Addressing Unmet Treatment Needs in POMPE DISEASE

Therapeutic Strategies for Pompe Disease

Enzyme Replacement Therapy

First-generation ERT

Alglucosidase alfa (ALA)
first approved in **2006**

Second-generation ERT

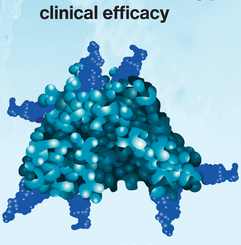
Avalglucosidase alfa (AVAL)
approved **2021/2022** (USA/EU)

Cipaglucosidase alfa with miglustat (CIPA + MIG)
submitted to FDA and EMA

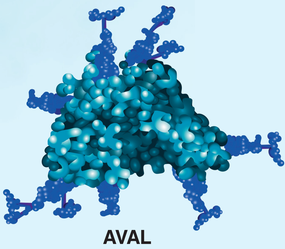
Second-Generation ERT

AVAL

- **Increased enzyme uptake through greater affinity for the M6P receptors on the cells of target tissues**
- **Aim is to enhance glycogen clearance and improve the clinical efficacy**



ALA

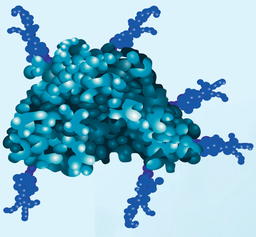


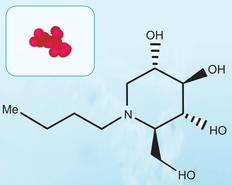
AVAL

COMET Study

- Treatment-naive patients with LOPD (N=100)
- AVAL led to clinically meaningful improvements in respiratory and motor functions over ALA through week 49
- Statistical analysis showed non-inferiority of AVAL to ALA
- Similar IgG antidrug antibody responses with both AVAL and ALA

CIPA + MIG





CIPA

- rhGAA with significantly higher M6P
- Approximately 10x higher bis-M6P
- Enables significantly better tissue uptake and lysosomal targeting
- Endogenous addition of structures retains ability for processing to mature and more active form of rhGAA after uptake

MIG

- Orally administered iminosugar stabilizer
- Reduces rhGAA protein denaturation and aggregation at neutral pH of plasma
- Stabilizes cipaglucosidase alfa in plasma during infusion to provide more active enzyme for uptake into tissues

PROPEL Study

- Pre-treated and treatment-naive patients with LOPD (N=125)
- CIPA + MIG led to improvements in measures of physical and lung function
- After week 52, the difference between groups in change in sitting FVC % predicted was significant (p=.023)
- Safety profile of CIPA + MIG was similar to ALA

Abbreviations

FDA: US Food and Drug Administration
FVC: force vital capacity
EMA: European Medicines Agency
ERT: enzyme replacement therapy
Ig: immunoglobulin
LOPD: late-onset Pompe disease
M6P: mannose 6-phosphate
rhGAA: recombinant human acid alpha-glucosidase

References

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