Abstract: PUB236

Nonclinical Safety and PK/PD of BION-1301, a Fully Blocking Antibody Targeting A PRoliferation Inducing Ligand (APRIL) for the Treatment of IgA Nephropathy

Session Information

- Publication Only

Category: Glomerular Diseases

- 1202 Glomerular Diseases: Immunology and Inflammation

Authors

- Kreijtz, Joost, Aduro Biotech Europe, Oss, Netherlands
- Van zandvoort, Peter, Aduro Biotech Europe, Oss, Netherlands
- Van de crommert, Johannes, Aduro Biotech Europe, Oss, Netherlands
- Mueller, Thomas, Aduro Biotech Inc, Berkeley, California, United States
- De greef, Rik, Certara, Oss, Netherlands
- van Elsas, Andrea, Aduro Biotech Europe, Oss, Netherlands

Background

IgA Nephropathy (IgAN) is a common form of glomerulonephritis and its pathogenesis is thought to consist of sequential pathogenic hits, including the critical production of galactose-deficient IgA1 (Gd-IgA1) and auto-antibody formation ultimately leading to immune complex deposition, inflammation and functional deterioration of the kidneys. Serum levels of APRIL (A PRoliferation Inducing Ligand, TNFSF13) and levels of Gd-IgA1 are correlated with severity of disease (Zhao et al, 2012). As a ligand for the receptors BCMA and TACI, APRIL is thought to regulate B cells and plasma cells. In nonclinical studies treatment with an anti-mouse APRIL antibody was reported to reduce serum IgA and halt proteinuria progression in the IgAN "grouped ddY" mouse model (Kim et al. 2015; Myette et al 2019). Here we describe the nonclinical safety assessment of BION-1301, a humanized anti-APRIL antibody, to support its clinical development for the treatment of IgA Nephropathy.

Methods

A 14wk repeat-dose safety and pharmacokinetic/pharmacodynamic (PK/PD) study in non-human primates (NHP) (Cynomolgus monkey) was performed by biweekly intravenous (i.v.) administration of BION-1301 at three different dose levels. To support a potential change in route of administration, a 4wk repeat-dose NHP bridging study was conducted with weekly subcutaneous (s.c.) administration of BION-1301 at three different dose levels.

Results

In both the 14wk i.v. study and the 4wk s.c. study, BION-1301 was evaluated for safety, PK and PD. For PK and PD, BION-1301 levels, uncomplexed APRIL levels and immunoglobulin levels (IgA, IgG, IgM) were quantified in serum. Immunophenotyping was performed on peripheral blood to assess the impact of BION-1301 on the B cell compartment.

Conclusion

Results of these extended nonclinical pharmacology and toxicology experiments add to the BION1301 safety, PK, PD assessments reported earlier (Dulos et al, ASN 2018) and inform the ongoing clinical program to develop BION1301 for the treatment of IgAN.

Funding

- Commercial Support