Abstract: PO2536

Iptacopan, a Novel Oral Complement Factor B (FB) Inhibitor, Significantly Reduces Proteinuria and C3 Deposit Scores in Native and Transplanted Kidneys C3 Glomerulopathy (C3G) Patients

Session Information

- Late-Breaking Clinical Trials Posters
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- 1002 Genetic Diseases of the Kidneys: Non-Cystic

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Background

C3G is a rare, inflammatory KD caused by genetic mutations or auto-AB that dysregulate the complement system.

With no approved therapies, progression to ESRD is frequent.
Iptacopan is a new, highly selective oral LMW inhibitor of FB, a key complement alternative pathway (AP) protease.
We report final Ph2 data [NCT03832114] for iptacopan in pts with native or recurrent C3G post kidney Tx.

Methods

Adults with biopsy-proven (Bx), native (CoA) or recurrent C3G post KTx (CoB) received iptacopan for 12 wks (W).
CoA had proteinuria >1g/24h despite ACEi/ARB, and all had low C3 levels.
Primary endpoints (pEP) were reduction in UPCR from baseline (BL) to W12 for CoA; change in C3 Deposit Score (DS) for CoB.
Pts were invited to continue iptacopan in a long-term extension trial [NCT03955445].

Results

All pts (N=16/11 in CoA/B) completed the trial.
BL mean age 26.1/34.5 yrs; geo-mean UPCR (24h) 401.9/36.2 g/mol; mean eGFR 70.1/52.2 mL/min in CoA/B; median C3 DS 3.0 in CoB.
Iptacopan was well tolerated without any drug-related serious AE.
CoA pEP met with -45% in UPCR from BL to W12 (p=0.0003) [**Fig 1A**].
CoB pEP met with significant reduction in C3 DS in kidney Bx from BL to W12 (p=0.0313) [**Fig 1B**].
A profound and sustained inhibition of the AP [**Fig 1C**] and normalization of C3 levels were observed [**Fig 1D**].
eGFR was stable with mean change from BL to W12 of +1.04 mL/min.

Conclusion

Treatment with iptacopan 200 mg bid in patients with native or recurrent C3G was well tolerated and resulted in statistically significant and clinically important reduction of UPCR, normalization of C3 levels, stabilization of eGFR, and significant reduction in histologic C3 DS in follow-up kidney Bx. Iptacopan is now tested in a pivotal Ph3 trial APPEAR-C3G [NCT04817618].

Funding

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