Exploratory objectives model, 2
Adverse events were mild in intensity with no clear dose dependency (Weber et al, 2012), is responsible for edema and a secondary increase in basal Ca²⁺ levels leading to myofiber necrosis and muscles degeneration (Burr et al, 2015)

Phase II/III prerequisites

Extensive Toxicology package did show that Rimeporide was safe
- Repeated oral toxicity studies up to 26-week in rats and up to 39-week in dogs showed the main target organ in both species to be fundic parietal cells (reversible mild parietal cells alteration).
- No mutagenic activity nor teratogenic potential were shown
- No impairment of male and female fertility
- No skin sensitizing properties
- No effect on cardiovascular hemodynamic parameters, no evidence of risk for any pro-arrhythmic effects
- No relevant effects on the central and peripheral nervous system, nor on the gastro-intestinal, renal and respiratory system

Rimeporide Clinical trial status update

A complete safety & PK in healthy adults and congestive heart failure patients
- Clinical pharmacology studies in over 166 healthy and CHF patients:
  - Single oral and IV administration
  - Multiple oral doses administration
  - Food interaction
  - Drug Drug Interaction with Digoxin
  - Safety, tolerability, PK in CHF patients with renal insufficiency
- Adverse events were mild in intensity with no clear dose dependency
  - headache (≥15%), dizziness (≥ 5%), chest discomfort (≥10%), paresthesias, vaso-vagal attacks, local skin reactions. No clinically relevant changes in vital signs, ECGs, Laboratory.
  - Similar events reported on Placebo and treated patients

PK profile in Adults

Predicted PK profile in Children

Ongoing Clinical development in patients with DMD (6 to 14 y)
- Primary objective: Determine safety & tolerability of Rimeporide after 4 weeks oral treatment
- Secondary objective : Evaluate the PK profile of rimeporide in plasma
- Exploratory objectives : NMRI indices (T2, Muscle Mass, FF) & Serum Biomarkers

Cohort 1 PK results
- In cohort 1:
  - 5 ambulant DMD patients aged 6 to 10 y, enrolled in France, received oral rimeporide for 4 W
  - No treatment-related adverse events, no significant modification of safety lab & tolerability issues
- In cohort 2: 5 patients (6-10 y) in Italy, Spain & UK completed, safety analysis ongoing
- PK: Visual Predictive Check shows that the adult model, incorporating allometric scaling, adequately reflects the PK in children

ODD Preclinical Poc
2015 2016 2017 2021
Scientific Advice Biomarkers strategy Launch of pivotal study(ies) NDA approval
Phase Ib in DMD patients Phase II/III preparation
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