

PENTA-ID and Pharma collaborations – Enpr-EMA 2013



The screenshot shows the PENTA-ID website interface. At the top right, there are logos for the European Union and the PENTA-ID project. Below these is a large orange banner with the text "PENTA-ID" in white. The main content area is divided into several sections:

- WHAT IS:** A list of navigation links including Home, What's new?, ID, Antibiotics, Antivirals, Antifungals, Tuberculosis, Vaccines, Pediatric Infections, Rapid diagnosis and immunodiagnosis, Education, The Foundation, and Links.
- Introduction:** A text block stating that PENTA was established in 1991 as a collaboration between paediatric HIV centres in Europe, which are principally funded by the European Commission, for governmental bodies in a number of European countries and by support from the pharmaceutical industry.
- Text:** A paragraph explaining that the PENTA foundation for the treatment and care of children with HIV serves as an umbrella for the PENTA clinical trials network, as well as for future work in testing and cohort collaborations.
- Text:** A paragraph discussing many questions about treatment for HIV that are answered in adult trials and if it is necessary to repeat all trials in children, noting the natural history of vertical HIV infection differs from that in adults in some important ways and the tolerability of drugs in children may also be different.
- Collaboration with EuroCoord:** A section titled "Collaboration with EuroCoord" describing PENTA as one of four projects now collaborating in EuroCoord, a European network of HIV/AIDS cohort studies to coordinate clinical research on HIV/AIDS at European and international levels. This initiative of the CATO206, COHERE, EuroCoord and PENTA projects has been funded by the EU seventh Framework Program.
- Research Update:** A box titled "RESEARCH UPDATE" with the heading "TO WHAT DOES IT LEAD?". The text states: "The COHERE (COhort in Europe) is evaluating whether zidovudine (AZT) is as safe and effective as HAART (HAZ) therapy. Participants from Europe, Thailand and South Africa are currently taking part in this study which is now aimed to recruitment. We published earlier..."

At the bottom of the page, there is a footer with the European Union logo, a disclaimer: "This content was produced by the project but does not necessarily reflect the views of the European Commission or the European Union. The site was developed by the project but does not necessarily reflect the views of the European Commission or the European Union.", and page navigation icons for "All Total" and "1/1".

PENTA-ID and Pharma collaboration

- Complex and wide ranging interactions
- Working with SME and large Pharma
- Phase I, II, III, IV
- Many good examples of collaborative interaction (HIV, HepC)
- Other examples where joint interaction could be improved (IMI)

KONCERT - PENTA 18



Half-strength, smaller, lopinavir/r tablet (100/25 mg) approved BID by the EMEA and FDA in 2008



- FDA: dosing based on body weight bands and BSA:

≥15 to ≤25kg, >25 to ≤35kg, >35 kg

- EMA: dosing based on body surface area:

230mg/m² BID

Differences in the number of tablets recommended for a child of a given weight/BSA

New protocol developed between PENTA and Abbott

KONCERT - Design

160 children aged <18 years, ≥ 15 kg

Screening visit

16 children per weight band allocated to PK group

Week 0

48 children undergo full PK

Children randomised (1:1) to OD or BID Kaletra

Week 4

80 children on OD Kaletra

24 children undergo full PK

Week 4

80 children on BID Kaletra

No further full PK

Follow-up

Clinic visits – weeks 8, 12, 24, 36, 48 and every 12 weeks until last patient reaches 48 weeks

If VL ≥ 50 repeat HIV-1 RNA viral load test within 4 weeks.

Hep C and PENTA-ID



**30 drugs – 5
companies**

**Individual patient-
data pooled
analyses**

**Developing
clinical cohorts**

**Collaboration
between
Pharma in PIP
development**

Paediatric HIV cohorts - Pharmacovigilance data merger



- Darunavir (Janssen) and Atazanavir (BMS) PV studies underway
- TDF (Gilead) – 3 year study (EMA approved 2012)
 - Are clinicians following the summary product characteristics (SmPC)
 - PV study of all children on TDF in Europe
 - Retrospective cohort of risk of low phosphate in UK/Ireland
- Etravirine (Janssen) – 5 year study (EMA approved 2013)
 - n=80 patients, aged <18 years ever on ETR
 - HDL/LDL cholesterol, AST, alkaline phosphatase
 - Additional info on non-serious AEs related to ETR
- Combivir (GSK) – one-off study, scored tablets 2008+
 - specific interest in choking/GI in patients taking 0.5AM/1PM

Scavenging pharmacokinetics – Antiretrovirals in Pregnancy – PANNA Study



Compounds under investigation

NNRTI

- Etravirine 200mg BID
- Efavirenz 600mg QD, UK/Ireland only
- Rilpivirine 25mg QD

NRTI

- **Emtricitabine** INCLUSION COMPLETED
- **Tenofovir** INCLUSION COMPLETED
- Abacavir 600mg QD / 300mg BID

PI

- **Atazanavir** INCLUSION COMPLETED
- Fosamprenavir 700mg/100mg RTV BID; 1400mg/200mg RTV QD
- **Darunavir** INCLUSION COMPLETED
- Tipranavir 500mg/200mg RTV BID
- Indinavir 800mg TID; 800mg/100mg RTV BID

Integrase inhibitor

- Raltegravir 400mg BID

Entry inhibitor

- Enfuvirtide 90mg BID
- Maraviroc 300mg BID / 150mg BID+PI

New Antibiotics – Most Phase 3 completed before PIPs started

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Review

New antibiotics for paediatric use: A review of a decade of regulatory trials submitted to the European Medicines Agency from 2000—Why aren't we doing better?

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ABSTRACT

New initiatives have been introduced in Europe and the USA to encourage more rapid development of antibiotics. The need to ensure these new antibiotics can be safely used in children, and especially neonates, is important owing to high antimicrobial resistance in these patient groups. This review aims to determine what lessons can be learnt from the recent regulatory processes to speed up access to new medicines for children, focusing on antibiotics licensed for adults by the EMA since 2000. For the 11 newly approved antibiotics, 31 clinical trials enrolling children in Europe were identified. However, many of these trials included both adults and children but did not provide a subset analysis for paediatrics, limiting the relevance of their findings. Some studies have been prematurely terminated and others are apparently active but are still not yet recruiting patients. Among paediatric-specific studies, 18 evaluate safety and efficacy of new compounds, 4 are pharmacokinetic studies, but only 2 focus on neonates. Nearly all studies with an agreed Paediatric Investigation Plan have just started or are not yet recruiting. For most antibiotics, despite adult phase 3 studies being completed, with specific concerns for particular drugs already noted, it will take another 3–5 years before adequate prescribing information becomes available for paediatricians. Evidence from this review suggests that we could do better. Lessons should be learnt from paediatric antiretroviral development, with neonatal and paediatric pharmacokinetic, clinical trial and pharmacovigilance drug development programmes being run directly in parallel with adult studies—not a decade behind.

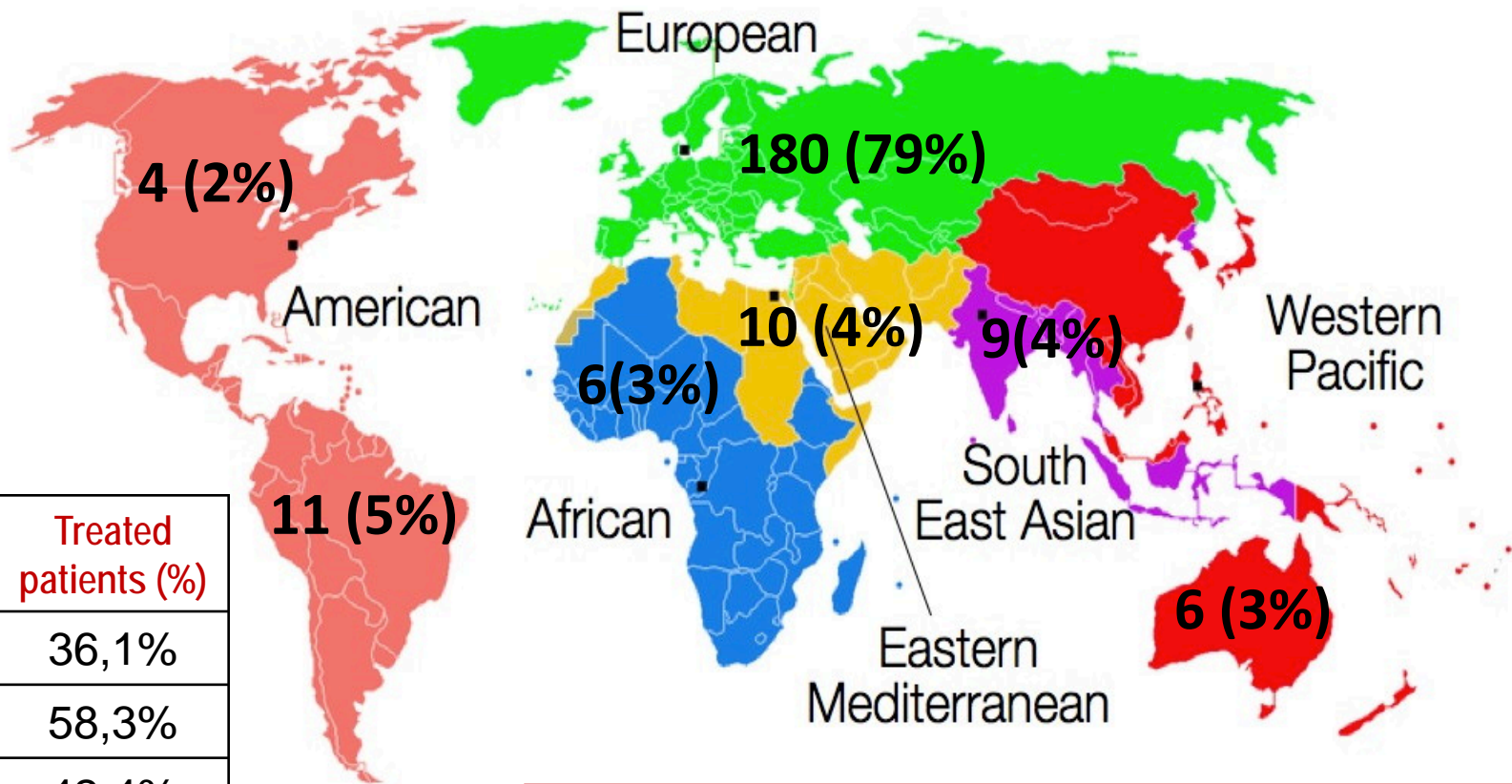
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Other examples

- NeoMero – Phase 3 – PUMA – Chiesi
- NeoVanc – Phase 2a – PUMA – Therakind – SME.
- Antifungals
- Antivirals
- COMBACTE – IMI AMR



The six regions of the World Health Organisation

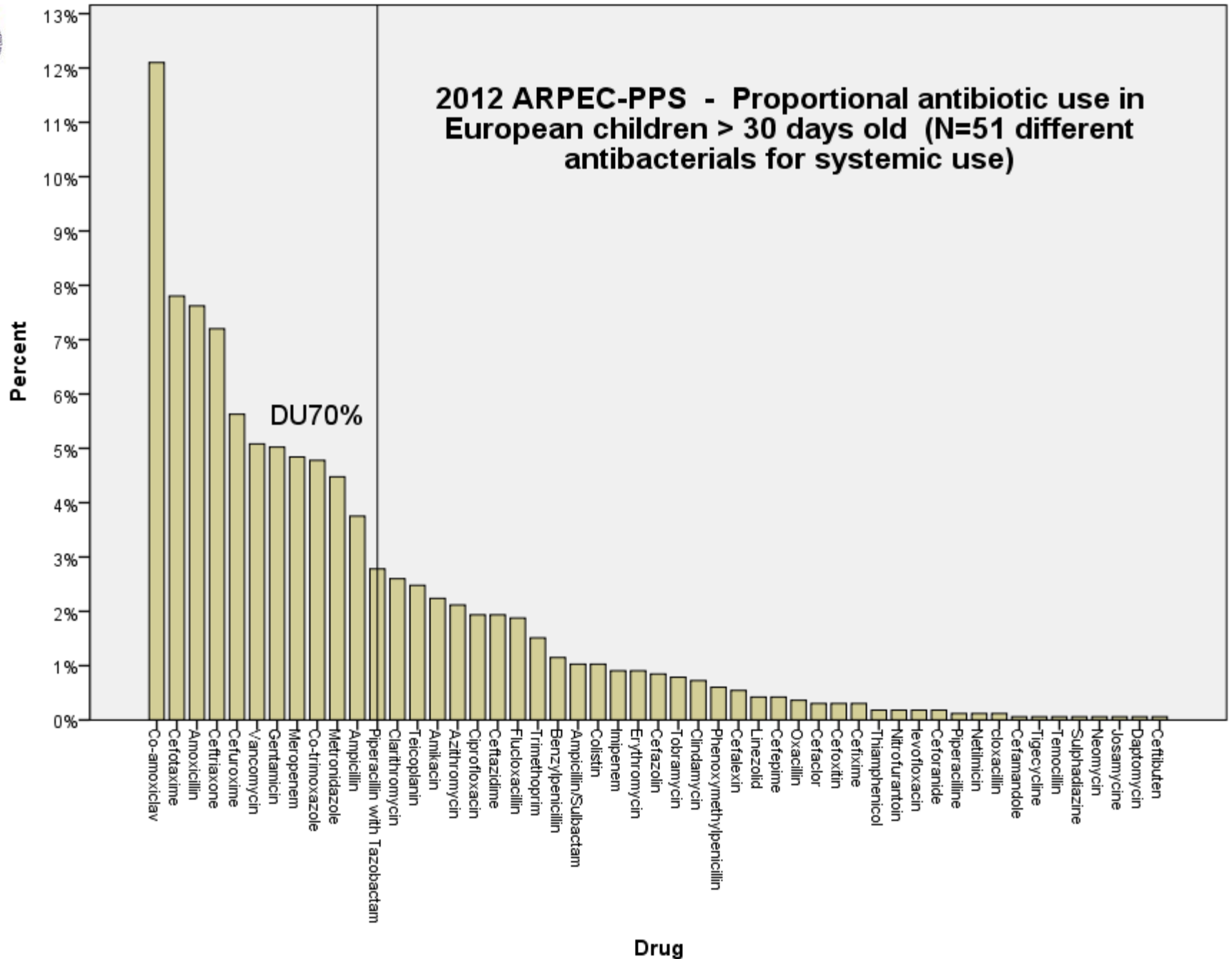


UN region	Treated patients (%)
Europe	36,1%
Asia	58,3%
Oceania	42,4%
Africa	50,3%
Latin America	52,1%
Northern America	40,1%

**Degree of participation
2012 ARPEC-PPS
(226 CENTERS)**



2012 ARPEC-PPS - Proportional antibiotic use in European children > 30 days old (N=51 different antibacterials for systemic use)



Summary

- Many examples of good practice
- Good relationship with a company in one area – different in other areas.
- Networks need to get more organised – developing a few centres that can deliver.
- Working with complex different overlapping clinical networks – neonatology/oncology – who benefits..?
- Core funding – Secretariat – study top slice..?
- Building relationships the key – more proactive with industry – searching their pipeline..