Jonathan Barratt, Brian Schwartz, Bess Sorenson, Suzanne Roy, Colleen Stormatt, Margaret MacDonald, Jerlyn Tolentino, Sai Prasad Iyer, Aaron Endsley, Jeannette Lo, Alan Glicklich

University of Leicester, Leicester, UK; Chinook Therapeutics, Inc.; Certara, Inc

Background and Aims

IgA nephropathy (IgAN) is the most common primary glomerulonephritis globally, with up to 45% of IgAN patients at risk of progressing to ESKD. There are currently limited treatment options for IgA nephropathy, especially for patients at high risk of disease progression. The initiating step in IgAN pathogenesis is the excess production of galactose-deficient IgA1 (Gd-IgA1) resulting in formation of pathogenic immune complexes that cause kidney inflammation and damage. A Proliferation-Inducing Ligand (APRIL), a TNF superfamily cytokine, is elevated in IgAN patients and correlated with higher levels of Gd-IgA1 and proteinuria, and lower eGFR. BION-1301 is a novel monoclonal antibody which blocks and blocks APRIL. The primary objective of Study ADU-CL-19 is to assess the safety and tolerability of BION-1301 in Healthy Volunteers (HV) and IgAN patients and to secondarily assess the PK, PD, immunogenicity, and preliminary clinical activity.

Introduction

Role of APRIL and BION-1301 in IgA Nephropathy (IgAN)

APRIL is a 38 kDa, 467 amino acid transmembrane/ secreted protein that functions as a ligand of the TNF superfamily receptor family, binds to TACI and BCMA, and upregulates B-cell survival and differentiation. BION-1301 is a humanized monoclonal antibody which binds and blocks APRIL.

Key Eligibility Criteria

- Age 18 years and older
- Urine protein excretion >0.5 g/24 hr
- eGFR >45 mL/min/1.73 m²

Methods

The Phase 1/2 study (NCT03945318) consists of 3 parts. Parts 1 and 2 were blinded, placebo-controlled single and multiple ascending dose designs in HV and have been completed. Part 3 is a multicenter (US, UK, South Korea) multicohort, open-label study in up to 40 patients with IgAN. Patients in Cohort 1 receive BION-1301 at 450 mg IV every 2 weeks for up to 1 year. Patients in Cohort 1 will transition from IV to receive 600 mg of BION-1301 SC biweekly after completing at least 24 weeks of IV dosing. Subsequent cohorts will be given BION-1301 via SC injection.

Part 1, SAD in healthy volunteers
- BION-1301 (400 mg)
- Part 2, MAD in healthy volunteers
- MAD Cohort 1: 50 mg SC, 40 mg IV Q2W for up to 2 weeks
- MAD Cohort 2: 200 mg SC, 150 mg IV Q2W for up to 2 weeks
- MAD Cohort 3: 500 mg SC, 375 mg IV Q2W for up to 2 weeks

Part 3, Optional additional cohorts in IgAN patients
- IV: 450 mg Q2W, up to 52 weeks
- SC: 600 mg Q2W, up to 52 weeks

RESULTS

Final HV data from Parts 1 and 2 have been presented at earlier conferences. Part 3 is ongoing, and interim data from Cohort 1 with IV dosing are being presented at the WCN 2022 (Abstract P WCN22-0485).

Conclusions

The current design of the Phase 1/2 study, incorporating SC dosing, provides for an improved patient experience, and will enable the generation of long-term safety, PK, PD, immunogenicity, and preliminary activity data for use of BION-1301 in IgAN patients.

References


ADU-CL-19: a Phase 1/2, Multicenter Trial to Investigate the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of BION-1301 in Healthy Volunteers and Adults With IgA Nephropathy

Jonathan Barratt, Brian Schwartz, Bess Sorenson, Suzanne Roy, Colleen Stormatt, Margaret MacDonald, Jerlyn Tolentino, Sai Prasad Iyer, Aaron Endsley, Jeannette Lo, Alan Glicklich

University of Leicester, Leicester, UK; Chinook Therapeutics, Inc.; Certara, Inc

Background and Aims

IgA nephropathy (IgAN) is the most common primary glomerulonephritis globally, with up to 45% of IgAN patients at risk of progressing to ESKD. There are currently limited treatment options for IgA nephropathy, especially for patients at high risk of disease progression. The initiating step in IgAN pathogenesis is the excess production of galactose-deficient IgA1 (Gd-IgA1) resulting in formation of pathogenic immune complexes that cause kidney inflammation and damage. APRIL is a Proliferation-Inducing Ligand (APRIL), a TNF superfamily cytokine, elevated in IgAN patients and correlated with higher levels of Gd-IgA1 and proteinuria, and lower eGFR. BION-1301 is a novel monoclonal antibody which blocks and blocks APRIL. The primary objective of Study ADU-CL-19 is to assess the safety and tolerability of BION-1301 in Healthy Volunteers (HV) and IgAN patients and to secondarily assess the PK, PD, immunogenicity, and preliminary clinical activity.

Introduction

Role of APRIL and BION-1301 in IgA Nephropathy (IgAN)

APRIL is a 38 kDa, 467 amino acid transmembrane/secreted protein that functions as a ligand of the TNF superfamily receptor family, binds to TACI and BCMA, and upregulates B-cell survival and differentiation. BION-1301 is a humanized monoclonal antibody which binds and blocks APRIL. The primary objective of Study ADU-CL-19 is to assess the safety and tolerability of BION-1301 in Healthy Volunteers (HV) and IgAN patients and to secondarily assess the PK, PD, immunogenicity, and preliminary clinical activity.

Key Eligibility Criteria

- Age 18 years and older
- Urine protein excretion >0.5 g/24 hr
- eGFR >45 mL/min/1.73 m²
- Stable on an optimized dose of ACE/ARB for 3 months prior to screening (or intolerant to ACE/ARB)
- No history of other chronic kidney disease or any transplantation
- No history of secondary forms of IgAN
- No Type 1 or 2 diabetes

Methods

The Phase 1/2 study (NCT03945318) consists of 3 parts. Parts 1 and 2 were blinded, placebo-controlled single and multiple ascending dose designs in HV and have been completed. Part 3 is a multicenter (US, UK, South Korea) multicohort, open-label study in up to 40 patients with IgAN. Patients in Cohort 1 receive BION-1301 at 450 mg IV every 2 weeks for up to 1 year. Patients in Cohort 1 will transition from IV to receive 600 mg of BION-1301 SC biweekly after completing at least 24 weeks of IV dosing. Subsequent cohorts will be given BION-1301 via SC injection.

Part 1, SAD in healthy volunteers
- BION-1301 (400 mg)
- Part 2, MAD in healthy volunteers
- MAD Cohort 1: 50 mg SC, 40 mg IV Q2W for up to 2 weeks
- MAD Cohort 2: 200 mg SC, 150 mg IV Q2W for up to 2 weeks
- MAD Cohort 3: 500 mg SC, 375 mg IV Q2W for up to 2 weeks

Part 3, Optional additional cohorts in IgAN patients
- IV: 450 mg Q2W, up to 52 weeks
- SC: 600 mg Q2W, up to 52 weeks

RESULTS

Final HV data from Parts 1 and 2 have been presented at earlier conferences. Part 3 is ongoing, and interim data from Cohort 1 with IV dosing are being presented at the WCN 2022 (Abstract P WCN22-0485).

Conclusions

The current design of the Phase 1/2 study, incorporating SC dosing, provides for an improved patient experience, and will enable the generation of long-term safety, PK, PD, immunogenicity, and preliminary activity data for use of BION-1301 in IgAN patients.

References