GENERAL INFORMATION

Project Title

Raro non vuol dire solo

Institutions in the Project

1. Division of Hemato-Oncology, Department of Childôs and Womanôs Health, University Hospital of Padua
2. Pediatric Surgery, Department of Childôs and Womanôs Health, University Hospital of Padua
3. Institute of Human Pathology, University of Padua
4. Clinical trials and Biostatistics Unit, Istituto Oncologico Veneto, Padua
5. CINECA (Inter-University Computing Centre), Bologna
6. Istituto Nazionale per la ricerca e la cura dei Tumori, Milan

Principal Investigator

Gianni Bisogno, M.D., Ph.D.
Date of birth: 20.11.1962

Pediatric Oncology Consultant, Head of the Solid Tumor Unit,
Clinica di Oncoematologia Pediatrica
Department of Childôs and Womanôs Health
Tel. 049 8211481, Fax: 049 8213510
e-mail: gianni.bisogno@unipd.it

Project duration

36 months

Budget

The total budget of the project is 113.000 Euro

PIANO DELLA RICERCA

Abstract (Inglese)

Background and rationale.
Very rare tumors in pediatric age (< 2 cases/million children/year) are orphan diseases which means that for a long time very little clinical and scientific interest or dedicated trials existed and the public or private financial support has been poor. Due to the low incidence the diagnosis and treatment of children with VRT can be difficult due to the lack of experience. The scarcity of medical information has a major impact for patients and families and they are often obliged to travel, sometime abroad, to give to their child the best care.
The Tumori Rari in Età Pediatrica (Rare Tumours in Paediatric Age [TREP]) project was launched in Italy in 2000 and represents a model of network dedicated to pediatric VRT. Among its major achievement are the creation of a Registry of patients with VRT and the establishment of treatment guidelines.
Project description.
This project will further develop the TREP experience with a special effort to assist patients and families to obtain a correct diagnosis and treatment and scientific-based, accurate information.
This will be achieved creating a system that will allow give a certain diagnosis through the implementation of a review of the diagnosis by an expert pathologist, assisting clinician with diagnostic and treatment recommendations and creating a system to obtain expert advice. A remote data entry to capture the data of patients with VRT will be created. The TREP website will be updated to increase the quality of information to patients and families using more modern way of communications (videos)
Finally the TREP project will be supported in its activity in order to expand on an international level experiences and data.
Objectives and expected results

a) to provide patients with a reliable diagnosis
b) to update the current diagnostic-therapeutic guidelines and elaborate new ones
c) to offer the possibility to Italian pediatric oncologists to receive an expert advice, also using videoconference and internet based tools and, if this will be the case, to promote the concentration of children with unusual tumors in few centres with the necessary expertise
d) to prospectively collect data on VRT
e) to increase the quantity and quality of information for patients with VRT and their families
f) to support the TREP Italian network activity and its participation to the European reference network dedicated to pediatric VRT .

This project will establish a model for a comprehensive care and collaborative action against orphan diseases and have significant impact to improve the quality of diagnosis and treatment of children and adolescents with VRT.

Abtract (Italiano)

Background e razionale.
I tumori rari in età pediatrica (<2 casi / milione di bambini / anno) sono da considerare malattie orfane, nel senso che per lungo tempo vi è stato poco interesse clinico e scientifico, non esistevano studi clinici dedicati e il sostegno finanziario di tipo pubblico o privato è stato minimo. La diagnosi e il trattamento dei bambini con tumore raro possono essere difficili a causa della mancanza di esperienza. La scarsità di informazioni mediche ha un impatto importante per i pazienti e le famiglie che sono spesso obbligate a viaggiare, a volte all'estero, per dare al loro bambino lôassistenza migliore.
Il progetto TREP (Tumori Rari in età Pediatrica è stato avviato in Italia nel 2000 e rappresenta un modello di rete dedicata ai bambini con tumori rari. Tra I risultati più importanti finora onseguiti figurano lœlaborazione di raccomandazioni per la diagnosi e il trattamento e la creazione di un Registro dei pazienti con tumore raro.
Descrizione del progetto.
Questo progetto svilupperà ulteriormente l'esperienza TREP affiancando alla parte più prettamente scientifica uno sforzo particolare per assistere pazienti e famiglie ad ottenere una corretta diagnosi, un trattamento adeguato ed informazioni accurate.
Questo obiettivo sarà raggiunto creando un sistema che permetterà la revisione della diagnosi da parte di un patologo esperto, la diffusione di raccomandazioni diagnostiche e terapeutiche e la possibilità per i medici che curano I bambini con tumore raro di ottenere la consulenza di esperti. Verrà inoltre creato un sistema online per la raccolta dei dati sulle caratteristiche della malattia e del trattamento dei pazienti con tumore raro. Il sito web del progetto TREP sarà aggiornato per aumentare la qualità delle informazioni ai pazienti e alle famiglie, anche utilizzando sistemi più moderni di comunicazione (video)
Infine, il progetto TREP sarà supportato nella sua attività di collaborazione internazionale in modo da poter condividere esperienza e dati a livello europeo.
Obiettivi e risultati attesi

a) fornire ai pazienti con una diagnosi affidabile
b) aggiornare le line guida formulate in passato e elaborarne ulteriori
c) offrire la possibilità di oncologi pediatrici italiani di ricevere un supporto da parte di esperti nella diagnosi e trattamento dei bambini con tumore raro. Questo obiettivo sarà raggiunto utilizzando anche strumenti di videoconferenza e internet-based (telemedicina). Sarà inoltre possibile, se questo sarà il caso, favorire la concentrazione dei bambini con tumore raro nei centri dove esistono le necessarie competenze.
d) per raccogliere in modo prospettico i dati sui tumori rari in età pediatrica
e) per aumentare la quantità e la qualità delle informazioni per i pazienti con tumore raro e le loro famiglie
f) sostenere l'attività del progetto TREP e la sua partecipazione al network europeo di dedicato ai tumori rari pediatrici.

Questo progetto mira a creare un modello di presa in carico dei pazienti e collaborazione a livello nazionale e internazionale contro le malattie orfane e ad avere un impatto significativo nel miglioramento della qualità della diagnosi e del trattamento di bambini e adolescenti con tumore raro.

BACKGROUND

Cancer in children is definitively rare (1) and, as other uncommon diseases, presents to doctors and patients additional challenges to the ones posed by the disease itself and the search for a certain diagnosis and the appropriate treatment may be demanding

In the past decades a national and international collaboration among pediatric oncology centers has been progressively established allowing many clinical trials and biological researches to be carried out. This increasing collaboration has paralleled the progressive improvement of the survival results in nearly all pediatric tumors. Examples are represented by the possibility of cure achieved by patients with lymphoblastic leukemia or localized Wilms tumor that approach 90% (2,3). Unfortunately, they still remain a small group of very uncommon tumors (incidence < 2 cases/million/children) for which national or international cooperative studies have rarely (or never) been developed. Children suffering from very rare tumors (VRT) have not benefited to the same extent of the enormous advances obtained in pediatric oncology.

In this respect rare pediatric cancers might be classified as orphan diseases. The establishment of meaningful clinical and biological research is also challenged by the heterogeneity of this group of tumors. Some of them are typical of the pediatric age, such as pleuropulmonary blastoma or pancreatoblastoma, others are more common in adulthood, but when they develop in children or in adolescents, they often present very different behaviors. This is the case for example for thyroid carcinoma, GIST, melanoma or renal carcinoma. Taken together, these tumors are not as rare as their name suggest, since they account for approximately 5% of all childhood cancers

Due to the low incidence of VRT the diagnosis and the choice of the best treatment can be difficult due to the lack of experience. Histological diagnosis may be challenging even for expert pathologists who may encounter one or two cases of VRT per year. It is therefore necessary to create a network of pathologists, each of whom with the expertise in at least one VRT that can review the pathology material and give the patient a reliable diagnosis that will allow a correct treatment.

Pediatric oncologists and surgeons only occasionally diagnose patients with these tumors. They therefore may feel unprepared to treat children with VRT due to their very limited or non existent experience. In these cases available diagnostic and therapeutic guidelines and the possibility to seek advice from more expert colleagues would be important to choose therapeutic strategies that are appropriate for that patient.

Finally, the limited amount of medical information available may have a major impact on patients and families in many aspects: the search for reliable, scientific based, information and for pediatric oncology centers that can deliver the best treatment can be difficult. Families are often obliged to travel, sometime abroad, to get the best care for their child. A proper diagnosis will assure families that the treatment received is the best available relieving them from a strong sense of uncertainty and isolation that is often felt.

In the last decade cooperative groups specifically dedicated to study VRT in the pediatric age have been founded. These initiatives were mainly nationally based but the necessity to search for international collaborations in order to partially overcomes the problem of low case numbers and in order to accelerate the research development became rapidly apparent.

The ñTumori Rari in Età Pediatricaò (Rare Tumours in Paediatric Age [TREP]) project was launched in Italy more than 10 years ago and represents a network working model dedicated to rare paediatric tumours. Among its major achievements are the setting up of a national Registry of patients with VRT and the establishment of treatment guidelines (4).

This project aims to further develop the TREP experience with a specific effort designed to assist patients and families, in order to obtain a correct diagnosis and treatment and a scientifically-based information.

PRELIMINARY RESULTS

The first cooperative group dedicated to pediatric VRT has been founded in Italy: the TREP (Tumori Rari in Età Pediatrica) project started in the year 2000, supported by the Associazione Italiana Ematologia Oncologia Pediatrica (AIEOP), and in collaboration with the Società Italiana Chirurgia Pediatrica (SICP) (4) This project was created with a dual purpose: prompting research, and providing all centers with practical diagnostic and therapeutic guidelines.

Between January 2000 and April 2014, 830 patients < 18 years of age were registered by 38 different Italian centers in the TREP database. Diagnostic and treatment recommendations have been created for 8 different rare tumors. The experience has increased over time allowing us to conduct a significant number of studies (ref). A dedicated website (http://trepproject.org) has been created in support of the project where networking Centers can retrieve documents and information.

The TREP project has been fundamental to stimulate an international cooperation and 4 European groups have been founded adopting a similar model (5)

The German rare tumor group ñSeltene Tumoren in der Pädiatrieò (STEP) was founded in 2006 with similar goals. STEP is a working group of the German Society of Pediatric Oncology and Hematology (GPOH) In October 2008, the active data accrual started in Germany, Austria and Switzerland (6)

The United Kingdomôs Childrenôs Cancer & Leukaemia Group (CCLG) founded a Rare Tumour Working Group in 1997, with the aim of developing guidance for management, diagnosis and treatment for several rare tumors. No dedicated registry was developed, but selected data were collected throughout the UK National Registry of Childhood Tumours.

The Polish rare tumor group has been active since 2002. They have been collecting data from 20 different centers on eight VRT. The Group provides consultation for difficult cases and recommendations have been circulated to national Centers (7).

In France the ñComité tumeurs rares » was created in 2006 and includes 32 pediatric oncology centers. Objectives are similar to those of the other Groups. The Comité has proposed guidelines on different VRT including melanoma, pleuro-pulmonary blastoma, pancreatoblastoma, and Frantz tumor. Presently a national registry, in collaboration with the French cancer register, is under development.

These Groups officially met in June 2008 in Padua to evaluate whether a European collaboration was possible. A new cooperative group was created denominated EXPeRT (European Cooeprative study for Pediatric Rare Tumors). As a first initiative, the Groups decided to combine the data collected in the different countries on some tumor entities included in the list of VRTs. For this purpose, a harmonized core data sheet for uniform documentation of clinical data of children with rare cancers was developed.

The analysis on pancreatoblastoma,a very rare pancreatic tumor typical of children, has been the subject of the first publication demonstrating that collaboration between European Groups is possible and fruitful. In fact, as a result of the study, a standard approach for pancreatoblastoma has been elaborated, including a standardized diagnostic work-up, a prognostically relevant surgical staging system and guidelines for multimodal treatment. It is hopeful that this experience could be progressively extended to other VRT (8)

Overall the EXPeRT network will aims to include 5 European countries, with more than 120 Centers of pediatric and surgical oncology and 5 Data Centers. In the future collaboration with other European and non European Institutions will also be possible (9).

Objectives

Aims of this project are

a) to provide patients with a reliable diagnosis
b) to update the current diagnostic-therapeutic guidelines and elaborate new ones
c) to offer the possibility to Italian pediatric oncologists to receive an expert advice, through the use of videoconferences and internet based tools and, if this will be the case, to promote the concentration of children with unusual tumors in few Centers with the necessary expertise
d) to prospectively collect data on VRT
e) to increase the quantity and quality of information for patients with VRT and their families
f) to support the TREP Italian network to expand its activity at an international level.

Expected Results

This project will establish a model for a comprehensive care and collaborative action against orphan diseases. It will also have a significant impact in order to improve the quality of diagnosis and treatment of children and adolescents with VRT. This may help to fill the gap accumulated over the years supporting epidemiological, clinical and basic research for the benefit of children and adolescents with VRT.

As measurable outcomes we expect:

a) to obtain that at least 70% of patients with VRT included in the TREP project had a diagnosis centrally reviewed by an expert Pathologist
b) to update the 8 existing guidelines and develop 5 new guidelines for additional VRT
c) the implementation of a procedure and tools in order to give experts advice for patients with VRT
d) the development of a remote data entry system that will substitute the existing Registry
e) the creation of documents and information available on internet for families/patients with VRT

Personnel in the project

	Role	Time in the project (%)
Dr. Gianni Bisogno	Project coordination. In particular he will overlook the set up of the TREP database, the creation of ñmedical adviceò system, the ideation and validation of diagnostic and treatment guidelines and the preparation of informative materials.	20
Prof. Giovanni Cecchetto	Responsible for all the aspects concerning surgery: preparation of surgical guidelines, surgical advice	10
Dr. Andrea Ferrari	Responsible for the preparation of diagnostic and therapeutic guidelines and informative materials	10
D.ssa Rita Alaggio	Responsible for the Pathologists network and main reviewer of the histological diagnosis	15
Study assistant (to be identified)	Responsible for managing the Remote data entry system (set up of database, input of data, queries to the participating Centers) and administrative aspects (i.e. relations with other Centers, documents for ethical authorities,é). He/She will be in charge of receiving advice requests, collect necessary materials (i.e. pathology and biology specimen, imaging, clinical and pathology reports). He/she will be responsible for managing and updating the TREP website, in specific developing the section dedicated to families/patients	100
Dr. Gian Luca De Salvo	Statistical support and data analysis	5

The principal investigator and all the other collaborators of the research team have already been involved in collaborative Groups and have worthy experience in the coordination of national and international studies. Gianni Bisogno, Giovanni Cecchetto and Andrea Ferrari are the founders of the TREP project that represents one of the most successful national projects on VRT. Evidence of its success lines in the significant number of research published on the subject of very rare tumors and the numerous invitations received at international Congresses to give key lectures on VRT (SIOP 2009-2013, ASCO 2010, ECCO 2011, SIOPE 2014).

In addition:
Prof. Giovanni Cecchetto is Associate professor of Pediatric Surgery Division of Padova. He is one of the most experienced Italian pediatric surgeons in the field of oncology. For many years prof. Cecchetto has been the coordinator of the GICOP (Gruppo Italiano di Chirurgia in Oncologia Pediatrica) and since 2012 is the President of IPSO (International Society of Pediatric Surgical Oncology).

Andrea Ferrari is a pediatric oncology consultant at the Istituto Nazionale Tumori of Milan. He is the principal investigator of the ongoing European protocol dedicated to non-rhabdo soft tissue sarcoma. He has been the coordinator of the AIEOP Very rare tumor Committee from 2006 to 2010.

Gian Luca De Salvo is the Head of the Clinical Trials & Biostatistics Unit, at the Istituto Oncologico Veneto ï I.R.C.C.S. Padua. He has been involved in the planning of projects on pediatric tumors since 2000 and has in-depth experience on handling the remote data entry collection. Throughout the years particular attention has been paid to make sure that all trial activity is carried out according to the Good Clinical Practice guidelines.

Related ongoing Project:
. Gianni Bisogno is actively involved as a work package leader in EXPO-r-NET, a European funded project that aims to establish rules for pediatric tumor boards on an international level (dr. Bisognoôs time in project 10%).

- *National Partner*

  - The Remote data Entry system will be develop in collaboration with CINECA, an inter-University Consortium (based near Bologna), founded in 1969 by the Ministry of Public Education as a non-profit consortium of 18 Italian universities for high performance computing and information processing. Its aim is to promote the use of the most advanced computing systems to support public and private scientific and technological research in different areas. At present CINECA is involved in many EU research projects in different sectors: pharmaceutical, medical, financial. A devoted system has been setup and developed to manage trials through telematics technology according to FDA and European standards. Currently this system provides a management service for several different clinical trials and pediatric epidemiological registries.

- *European Partners:*

  - Dr. Bernadette Brennan, coordinator of the United Kingdomôs Childrenôs Cancer & Leukaemia Group Rare Tumour Working Group
  - Dr. Dominik Schneider, dr. Ines Brecht coordinators of The German rare tumor group: ñSeltene Tumoren in der Pädiatrieò (STEP)
  - Dr. Jan Godzinsky coordinator of the Polish Paediatric Rare Tumours Study Group
  - Dr. Daniel Orbach, Dr. Ives Reguerre coordinators of ñFRACTUREò (groupe FRAnCais des TUmeurs Rares de lôEnfant)

METHODS

The project includes a scientific part and, in parallel, activities that focus on patients/families. The timeline for the different achievements is described in figure 1.

a) An office will be setup with the aim of managing the submission of material for histopathological diagnosis review, circulate biological material for molecular characterization, if necessary. The office will collect advice request and organize the material that needs to be revised by the experts.
b) A national expert will be identified for each VRT and will be in charge of analyzing the data included into the TREP database, review medical literature and prepare documents that contain recommendations for the diagnosis and treatment of each VRT.
c) A procedure for medical advice requests and answer will be setup. This will include the creation of a dedicated videoconference system dedicated that will be used to discuss difficult cases. This will allow the clinician responsible for the childôs care to have a face to face discussion with the experts: information and investigation results (including tumor samples and imaging) will ñvirtually travelò rather than patients and families
d) The existing TREP registry needs to be updated. The flux of information is based on paper forms sent by Italian Pediatric Oncology Centres to the Coordinating Centre in Padova. The creation of a Remote data entry system that will allow a more accurate data collection, with different datasheets according to the different tumors and the implementation of an online data quality control. This will represent a major improvement in the collection of data for patients with VRT. The remote data entry system will be in English and will also provide the possibility of extending the data collection to other European countries.
e) A dedicated website for VRT has already been created by our group (www.treproject.it). The website offers limited information for doctors and families. New information will be prepared or updated if already available. The possibility to made videos dedicated to pediatric rare tumors has already been considered by our Group (10) and a video discussing VRT has already been made (https://www.youtube.com/watch?v=qWHLDOwGcVI). Videos dedicated to the different VRT will be prepared and made public using available internet tools. In addition, information on how to have a diagnosis reviewed and on how doctors can ask the expert for clinical advice will be prepared and made available. The support of Fondazione Celeghin will be acknowledged in all these documents. It may also be possible to create a link between the documents and videos that will be prepared and the Fondazione Celeghin website.
f) A national meeting will be held once a year to go over all the project progress. All the representative of the Centres participating in the project will be invited and involved 8see in additional information the list of Centres participating to the TREP project)

Timelines of the different milestone of the Project

VRT Office						
Organization of Panels for diagnosis review and clinical advice						
Dedicated Video conferencing system						
Diagnosis review and clinical advice						
Remote data entry set up						
Online Data collection						
Information to patients and families				Online leaflets		Videos
VRT meeting						
Months	*6*	*12*	*18*	*24*	*30*	*36*

BUDGET

	1st year	2nd year	3rd year	Total
Consumables, cost for material shipping, histological analysis (immunohistochemistry, molecular biology tests) documents and video costs	5.000	8.000	8.000	21.000
Tools necessary for the Remote data entry system*, the website management and the videoconferencing system	4000	2.000	2.000	8.000
Personnel costs	25.000	25.000	25.000	75.000
Meeting organization and travel costs	2000	2000	2000	6.000
Other	1.000	1.000	1.000	3.000
TOTAL COST / YEAR	37.000	38.000	38.000	
TOTAL COST				113.000

* Part of the costs to establish the Remote data entry system is covered by an agreement by CINECA and AIEOP.

Scientific Coordinator information

Gianni Bisogno, M.D., Ph. D.

Birth date: 20.11.62

Work Address Clinica di Oncoematologia Pediatrica,
Department of Womanôs and Childôs Health, University Hospital of Padova,
via Giustiniani 3, 35128 Padova - Italy.
Tel. 0039-49-8211481 Fax 0039-49-8211462. email: gianni.bisogno@unipd.it

Education and Training:

1995-97: Ph. D. in Pediatric Oncology, University of Padova, Italy.
9.95-3.96 Fellowship in Pediatric Oncology - Section of Paediatric Oncology and Laboratory of Paediatric Oncology, Royal Marsden Hospital, Sutton, Surrey, U.K.
1992-93 and 1993-94: Fellowship in Paediatric Oncology - Hematology-Oncology Division, Paediatric Department University of Padova, Padova
5/94 Visiting Doctor- Hematology Oncology Division, Emma Children's Hospital / The Children's Academic Medical Centre, Amsterdam, The Netherlands.
9/89-2/90: Fellowship in clinical trial methodology at Pharmacology Laboratory - Pharmacological Research Institute "Mario Negri" Milan, Italy.
1988-92: Residency in Paediatrics - Paediatric Department University of Padova, Italy
1988 Medical Degree (Medical School University of Padova, Italy).

Research activities

The activity is manly dedicated to patients with pediatric solid tumors, and in particular Soft tissue sarcomas, Very rare tumour and Wilms tumor.
Since 2008 dr. Bisogno ha created a group specifically dedicated to the clinical investigations of new drugs in pediatric oncology

National Activity

- *Since 2004:* Coordinator of the soft tissue committee affiliated to the Associazione Italiana di Onco-Ematologia Pediatrica (AIEOP)
- *1999-2005:* Principal investigator of the RMS4.99 national protocol dedicated to children and adolescents with metastatic rhabdomyosarcoma
- *Since 2000:* Founder and coordinator of the TREP (tumori rari in età pediatrica) project
- *Since 2004:* Member of the AIEOP Germ Cell Tumor Scientific Committee
- *Since 2010:* Member of the AIEOP/ISG Bone Tumor Scientific Committee
- *Since 2010*: Member of the AIEOP Clinical pharmacology Committee
- *Since 2002:* Founder and Coordinator of the Regional Network dedicated to thrombocytopenia in pediatric age

International Activity

- *Since 2004:* Member of the European paediatric Soft tissue sarcoma Study Group (EpSSG) Board. On *December 2013* he has been elected Chair of the Group.
- *Since 2005:* Principal Investigator of the EpSSG RMS2005 protocol dedicated to children and adolescents with rhabdomyosarcoma.
- *Since 2008:* Founder Member of EXPeRT (European cooperative study group for pediatric rare tumors)
- *2001-2010:* Member of the International Society of Pediatric Oncology Wilms Tumor Scientific Committee
- *2010-2012:* Member of the Europe Clinical Trial Group
- *Since 2010:* Member of ITCC (Innovative Therapy for Children with Cancer)
- *Since 2012:* Member of the Steering Committee of the European Clinical Research Council for paediatric and adolescent oncology
- *2008-2010:* Member of the Scientific Board of Deutsche Forschungsgemeinschaft (German Research Foundation)

Projects

Since 1999 dr. Bisogno has been involved as Principal Coordinator or Partner with his own budget in 14 projects supported by different Institutions (Veneto Region, Città della Speranza Foundation, Italian Ministry of Health, European Community).
He has been involved as collaborator in 3 additional projects
He is (or has been) Principal Investigator in 17 projects investigating new agents sponsored by Pharmaceutical Companies or Research Institutes.

Appointments

1/2011-until now: Head of the Solid Tumor Unit. Division of Hematology-Oncology, Department of Womanôs and Childôs Health, University Hospital of Padova
1/2007- until now: Lecturer in the Pediatric Medical School of Padova and, *from 2011*, Honorary Professor. Specialty School of Pediatrics, University of Padova
8/2000-2/2001: Consultant Pediatric Oncologist in the Childrenôs Department of the Royal Marsden Hospital Sutton, Surrey, UK
1/1998- until now: Consultant Pediatric Oncologist. Division of Hematology-Oncology, Department of Womanôs and Childôs Health, University Hospital of Padova

Publications (from 1997 to May 2014)

- 141 papers published on international Journals and indexed on PubMed.
- 15 papers published on Italian Journals
- 214 abstracts presented to international and national Congresses
- 9 book chapters

- Total Impact factor: 441.690
- H index: 25 (source: ISI web of science); 27 (source: Scopus)

Publication most relevant to the present project (30 papers selected from 72 papers published since 2009)

1. *Bisogno G*, Brennan B, Orbach D, Stachowicz-Stencel T, Cecchetto G, Indolfi P, Bien E, Ferrari A, Dommange-Romero F. **Treatment and prognostic factors in pleuropulmonary blastoma: an EXPeRT Report.** Eur J Cancer. 2014;50(1):178-84.

2. *Bisogno G*, Tagarelli A, Schiavetti A, Scarzello G, Ferrari A, Cecchetto G, Alaggio R. **Myoepithelial carcinoma treatment in children: A report from the TREP project.** Pediatr Blood Cancer. 2014;61(4):643-6.

3. Ferrari A, *Bisogno G*, Cecchetto G, Santinami M, Maurichi A, Bono A, Vajna De Pava M, Pierani P, Bertolini P, Rossi CR, De Salvo GL. **Cutaneous melanoma in children and adolescents: the italian rare tumors in pediatric age project experience**. J Pediatr. 2014;164(2):376-82. e1-2.

4. Virgone C, Cecchetto G, Alaggio R, Ferrari A, Bisogno G, Conte M, Inserra A, Fagnani AM, Indolfi P, Salfi N, Dall'igna P. **Appendiceal Neuroendocrine Tumours in Childhood: Italian TREP Project.** J Pediatr Gastroenterol Nutr. 2014;58(3):333-8.

5. Bausch B, Wellner U, Bausch D, Schiavi F, Barontini M, Sanso G, Walz MK, Peczkowska M, Weryha G, Dall'igna P, Cecchetto G, *Bisogno G*, Moeller LC, Bockenhauer D, Patocs A, Rácz K, Zabolotnyi D, Yaremchuk S, Dzivite-Krisane I, Castinetti F, Taieb D, Malinoc A, von Dobschuetz E, Roessler J, Schmid KW, Opocher G, Eng C, Neumann HP. **Long-term prognosis of patients with pediatric pheochromocytoma**. Endocr Relat Cancer. 2013;21(1):17-25.

6. Orbach D, Brennan B, Casanova M, Bergeron C, Mosseri V, Francotte N, Van Noesel M, Rey A, *Bisogno G*, Pierron G, Ferrari A. **Paediatric and adolescent alveolar soft part sarcoma: A joint series from European cooperative groups.**Pediatr Blood Cancer. 2013;60(11):1826-32.

7. Bonvini P, Zin A, Alaggio R, Pawel B, *Bisogno G*, Rosolen A. **High ALK mRNA expression has a negative prognostic significance in rhabdomyosarcoma.**Br J Cancer. 2013;109(12):3084-91.

8. *Bisogno G*, Compostella A, Ferrari A, Pastore G, Cecchetto G, Garaventa A, Indolfi P, De Sio L, Carli M. **Rhabdomyosarcoma in adolescents: a report from the AIEOP Soft Tissue Sarcoma Committee**. Cancer. 2012;118(3):821-7.

9. Magro G, Esposito G, Cecchetto G, Dall'Igna P, Marcato R, Gambini C, Boldrini R, Collini P, D'Onofrio V, Salfi N, d'Amore E, Ferrari A, *Bisogno G*, Alaggio R. **Pediatric adrenocortical tumors: morphological diagnostic criteria and immunohistochemical expression of matrix metalloproteinase type 2 and human leucocyte-associated antigen (HLA) class II antigens. Results from the Italian Pediatric Rare Tumor (TREP) Study project**. Hum Pathol. 2012;43(1):31-9.

10. Casanova M, *Bisogno G*, Gandola L, Cecchetto G, Di Cataldo A, Basso E, Indolfi P, D'Angelo P, Favini F, Collini P, Potepan P, Ferrari A; Rare Tumors in Pediatric Age Group. **A prospective protocol for nasopharyngeal carcinoma in children and adolescents: the Italian Rare Tumors in Pediatric Age (TREP) project.** Cancer. 2012;118(10):2718-25.

11. *Bisogno G*, Pastore G, Perilongo G, Sotti G, Cecchetto G, Dallorso S, Carli M. **Long-term results in childhood rhabdomyosarcoma: a report from the Italian Cooperative Study RMS 79.** Pediatr Blood Cancer. 2012;58(6):872-6.

12. Ferrari A, De Salvo GL, Oberlin O, Casanova M, De Paoli A, Rey A, Minard V, Orbach D, Carli M, Brennan B, Vannoesel MM, Morosi C, Stevens MC, *Bisogno G*. **Synovial sarcoma in children and adolescents: A critical reappraisal of staging investigations in relation to the rate of metastatic involvement at diagnosis. Eur J Cancer.** 2012;48(9):1370-5.

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Additional Information

List of Very Rare pediatric Tumors included in the TREP project

- Carcinoma indifferenziato del rinofaringe
- Blastoma pleuropolmonare
- Tumori maligni del pancreas
- Carcinoma adrenocorticale
- Carcinoide dellôappendice
- Tumori gonadici non germinali
- Feocromocitoma
- Carcinoma del rene
- Melanoma e altri tumori della cute
- Carcinoma della tiroide
- Neoplasie timiche
- Tumori epiteliali delle ghiandole salivari
- Mesotelioma
- Carcinoma Mioepiteliale
- Carcinoma della vescica
- Carcinoma intestinale
- Altri tumori rari

List of Pediatric Oncology/pediatric Surgery Centres participating in the TREP Project

CENTRO	***Referente***
Ancona	*Dr. P. Pierani*
Aviano	*Dr. M. Mascarin*
Bari	*Dr. N. Santor*
Bergamo	*Dr. M. Provenzi*
Brescia	*Dr. F. Porta*
Cagliari	*Dr.ssa L. Casula*
Catania	*Dr. A. Di Cataldo*
Catanzaro	*Dr.ssa E. Galea*
Cosenza	*Dr. D. Sperlì*
Firenze	*Dr.ssa A. Tamburini*
Genova	*Dr. M. Conte Massimo*
Milano INT	*Dr. A. Ferrari/ Dr.ssa M. Casanova*
Milano "De Marchi"	*Dr. D. Portaleone/d.ssa A. Fagnani*
Milano ñNi Guardaò	*Dr. F. Fedeli*
Modena	*Dr.ssa M. Cellini*
Napoli	*Dr. P. Indolf*
Padova	*Dr. G. Bisogno/prof. G. Cecchetto*
Palermo	*Dr. P. DćAngelo*
Parma	*D.ssa P. Bertolini*
Pisa	*Dr. C. Favre*
Rimini	*Dr.ssa R. Pericoli*
Roma B.G. oncol.	*Dr. R. Cozza/ Dr. A. Inserra*
Roma Gemelli oncol.	*Dr. A. Ruggiero*
Roma L.S. oncol.	*Dr.ssa A. Schiavetti*
Torino	*D.ssa E. Basso*
Trieste	*Dr. G. Zanazzo*
Verona	*Dr. S. Cesaro*

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Padova, 22.9.2014

dr. Gianni Bisogno