

Single dose of iptacopan treatment rapidly decreases plasma complement Bb levels

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Introduction

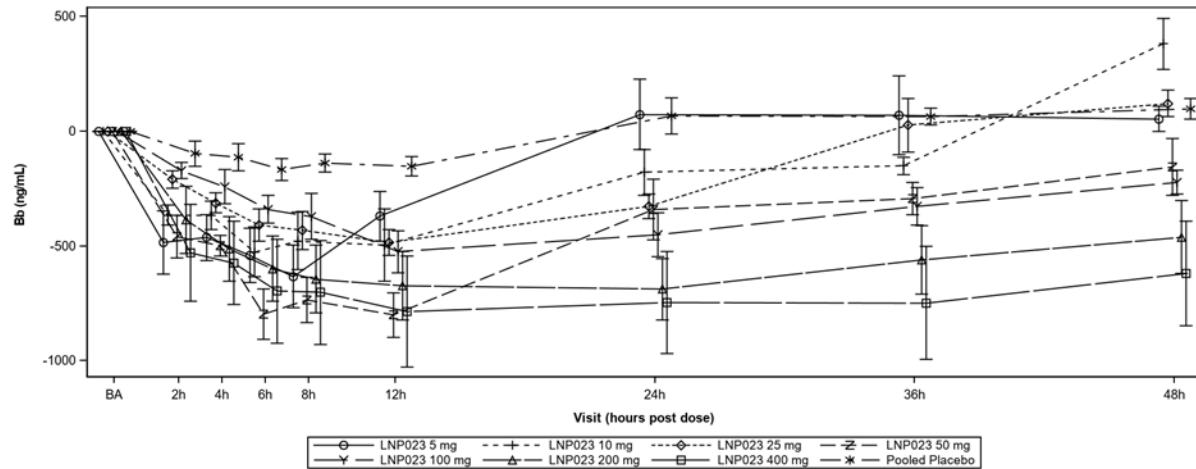
Iptacopan (LNP023) is an oral, first-in-class, low molecular weight inhibitor of Factor B in clinical development for treatment of diseases associated with activation of the alternative complement pathway. Phase 3 studies of iptacopan are ongoing in paroxysmal nocturnal hemoglobinuria, C3 glomerulonephritis, IgA nephropathy, and atypical hemolytic uremic syndrome. The complement fragment Bb, a biomarker of alternative pathway (AP) activity, was measured in healthy subjects to determine the effect of a single dose of iptacopan on the AP.

Methods

In this randomized, blinded study, 56 healthy participants were enrolled into 7 treatment groups to receive a single dose of iptacopan (5–400 mg; n=6 per group) or placebo (n=14). Plasma Bb was measured at baseline and at 8 on-treatment timepoints over 48 hours using a validated immunoassay (LLOQ=484 ng/mL).

Results

Treatment with iptacopan was well tolerated. Mean (\pm SE) change in plasma Bb from baseline in the 8 groups over time is shown (Figure). At baseline, mean plasma Bb was 1324–2180 ng/mL. In contrast to the placebo group, participants in the 7 iptacopan treatment groups exhibited a rapid decrease in plasma Bb at 2 hours post dose. A dose-dependent, persistent effect was seen at 24 hours post dose, with the highest mean decrease in Bb (approximately 700 ng/mL; ~50%) seen with 200 and 400 mg iptacopan.



Conclusion

Similar to previously reported Wieslab data, iptacopan treatment resulted in a rapid, substantial and dose-dependent decrease in Bb. These results support the iptacopan clinical dose of 200 mg twice daily and indicate that oral iptacopan provides durable AP inhibition.

This abstract was also submitted for the NKF'23 congress. By submitting the abstract to WCN'24, abstract authors declare that re-submitting the abstract is permitted by the organizers of the previous meeting.

Theme

The Kidney Losing Function: Dialysis, CKD-MBD, Anemia and Interventional Nephrology

Topic

CKD, experimental models, biomarkers , precision medicine

Key words (5 maximum)

complement, iptacopan, Factor B, IgAN, C3G

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