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## 30th PRINTo newsletter | December 2019

### Table of contents

PRINTo news

PRINTo ongoing projects

- JIA classification study
- The STARS Trial
- PharmaChild
- Eurofever
- Conect4children (c4c)
- MYPAN

Latest PRINTo papers

PRINTo membership

PRINTo advisory council & contacts

### PRINTo news

#### **PRINTo Paediatric Rheumatology Day | 21-22 March 2020**

It is with great pleasure that we wish to invite you in Genoa **on the 21st of March 2020** to participate in a two-day event **in honor of Alberto**, who has left his service from the Gaslini Hospital and the University of Genoa in the end of October 2019.

To celebrate his outstanding contribution in Pediatric Rheumatology, we have decided to organize **an international meeting** and to invite some key leaders in the field and Alberto's fellows most active in research. The event will focus on the state of the art and the most recent developments on **pathogenesis, diagnosis and treatment of juvenile idiopathic arthritis and of auto-inflammatory diseases** and we will highlight our current research plans in this exciting field.

Please click [here](#) to download the provisional program of the event.

If you would like to attend the congress, please contact PRINTo cc at [printo@gaslini.org](mailto:printo@gaslini.org).

We look forward to welcoming in Genoa in March 2020!

With our warmest personal regards

Angelo, Nicola and Marco

#### **2019 call for projects within the PReS Working Parties 2.0**

With the aim of expanding the research activities of PReS (<https://www.pres.eu/>), **the Council envisaged a novel format of projects based on a tight collaboration with PRINTo**. This novel PReS/PRINTo collaboration will consist in **annual calls for projects within the PReS Working Parties 2.0 (WP2.0)** and with the technical assistance from PRINTo.

In the 2019 call, one project will be funded for a total of 3 years. PReS will grant a financial contribution to the winner of 10,000€/year (total 30,000€), and the equivalent in manpower for technical assistance and implementation of international collaborative studies (30,000€) will be provided by PRINTo. Funding will cover primarily personnel, meetings and networking costs with volunteer participation from centres.

**The requirements to participate** are the following:

1. A PI and co-PI (co-PI under 40 years of age) who are members of a PReS WP2.0 and hold a valid PReS membership;

2. A PI and co-PI who are members of PRINTO (please visit <https://www.printo.it/contact/apply-membership> or contact [printo@gaslini.org](mailto:printo@gaslini.org) for further information);
3. The proposed project must not have other sources of funding from other organizations/entities;
4. The involvement of at least 3 different countries is highly recommended;
5. The technical support requested to PRINTO must be clearly stated in the proposal.

**Application deadline is December 15th, 2019!**

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## PRINTO ongoing projects

### JIA classification study

The **JIA Classification study** is a translational research that aims to validate, in a prospective collection of at least 1,000 patients at disease onset, the proposed PRINTO consensus classification criteria . This will entail also the collection of biologic samples for ANA, anti CCP, RF, HLA B27 determinations and DNA analysis.

As of today, out of the **146 participating sites** , **66 have obtained the EC approvals** , and **80 are in progress** . Globally, **288 patients** have been enrolled **from 34 sites**.

**WEBSYSTEM:** please note that we have recently modified the password system for the login into all of our websystem. If you have not done this yet, please use the *Forgot your password* function to change your personal password. You will receive a link via email that will allow you to choose your own password (which must contain numbers, capital letter and special characters). Please note that the link you will receive to change your password expires after one hour!

**Next scheduled PRINTO remote trainings** for the use of the websystem:

- Wednesday 18th December 2019 at 11 am Italian Time (CET)
- Thursday 19th December 2019 at 3.00 pm Italian Time (CET)

Please contact the PRINTO staff if you wish to participate.

**ENROLLMENT TIP** : We recommend you to schedule the **Month 0 during the first visit at your site** . The ideal situation would be to have a first visit = M0.

**BIOLOGIC SAMPLES:** PRINTO will provide the kits for the visits requiring samples collection and laboratory instruction containing also storage and shipment information. If you need more kits please contact PRINTO and we will provide you with a refilling of the necessary material.

We remind you that the **biologic samples** should be **collected** at **Month 0 and after 3 months**.

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### The STARS Trial

The comparison of **STep-up and step-down therapeutic strategies in childhood ARthritis trial (STARS)** is a new **interventional trial** financed by AIFA (Agenzia Italiana del Farmaco) and by the Italian Foundation Compagnia di San Paolo that will be conducted by PRINTO only in the Italian centres. This clinical trial has the aim **to investigate whether an early aggressive therapeutic intervention in children with JIA** , based on the initial start of synthetic and biologic DMARDs (Step-down strategy), **is superior to an approach based on treatment escalation conducted following the treat-to-target principle** (Step-up strategy). The effectiveness of the two strategies will be assessed by comparing their ability to induce sustained clinical disease remission on/off treatment.

As of today, out of the **25 participating sites** , **9 centres obtained their EC approvals** and **16 centres are currently in progress**. **The first 7 patients have been enrolled at the coordinating centre in Genoa** .

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### PharmaChild

**Pharmachild** is a **pharmacovigilance project** which aims at observing children with JIA for 3-10 years undergoing treatment with MTX or biologic agents in order to collect moderate, severe or serious adverse events occurred. Pharmachild was started in 2011 thanks to a European

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Union (EU) grant within the FP7 framework and has obtained the ENCePP Study Seal ([ENCePP](#)).

As of today, **almost 9,000 patients have been enrolled from 85 centres in 31 countries** .

PRINTO has recently finalized a **second manuscript** aiming at the analysis of the **opportunistic infections in the immunosuppressed patients with Juvenile Idiopathic Arthritis** enrolled in PharmaChild.

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### Eurofever

The Eurofever Registry was promoted in 2008 by the work group of autoinflammatory diseases of the Paediatric Rheumatology European Society (PRES) and was supported by the Executive Agency for Health and Consumers (EAHC). The main objective of the project has been the **creation of a registry of autoinflammatory diseases** .

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We are now proud to announce that **PRINTO has recently launched the new Eurofever data collection webservice** at the link <https://registry.printo.it/>

This webservice is used not only for the data collection of the Eurofever Project, but also for all other current projects coordinated by PRINTO.

The main features of the new webservice are:

- Increased data security (GDPR)
- Improved graphic display for mobile devices (tablets, smartphones)
- Possibility to collect data for all PRINTO studies using only one webservice
- Better programming code management

**All data collected within the Eurofever registry have been transferred to the new system.**

Your access to the new webservice is granted:

- **Through your Member Area of the PRINTO website:**

[www.printo.it](http://www.printo.it)

or

- **Through a direct link:**

<https://registry.printo.it/>

Before entering new data, we suggest the investigators to read the pdf instructions document that can be found in the Homepage of the new webservice.

The PRINTO coordinating centre staff remains at your disposal for any question or if you need assistance.

Below is the list of the **32 conditions collected as of today by the Eurofever Registry**.

### Monogenic autoinflammatory diseases

1. Blau's disease/Early onset Sarcoidosis
2. NLRP3-associated autoinflammatory diseases (NLRP3-AID: CINCA/ Muckle Wells/ FCAS)
3. Deficiency of IL-1 receptor antagonist (DIRA)
4. Familial Mediterranean Fever (FMF)
5. Mevalonate kinase Deficiency (MKD or Hyper IgD syndrome)
6. NLRP12-related disease
7. PSTPIP1-associated Pyoderma gangrenosum, acne, pyogenic arthritis syndrome (PAPA)
8. Periodic fever associated to TNFRSF11A (TRAPS11)
9. TNF receptor associated periodic syndrome (TRAPS)
10. Chronic atypical neutrophilic dermatosis with lipodystrophy and elevated temperature syndrome/proteasome-associated autoinflammatory syndromes (CANDLE/PRAAS)
11. Deficiency of the IL-36 receptor antagonist (DITRA syndrome)
12. Majeed syndrome
13. Deficiency of Adenosine Deaminase 2 (DADA2)
14. STING-associated vasculopathy with onset in infancy (SAVI)
15. CARD14 mediated psoriasis (CAMP5)
16. IL-10 deficiency-associated Inflammatory bowel disease
17. Autoinflammation with infantile enterocolitis (NLRC4 – AIFEC)
18. Autoinflammation, Panniculitis, And Dermatitis Syndrome (OTULIN – AIPDS)
19. PLCG2-associated antibody deficiency and immune dysregulation (PLAID)
20. Autoinflammation with arthritis and dyskeratosis **\*new**
21. LACC1-associated familial arthritis **\*new**

22. Familial acne inversa (Pyoderma gangrenosum, Acne and Suppurative Hidradenitis, PASH) **\*new**
23. TNFAIP3-associated autoinflammatory syndrome, familial, behcet-like (AISBL) **\*new**
24. Autoimmune interstitial lung, joint and kidney disease (COPA) **\*new**

#### **Multifactorial auto inflammatory diseases**

25. Behcet's disease
26. Chronic non bacterial osteomyelitis/osteitis (CNO or Chronic recurrent multifocal osteomyelitis CRMO)
27. Periodic fever, aphthous stomatitis, pharyngitis and adenitis (PFAPA or Marshall's syndrome)
28. Schnitzler syndrome
29. Recurrent idiopathic pericarditis **\*new**
30. Systemic onset juvenile idiopathic arthritis **\*new**
31. Undefined Autoinflammatory disease
32. Systemic undefined recurrent fever (SURF) **\*new**

The PI Dr. Marco Gattorno thanks all the **116 centers in 42 countries** that collected information of **more than 4000 patients** with Autoinflammatory diseases.

We are more than happy to receive any proposal for possible studies based on the Eurofever data! You may send your proposal to [printo@gaslini.org](mailto:printo@gaslini.org) and we will submit it to the Steering Committee (M. Gattorno, J. Frenkel, S. Ozen, N. Ruperto, H. Lachmann).

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#### **Conect4children (c4c)**

PRINTO is partner of the “**conect4children**” (c4c) initiative ; the collaborative network for European clinical trials for children, (c4c) is a consortium that aims to enhance the competitiveness of Europe as a critical region for developing medicines for children by using existing expertise, patient access and developing common processes to be applied to disease natural history studies, registries, studies of new therapies and comparisons of existing therapies. **The consortium is a novel collaboration between academic and private sectors** that includes **33 academic and 10 industry partners from 20 European countries, more than 50 third parties and around 500 affiliated partners.**

The six-year project, comprised of a multidisciplinary public-private consortium, brings together key stakeholders across academia and industry. It is a pioneering opportunity to build capacity for the management of multinational paediatric clinical trials across Europe whilst ensuring the voices of children, young people and their families are heard. Strong links with regulators will be established.

This project has received funding from the Innovative Medicines Initiative 2 Joint Undertaking under grant agreement No 777389. The Joint Undertaking receives support from the European Union’s Horizon 2020 research and innovation program and EFPIA.

For more info, please visit <https://conect4children.org/>

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#### **MYPAN**

The MYPAN trial is an Open Label Randomised Controlled Trial of Mycophenolate Mofetil (MMF) Versus Cyclophosphamide (CYC) for the Induction of Remission of childhood PAN, sponsored by University College London and coordinated by the Children Hospital in Liverpool and PRINTO (PI Dr P. Brogan).

**MYPAN investigates the comparative efficacy and safety of MMF (experimental treatment) vs CYC (standard treatment) for induction of remission of childhood PAN.** This is the first ever randomized trial for childhood PAN.

The enrollment period was officially closed on June 30th, 2018: **11 patients** have been globally **enrolled** and the Last Patient Last Visit was scheduled for November 2019.

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#### **Latest PRINTO papers**

Dolezalova P, Anton J, Avcin T, Beresford MW, Brogan PA, Constantin T, Egert Y, Foeldvari I, Foster HE, Hentgen V, Kone-Paut I, Kummerle-Deschner JB, Lahdenne P, Magnusson B, Martini A, McCann L, Minden K, Ozen S, Schoemaker C, Quartier P, Ravelli A, Rumba-Rozenfelde I, Ruperto N, Vastert S, Wouters C, Zulian F, Wulffraat NM for SHARE Consortium and the Paediatric Rheumatology International Trials Organisation (PRINTO)

**The European network for care of children with paediatric rheumatic diseases: care across borders**

Rheumatology 2019 Jul 1;58(7):1188-1195 [PubMed](#)

Rosina S, Consolaro A, van Dijkhuizen P, Pistorio A, Varnier GC, Bovis F, Nistala K, Maillard S, Civino A, Tsitsami E, de Inocencio J, Jelusic M, Vojinovic J, Espada G, Makay B, Katsicas MM, Pratsidou-Gertsis P, Lazarevic D, Rao AP, Pires Marafon D, Martini A, Pilkington C, Ruperto N, Ravelli A. for the Pediatric Rheumatology International Trials Organization (PRINTO)

**Development and validation of a composite disease activity score for measurement of muscle and skin involvement in juvenile dermatomyositis**

Rheumatology 2019 Jul 1;58(7):1196-1205 [PubMed](#)

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Minoia F, Bovis F, Davì S, Horne A, Fischbach M, Frosch M, Huber A, Jelusic M, Sawhney S, McCurdy DK, Silva CA, Rigante D, Unsal E, Ruperto N, Martini A, Cron RQ, Ravelli A; Pediatric Rheumatology International Trials Organization (PRINTO), the Childhood Arthritis & Rheumatology Research Alliance, the Pediatric Rheumatology Collaborative Study Group and the Histocyte Society.

**Development and initial validation of the MS score for diagnosis of macrophage activation syndrome in systemic juvenile idiopathic arthritis.**

Ann Rheum Dis 2019 Oct;78(10):1357-1362 [PubMed](#)

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Ter Haar NM, Eijkelboom C, Cantarini L, Papa R, Brogan PA, Kone-Paut I, Modesto C, Hofer M, Iagaru N, Fingerhutová S, Insalaco A, Licciardi F, Uziel Y, Jelusic M, Nikishina I, Nielsen S, Papadopoulou-Alataki E, Olivieri AN, Cimaz R, Susic G, Stanevica V, van Gijn M, Vitale A, Ruperto N, Frenkel J, Gattorno M; Eurofever registry and the Pediatric Rheumatology International Trial Organization (PRINTO)

**Clinical characteristics and genetic analyses of 187 patients with undefined autoinflammatory diseases**

Ann Rheum Dis 2019 Oct;78(10):1405-1411 [PubMed](#)

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Giancane G, Ruperto N for the Paediatric Rheumatology International Trials Organisation (PRINTO)

**Treatment of juvenile idiopathic arthritis: what is new?**

Curr Opin Rheumatol 2019 Sep;31(5):428-435 [PubMed](#)

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Pardeo M, Wang J, Ruperto N, Alexeeva E, Chasnyk V, Schneider R, Horneff G, Huppertz HI, Minden K, Onel K, Zemel L, Martin A, Koné-Paut I, Siamopoulou-Mavridou A, Silva CA, Porter-Brown B, Bharucha KN, Brunner HI, De Benedetti F, for the Paediatric Rheumatology International Trials Organisation (PRINTO) and the Pediatric Rheumatology Collaborative Study Group (PRCSG)

**Neutropenia During Tocilizumab Treatment Is Not Associated With Infection Risk in Systemic or Polyarticular-Course Juvenile Idiopathic Arthritis**

J Rheumatol 2019 Sep;46(9):1117-1126 [PubMed](#)

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Giancane G, Lavarello C, Pistorio A, Oliveira SK, Zulian F, Cuttica R, Fischbach M, Magnusson B, Pastore S, Marini R, Martino S, Pagnier A, Soler C, Sta?vicha V, Ten Cate R, Uziel Y, Vojinovic J, Fueri E, Ravelli A, Martini A, Ruperto N for the Paediatric Rheumatology International Trials Organisation (PRINTO)

**The PRINTO evidence-based proposal for glucocorticoids tapering/discontinuation in new onset juvenile dermatomyositis patients**

Pediatr Rheumatol Online J 2019;17(1):24. [PubMed](#)

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Gattorno M, Hofer M, Federici S, Vanoni F, Bovis F, Aksentijevich I, Anton J, Arostegui JI, Barron K, Ben-Cherit E, Brogan PA, Cantarini L, Ceccherini I, De Benedetti F, Dedeoglu F, Demirkaya E, Frenkel J, Goldbach-Mansky R, Gul A, Hentgen V, Hoffman H, Kallinich T, Kone-Paut I, Kuemmerle-Deschner J, Lachmann HJ, Laxer RM, Livneh A, Obici L, Ozen S, Rowczenio D, Russo R, Shinar Y, Simon A, Toplak N, Touitou I, Uziel Y, van Gijn M, Foell D, Garassino C, Kastner D, Martini A, Sormani MP, Ruperto N, for the Eurofever Registry and the Paediatric Rheumatology International Trials Organisation (PRINTO)

**Classification criteria for autoinflammatory recurrent fevers**

Ann Rheum Dis 2019;78:1025–1032 [PubMed](#)

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Nordal E, Pistorio A, Rygg M, Giancane G, Maghnie M, Di Iorgi N, Flemming K, Hofer M, Melo-Gomes JA, Bica BERG, Brunner J, Dannecker G, Gerloni V, Harjacek M, Huppertz HI, Pratsidou-Gertsis P, Nielsen S, Stanevicha V, Ten Cate R, Vougiouka O, Pastore S, Simonini G, Ravelli A, Martini A, Ruperto N. for the Paediatric Rheumatology International Trials Organisation (PRINTO)

**Growth and puberty in juvenile dermatomyositis: a longitudinal cohort study.**

Arthritis Care Res [Epub ahead of print] [PubMed](#)

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## PRINTO membership

As of today, PRINTO has reached 1433 effective members in 661 centres from 91 countries.

If you wish to become a PRINTO member  
and receive regular updates about our research activity and invitations to our projects  
please go to:

<https://www.printo.it/contact/apply-membership>

Your cooperation will be more than welcome  
and your effort will be essential for the research in the field of paediatric rheumatic diseases.

**WELCOME ABOARD!**

## PRINTO advisory council & contacts

### **Chairman**

**Alberto Martini, MD, Prof - Genoa, Italy**

### **Counsellors**

**Tadej Avcin, MD, PhD - Ljubljana, Slovenia**

**Michael Hofer, MD, Prof - Lausanne, Switzerland**

**Seza Ozen, MD, Prof - Ankara, Turkey**

**Pierre Quartier, MD - Paris, France**

**Claudia Saad Magalhães, MD, Prof - Botucatu, Brazil**

**Joos Swart, MD - Utrecht, The Netherlands**

### **Senior Scientist**

**Nicolino Ruperto, MD, MPH - Genoa, Italy**

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