PRINTO

The Paediatric Rheumatology INternational Trials Organisation (PRINTO at www.printo.it) is a not for profit, non-governmental, international research network founded by Alberto Martini and Nicolino Ruperto in 1996. PRINTO initially included 14 European countries (550 centres worldwide with 1200 members today), with the goal to foster, facilitate and co-ordinate the development, conduct, analysis, and reporting of multi-centres, international clinical trials and/or outcome standardisation studies in children with paediatric rheumatic diseases (PRD).

intestazione foto

PRINTO also fosters the training of young fellows in Pediatric Rheumatology through different education fellowship programs.

The PRINTO Academic Research Activities

PRINTO acts as an international academic research service to the paediatric rheumatology community for the implementation of non-for profit trials and other investigator's initiated studies (consensus projects, cross-cultural adaptation of questionnaires, training, standardized information to families etc). Many projects coordinated by the network have been funded by the European Union or other public bodies (The Methotrexate trial in JIA ,The quality of life project for the PRD, JDM and JSLE diagnosis criteria, A website for families of children with pediatric rheumatic diseases, Research Training in pediatric rheumatology, Pharmachild registry, Abirisk registry, INSAID and EuroFever registry).

The PRINTO Academic Research Activities

These are the ongoing academic projects coordinated by the network:

Pharmachild: pharmacovigilance JIA registry;

Eurofever: registry of patients (children and adults) with autoinflammatory diseases;

EPOCA: epidemiology and outcome of children with JIA around the world;

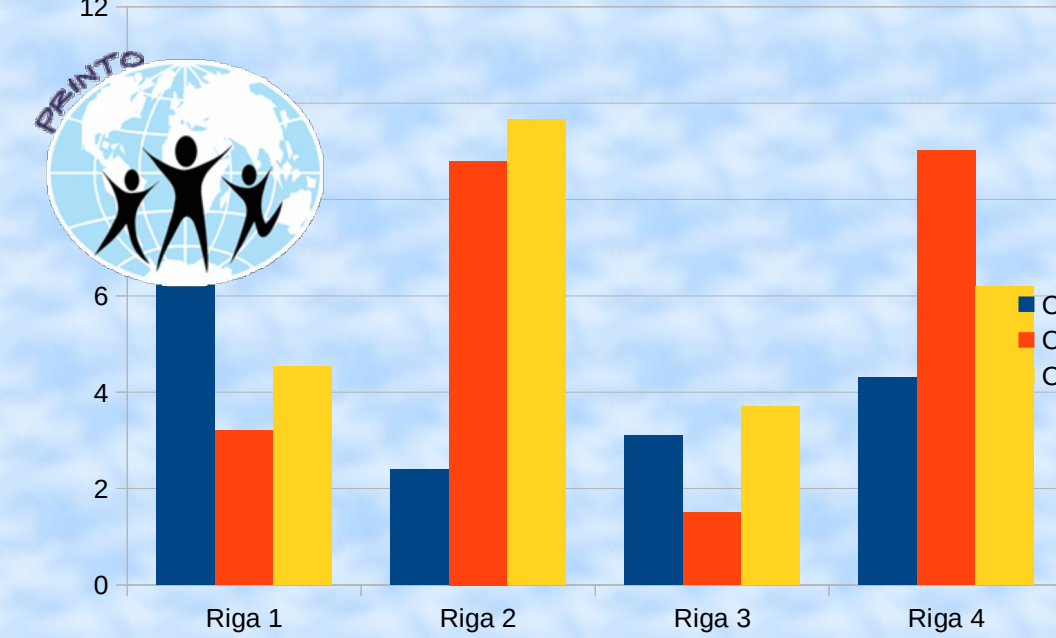
Abirisk: evaluation of the presence of antibodies against biologic drugs in JIA;

Share: update of the families' website containing information on pediatric rheumatic diseases, on pediatric rheumatology centers and on family associations;

MyPan: randomised trial on childhood polyarteritis nodosa.

As a result of academic initiatives a total of over **37,500** patients have been enrolled from about **300 centres** in **67** different countries.

A total of over 135 manuscripts have been published with over 685 authors with 40% of them in multiple publications.



INSERIRE GRAFICO CENTRI CON PERFORMANCE ARRUOLAMENTO

The network is coordinated by the International Coordinating Centre located at Genoa,Italy. The coordinating centre is supervised by the Scientific Responsible Dr. Nicolino Ruperto. The chief function of the International Co-ordinating Centre is to facilitate the flow of logistic and scientific details needed to design, launch and manage multi-centred, multi-national, collaborative studies.

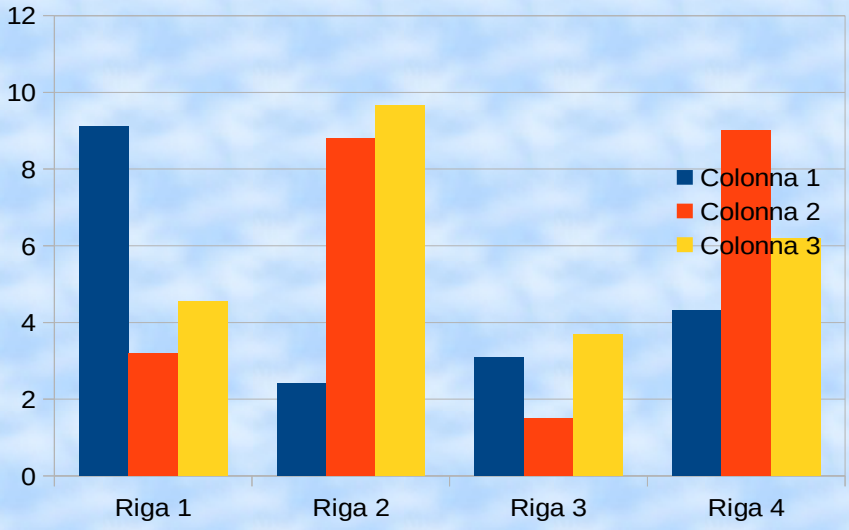
The International Co-ordinating Centre can assist the Principal Investigator in the design of the protocol, statistical analysis and generation of the final report and of the manuscript. It is located in Genova, Italy, at the Istituto di Ricovero e Cura a Carattere Scientifico (IRCCS) G. Gaslini Institute, the biggest paediatric hospital in Italy.

7 research assistants
3 web-designers

Collaboration with Pharmaceutical companies

PRINTO collaborates with several pharmaceutical companies in the pediatric investigation plan (PIP), protocol and case report form development, site selection through dedicated feasibilities among PRINTO members, training, monitoring, analysis and reporting of clinical trials.

As a result of this collaboration over **3,000** patients have been enrolled from more than **250** centres in **39** different countries.



Collaboration with Pharmaceutical companies

Why pharmaceutical companies should choose PRINTO as vendor?

-scientific expertise

-monitoring of data quality

-xdfdf

-sfsfsdf

-sfsfs

-sfsfs

It is well known that data management in clinical trials performed by academic trial units still faces many difficulties (e.g. heterogeneity of software products, deficits in quality management, limited human and financial resources and the complexity of data collection).

We think that relying on the twenty-years experience of PRINTO that since years has developed procedures of data management in multinational clinical trials could be an added value for the pharmaceutical companies who need to perform mutinational clinical trials in Pediatric Rheumatology.

In the next pages you can find a list of all the services provided by the PRINTO International Coordinating Centre

Collaboration with Pharmaceutical companies

1. WEB-BASED FEASIBILITY SURVEY

PRINTO web-designers develop a web-based system customized according to company's requirement aimed to submit a feasibility survey by approaching selected PRINTO members to assess their interest, their ability and their availability to participate in the study protocol.

Our research assistant will assist you during all the design and conduct phase.

Of the feasibilities conducted so far the xxx% of the sites selected by the companies are PRINTO affiliates.

All the PRINTO sites participating into industry-sponsored clinical trials are GCP compliant and respect all the national and international standard requirements for data management in multinational clinical trials.

Collaboration with Pharmaceutical companies

2. CONSULTANCY SERVICES

The decades-old experience in the field of pediatric rheumatology by Prof. Alberto Martini (PRINTO Chairman) and Dr. Nicolino Ruperto (PRINTO Senior Scientist) is available to pharmaceutical companies.

The following is a non-exhaustive list of services we might provide:

- Help in the design of the study
- In the event of a centre having to be replaced (due to lack of participation, repeated protocol violations, dissolution of the centre etc,) make recommendations for a suitable replacement.
- Assist in decisions about early termination or “mid-course” corrections.
- Assist in the review of the eligibility of patients who investigators are considering entering the Trial.
- Actively support recruitment, i.e. will encourage investigators to recruit patients into the Trial because of an unsatisfactory recruitment status.
- Answer day-to-day study related questions of investigators about the interpretation of the protocol and case report forms from all participating centres via phone and fax lines and or e-mails.
- Assist in collecting information about side effects that require reporting and in accordance with company current reporting procedures and policies.
- Be available for and provide active support of investigator meetings by participation and contribution, e.g. making presentations etc.
- Assist in the data analysis and preparation (in collaboration with company and a panel of selected investigators as detailed in the Trial protocol) of abstracts and full publications of the Trial results for presentation at professional meetings and the final manuscript for publication in a professional journal.

Collaboration with Pharmaceutical companies

3. Independent evaluation for ACR pediatric 30/50/70/90, flare, disease activity and inactive disease status, steroid tapering, juvenile arthritis disease activity score (JADAS) and juvenile arthritis damage index (JADI) in collaboration with the PRCSG for JIA, JSLE or JDM

Proposal assumptions:

The proposal is relevant for all kind of study design (withdrawal design classic parallel studies, etc)since it is known from previous PRINTO experience that the quality of the data reported through theregular monitoring process of CRO might contains up to 30% missing data. This high rate of missingdata is due to the fact that monitoring normally occurs few weeks after the visit has been done making impossible to retrieve data that by error have not been collected by the centre. As detailed below this proposal on the contrary assume evaluation of the quality of the data at the time of the visit (real time remote monitoring) by the PRINTO coordinating centre.

This proposal is particularly relevant in withdrawal design studies when the evaluation of ACR pediatric 30 response has to be done in a timely manner since it is critical for the randomisation process. Similarly the determination of flare status is critical during the double blind portion of the trial. The proposal is also relevant for classic parallel studies.

Determinations of responder/non-responder and flared/non-flared status, disease activity and inactive disease status and steroid tapering will be completed and communicated to appropriate sources for each study subject at appropriate study visits within 1 hour after complete and readable WEB based CRF are received at PRINTO coordinating centre.

Determinations for sites will be based on review and analysis of data recorded on line at the secured PRINTO web site with username and access password.

Review and determination of responder/non-responder and flared/not-flared status; steroid tapering, will be determined by independent review of CRF pages by 2 individuals within the CC who will then confer on consensus assessment of status

Collaboration with Pharmaceutical companies

3. Independent evaluation for ACR pediatric 30/50/70/90, flare, disease activity and inactive disease status, steroid tapering, juvenile arthritis disease activity score (JADAS) and juvenile arthritis damage index (JADI) in collaboration with the PRCSG for JIA, JSLE or JDM

Proposal assumptions:

Detailed training of adequate staff (12 at PRINTO and 2 at PRCSG CC depending on the sample of the study) to provide adequate backup staffing for performance of CC functions despite CC staff illness, travel, etc. PRINTO staff will also include Spanish speaking personnel.

CC staff will carry a cell phone to provide study sites access to CC outside of regular business hours (up to 10 pm local time on regular working days) or in event of fax machine failures.

CC will develop oral presentations and written instructional materials relating to logistics of responder/non-responder and flared/not-flared status and steroid tapering determinations to be used at Investigators meetings and Investigators Binders. These materials will be developed by

CC staff in adequate time for company review before investigators meetings. Company will print these instructional materials for use at the Investigators meetings.

Determinations of CC will be documented, stored, protected and reported in a format that is in compliance with all GCP, HIPAA, FDA and European Regulatory agencies' requirements.

Use of the same computerized algorithm for determination of responder/non-responder and flared/not-flared; and steroid tapering status will be used at both CCs. In addition the database output resulting from the use of this computerized algorithm will be sent to Company at intervals to be determined.

Collaboration with Pharmaceutical companies

4. PRINTO CC administrative support to Italian sites for Ethics Committee (EC) and Regulatory Authorities approvals

Collaboration with Pharmaceutical companies

5. PRINTO CC design and development of cross-culturally adapted Patient Reported Outcome Tools

Collaboration with Pharmaceutical companies

6. Central reading of wrist/hand x-Ray

For the evaluation of joint erosion over time.

To this regard please notice that in the past 2 Phase III trials on going within the PRINTO membership the evaluation of joint erosion has become standard.

Collaboration with Pharmaceutical companies

7. Assistance in wiriting process of scientific results