Moderated 04

Lomitapide for the treatment of paediatric homozygous familial hypercholesterolaemia patients - Results from the efficacy phase of the APH-19 study

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Aim: To assess the efficacy and safety of lomitapide in pediatric patients with homozygous familial hypercholesterolemia (HoFH).
Methods: APH-19 (NCT04681170) is an ongoing phase 3, open-label, single-arm trial of lomitapide in paediatric patients with HoFH receiving standard of care lipid-lowering therapy. The study consisted of a run-in period, followed by a 24-week efficacy phase, 80-week safety phase and follow-up period. Patients were stratified by age into three dose escalation groups: 5 – 10, 11 – 15 and 16 – 17 years, where maximum daily doses were 20, 40 and 60 mg, respectively. Patients were titrated to maximum tolerated doses from a starting dose of 2 mg (patients 5 – 15 years) or 5 mg (patients 16 – 17 years).
Results: Forty-three patients were treated (Female: 55.8%; mean age: 10.7 years). APH-19 met its primary endpoint; mean change from baseline in LDL-C at Week 24 was -53.5% (95% CI -61.6 – -45.4, p<0.0001), with results similar between patients aged 5 – 10 and 11 – 17 (Figure 1). Mean reductions were also observed at Week 24 for non-high-density lipoprotein C (-53.9%; 95% CI -61.7 – -46.1, p<0.0001), total cholesterol (-50.1%; 95% CI -57.6 – -42.5, p<0.0001) and very-low-density lipoprotein cholesterol (-50.2%; 95% CI -59.1 – -41.2, p<0.0001).
Patients reported mild (48.8%), moderate (30.2%) and severe (11.6%) adverse events (AEs). One patient experienced a life-threatening AE (MACE; treatment-unrelated). No serious AEs led to discontinuation.
Conclusions: This study demonstrated that lomitapide significantly reduced LDL-C levels in paediatric HoFH patients. Safety was consistent with the known profile of lomitapide, with no new signals identified.

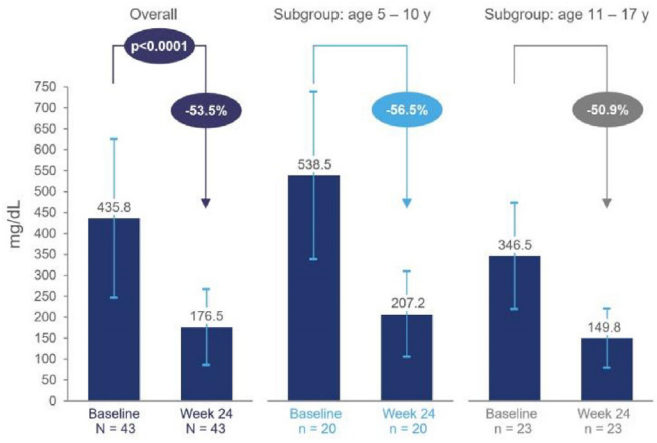

Figure. Mean (SD) change from baseline in LDL-C (mg/dL) at Week 24: Overall population and by age group.

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Moderated 05

How many FH genetic tests were performed by the UK Genetic Laboratory Hubs in 2022?

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Background: The NHS 2019 Long Term Plan (LTP) set an ambition of "identifying 25% of the predicted 150,000 FH patients in England, of whom only ~7% were currently known". To monitor progress towards achieving this target, The FH Oversight Delivery Board has requested the Genomic Laboratory Hubs (GLHs) to provide twice yearly data on the number of FH index case tests (R134) and relative tests carried out, and the proportion where an FH-causing variant has been identified,
Methods: Data was collected from all 7 GLHs (and the NHSE diagnostic laboratories in Scotland and Wales+Northern Ireland) using a standard template for the monthly number of reported tests over the period August 2021 – September 2022.
Results: Over this period the total number of index case tests was 9522 of which 1662 (17.5%) carried an FH-causing variant (FH+ve). The total number of relative tests was 1733 of which 892 (51.5%) carried the family variant. This equates to 680 index case tests and 123 relative tests per month in the 7 England GLHs, with 1.0 relative tests being carried out per FH+ve index case. In the Scotland and Wales diagnostic laboratories an additional 936 index tests were carried out with 279 (30%) being FH+ve and 432 relative tests carried out with 198 (46%) being FH+ve**.** Overall in the UK, for those where an FH-causing variant was found, 81.8% were in *LDLR*, 14.4% in *APOB*, 2.2% in *PCSK9* and 1.5% in *APOE*. On average, in 0.9% of index case tests a "Hot" Variant of Uncertain Significance was reported (defined as being potentially clinically significant and warranting further testing such as segregation analysis).
Conclusion: Achieving the NHS LTP 25% ambition requires the identification of at least ~37,500 individuals of whom ~8000 are currently known. Based on the current rate of identification, achieving the LTP ambition will take ~13 years, but if the number of tested relative could be increased 3-fold this would reduce to ~8 years.

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Moderated 06

Statin treatment is associated with greater hyperglycaemic response to a glucagon challenge

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Background: Statin treatment is associated with an increased risk of developing type 2 diabetes mellitus (T2D). We have previously demonstrated using pre-clinical models that hepatic cholesterol levels inversely correlate with glucagon sensitivity.
We aimed to determine if treatment with statins is associated with an increased hyperglycaemic response to a glucagon challenge in patients with minimal pancreatic insulin secretion.
Methods: We retrospectively analysed data collected from patients