The Role of Enpr-EMA
-
A Neonatal Network‘s Perspective

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KLINIK FÜR KINDER- UND JUGENDMEDIZIN

GNN
German Neonatal Network

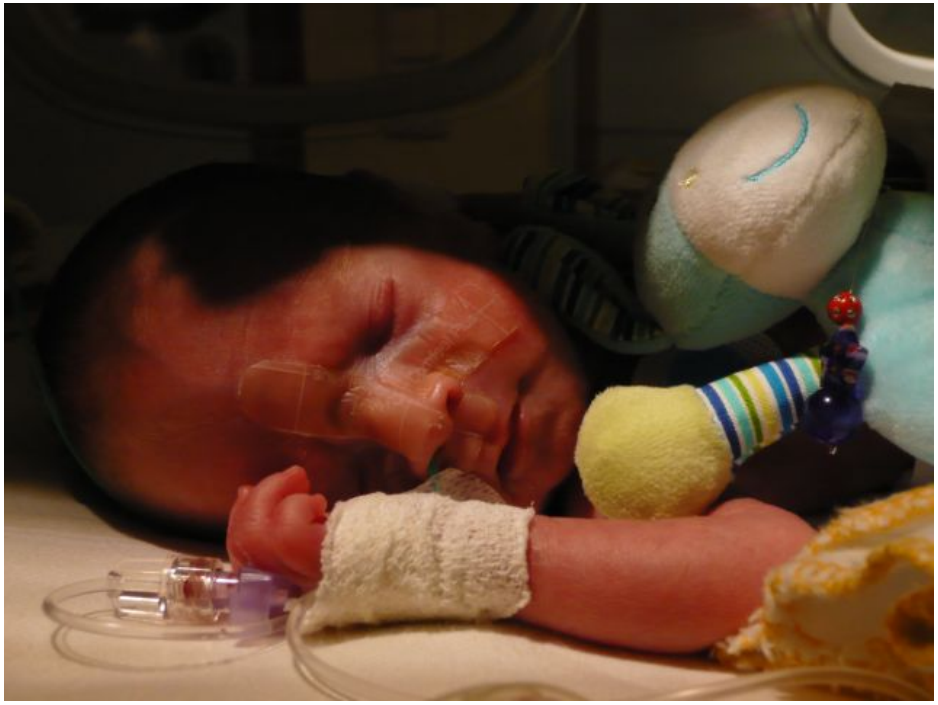
Expectations for Enpr-EMA – A Neonatal Network‘s perspective

Who we are

- 40 Neonatal Intensive Care Units from Germany.
- Funding by the Federal Ministry for Education and Research since 2009.
- Last GNN-network meeting in February 2011.

Expectations for Enpr-EMA – A Neonatal Network‘s perspective

Aim of our network



To improve

- **the long term outcome**
- **of preterm infants with a birth weight below 1500 grams**

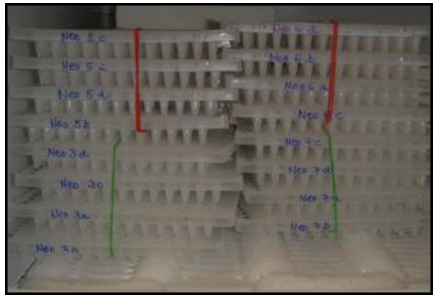
by

- **Identification of clinical and genetic risk factors.**
- **Analysis of centre specific treatment strategies.**
- **Supporting clinical trials.**

Expectations for Enpr-EMA – A Neonatal Network's perspective

What we do

Logistics



Biobank

Genotyping

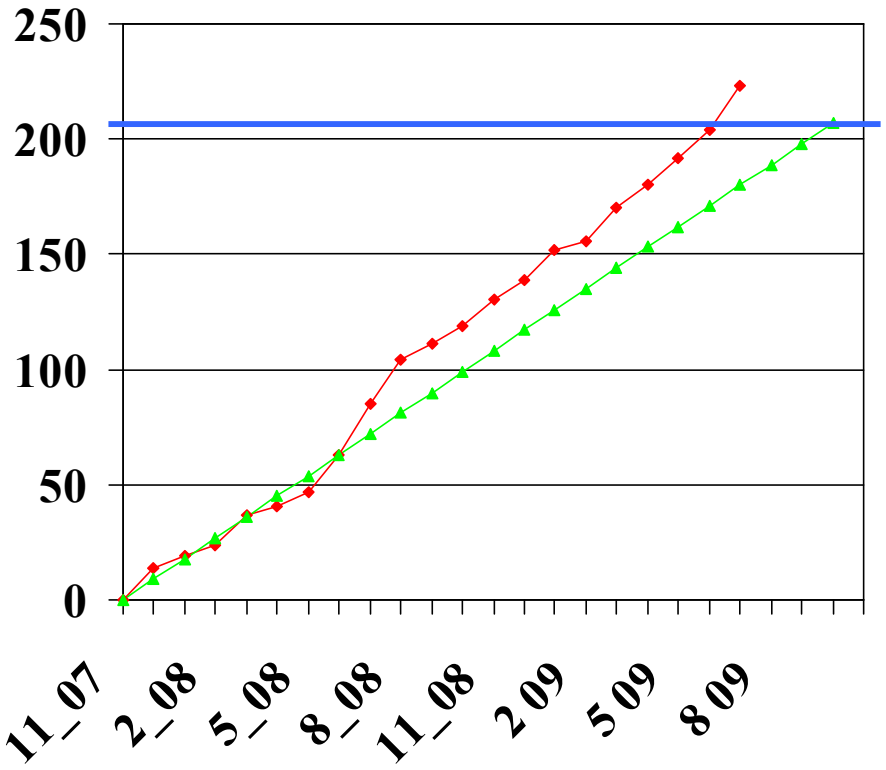
Reports

RCT

- **Logistics:**
  Transfer and storage of biosamples for more than 40 neonatal intensive care units.
- **Biobank:**
  Phenotypes and DNA-samples of more than 7000 very low birth weight infants (5000 mother/infant pairs).
- **Genotyping:**
  - **Genome wide association studies in preterm infants in 2011.**
  - **Single Nucleotide Polymorphism genotyping facility for confirmation studies (>2000 SNPs/day)**
- **Clinical data:**
  Regular reports for all participating centres.
- **Randomised controlled trials:**
  The first GNN-investigator initiated trial was completed in 2010. Another will complete enrolment in 2011/2.

Expectations for Enpr-EMA – A Neonatal Network‘s perspective

Problems with clinical trials

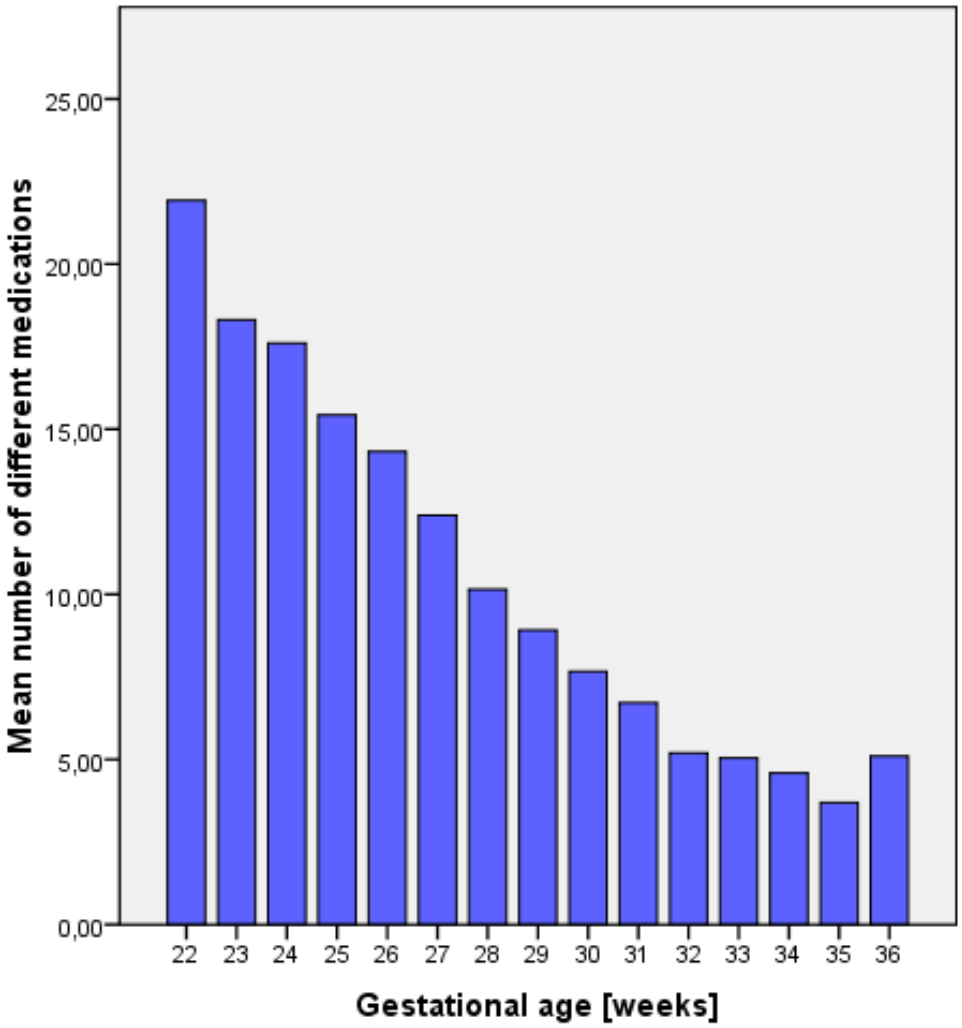


Enrolment of patients in the AMV-trial:
Green line: planned enrolment
Red line: achieved enrolment

Problems of neonatologists with clinical trials:

- Is there a chance, that the medication studied is really beneficial?
- No sufficient infrastructure for clinical trials (e.g. study nurses).
- Overwhelming documentation (CV, CRF, SAE…); some within 24 hours.

Why are clinical trials in newborns and preterm infants so important?



- In a UK study, 90% of all babies on a neonatal intensive care ward received a drug that was either unlicensed or used „off label“ (Arch Dis Child 1999; 80:F142-5).

This is a severe problem since newborns are special:

- Side effects are underreported.
- Drug absorption via the gastrointestinal tract is variable.
- Their total body water is much higher than in adults.
- Many enzymes involved in drug metabolism have a reduced activity in newborns.
- Renal function – which is crucial for the excretion of many drugs – depends on gestational and postnatal age.
- Drug interactions might be excessive, especially in preterm infants (figure, n=4853).

Expectations for Enpr-EMA – A Neonatal Network‘s perspective

Expectations I: Trials

NEOOPIOD	SW	Fentanyl, Morphine	2008
TINN	FR	Fluconazole Ciprofloxacin	2008
NEMO	UK	Bumetanide	2009
THE HIP TRIAL	IR	Dopamine, Adrenaline	2010
NEUROSIS	D	Beclomethasone	2010
NEOMERO	I	Meropenem	2010
TINN2	FR	Azithromycin	2011
NeoCirc	UK	Dobutamine	2011

- Support clinical studies on drugs which are already in use – although not licensed (FP7-trials see table).
- Support licensing and clinical studies for new medications which might be beneficial for newborns (e.g.: analgesics with less side-effects, new antibiotics)
- Support interaction between groups studying drugs in newborns (e.g. face to face meetings of FP7 projects).

Expectations II: Monitoring and Documentation

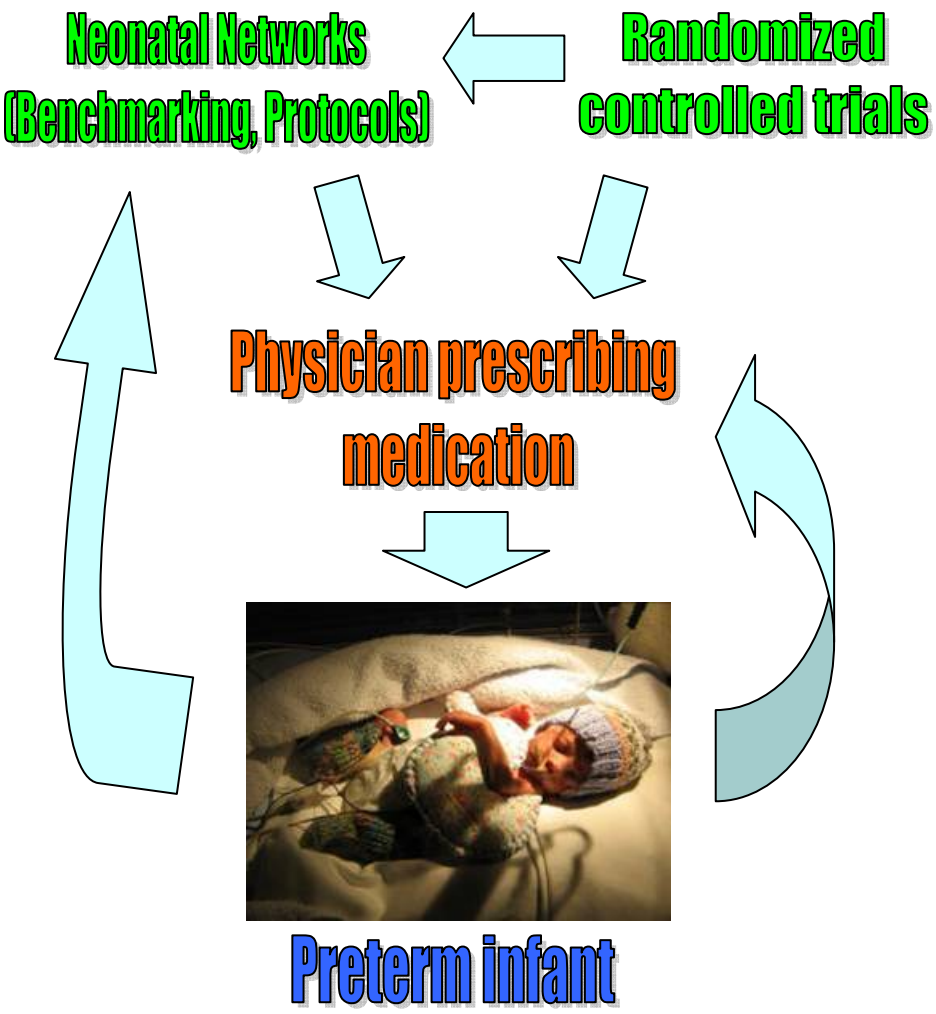
KISS: Keep It Simple and Smart

- Simple methods for collecting, storage and analysis of biosamples.
- Simple methods for documentation of exposures, endpoints and severe adverse events (SAEs).
- Smart methods for drug monitoring and pharmacokinetics.
- Limit/reduce bureaucracy (especially for investigator sponsored trials).

Expectations III: Challenges of the future

- We need data from very large cohorts of preterm infants.
- Translational medicine in Neonatology:
  - Transfer of study data into clinical practice.
  - Transfer of best-centre data into treatment protocols
- Personalised medicine will be much more relevant than nowadays, especially for drug prescription in neonates and preterm infants:

  Individual dosing including
  - Analysis of monitoring data
  - Pharmacogenetics
  - Drug interactions
  - Mikrobiom analysis



Personal Conclusions

- It is very important to communicate, that research is helpful to improve neonatal care.
- In the forthcoming years, the German Neonatal Network will focus its efforts on translational and personalised medicine.
  - Translational Medicine
    - Transfer of new RCT-data.
    - Development of suitable protocols.
  - Personalised Medicine
    - Analysis of large cohorts.
    - Reduce costs of sampling and biobanking.
    - Reduce costs of phenotyping.
- The GNN is keen to learn from other paediatric networks and to share its expertise with Enpr-EMA.
- Finally, neonates and their parents should benefit from all our efforts.