
Paediatric Rheumatology **InterNational Trials Organization** **PRINTo**

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Outline

- ◆ PRINTo outline
- ◆ Open questions for international collaboration
 - An academic point of view
 - An industry point of view

www.printo.it

PRINTO
Paediatric Rheumatology International Trials Organization

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INFORMATION ON PAEDIATRIC RHEUMATIC DISEASES

Pediatric Rheumatology International Trials Organisation (PRINTO)

The Paediatric Rheumatology International Trials Organisation (PRINTO) is a non governmental international network founded by [Alberto Martini](#) and [Nicolino Ruperto](#) in 1996, and initially included 14 European countries (now 46 countries and more than 200 centres worldwide), 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).

To learn more about PRINTO [click here](#)

IN THE SPOTLIGHT

16-AUG-2005
A new version of the website is online

16-AUG-2005
The websurvey about the JSLE and JDM trials is online

Use the SITE MENU on the left to get informations about the structure of PRINTO, past and ongoing projects, publications or to get in touch with the PRINTO co-ordinating centres. For paediatric rheumatology researchers interested in becoming members of PRINTO click the section "[apply for membership](#)".

If you are already member of PRINTO please login to access the area reserved to member.

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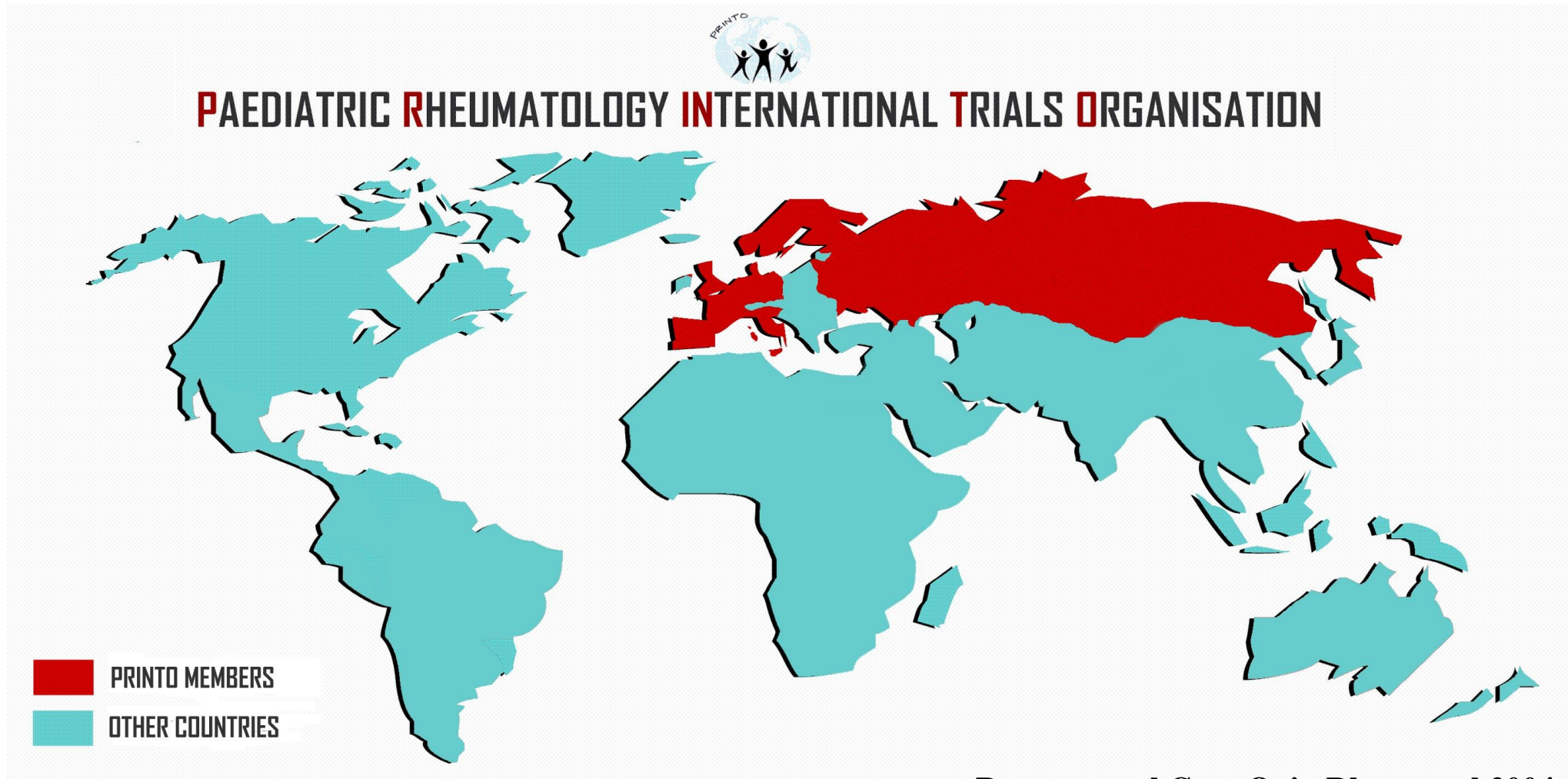
“...to foster, facilitate, and conduct high quality research in the field of paediatric rheumatology...”

PRINTO bylaws

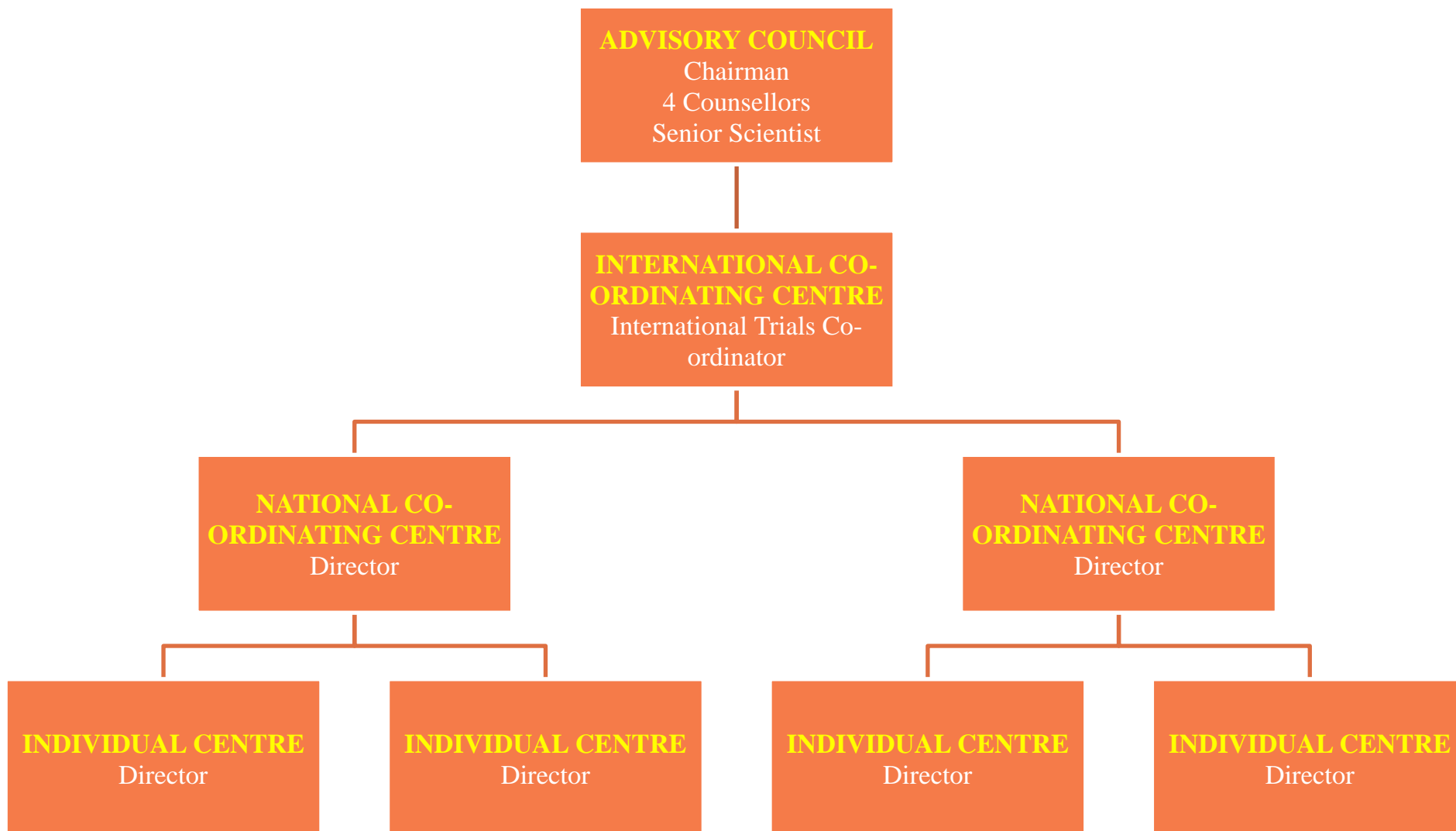
Italy, May 1996



PRINTO members (14 countries) 1996



PRINTo Organisation Chart



Open questions

- ◆ Is there a role for academia for drug approval?

PRINTo bottom up approach

- ◆ **Standardized criteria to evaluate response to therapy in JIA, JSLE and JDM**
 - ACR pediatric criteria in JIA (FDA, EMEA, ACR)
- ◆ Standardised web information to families
- ◆ Non for profit clinical trials (JIA, JDM, JSLE)
- ◆ Training to young researchers
- ◆ Liaisons with pharmaceutical industries
- ◆ Main source of funding European Union, AIFA, pharmaceutical companies

Response to therapy

◆ ACR JIA criteria (FDA, EMA)

- Giannini et al. Arthritis Rheum 1997

◆ PRINTo/ACR juvenile SLE criteria

- Ruperto et al Rheumatology 2003 Arthritis Rheum 2005, 2006

◆ PRINTo/ACR/EULAR JDM criteria

- Ruperto et al Rheumatology 2003, Arthritis Rheum 2008, Arthritis Care Res 2010

JIA core set and response criteria

◆ JIA core set

1. Physician global assessment of overall disease activity
2. **Parent or patient global assessment of overall well-being**
3. **Functional ability (CHAQ)**
4. Number of joints with active arthritis
5. Number of joints with limited range of motion
6. Index of inflammation: ESR or CRP
7. (FEVER for systemic JIA)

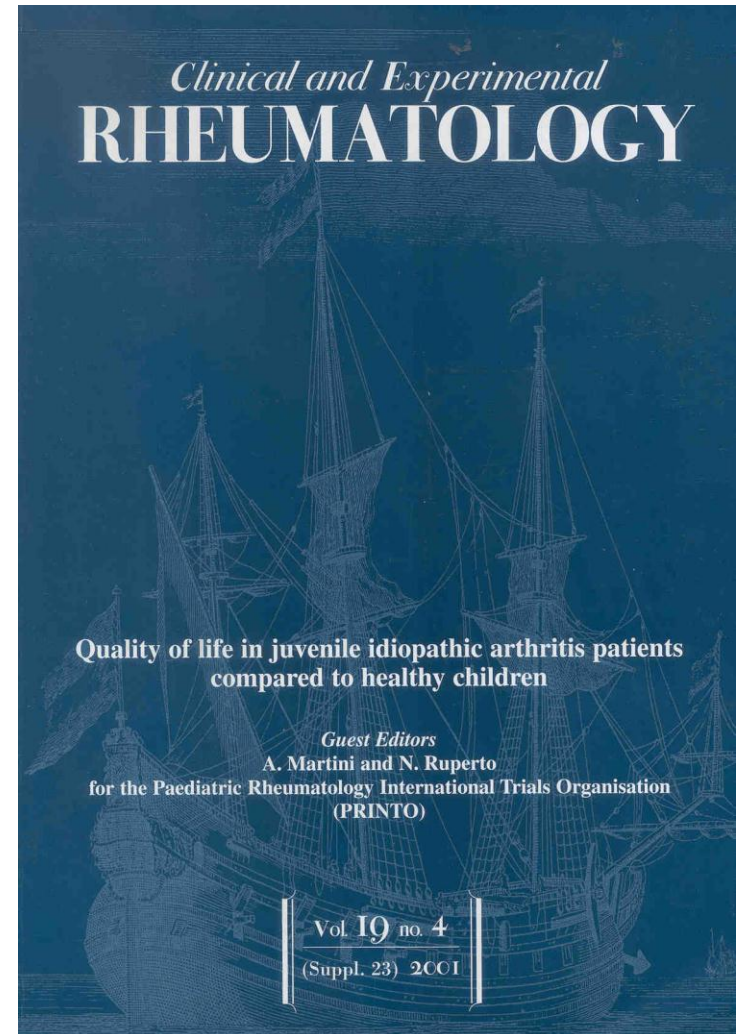
- ◆ **ACR Criteria:** 3/6 core set variables improved $\geq 30\%$ (50%, 70%, 90%, 100%) with no more than 1/6 worsened by $>30\%$ **(AND NO FEVER)**

◆ FDA and EMA accepted

Quality of life in JIA

Translations of the CHAQ/CHQ
available in **32** languages and
6,443 patients collected

(Argentina, Austria, Belgium, Brasil,
Bulgaria, Chile, Croatia, Czech Republic,
Denmark, Finland, France, Georgia,
Germany, Greece, Hungary, Israel, Italy,
Korea, Latvia, Mexico, Netherlands,
Norway, Portugal, Poland, Russia, Slovakia,
Spain, Sweden, Switzerland, Turkey, United
Kingdom, Yugoslavia)



The paradox of Methotrexate

- ◆ Mainstream for treatment, proven efficacy and safety
 - NEJM 1992, Arthritis Rheum 2005, **PRINTO Arthritis Rheum 2005-JAMA 2010**
- ◆ Used in combination in several biologic agents trials (infliximab, adalimumab, abatacept, etc)
- ◆ No interest from companies (off patent, low cost)
- ◆ **Not approved for use in JIA in most countries**
- ◆ **Patients treated with biologics are required to fail MTX!!**

Open questions

- ◆ Is there a role for academia for drug approval?
- ◆ Where are the paediatric centres?

www.pediatric-rheumatology.printo.it



PRINTO

SUPPORTED BY
THE EUROPEAN UNION



PRINTO paediatric
rheumatology
european
society

Избирате
בחר **choisissez**
select
اختار **seleciona**
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Επιλέξετε

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 Cuba	 Česká R.	 Danmark	 Deutschland	 مصر	 España	 France	 საქართველო
 Ελλάδα	 Hrvatska	 India	 ایران	 Ireland	 ישראל	 Italia	 日本
 Latvija	 Lietuva	 Luxembourg	 Magyarország	 México	 Nederland	 Norge	 Österreich
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Information on paediatric rheumatic diseases

To be listed on this website
please download the **SURVEY**

For any inaccuracy **CONTACT us**

LINKS to related websites

www.pediatric-rheumatology.printo.it

Pediatric Rheumatology Diseases - Microsoft Internet Explorer

File Modifica Visualizza Preferiti Strumenti ?

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Indirizzo <http://www.printo.it/pediatric-rheumatology/pediatricrheumatology/index.asp?Lingua=Italy&Paese=Italy> Val Collegamenti

Cerca nel Web Blocco popup Opzioni






Italia
12/2003

Questo sito è stato realizzato da PRINTO ("Paediatric Rheumatology International Trials Organisation") in italiano "Rete Internazionale per gli Studi sui Farmaci in Reumatologia Pediatrica") in collaborazione con PRES ("Paediatric Rheumatology European Society" in italiano "Società Europea di Reumatologia Pediatrica") e grazie ad un finanziamento dell'Unione Europea (contratto n. 2001CVG4-808).

PRINTO è una rete di ricerca internazionale senza fini di lucro creata nel 1996 da 14 paesi europei (ora 43 paesi europei ed extra europei). L'obiettivo principale di PRINTO è di promuovere, facilitare e coordinare lo sviluppo, la gestione e l'analisi di studi per valutare l'efficacia e la sicurezza dei farmaci e la qualità di vita dei bambini con malattie reumatiche. Fanno parte di PRINTO università ed ospedali attivamente impegnati nella ricerca e nella cura clinica dei bambini con malattie reumatiche.

PRES è una società scientifica internazionale per il personale sanitario europeo (e non europeo come membri associati) che si occupa di reumatologia pediatrica. La missione di PRES è di promuovere la conoscenza sulle malattie pediatriche reumatiche, stimolare la ricerca nel campo, disseminare informazioni tramite congressi e pubblicazioni, fornire linee guida e standard per la crescita professionale del personale sanitario. Inoltre PRES si occupa di coordinare le attività connesse alle reumatologia pediatrica in Europa; ad esempio il presidente di PRINTO e il Presidente dell'EULAR hanno una posizione permanente nel consiglio direttivo di PRES.

Il sito è suddiviso in tre sezioni:

La **prima sezione**, chiamata "informazioni" ha l'obiettivo di fornire notizie utili per le famiglie dei bambini con malattie reumatiche; in questa sezione troverete informazioni sulle caratteristiche più importanti delle principali malattie reumatiche (che cos'è, come si cura ecc). Nella **seconda sezione**, chiamata "centri" troverete l'elenco, ed il relativo indirizzo, dei centri di reumatologia pediatrica i cui medici sono soci di PRINTO e/o di PRES. L'elenco dei centri verrà aggiornato periodicamente e non pretende di essere completo. Infine, nella **terza sezione**, chiamata "famiglia", troverete gli indirizzi delle associazioni di sostegno alle famiglie alle quali potete rivolgervi. L'obiettivo principale di queste associazioni è di dare consigli per affrontare al meglio i problemi di vita quotidiana delle famiglie di bambini con malattie reumatiche. Anche questo lista verrà aggiornata periodicamente e non pretende di essere completa.

Le informazioni fornite con questo sito web sono state raccolte tramite un questionario ideato da PRINTO ed approvato da PRES ed inviato a centri di reumatologia pediatrica in diversi paesi.


informazioni
 informazioni sulle
 malattie reumatiche
 del bambino
 


i centri
 i centri pediatrici a cui
 rivolgerti
 

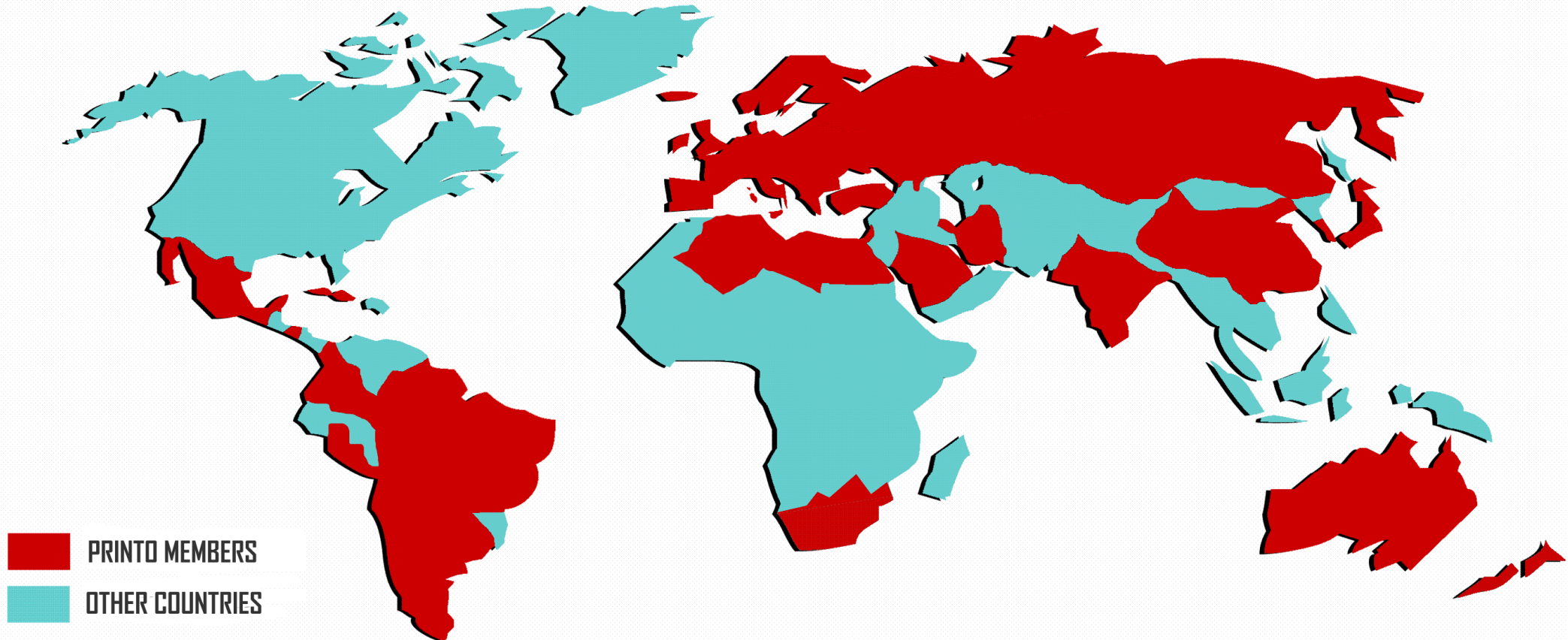

famiglia
 le associazioni di
 sostegno alle famiglie
 

>11.000 people/day from over 130 countries

PRINTO members (56 countries)



PAEDIATRIC RHEUMATOLOGY INTERNATIONAL TRIALS ORGANISATION



Open questions

- ◆ Is there a role for academia for drug approval?
- ◆ Where are the paediatric centres?
- ◆ Do we need standardised clinical trial training?

Research training

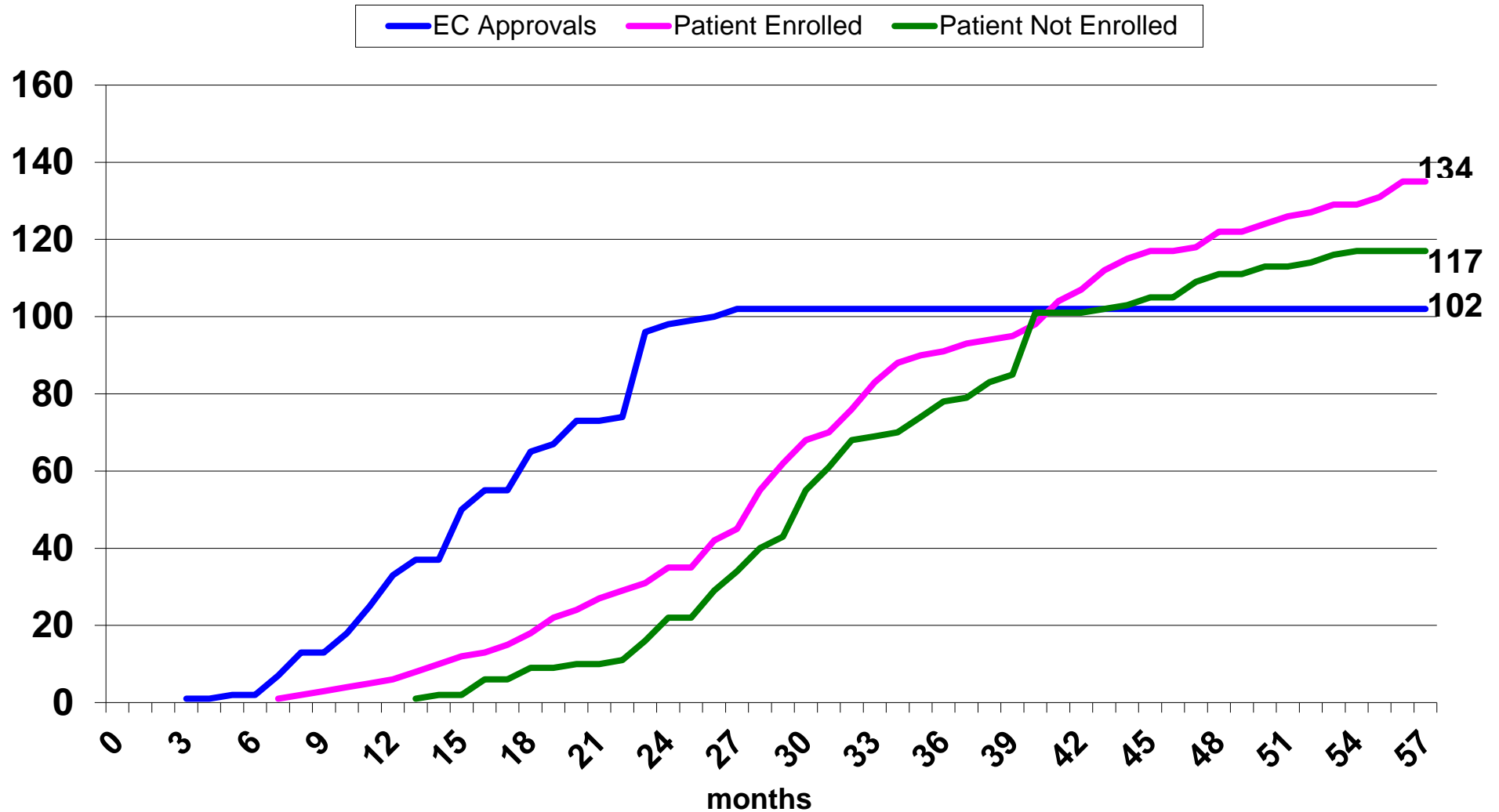
- ◆ Fellowships (1-12 months)
 - > 80 physicians from 24 countries
 - Funding: EU, EULAR, Government, self-financing
 - International PhD on-going

- ◆ PRINTO joint assessor certificate (required by FDA for clinical trials)

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PRINTo JDM trial





Ethics Committee submission

Country	National approval	Local approval	CA approval	Insurance	GCP monitoring	Drug supply/no authorization on off-label	EudraC T	Financial Agreement	EC payment
Austria		X							
Belgium	X	X	X				X		
Bulgaria	X	X		X	X				
Croatia	X	X				X			X
Czech Republic		X							
Denmark	X		X				X		
Finland	X	X	X						
France	X		X	X			X		X
Germany		X		X					X
Greece		X							
Hungary		X	X			X			
Italy		X		X			X	X	

PRINTO no profit studies

	Western Europr	Eastern Europe	LatinaA merica	North America	Other	Total
MTX	492	55	66	8	12	633
QOL	3,988	1,388	903		365	6,644
JSLE	243	102	150	37	21	553
JDM	162	37	78	18	3	298
CSA	203	27	25	85	4	344
MTX2	180	80	90		10	360
Vascul.	599	353	260	6	181	1399
Autoin	1505	266	48		192	2011
JDM	94	12	15	1	2	134

PRINTo publications

- ◆ 95 papers
- ◆ 483 authors
 - 175 (36%) multiple publications

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- ◆ Is there a role for an “academic” CRO?

Liaisons with pharma companies

- ◆ **PIP/Protocol/CRF drafting, feasibility for site selection, training, PRINTo/PRCSG primary outcome evaluation, monitoring, analysis, reporting**
- ◆ **Clinical trials:**
 - NSAIDs: meloxicam, rofecoxib
 - Biologic agents:
 - **Approved: etanercept (approved), adalimumab, abatacept**
 - On-going: tocilizumab, canakinumab, golimumab, certolizumab, belimumab, JAK3.
 - Not approved: infliximab,
- ◆ **Starting point: FDA, EU pediatric legislation**

Phase II/III trial with pharma

	West Europe	East Europe	Latin America	North America	Total
Etanercept				69	69
Infliximab	61	10	28	11	110
Adalimumab	57	26		88	171
Abatacept	75		108	31	214
Tocilizumab	59	7	22	24	112
Tocilizumab	54	50	60	24	188
Canakinumab	26				26
Canakinumab	141	13	17	19	190

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- ◆ Do we need templates for pharmas for consent/assent, contract negotiation, drug provision?

The PRINTO/pharma “ethical” approach

- ◆ Provision of drug to patients until beneficial to child or local paediatric approval (whichever last)
- ◆ Central contract negotiation (e.g. minimum per patient fee for all participating countries)
- ◆ Family reimbursement for travel related expenses
- ◆ Authorship for collaborative publication (>80 papers with more than 450 co-authors)
- ◆ **Reinvestment of funding for no profit research**

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- ◆ (Enpr-EMA) role for funding (e.g. paediatric IMI)?

The issue of public funding

- ◆ 3 millions € in public grants from 1998
 - PRINTO as support for academic research with reinvestment of funding coming from pharmaceutical industries

- ◆ CARRA (North American network) 33 million \$ in 2 years!

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