Eledon Pharmaceuticals

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Tegoprubart for the treatment of patients with IgA nephropathy: a snapshot of emerging data from an ongoing trial

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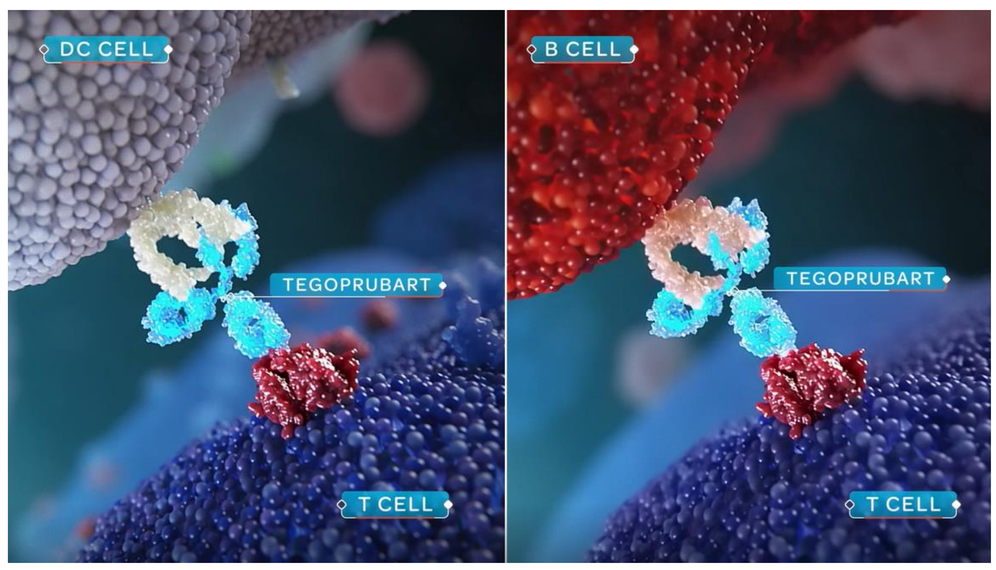
Background

IgA nephropathy (IgAN) is the most common autoimmune nephropathy, with a young age of onset and a slow progressive course. ~40% of affected patients progress to kidney failure within 20 years of diagnosis. Therapeutic options that delay progression are limited, and more options are needed. Tegoprubart is a next generation monoclonal antibody directed against CD40 ligand (CD40L; CD154), a target important in both cell and antibody mediated immunity. Inhibiting CD40L is expected to disrupt the pathophysiology of IgAN both upstream, by blocking antibody and immune complex formation, and downstream, by interfering with the cell based inflammatory response in the glomeruli.

Tegoprubart binds to CD40L on the cell surface of T lymphocytes and prevents this ligand from binding it's receptor (CD40) which is expressed on both the cell surface of both antigen presenting cells (e.g. dendritic cells, macrophages) and the cell surface of B cells. Blocking the interaction between the T cells and antigen presenting cells, prevents T cell activation, and results in the T cells adopting a regulatory T cell phenotype. Blocking the interaction between T cells and B cells, prevents B cell activation, clonal expansion and the production of antibodies.

A Phase 2a dose-finding, open-label study, AT-1501-N205, to evaluate the safety and efficacy of tegoprubart in patients with IgAN is underway. The study is designed to assess whether tegoprubart can decrease urine protein at Week 24 and slow the decline in eGFR at Week 96. A total of 42 participants are planned.

Tegoprubart Mechanism of Action



Methods

42 adult participants with biopsy proven IgAN and proteinuria ≧0.75g/24h despite the use of angiotensin converting enzyme inhibitors or angiotensin receptor blockers for at least 90 days will be enrolled into 2 sequential open-label cohorts assessing the efficacy of 10mg/kg and 5mg/kg of tegoprubart administered IV every 3 weeks. The cohorts are staggered such that the 5mg/kg cohort will not proceed if futility is seen with the 10mg/kg cohort. The cohorts have the same inc/exc criteria, visit schedule and endpoints. The primary endpoint is change from baseline of urine protein to creatinine ratio after 24 weeks of therapy. The study will continue through Week 96 to assess change in eGFR. Prior IgA vasculitis is permitted provided that the kidney is the only current organ affected (no skin, joint or GI tract involvement). Use of concurrent corticosteroids or other immunosuppressants is prohibited.

The study is ongoing. Data summarized below is through February 27, 2023

Results

Disposition

	Participants
Enrolled	16
Ongoing	16
Completed	0
Early Discontinuation	0
Completed 12 Weeks	9
Completed 24 Weeks	4

Demographics

Parameter	
Age	34.2 (18, 53) y.o.
Gender	Male: 5 (31.3%) Female: 11 (68.8%)
BMI	28.5 (18.3, 37.7) kg/m^2
Mean Time from Diagnosis	2.6 (0, 10.4) years
History of IgA Vasculitis	2 (12.5%)
Previous Corticosteroid Treatment	6 (37.5%)

Overview of Safety

	Number
Number of TEAEs Reported	11
Number of Participants with at Least 1 TEAE	8 (50%)
Number of Serious TEAEs Reported	0
Number of Participants with Drug-Related TEAEs	2
Participants TEAEs by Maximum Grade:	
Grade 1	5 (31.3%)
Grade 2	3 (18.8%)
Grade 3	0
Grade 4	0
Grade 5	0
Number of Participants with TEAEs Leading to Drug Withdrawal	0
Number of Participants with TEAES Leading to Death	0

Related TEAES: Alanine aminotransferase increased and musculoskeletal pain
Grade 2 TEAES: Alanine aminotransferase increased, gout and urinary tract infection

Treatment Emergent Adverse Events

System Organ Class Preferred Term	Number of TEAEs
Infections and Infestations	2 (12.5%)
Pharyngotonsillitis	1 (6.3%)
Urinary Tract Infection	1 (6.3%)
Gastrointestinal Disorders	1 (6.3%)
Haemorrhoids	1 (6.3%)
General Disorders and Administration Site Conditions	1 (6.3%)
Pyrexia	1 (6.3%)
Investigations	1 (6.3%)
Alanine Aminotransferase Increased	1 (6.3%)
Metabolism and Nutrition Disorders	1 (6.3%)
Gout	1 (6.3%)
Musculoskeletal and Connective Tissue Disorders	1 (6.3%)
Musculoskeletal Pain	1 (6.3%)
Nervous System Disorders	1 (6.3%)
Migraine	1 (6.3%)
Skin and Subcutaneous Tissue Disorders	2 (12.5%)
Rash	2 (12.5%)
Vascular Disorders	1 (6.3%)
Hypertension	1 (6.3%)

Discussion

This study is the first conducted with tegoprubart in patients with IgAN. It is designed to assess the safety and efficacy of tegoprubart in this population. This snapshot of the data looks at the safety in the first 16 enrolled participants, all in the 10 mg/kg dosing cohort. The available data suggests that tegoprubart is safe and well tolerated at this dose in this patient population. All 16 enrolled participants are ongoing in the trial, with 4 participants having completed at least 24 weeks on treatment and 5 others having completed at least 12 weeks. No one has discontinued early. There have been no serious nor severe adverse events reported. No new safety signals are emerging as each event reported has only occurred in 1-2 participants. The study remains ongoing.