Interim analysis of a Phase 2 dose ranging study to investigate the efficacy and safety of iptacopan in primary IgA nephropathy

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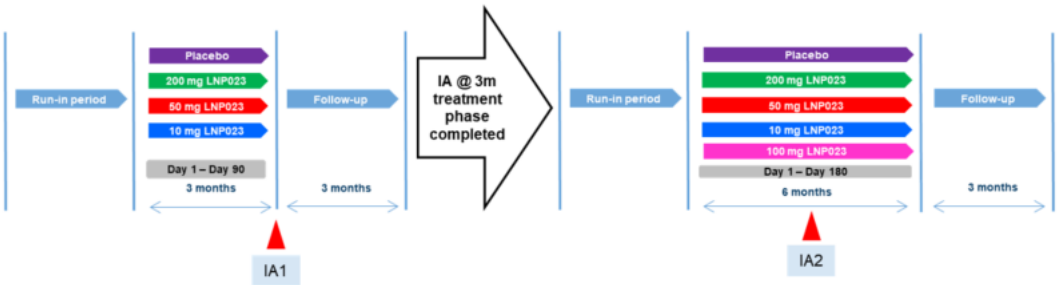
IgA nephropathy (IgAN) is cause of kidney failure with No treatments approved. Alternative complement (AC) pathway has a role in glomerular inflammation and worsening. Iptacopan is a potent selective inhibitor of factor B and AC. We conducted a randomized, double-blind, placebo-controlled, dose-ranging, parallel-group adaptive design phase 2 study of Iptacopan in adult IgAN pts.

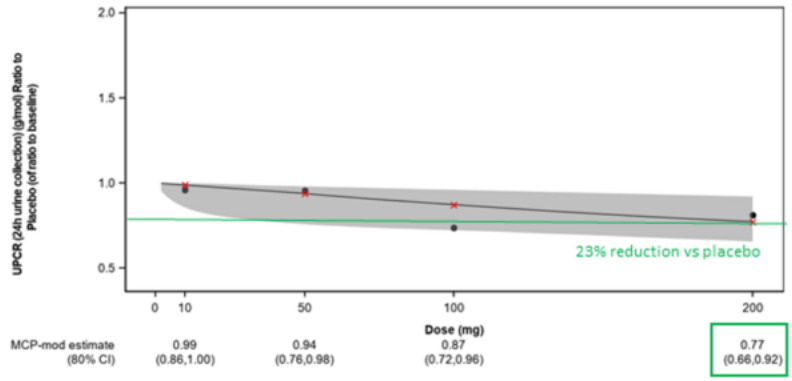
Part 1: 46 pts, 3 doses of Iptacopan or placebo (90 days); interim analysis (IA1) lead to add more pts to Part 2: 66 pts, 4 doses of Iptacopan or placebo (180 days). Second IA Primary goal: dose response effect of Iptacopan on UPCR 24h reduction (90 days).

112 patients were randomized with 4 Treatment discontinuations. Primary analysis: statistically significant dose response (1-sided p=0.038) of iptacopan versus placebo with a 90 day 23% UPCR 24h reduction in the 200 mg b.i.d. arm vs placebo (Fig 2); trends to eGFR stabilization (Fig 3); dose-dependent reduction in serum levels of the Wieslab assay; fall in urine excretion of soluble C5b-9 (creatinine-normalized) and plasma levels of Bb, from Day 8. No severe AEs and deaths reported.
This is the first study on safety and efficacy of selective AP inhibition in IgAN. Iptacopan was well tolerated and resulted in a dose dependent inhibition of measures of AP activity, associated with a significant dose-dependent reduction in UPCR and a trend to eGFR stabilization. These data support further evaluating iptacopan in IgAN in Phase 3 trial.

IgAN Phase 2 (LNP023X2203) – Adaptive, seemless design



Estimated UPCR 24h ratio to placebo (of ratio to baseline) and dose response relationship at Day 90 (Part 1 and Part 2 combined)



Adjusted arithmetic means (80% CI) of change from baseline in eGFR by LNP023 dose over time (Part 1 and Part 2 combined up to 90 days)