

Clinical Pharmacology, Efficacy, and Safety of the Anti-Hepcidin Spiegelmer[®] Lexaptetid Pegol (NOX-H94)

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Disclosures

Employment

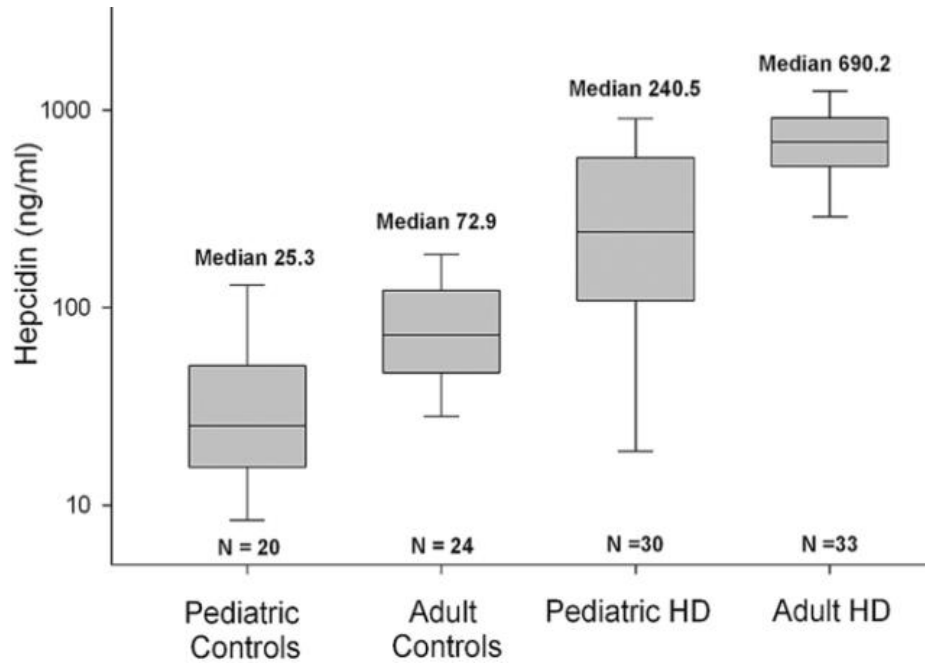
- NOXXON Pharma AG

Funding

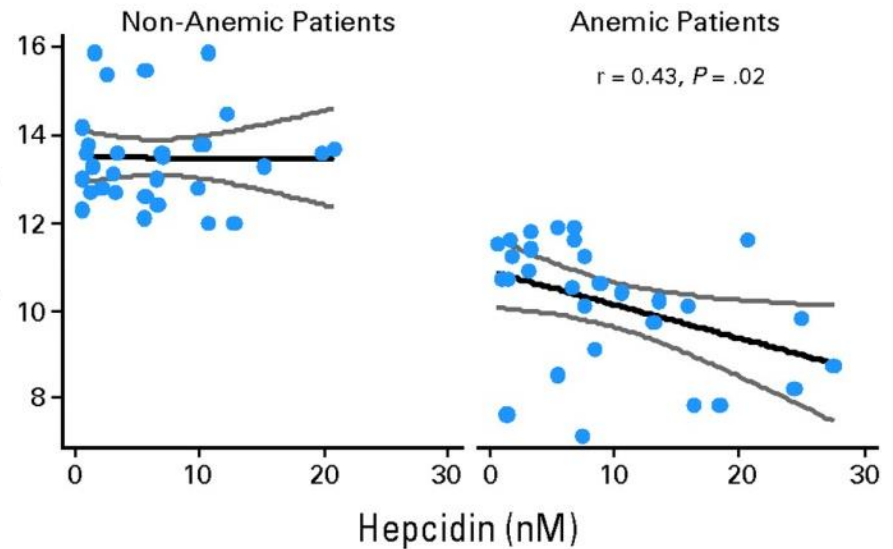
- NOXXON Pharma AG
- Bundesministerium für Forschung und Technologie

High Hepcidin Causes Anemia of Chronic Disease

Hepcidin levels in patients on hemodialysis and in controls
(Zaritsky 2010)



Hemoglobin and Hepcidin levels in patients with Hodgkin's disease
(Hohaus 2010)

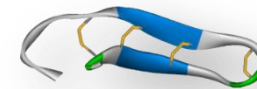


Lexaptepid Pegol

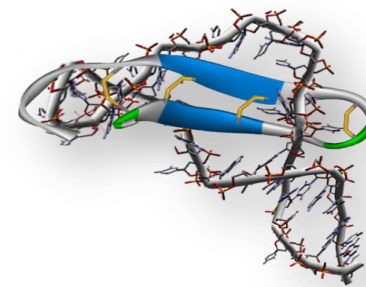
- Single-stranded structured L-RNA oligonucleotide with 44 nucleotides
- Conjugation to 40kDa Polyethylene Glycol (PEG)
- Binds and inactivates human hepcidin



**Secondary structure of
lexaptepid pegol (NOX-H94)**



Hepcidin



**Hepcidin bound to
lexaptepid pegol**

Three Clinical Trials Completed

Phase I:

Safety, pharmacokinetics, pharmacodynamics in healthy subjects

- Single ascending IV doses
- Repeated ascending IV doses
- Repeated SC doses

Phase I:

Pharmacodynamics in endotoxemia

- PK/PD in endotoxemia (single IV dose)

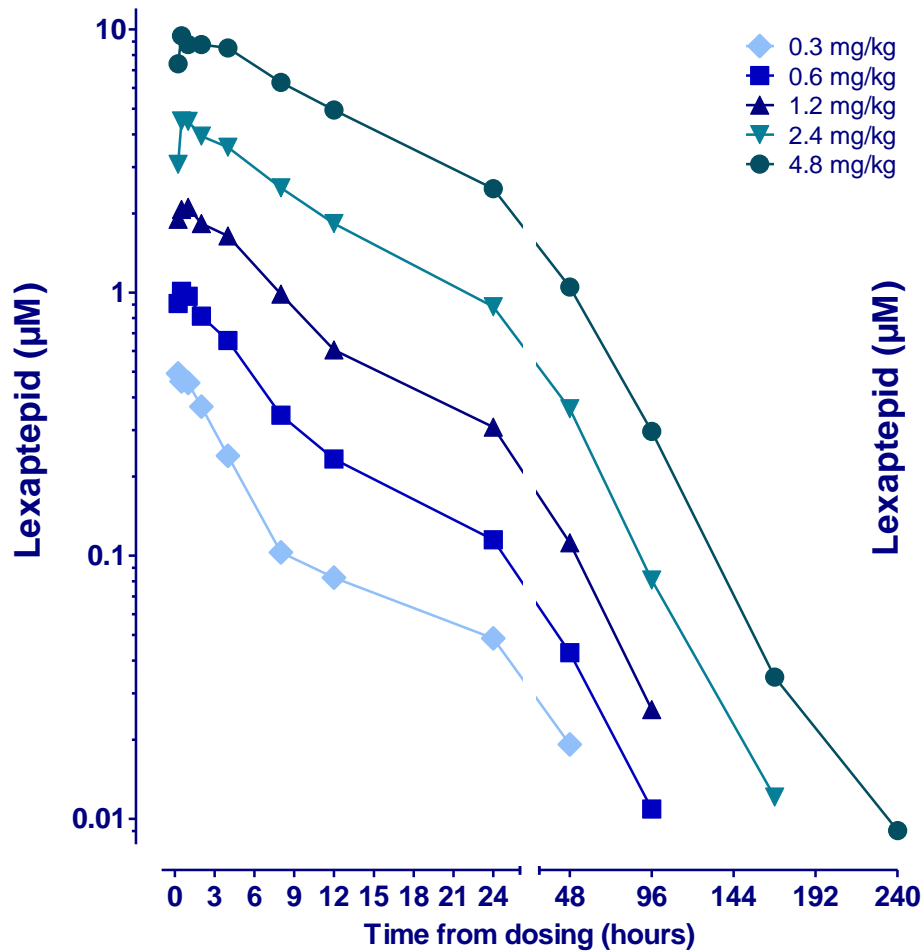
Phase II:

Proof of concept study in patients with cancer

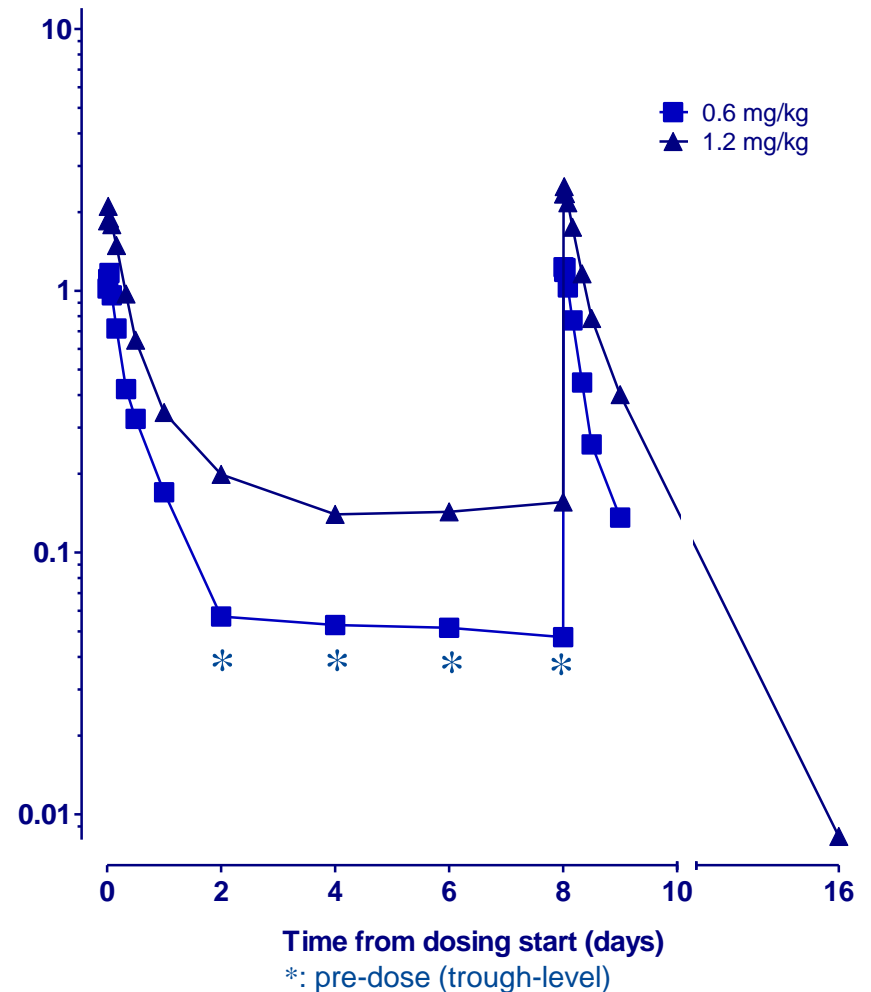
- Efficacy on anemia of chronic disease (4-week IV treatment)

Pharmacokinetics in Healthy Subjects

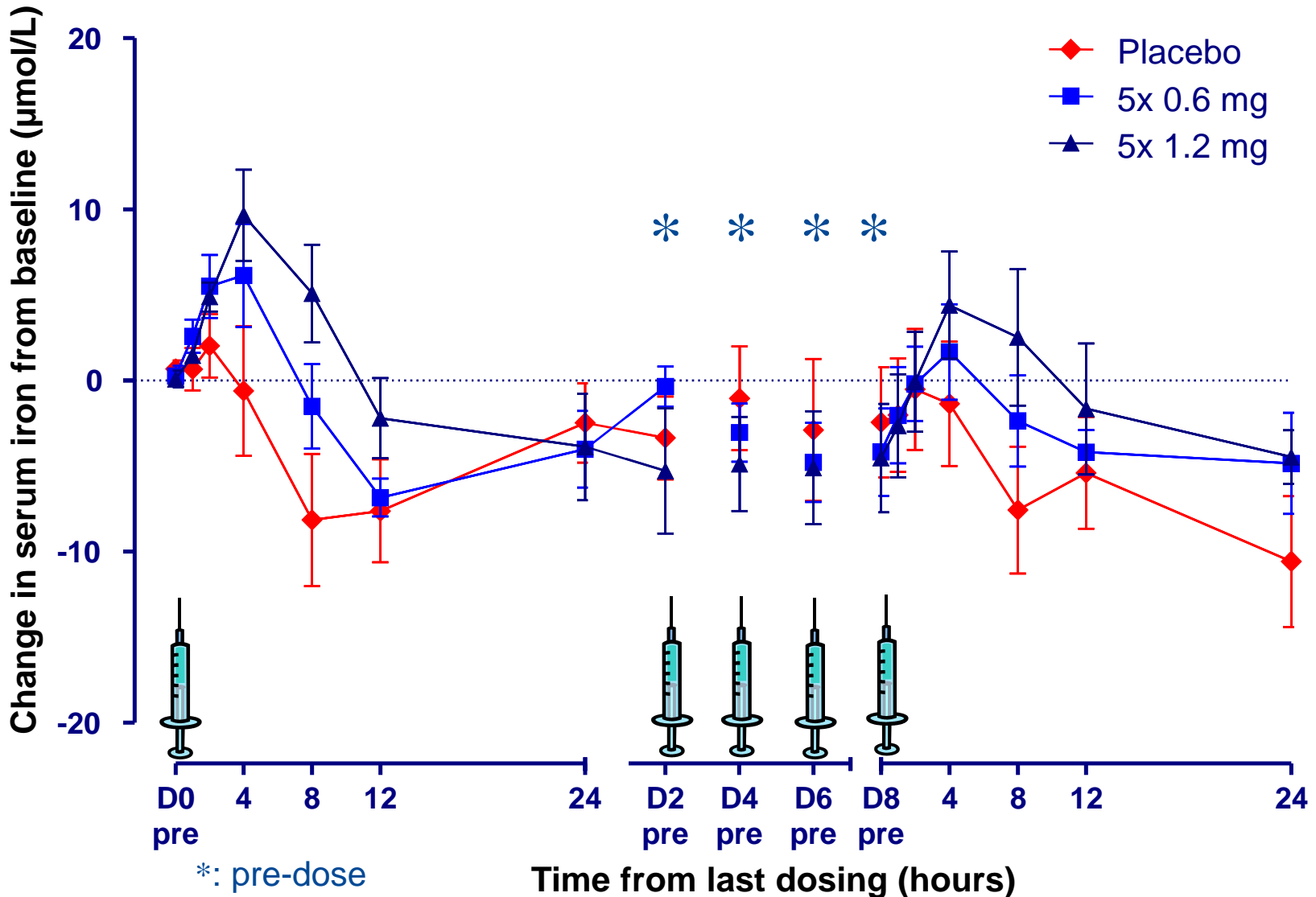
Single IV doses



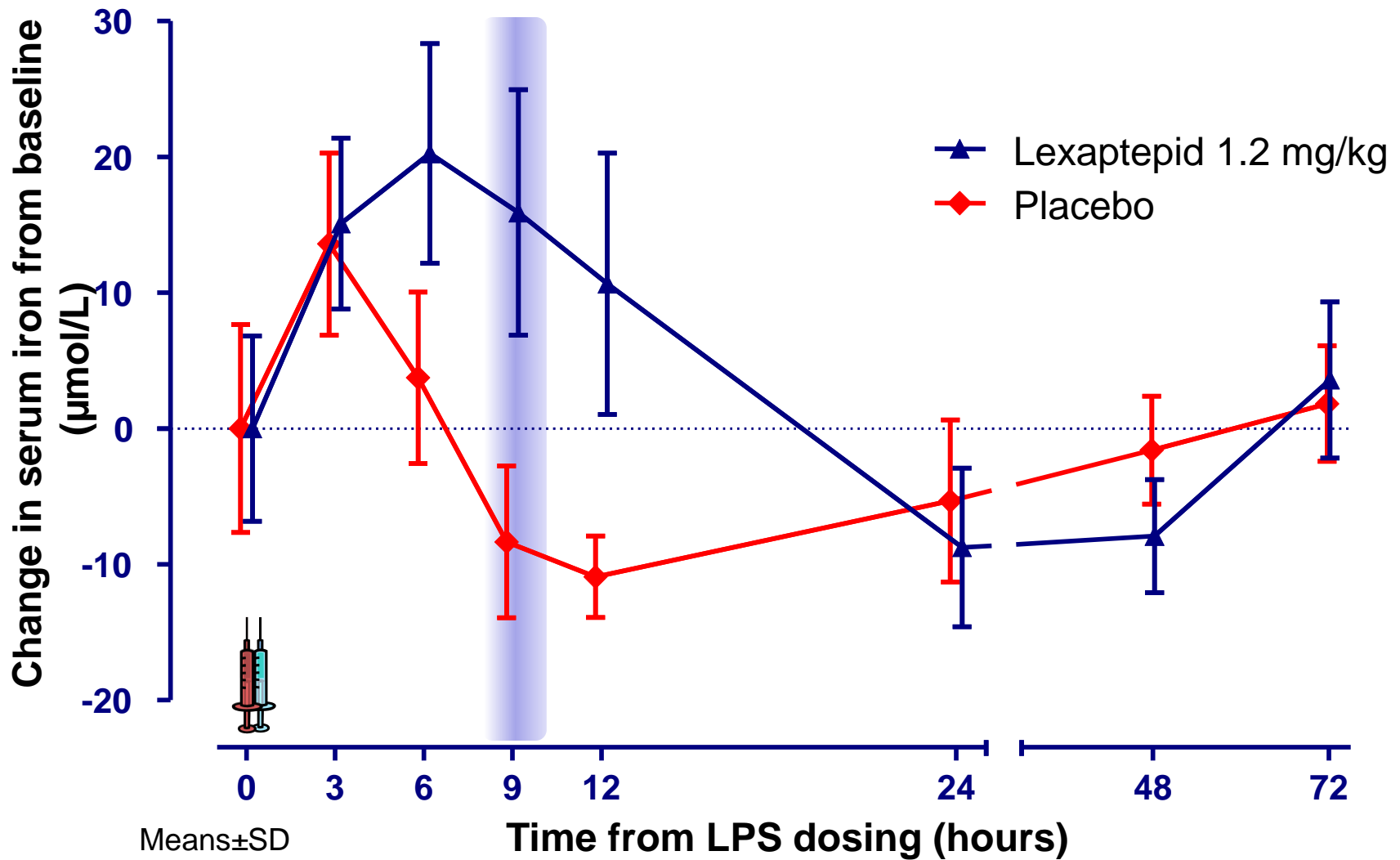
Repeated IV doses



Lexaptepid Increases Serum Iron in Healthy subjects



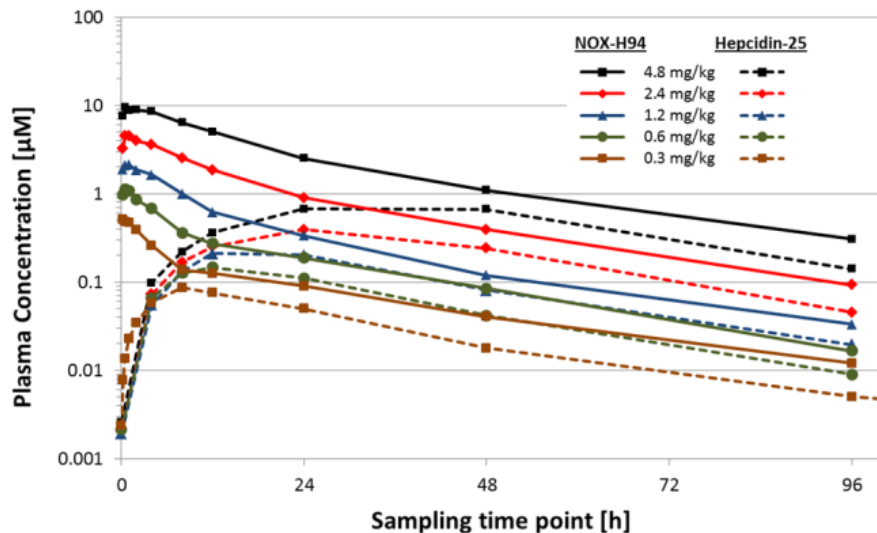
Lexaptepid Increases Serum Iron in Inflammation



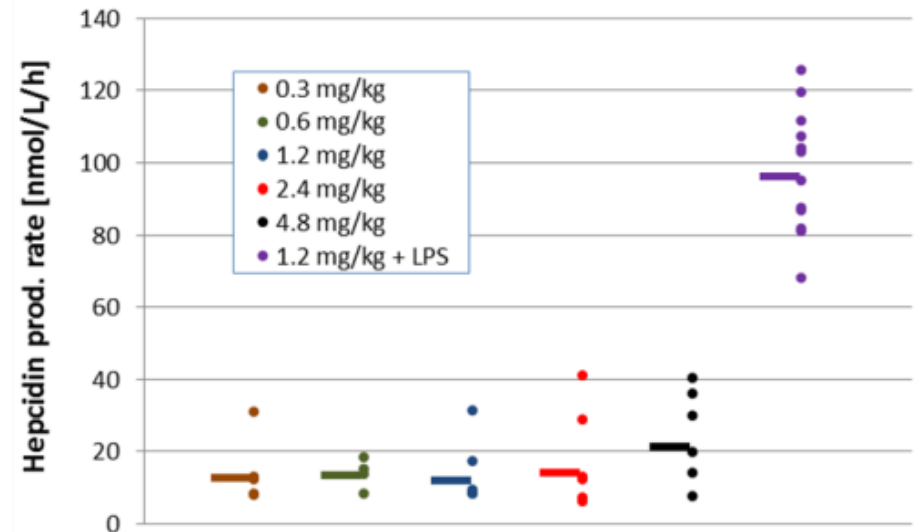
Plasma Hepcidin-25

- Analyzed by validated MALDI-TOF in Plasma
- Assay detects the sum of free and bound hepcidin
 - Hepcidin concentrations, bound hepcidin, increase in presence of lexaptetid
 - Production rate independent from lexaptetid dose
- Lexaptetid does not increase hepcidin production but decreases the excretion of bound hepcidin

A: Hepcidin and LXP after single IV dose



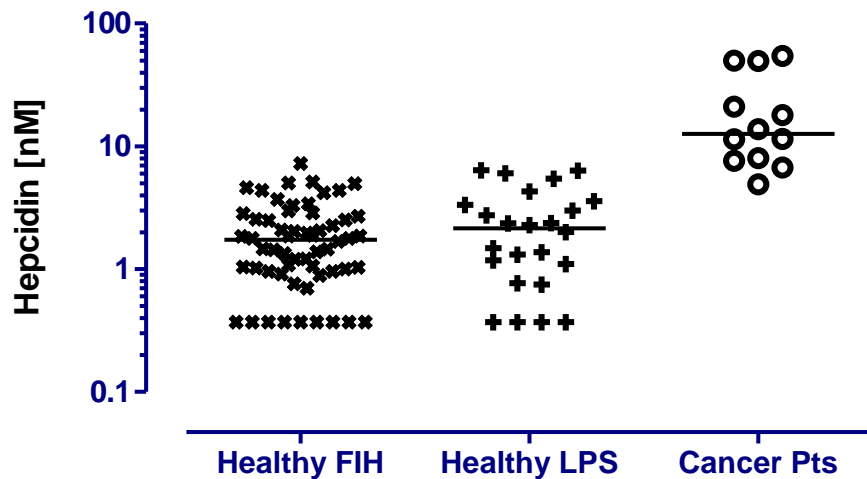
B: Hepcidin production rates after LXP ± LPS



Efficacy in Cancer Patients

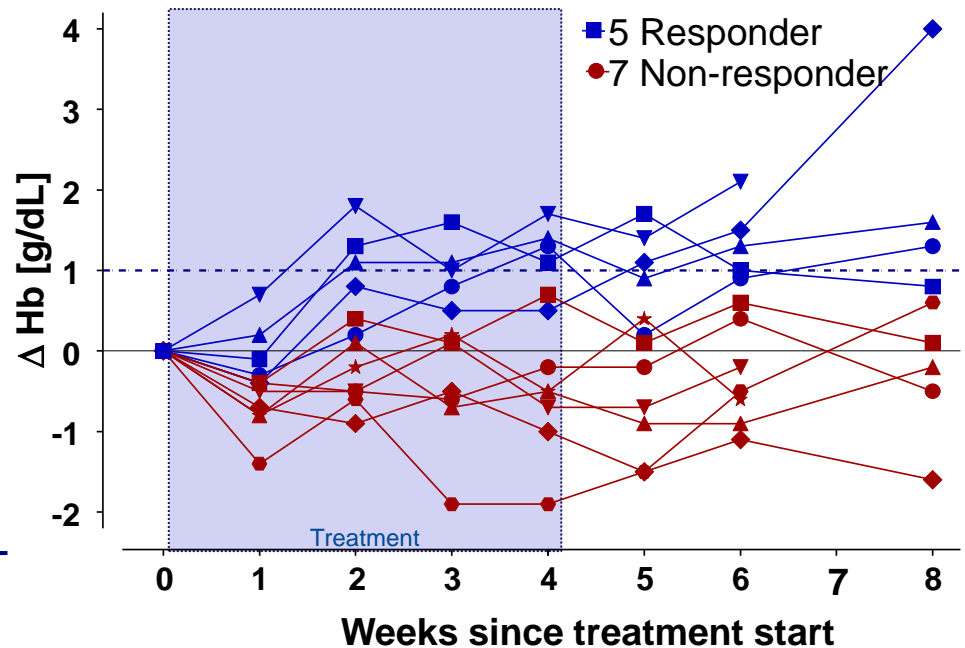
- Pilot group of 12 patients with multiple myeloma / lymphoma
- Anemia 8.0 - 10.7 g/dL;
- Functional iron deficiency TSAT 6.5-25.2%, Ferritin 193-2800 $\mu\text{g/L}$

Basal hepcidin in healthy subjects and patients



Individual data, medians

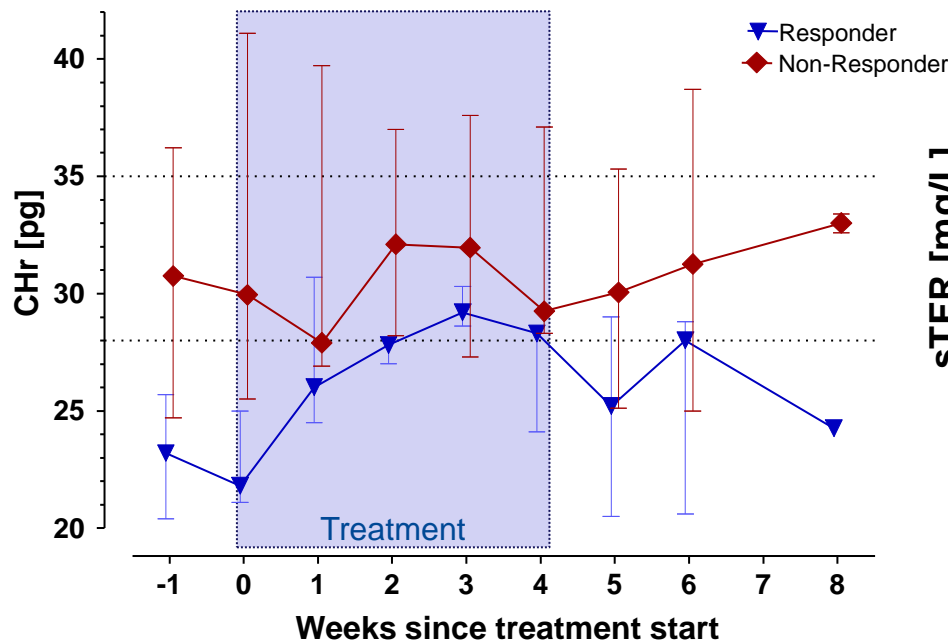
Hb increase after lexaptepid treatment



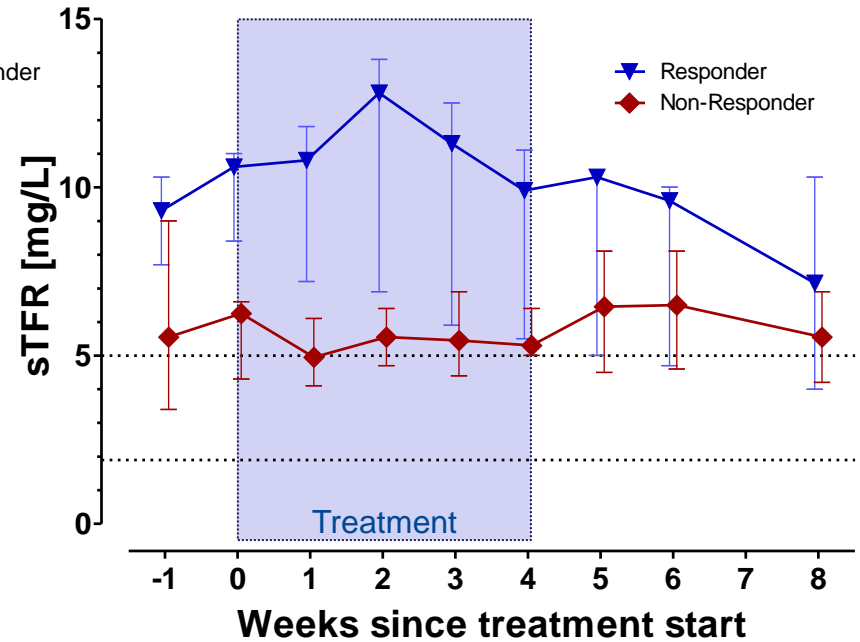
Individual data

Efficacy in Cancer Patients

Reticulocyte hemoglobin



Soluble transferrin receptor



Safety

- Healthy subjects
 - Only typical phase I adverse events
 - Local reactions after SC injection
 - Mild (<2x ULN) and transient ALT/AST increases at high doses
- Patients
 - No relevant adverse event
- Lexaptepid was safe and well tolerated

Summary and Outlook

Lexaptepid inhibits hepcidin activity in humans

- Pharmacodynamic activity in healthy subjects
- Pharmacodynamic activity in inflammation model

First signs of efficacy in cancer patients with functional iron deficiency

- Supported by pharmacodynamic markers
- Favorable safety profile
- ↩ **Pilot study in dialysis patients ongoing**

Thanks to: Investigators, Colleagues, Subjects, Patients



Hammersmith
Medicines Research



NOXXON

| P H A R M A A G



Hepcidinanalysis.com
service in mass
spectrometry



King's College Hospital
NHS Foundation Trust



Radboudumc
university medical center

