Paediatric Clinical Trial Networks

The Paediatric Rheumatology InterNational Trials Organization (PRINTO) perspective

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ENPrEMA category network 1

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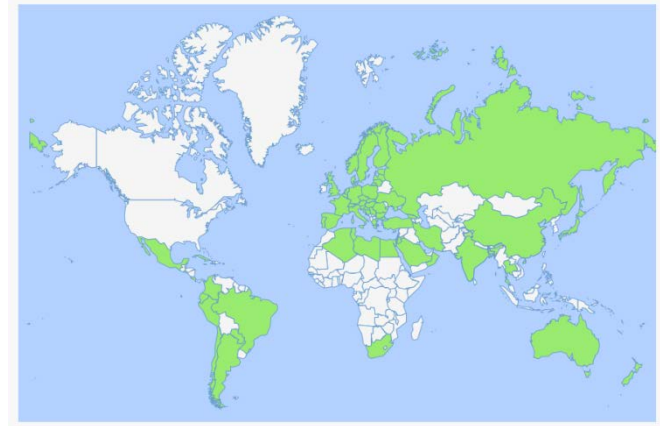
Outline

- PRINTO outline
  - academic projects and
  - trials with pharmaceutical companies

- Clinical and scientific expertise at specialty level is needed to design and implement scientifically-sounded paediatric trials and academic projects

www.printo.it (>80 countries, >500 centres)

www.pediatric-rheumatology.printo.it



- ***EULAR Centre of Excellence in Rheumatology 2008-2018***
- ***Category 1 ENPrEMA***

Italy, May 19, 1996

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

PRINTO bylaws

Ann Rheum Dis. 2005 Arch Dis Child 2011-2012

>4,000 people/day from over 180 countries

PRINTO not-for-profit studies

(>37,500 pts in 300 centres in 67 countries)

	No centres / countries 300/67	West Europe	East Europe	Latin America	North America	Others	Totals
MTX1	56/20	492	55	66	8	12	**633**
HRQOL	32/32	3,988	1,388	903		365	**6644**
JSLE	108/39	247	102	150	37	21	**557**
JDM	95/36	159	37	78	17	3	**294**
Cyclosporine	56/22	203	27	25	85	4	**344**
MTX2	61/29	193	80	80		11	**364**
Vasculitis	93/36	599	353	260	6	181	**1399**
JDM	53/20	89	10	39	1		**139**
Eurofever	100/35	2981	349	68	1	185	**3584**
EPOCA	120/49	6044	3635	1308	723	2175	**13885**
MAS	90/31	659	99	74	148	131	**1111**
Pharmachild	86/32	5252	2401	576		219	**8448**
Abirisk	24/12	115	33				**148**

PRINTO-PRCSG Enrollment

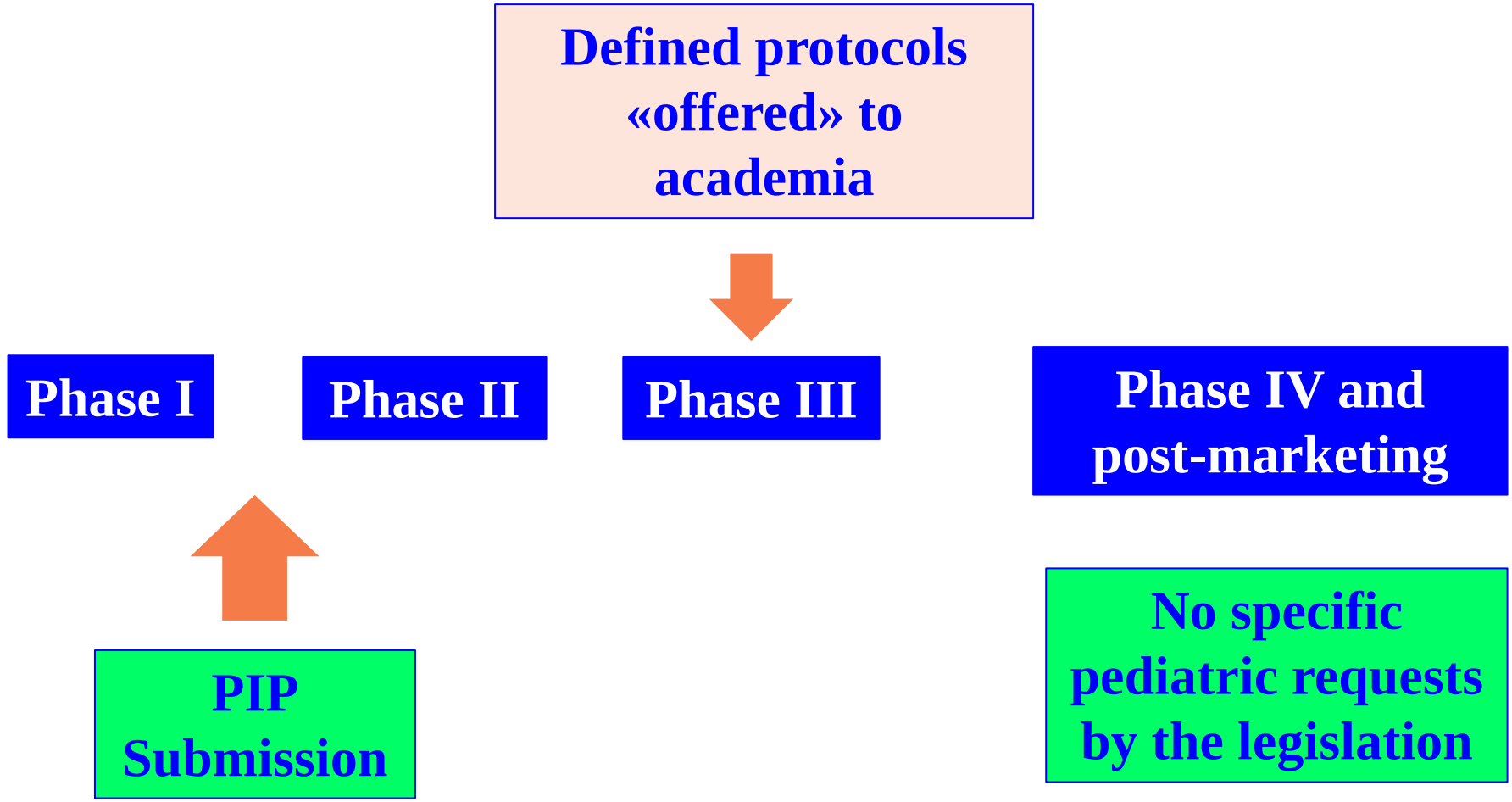
(3495 patients in 268 centres in 40 countries)

	No centres / countries 268/40	West Europe	East Europe	Latin America	North America	Others	Totals
Etanercept	9/2				69		**69**
Etanercept	38/19	43	75	5		4	**127**
Infliximab	31/14	62	10	28	23		**123**
Adalimumab	31/8	57	26		88		**171**
Abatacept iv	43/12	69		94	27		**190**
Abatacept sc	48/12	97	5	63	23	19	**207**
Tocilizumab syst	42/18	54	7	22	24	5	**112**
Tocilizumab poly	58/15	50	50	60	24	4	**188**
Canakinumab PII	5/5	23					**23**
Canakinumab P III	63/22	128	27	16	19		**190**
Golimumab	33/13	69	46	30	28		**173**
Meloxicam	31/7	130	96				**226**
Adalimumab registry	90/17	274	60	5	505	5	**849**
Abatacept registry	23/14	151	26	3		14	**194**
Rilonacept	59/22	134	35	82	69	7	**327**
Certolizumab Pegol	34/7		44	39	80		**163**
Tofacitinib poly	49/10	13	38	24	84	4	**163**

10 years of the EU Paediatric regulation

- The last 10 years have seen some considerable progress …. **Rheumatology or infectious diseases are often referred to as prime examples.** The significant surge of new treatments for children with rheumatologic diseases following the completion of PIPs has transformed a sector, which was previously neglected.

Drug development: «the central paradigm»



PRINTO liaisons with pharma companies

- **Scientific collaboration:**
  - **PIP (over 20)**/Protocol/CRF drafting
    - Study design, inclusion/exclusion criteria
  - Pediatric rheumatology concerns (drug prioritization)
- Service to companies
  - feasibility for site selection (deep knowledge of the centres)
  - Training and investigator certification (Joint assessor certif)
  - PRINTO/PRCSG primary outcome evaluation Analysis and reporting
- **Publications** (over 200 manuscripts)

Drug development: «the PRINTO paradigm»

PRINTO collaboration with pharmaceutical companies

PRINTO academic pharmacovigilance pharmachild

Phase I

Phase II

Phase III

Phase IV and post-marketing

PRINTO pre-PIP

PIP Submission

Protocol (PIP) Revision

No specific pediatric requests by the legislation

Open problems

Viewpoint

Impact of the European paediatric legislation in paediatric rheumatology: past, present and future

Nicolino Ruperto,[1] Richard Vesely,[2] Agnes Saint-Raymond,[2] Alberto Martini,[1,3] for the Paediatric Rheumatology International Trials Organisation (PRINTO)

To cite: Ruperto N, Vesely R, Saint-Raymond A, *et al. Ann Rheum Dis* 2013;**72**:1893–1896.

- **Paradox:** too many studies too few patients
  - **Me-too-drugs:** perform «just» pk-dose findings/safety open label trials
  - **Biosimilars:** missing point in the legislation; perform «at least» pk-dose findings/safety open label trials
- **Study prioritisation:** not all studies are scientifically sounded→greater intervention from academia

Greater use of extrapolation

- **The ethical case of drug provision after trial end**

Enpr-EMA

- C1: Research experience and ability
- C2: Network organisation and processes
- C3: Scientific competencies and capacity to provide expert advice
- C4: Quality management
- C5: Training and educational capacity to build competences
- C6: Involvement of patients, parents or their organisations in trials

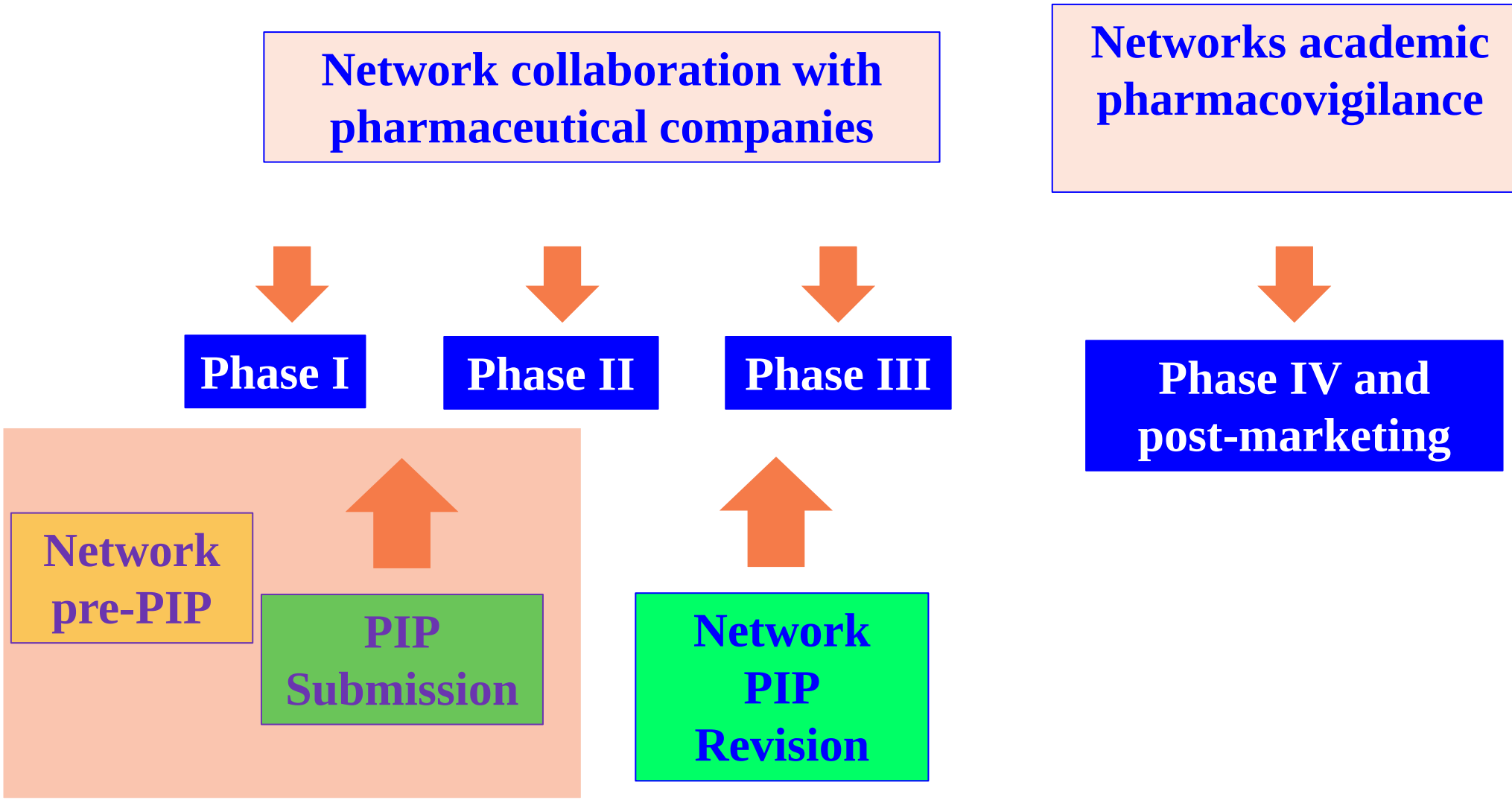
A European Network of Paediatric Research at the European Medicines Agency (Enpr-EMA)

Nicolino Ruperto,[1] Irmgard Eichler,[2] Ralf Herold,[2] Gilles Vassal,[3] Carlo Giaquinto,[4] Lars Hjorth,[5] Adolf Valls-i-Soler,[6] Christina Peters,[7] Peter J Helms,[8] Agnès Saint Raymond[2]

Arch Dis Child March 2012 Vol 97 No 3

- **Category 1**: Networks fulfilling all minimum criteria for membership
- **Category 2**: Networks potentially fulfilling all minimum criteria – but in need to clarify some issues before becoming a member of Enpr-EMA.
- **Category 2**: Networks currently not yet fulfilling minimum criteria

The networks paradigm via Enpr-EMA

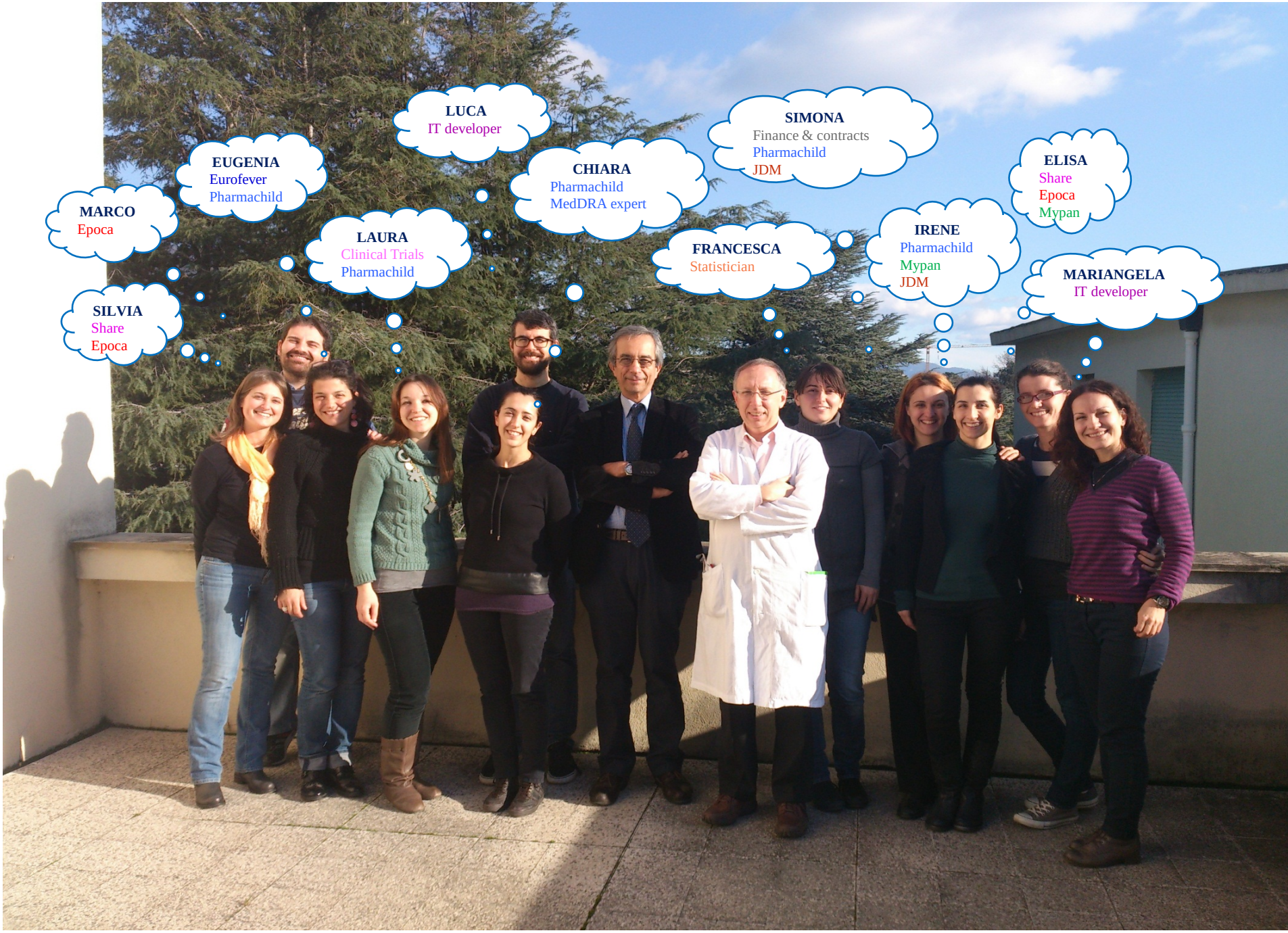


Network «perspective»: a simplified practical approach

- **Early and repeated intervention by academia**
  - **Pre-PIP (attention to pK-dose finding)**
  - Drug and studies prioritization
  - Pre-protocol finalisation
  - Revision of definitive protocol and CRF
  - Feasibility for centre identification
  - Assistance during the conduct of the trial (e.g. recruitment facilitation, outcome evaluation etc)

Network Clinical/Scientific Advisor(s)

- Pre-PIP involvement of health professionals(s)/families with **clinical expertise**
  - Knowledge of treatment paradigms
  - Revision of inclusion/exclusion criteria
  - (Clinical trial methodology)
- **Continuous collaboration with pharma** from PIP to trial implementation
  - Centre knowledge for feasibility (peer-to-peer)
  - Protocol and CRF revision
- **Facilitation by Enpr-EMA (WG interaction network-industry-regulators by S. Tansey)**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