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BASELINE CHARACTERISTICS OF THE ALIGN TRIAL: A PHASE 3 RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED CLINICAL TRIAL OF ATRASENTAN IN PATIENTS WITH IGAN

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Introduction: Endothelin A (ETA) receptor activation drives proteinuria, kidney inflammation and fibrosis in IgA nephropathy (IgAN). Atrasentan, a potent and selective ETA receptor antagonist, is a potential therapy to reduce proteinuria and preserve kidney function in patients with IgAN. Interim results from the IgAN cohort of the open-label AFFINITY study demonstrated atrasentan was well tolerated and resulted in clinically meaningful proteinuria reductions at 12 and 24 weeks. The ongoing ALIGN study (NCT04573478) is a global, phase 3, randomized, double-blind, placebo-controlled clinical trial of atrasentan in patients with IgAN at high risk of kidney function loss. Demographics and baseline characteristics will be presented.

Methods: Eligibility criteria for the ALIGN study include biopsy-proven IgAN, total protein excretion ≥ 1 g/d, eGFR ≥30 mL/min/1.73 m2 and receiving a maximally tolerated and stable dose of a renin-angiotensin system inhibitors (RASi). An additional stratum of patients also receiving a stable dose of sodium glucose cotransporter-2 inhibitors (SGLT2i) for at least 12 weeks are eligible. After randomization, patients receive 0.75 mg atrasentan or placebo daily for 132 weeks. The primary outcome is proteinuria change from baseline to Week 36. Key secondary and exploratory endpoints include eGFR change from baseline to week 136, safety and tolerability, and quality of life.

Results: The pre-specified interim analysis population included the first 270 patients enrolled in the main stratum. An additional 64 patients were enrolled in the exploratory SGLT2i stratum. Demographics and baseline characteristics were similar across both strata and will be presented at the time of the conference.

Conclusions: The global ALIGN trial has recruited patients with IgAN that are representative of a typical IgAN patient population. The inclusion of patients receiving maximally tolerated RASi and a stratum of patients receiving SGLT2i in addition to RASi reflects the current treatment paradigm in IgAN. This trial is ongoing and will report results at a future date.

I have potential conflict of interest to disclose.

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THE CLINICOPATHOLOGICAL SPECTRUM OF IGA DOMINANT/CODOMINANT GLOMERULONEPHRITIS DIAGNOSED AT AN ACADEMIC CENTRE IN SRI LANKA

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Introduction: IgA nephropathy is the most common primary glomerular disease in the world. There is limited data on IgA nephropathy in Sri Lanka.

Methods: The records of all kidney biopsies reported at the Department of Pathology, Faculty of Medicine, University of Colombo Sri Lanka from 2018 to 2023 in which light microscopy (LM) and immunofluorescence (IF) results were available were reviewed. The clinicopathological details of cases that showed IgA dominance or co-dominance on IF were analysed.

Results: Both LM and IF results were available in 468 of 1975 kidney biopsies handled during this period. 19.3% (n=93) showed IgA dominance/co-dominance which was the commonest IF pattern of the glomerulonephritides. 51.1%(n=47) were male. The median age was 32 years (IQR =24-44 years). Thirteen were below 16 years of age. The presentations included sub nephrotic range proteinuria(n=43;46.2%), nephrotic syndrome/nephrotic range proteinuria(n=36;38.7%), nephrotic/nephritic mixed picture (n=4;4,3%), acute kidney injury (n=5;5.3%), chronic increase in serum creatinine (n=3;3.2%) and nephritic picture (n=2;2.2%). IgA dominant GN was the second commonest cause (13.7%) for nephrotic syndrome/nephrotic range proteinuria, second to minimal change disease. Co-existing diabetes, hypertension and systemic lupus erythematosus were present in 24.4% (n=12), 47.3% (n=43) and 10.3% (n=5) respectively.

The majority showed a mesangioproliferative pattern(n=45;48.4%) on biopsy with smaller numbers showing minimal changes (n=12;12.9%), mild non-specific changes (n=7; 7.5%), an endocapillary proliferative glomerulonephritis (n=8;8.6%) and chronic changes with moderate to severe glomerulosclerosis, interstitial fibrosis and tubular atrophy (n=7;7.5%). Crescents involving less than 50% of the glomeruli were identified in 18 cases. Three showed necrotising glomerulonephritis. Four cases were associated with IgA vasculitis and five cases were possibly infection related. Four patients showed an elevated Anti streptolysin-O-titre. The clinical presentation and morphology are summarised in Table 1.

Conclusions: IgA nephropathy was the most common primary glomerular disease identified among all diagnosed glomerular diseases. The commonest presentations were nephrotic or sub nephrotic range proteinuria. The majority showed a mesangioproliferative pattern on light microscopy.

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TRF-BUDESONIDE AND SPARSENTAN AS AN INITIAL THERAPY FOR PRIMARY IGA NEPHRITIS

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Introduction: Primary immunoglobulin A nephropathy (IgAN) is one of the most common primary glomerulonephritis. IgAN is an autoimmune disorder with decreased O-linked galactosylation of the IgA1 hinge region leading to increased galactosedeficient IgA1 (Gd-IgA1) molecules in the circulation. This leads to the production of autoantibodies against Gd-IgA1, forming circulating immune complexes which deposit in the glomerular mesangium causing renal damage. Patients with primary IgAN who are at low risk for progressive renal dysfunction are managed conservatively with angiotensin inhibition, SGLT2 inhibitors, good blood pressure control and lifestyle changes. Patients at increased risk for progressive renal dysfunction with high oxford classification scores, do require management with immunosuppressive agents. Both sparsentan and targeted-release formulation (TRF) budesonide have been recently granted accelerated FDA approval for management of patients with primary IgAN.

Methods: