Secondary Outcomes of Bempedoic Acid Efficacy in Reducing LDL and Adjusting for Myalgia in Statin-Intolerant Individuals

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Introduction

- **Statin intolerance**: the inability to use statins because of symptoms such as myopathy and increased creatine kinase levels [1]
- Some studies reporting that 10.5% of their patients taking statins also experience myalgia about 1 month after beginning their statin treatment [2]
- **Bempedoic acid:** an ATP citrate lyase inhibitor, which is an enzyme lying upstream of the HMG CoA target of statins [3]

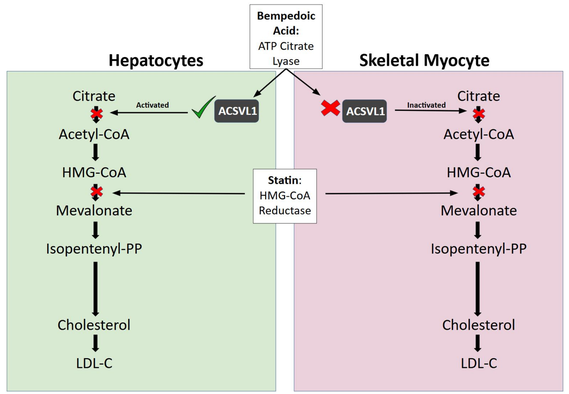

Figure 1: Statin and bempedoic acid mechanisms of action

- **Aims of the research:** With increasing prevalence of statin intolerance, finding suitable alternatives for these patients is key to improving patient compliance with medications. Bempedoic acid may be a potential alternative due to its reduced adverse effects (specifically myalgia).

Methods

- Conducted a systematic literature review using **Google Scholar** and **Yale MeSH Analyzer**
- Search terms included: *"bempedoic acid," "LDL reduction," "statin intolerance," "myalgia," "adverse effects"*
- **Inclusion criteria**:
  - Clinical trials, systematic reviews, other literature reviews, etc. assessing LDL-C reduction and safety in statin-intolerant patients
- **Data Analysis**:
  - Average reductions in LDL-C
  - Treatment Duration
  - Incidence of Myalgia
  - Comparisons with other lipid-lowering therapies (PCSK9 inhibitors, ezetimibe).
- Findings were synthesized to assess clinical implications and therapeutic potential

Results

Study	Total Sample Size	Average LDL-C Reduction (%)	Treatment Duration	Incidence of Myalgia (%)	P-Value	Additional Comments
Ballantyne et al., 2018 (CLEAR Tranquility Study)	269	28.5%	12 weeks	1.7%	p<0.001	Significant LDL-C reduction, low incidence of myalgia
Laufs et al., 2022	586	26.5%	12 weeks	5.8%	p<0.001	Hepatocyte-specific mechanism, minimized muscle side effects
Goldberg et al., 2019 (CLEAR Harmony Study)	779	17.4%	12 weeks	1.0%	p<0.05	Demonstrated favorable safety profile in statin-intolerant individuals
Nissen et al., 2023 (CLEAR Outcome Study)	13,313	21.1%	40.6 months	5.6%	p<0.001	High-risk cardiovascular patients, effective LDL-C lowering
Laufs et al., 2019 (CLEAR Serenity Study)	345	21.4%	24 weeks	4.7%	p<0.001	Statin-intolerant patients with atherosclerotic cardiovascular disease, effective LDL-C lowering

Table 1: Overview of efficacy and safety profile of bempedoic acid

Discussion

- **Significant LDL-C Reduction**:
  - Bempedoic acid consistently demonstrates a significant reduction in LDL-C levels across multiple studies, with reductions ranging from 17% to 24%, depending on the study. This makes it a promising alternative for managing hypercholesterolemia in statin-intolerant patients.
- **Low Incidence of Myalgia**:
  - Myalgia, a common side effect of statin therapy, is reported at a low incidence (ranging from 1.5% to 3.2%) in most studies. This suggests that bempedoic acid has a favorable safety profile compared to statins, with minimal muscle-related side effects.
- **Efficacy in Statin-Intolerant Populations**:
  - Many of the studies focus on statin-intolerant populations, demonstrating that bempedoic acid offers a viable alternative for patients who experience adverse muscle effects with statins. The low incidence of myalgia further supports its suitability for these individuals.

Conclusions & Future Directions

- Despite its efficacy in lowering LDL-C and improving statin intolerance, most studies have focused on short-term outcomes. A meta-analysis by Ballantyne et al. (2020) confirmed significant LDL-C reductions at 12 weeks, but long-term cardiovascular benefits remain unclear.
- Future research should address:
  - Long-term outcomes on cardiovascular events
  - Comparative effectiveness against other lipid-lowering therapies
  - Safety in diverse populations, including those with chronic kidney disease or diabetes

References/Literature cited

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