PENTA-ID and Pharma collaborations – Enpr-EMA 2013

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

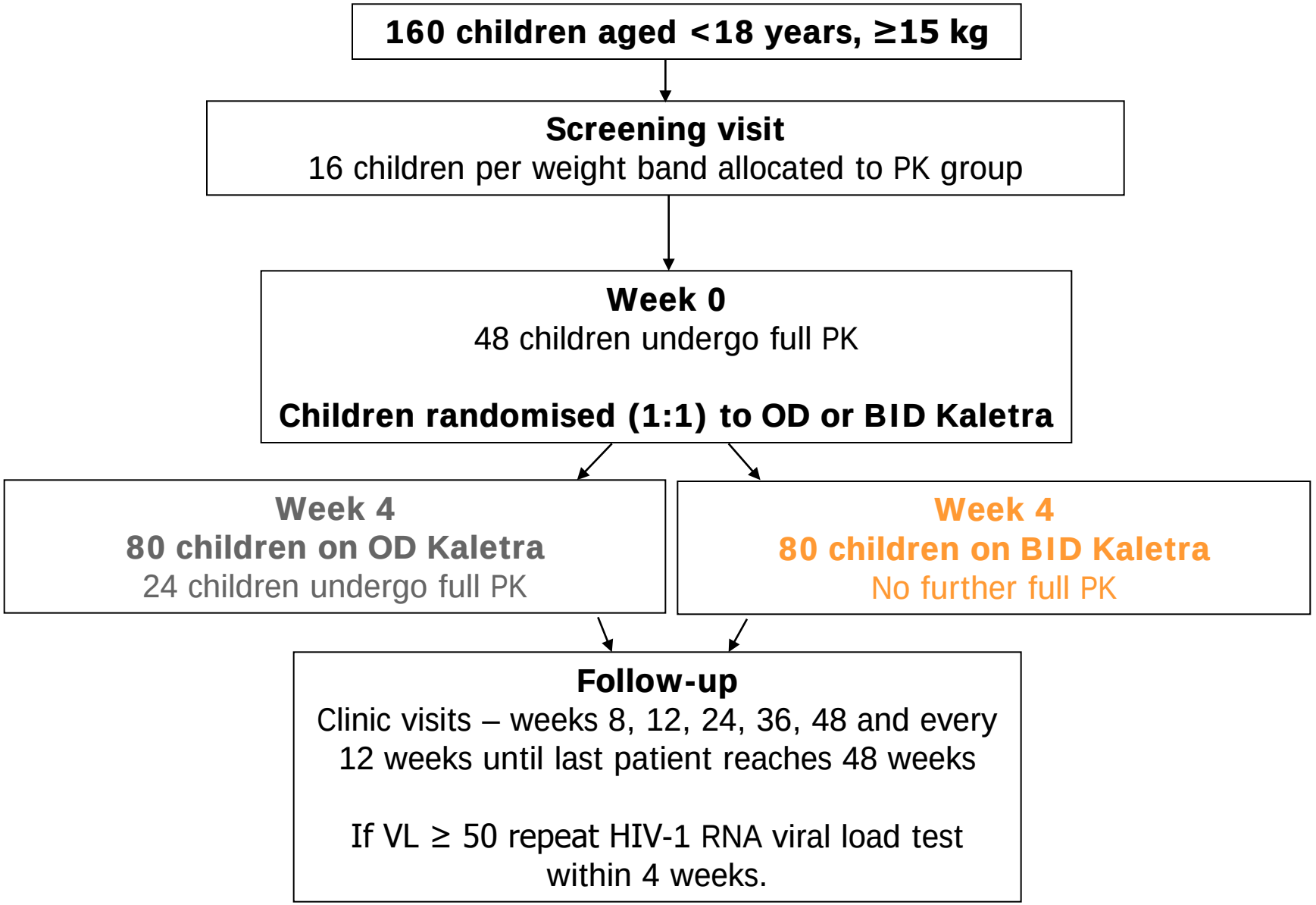
- EMA: dosing based on body surface area:

  230mg/m^2 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



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

panna

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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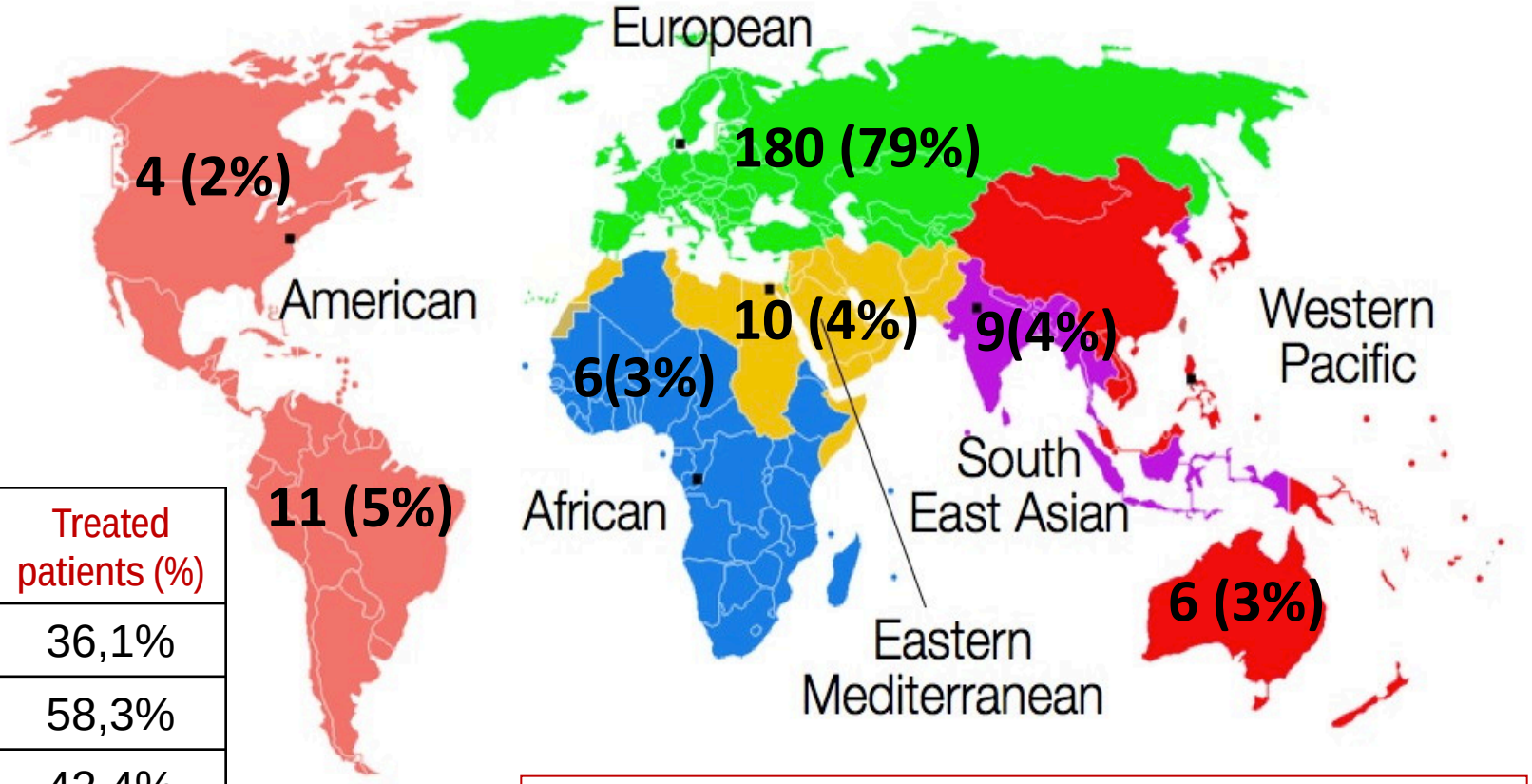
ABSTRACT

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.

Other examples

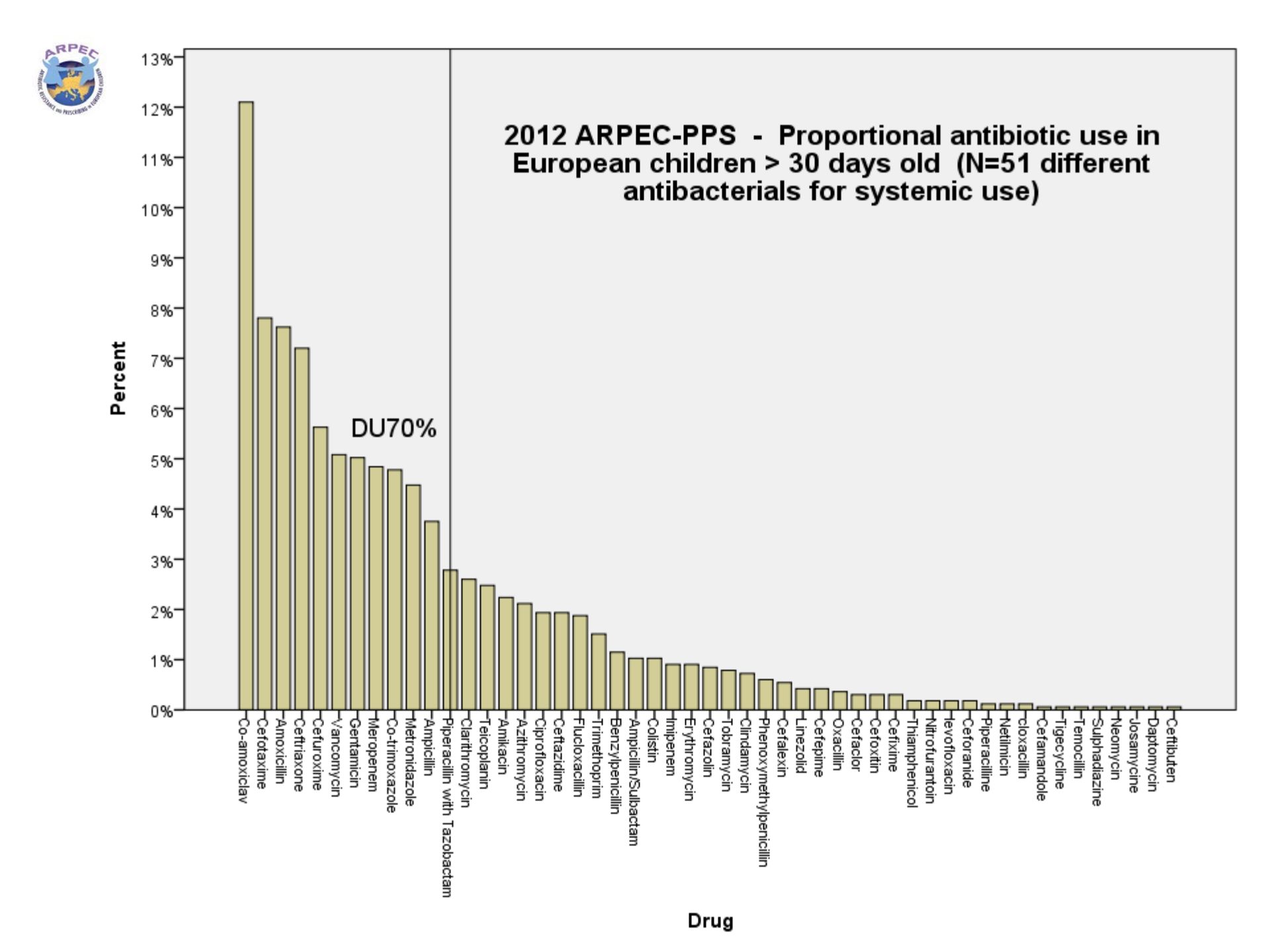
- NeoMero – Phase 3 – PUMA – Chiesi
- NeoVanc – Phase 2a – PUMA – Therakind – SME.
- Antifungals
- Antivirals
- COMBACTE – IMI AMR

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)
Percent
13%
12%
11%
10%
9%
8%
7%
6%
5%
4%
3%
2%
1%
0%
DU70%
Co-amoxiclav
Cefotaxime
Amoxicillin
Ceftriaxone
Cefuroxime
Vancomycin
Gentamicin
Meropenem
Co-trimoxazole
Metronidazole
Ampicillin
Piperacillin with Tazobactam
Clarithromycin
Teicoplanin
Amikacin
Azithromycin
Ciprofloxacin
Ceftazidime
Flucloxacillin
Trimethoprim
Benzylpenicillin
Ampicillin/Sulbactam
Colistin
Imipenem
Erythromycin
Cefazolin
Tobramycin
Clindamycin
Phenoxymethylpenicillin
Cefalexin
Linezolid
Cefepime
Oxacillin
Cefaclor
Cefoxitin
Cefixime
Thiamphenicol
Nitrofurantoin
levofloxacin
Ceforanide
Piperacilline
Netilmicin
cloxacillin
Cefamandole
Tigecycline
Temocillin
Sulphadiazine
Neomycin
Josamycine
Daptomycin
Ceftibuten
Drug

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..