappropriate surgery.

3. **SURGICAL MANAGEMENT OF EXTREMITY RHABDOMYOSARCOMA: A CONSENSUS OPINION FROM THE CHILDREN'S ONCOLOGY GROUP, EUROPEAN PEDIATRIC SOFT TISSUE SARCOMA STUDY GROUP, AND THE COOPERATIVE WEICHTEILSARKOM STUDIENGRUPPE** Pediatr Blood Cancer 2020 Aug 9;e28608. doi: 10.1002/pbc.28608.

Morris CD, Tunn P, Rodeberg DA, van Scheltinga ST, Binitie O, Godzinski J, Dall'Igna P, Million L, Hawkins DS, Koscielniak E, Bisogno G, Rogers T.- 28.

The treatment of extremity rhabdomyosarcoma remains a challenge due to several adverse prognostic factors frequently associated with this tumor site. The International Soft-Tissue Sarcoma Database Consortium (INSTRuCT) is a collaboration of the Children's Oncology Group Soft-Tissue Sarcoma Committee (COG), the European Pediatric Soft-Tissue Sarcoma Study Group (EpSSG), and the Cooperative Weichteilsarkom Studiengruppe (CWS). The INSTRuCT surgical committee developed an internationally applicable consensus opinion document for the surgical treatment of extremity rhabdomyosarcoma. This document addresses surgical management, including biopsy, nodal staging, timing of therapy, resection and reexcision, reconstruction, and surgical approach at relapse.

4. **LOCAL STAGING AND TREATMENT IN EXTREMITY RHABDOMYOSARCOMA. A REPORT FROM THE EPSSG-RMS2005 STUDY** Cancer Med. 2020 Oct;9(20):7580-7589. doi: 10.1002/cam4.3365.

Terwisscha van Scheltinga S, Marc H. W. A. Wijnen MHWA, Martelli H, Rogers T, Mandeville H, Gaze MN, McHugh K, Corradini N, Orbach D, Jenney M, Kelsey A, Chisholm J, Gallego S, Glosli H, Ferrari A, Zanetti I, De Salvo GL, Minard-Colin V, Bisogno G, van Noesel M, Merks JHM.

Pediatric patients with localized rhabdomyosarcoma of the extremity included in the EpSSG-RMS2005 study between 2005 and 2014 were evaluated for staging, treatment, and survival. The outcome was compared to the preceding European SIOP-MMT studies. Even if the lymph node staging was not always complete according to the RMS2005 protocol, node sampling changed lymph node status in a significant number of patients. Despite the higher rate of patients treated with locoregional radiotherapy, survival in RMS2005 did not improve compared to the previous European SIOP-MMT95 study.

5. **ALVEOLAR RHABDOMYOSARCOMA WITH REGIONAL NODAL INVOLVEMENT: RESULTS OF A COMBINED ANALYSIS FROM TWO COOPERATIVE GROUPS.** Pediatr Blood Cancer. 2020 Nov 27; e28832. doi: 10.1002/pbc.28832.

Gallego S, Chin YY, Zanetti I, Li M, Merks JHM, Rodeberg DA, van Scheltinga ST, Mascarenhas L, Orbach D, Jenney M, Million L, Minard-Colin V, Wolden S, De Salvo GL, Parham D, Mandeville H, Venkatramani R, Bisogno G, Hawkins DS.

Treatment of children and adolescents with alveolar rhabdomyosarcoma (ARMS) and regional nodal involvement (N1) have been approached differently by North American and European cooperative groups. To define the best therapeutic strategy we analyzed two studies conducted between 2005 and 2016 by the European paediatric Soft tissue sarcoma Study Group (EpSSG) and Children's Oncology Group (COG). The outcome of patients with Alveolar RMS N1 was similar using different schemas of chemotherapy. However, patients with FOXO1 fusion-negative tumors enrolled in RMS2005 showed a significantly better outcome suggesting that a subgroup of them can benefit from the EpSSG strategies including maintenance chemotherapy.

NRSTS COMMITTEE (BY DR. ANDREA FERRARI)

The EpSSG NRSTS Committee is working to the development of the new protocol dedicated to NRSTS.
This should be the **MYKIDS - Molecular Identification and Characterization of non-Rhabdomyosarcoma Soft Tissue Sarcoma in Kids, Adolescents and Young Adults: an EpSSG NRSTS study**.
The MYKIDS study should be 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 prognostication, and d) use molecular diagnostics to study non-invasive diagnosis (liquid biopsies). Co-principal investigators of the study are Max van Noesel (Princess Máxima Center, Utrecht), Daniel Orbach (Institute Curie, Paris) and Andrea Ferrari (Istituto Nazionale Tumori, Milan).
In parallel, the NRSTS group is joining forces with the German CWS group to explore the feasibility of a clinical trial dedicated to desmoid-type fibromatosis (DESMOVER, PI – Nadege Corradini, Leon Berard, Lyon).

Meanwhile, in 2020 various analyses have been published on previous series.
In particular:

Brennan B, et al. Dermatofibrosarcoma Protuberans in children and adolescents: the European Paediatric Soft Tissue Sarcoma Study Group prospective trial (EpSSG NRSTS 2005). Pediatr Blood Cancer. 2020;67:e28351. doi: 10.1002/pbc.28351.
The series included 46 patients with localised disease enrolled in the EpSSG NRSTS 2005 study, most having tumor smaller than 5 cm (93%) classified as IRS group I due to initial complete resection (76%). These patients had an excellent outcome, with 5-year EFS of 92.6% and OS of 100%.

Casanova M, et al. Inflammatory myofibroblastic tumor: the experience of the European paediatric Soft Tissue Sarcoma Study Group (EpSSG). Eur J Cancer. 2020 Mar;127:123-129. doi: 10.1016/j.ejca.2019.12.021.
This series included 60 patients (59 with localized and 1 with multifocal/metastatic disease); the lung was the primary site in 14 cases; 40 cases were ALK-positive, and 20 were ALK-negative. This study demonstrated a good overall prognosis for IMT, even for initially unresectable disease and in ALK-negative cases. Overall, 5-year EFS and OS were 82.9% and 98.1%, respectively. The overall response to systemic therapy was 64%: 8/10 cases responded to vinblastine-methotrexate chemotherapy, and 5/5 to ALK-inhibitors. The study suggested that chemotherapy is still a valid option for advanced disease; while larger studies involving both pediatric and adult patients are needed to clarify the role of ALK inhibitors.

Ferrari A, et al. Outcomes of metastatic non-rhabdomyosarcoma soft tissue sarcomas (NRSTS) treated within the BERNIE study: a randomised, phase II study evaluating the addition of bevacizumab to chemotherapy. Eur J Cancer. 2020 May;130:72-80. doi: 10.1016/j.ejca.2020.01.029.
This study analysed the cohort of metastatic NRSTS treated in the BERNIE protocol, i.e. open-label, multicentre, randomised phase II study evaluating the role of bevacizumab (2008-2013). The study included 49 NRSTS patients, 26 treated in the standard arm and 23 in the bevacizumab arm.
Objective response rate was seen in 10/36 evaluable cases (27.7%), i.e. 4/18 standard arm cases and 6/18 bevacizumab arm cases.
Two-year EFS was 27.3% for all NRSTS patients, i.e. 34.9% for bevacizumab arm and 22.9% for standard arm (p-value 0.19). Three-year OS was 35.2%, with no differences in the two arms.

Patients not receiving any local treatment on primary disease had a worse outcome as compared to others. Treatment results were better for patients receiving surgical resection and worse for those who did not receive any specific treatment.
This study describes the first series of paediatric patients with metastatic NRSTS prospectively treated in a randomised phase II trial including a biologic agent. Though it showed that the addition of the anti-angiogenic agent to the standard chemotherapy did not show statistically significant improvement in survival in metastatic NRSTS, this series may be considered benchmark for this disease category, in particular regarding the development of future investigational studies.

Orbach D, et al . Spotlight on the treatment of infantile fibrosarcoma in the era of neurotrophic tropomyosin receptor kinase inhibitors: International consensus and remaining controversies. Eur J Cancer. 2020 Sep;137:183-192. doi: 10.1016/j.ejca.2020.06.028.
This paper discussed the role of TRK inhibitors as highly specific therapeutic option for patients with IFS carrying the NTRK gene translocation, with the aim to define international recommendations. Data on joint series from EpSSG, CWS and COG were reported. The authors discussed how conventional conservative strategies before the era of targeted therapy, even in the case of extensive tumors, demonstrated efficacy in IFS, but were associated with acute and some chronic side effects. TRK inhibitors have demonstrated very rapid responses in the vast majority of children with IFS with limited acute toxicity. The study concluded that, with the current state of knowledge, both conventional chemotherapy and TRK inhibitors should be regarded as options for patients with localised disease; TRK inhibitors should be considered in patients with metastatic disease, and before mutilating surgery when conventional chemotherapy fails. Outside a clinical trial, additional data are needed to resolve the lack of consensus about front-line use of conventional chemotherapy versus versus TRK inhibitors in patients with localised disease.

In addition, the NRSTS Committee was involved in the international consensus on the treatment of infantile fibrosarcoma.

EARLY PHASE TRIALS COMMITTEE (BY MICHELA CASANOVA AND SUSANNE GATZ)

VIT 0910

The results of the VIT 0910 study (randomised phase II study of vincristine and irinotecan (VI) +/- temozolomide (T) in refractory/relapsed RMS), presented at ASCO 2019 and SIOP 2019, defined the new standard treatment for relapsed RMS in EpSSG.

Overall, 120 patients (60 per arm) were recruited in 37 centers; 89% patients had a relapsed RMS. ORR was 44% (24 of 55 evaluable patients) for VIT versus 31% (18/58) for VI; adjusted odds ratio, adj-OR=0.50, 95%CI, 0.22-1.12, p=0.09.

Compared to the VI arm, the VIT arm resulted to be associated with a large and significant reduction in the risk of death; median overall survival was 15.0 months (95%CI, 10.0-21.2) in the VIT arm and 10.3 months (95%CI, 7.1-12.6) in the VI arm. The Progression-Free Survival benefit was nearly significant (HR=0.68; 95%CI, 0.46-1.01; P=0.059). Overall, patients experienced adverse events ≥ grade 3 more frequently with VIT than VI (98% versus 78%, respectively; p=0.009), including a significant excess of hematological toxicity (81% versus 61%; p=0.025).

The final manuscript was prepared and submitted for publication.

REGORAFENIB

The results phase 1b expansion cohort to evaluate safety and tolerability of regorafenib combined with vincristine/irinotecan (VI) in patients with relapsed/refractory RMS and other solid tumors were presented at ASCO 2020 and SIOP 2020. The study, conducted at 10 study centers in four countries (France, Italy, Spain and the United Kingdom) was agreed with PDCO in the context of Stivarga PIP. Two different dosing schedule were evaluated: vincristine 1.5 mg/m^2 (Days 1 and 8) and irinotecan 50 mg/m^2 (Days 1-5) were combined with daily oral regorafenib either on Days 1-14 (concomitant schedule) or on Days 8-21 (sequential schedule) in a 21 day cycle.

A total of 21 patients with a median age of 10 years (range 2 to 17 years) including 12 RMS, 5 Ewing sarcoma, 3 neuroblastoma and 1 Wilms tumor, were treated; 2 in the concomitant schedule and 19 in the sequential schedule. Concomitant dosing was discontinued when several grade 3 dose-limiting toxicities were reported in both patients (peripheral neuropathy and liver injury; pain, vomiting, febrile aplasia). Toxicities observed were among those expected with no new types of toxicities reported although greater incidence of grade 3-4 haematologic toxicities was seen with the combination. The most common grade ≥3 treatment-emergent AEs were neutropenia (71%), thrombocytopenia (33%), leukopenia (29%), anaemia (24%), and an increased ALT (24%). Irinotecan had to be reduced in 62% of the patients due to toxicity. The maximum tolerated dose and recommended phase 2 dose of regorafenib in the sequential schedule was 82 mg/m^2.

Radiological responses were observed in 7 of 12 patients with RMS (1CR, 6PR). Responses were seen in patients with both embryonal and alveolar histology and also in patients who previously received irinotecan chemotherapy. Two patients remain on treatment for more than 1 year.

Overall, the level of activity seen for the new combination was considered sufficient and worth proceeding to the randomized phase 2 stage against standard VIT chemotherapy within FaR-RMS.

The FaR-RMS amendment including the Regorafenib randomisation is planned in 2021; in conjunction also a biomarker proposal has been developed which will be funded by BAYER.

VOLASERTIB

There are ongoing efforts on the proposal to include volasertib in FaR-RMS. The protocol synopsis has been finalised and the aim is to include a Phase Ib study of volasertib in combination with vincristine in the relapsed/refractory setting at a later stage. Negotiations with Oncoheroes are ongoing.

The early phase trials committee continues to work with pharma and the EpSSG Biology Committee to facilitate access to new agents for the FaR-RMS trial and other indications. The group held a successful workshop jointly with the biology committee as an open meeting on 30/11/2020 which aimed at discussing novel drug targets and drugs for RMS from the preclinical and clinical aspect. Targets/pathways discussed were: FGFRs, AURKA and BCL-XL, Neddylation, Hippo and HDAC/BET dependency/inhibitiors. A second such meeting

is planned prior to the EpSSG meeting in April 2021.

The group has developed an **early Phase study table** for STS which is listed in the members section of the EpSSG webpage.

FINANCIAL STATEMENT 2020 (BY DR. A. FERRARI)

Total income for the association in 2020 was €15.550, mainly from members' fees and meeting registration. Interest on accounts and investments was €2050,00.

Total expenses were almost €7.300; Annual and Board meeting and travel costs were €4.000, accountant's costs (€2200), banking costs (€1000) and website costs (€2000).

For 2021 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.

An accountancy and treasurer's Report of the final year's account was presented and approved during the EpSSG Spring meeting Assembly held virtually in April 2021.

Funding Sources: The EpSSG is indebted to the Kick Cancer Foundation, founded by one of our parents, Delphine Heenen and King Baudouin Foundation for supporting a new EpSSG data manager and for supporting preclinical pilot research directly supporting the biological studies planned within the EpSSG FaR-RMS study till 31st December 2020. Grateful to those who help implementing work resources in research.

WORKPLAN in 2021

1. Implement the FaR-RMS study across countries and invite new countries to participate.
2. Launch sub-studies to FaR-RMS including Imaging and Biology Biomarker studies
3. Finalize the Myckids Study and initiate the study across EpSSG countries.
4. Further develop the Desmover study to strive for opening of the study in 2022
5. Efficient preparation of reports by the International Data Center (IDC) in close collaboration with PI of each project leading to timely delivery of manuscript.
6. Consolidate funding for EpSSG IDC and secretariat activities
7. Optimize collaboration with parents through involvement at meetings and in projects
8. Optimize communication with members through our EpSSG website and mailings on important EpSSG developments

Aim for a live Winter meeting in Rome to nurture our important professional network

Help support the EpSSG Association

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

photograph taken by dr.Ferrari

DONATE to EpSSG

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. 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.

Association meetings - Calendar 2020-2021

DATE	MEETING	LOCATION	NOTES
2020			
May 4-8 (Mo-Fri)	EpSSG Spring Meeting & Association Assembly	SIOPE Congress, Valencia Spain	NOT HELD! Pandemic emergency
December 3-4 (Th-Fr)	EpSSG Winter Meeting & Association Assembly	Virtual Meeting	Virtual Meeting due to Pandemic emergency
2021			
April 26-30 (Mo-Fri)	EpSSG Spring Meeting & Association Assembly	SIOP Europe 2021 2nd Annual Meeting Virtual	Confirmed
December 1-3(We-Fri)	EpSSG Winter Meeting & Association Assembly	Rome	To be confirmed

Prepared by:

Nadege Corradini

Julia Daragjati

Marit Borger –Winkelman

Meriel Jenney

Julia Chisholm

Heidi Glosli

Angelika Sandakly

Gianni Bisogno

Andrea Ferrari,

Michela Casanova

Timothy Rogers

Henry Mandeville

Hans Merks

and with the great collaboration of all EpSSG Members