Felzartamab (anti-CD38) antibody for the Treatment of Lupus Nephritis – An Open Label Phase 1b Study

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Lupus Nephritis (LN) and the potential for anti-CD38 therapy

- LN is the most common major organ-threatening manifestation of systemic lupus erythematosus (SLE) that affects ~35-60% of SLE patients
- Only 30-40% of LN patients achieve complete renal response with current standard of care therapy
- A hallmark of LN is high-titer autoantibodies (eg, anti-dsDNA, anti-Smith) which are predominantly produced by CD38+ plasma cells
- CD38 expression is also induced on plasmacytoid Dendritic Cells (pDCs), the primary source of Type I IFN that has been also implicated in the pathogenesis of SLE
- CD38 is thus a compelling target for depletion of pathogenic cells in LN, supported by emerging clinical data that anti-CD38 therapy in LN is well tolerated with evidence of disease improvement or resolution.

Felzartamab Proposed Mechanism of Action in LN

- Felzartamab is a recombinant human IgG mAb that binds the CD38 cell surface antigen with high affinity
- Felzartamab depletes CD38 high antibody-producing cells such as plasma cells/plasmablasts primarily via antibody-dependent cell-mediated cytotoxicity (ADCC) and antibody-dependent cell-mediated phagocytosis (ADCP), with minimal impact of complement-dependent cytotoxicity (CDC)
- In SLE/LN, felzartamab may also deplete plasmacytoid dendritic cells (pDCs) that contribute to disease via Type I Interferon production
- Beyond LN, felzartamab is in development for several immune mediated kidney diseases, including primary membranous nephropathy (PMN), IgA nephropathy, and Ab-mediated kidney transplant rejection
- Felzartamab is well tolerated across clinical studies in immune mediated diseases with encouraging evidence of CD38+ cell depletion and lowering autoantibodies, while maintaining the ability for patients to mount humoral response to vaccines
- In studies of high risk PMN pts, felzartamab resulted in rapid, deep, and durable aPLA2R autoantibody responses with associated improvements in proteinuria and serum albumin.

For further information on felzartamab, see:

- Oral Presentation: “Targeting CD38 with Daratumumab in Refractory Systemic Lupus Erythematosus. November 2, 2023; from 5:24 PM to 5:33 PM; Room 103
- Poster Presentation: "Felzartamab reduces aPLA2R autoantibodies by selectively depleting CD38+ plasma cells and plasmablasts. The main pathogenic cellular driver of disease in Primary Membranous Nephropathy (PMN)." November 4, 2023; from 10:00 AM to 12:00 PM.

For more information about the trial, scan here:

- Acknowledgments and Disclosures

This study is supported by grants from the Kidney Health Initiative. Dynavax Technologies, Inc., is conducting a phase 2b clinical trial that has completed enrollment of patients. Dynavax maintains a research and development license for Felzartamab from MedImmune LLC, which was acquired by AstraZeneca in 2016. Dynavax received $25 million from AstraZeneca for the acquisition of Galapagos AS, in 2018. Dynavax has a pending patent application for use of Felvartamab in the treatment of SLE in children and adolescents. Dynavax has a pending patent application for use of Felvartamab in normal or healthy individuals. Dynavax is conducting clinical trials for both lupus nephritis and kidney transplant patients. Dynavax has a pending patent application for use of Felvartamab in normal or healthy individuals.