Mini Oral# MO209

# Baseline Characteristics of Patients Enrolled in the Ongoing Phase 3 Randomized, Double-Blind, Active-Control Trial of Sparsentan for the Treatment of Immunoglobulin A Nephropathy (PROTECT)

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TRAVERE THERAPEUTICS

- 20% to 40% of patients diagnosed with IgAN progress to chronic kidney failure requiring dialysis or kidney transplantation within 10-20 years despite optimized standard of care treatment with an ACEi and/or ARB,[1-3] seriously affecting QOL and mortality[4-6]
- Sparsentan is a novel single molecule Dual Endothelin Angiotensin Receptor Antagonist (DEARA) being investigated for IgAN[7]
- The ongoing Phase 3 PROTECT study is examining the long-term antiproteinuric and nephroprotective efficacy and safety of sparsentan compared with an active control, the ARB irbesartan, in adults with IgAN with overt proteinuria ≥1 g/day despite receiving maximized treatment with an ACEi and/or ARB

## Objective

- To report the blinded and aggregated baseline characteristics for all patients enrolled in the PROTECT trial

**1**. Manno C, et al. *Am J Kidney Dis*. 2007;49:763-75. **2**. Tesar V, et al. *J Am Soc Nephrol*. 2015;26:2248-58. **3**. Berthoux F, et al. *J Am Soc Nephrol.* 2011;22:752-61. **4.** Kwon CS, et al. *JHEOR*. 2021;8:36-45. **5.** Lai KN, et al. *Nat Rev Dis Primers*. 2016;2:16001. **6.** Jarrick S, et al. *J AM Soc Nephrol*. 2019;30:866-876. **7.** Barratt J, et al. *Kidney Int Rep*. 2019;4:1633-1637.

METHODS

# PROTECT Study Design

- Ongoing, global, Phase 3, multicenter, randomized, double-blind, parallel-group, active controlled study (the final patient visit will be Fall of 2023; EudraCT number: 2017-004605-41; US ClinicalTrials.gov identifier: NCT03762850)
- Double-blind period of 114 weeks followed by open-label extension up to 156 weeks
- Primary efficacy endpoint is the change from baseline in urine protein/creatinine ratio based on a 24-hour urine sample at Week 36
- Patients were randomized 1:1 to sparsentan (2-week titration to the target dose 400 mg/day) or irbesartan (2-week titration to the target dose 300 mg/day) stratified by screening eGFR and urine protein excretion values

# Patient Key Inclusion Criteria

- Male or female aged ≥18 years; biopsy-proven IgAN; at screening: urine protein excretion value ≥1 g/day, eGFR ≥30 mL/min/1.73m$^2$, systolic blood pressure ≤150 mmHg, diastolic blood pressure ≤100 mmHg
- On a maximized stable dose of ACEi and/or ARB for ≥12 weeks prior to screening that is (A) patient's maximum tolerated dose **AND** (B) ≥50% the maximum labeled dose (MLD)

ACEi, angiotensin converting enzyme inhibitors; ARB, angiotensin receptor blockers; eGFR, estimated glomerular filtration rate (determined using the CKD-EPI equation); IgAN, immunoglobulin A nephropathy.

RESULTS

# Baseline Characteristics of Patients Enrolled in PROTECT

| | Patients[a] (N=404) |
|---|---|
| **Age at informed consent, years, median (IQR)** | 46.0 (37.0, 56.0) |
| **Female, n (%)** | 122 (30) |
| **Race, n (%)** | |
| White | 272 (67) |
| Asian | 115 (28) |
| Black or African American | 4 (1) |
| Other | 13 (3) |
| **Not Hispanic or Latino, n (%)** | 368 (91) |
| **History of hypertension, n (%)** | 309 (76.5) |
| **Systolic / diastolic blood pressure, mmHg, mean±SD** | 129.0±13.5 / 82.4±10.6 |
| **BMI, kg/m$^2$, mean±SD** | 28.4±5.4 |
| **Serum albumin, g/L, mean±SD/median (IQR)** | 41.5±3.8 / 42.0 (40.0, 44.0) |
| **UP/C, g/g, median (IQR)** | 1.2 (0.8, 1.8) |
| **Urinary protein excretion, g/day, median (IQR)** | 1.8 (1.3, 2.8) |
| **Nephrotic range proteinuria, (>3.5 g/day), n (%)** | 49 (12.1) |

| | Patients[a] (N=404) |
|---|---|
| **Urine albumin/creatinine ratio, g/g, median (IQR)** | 1.05 (0.7, 1.5) |
| **Urinary albumin excretion, mg/day, median (IQR)** | 1493.0 (1072.5, 2279.5) |
| **eGFR, mL/min/1.73m$^2$, mean±SD/median (IQR)** | 57.0±24.0 / 50.0 (39.0, 70.0) |
| **eGFR, mL/min/1.73m$^2$, n (%)** | |
| ≥90 | 51 (12.6) |
| ≥60 - <90 | 97 (24.0) |
| ≥45 - <60 | 94 (23.3) |
| ≥30 - <45 | 142 (35.1) |
| ≥15 - <30 | 20 (5.0) |
| **RAAS inhibitors at screening, n (%)** | |
| ACEi at MLD | 104 (26) |
| ARB at MLD | 161 (40) |
| ACEi and ARB at MLD | 9 (2) |
| **Baseline medication use, n (%)** | |
| Non-RAASi antihypertensive medications | 171 (42) |
| Lipid-lowering medications | 223 (55) |

[a]The primary analysis set included all patients who were randomized and received at least one dose of study drug or control.

# CONCLUSIONS

- The PROTECT trial enrolled patients with IgAN (excluding IgAN secondary to another condition or Henoch-Schonlein purpura) at high risk of progression to chronic kidney failure despite maximum standard of care treatment[1]
- PROTECT is one of the largest trials in biopsy-confirmed IgAN to enroll patients across three different geographic regions with well represented differing racial backgrounds, an important consideration as there have been reports of differential prognosis and therapeutic response in patients with IgAN based on race
- At baseline, patients enrolled in the PROTECT trial displayed a broad range of eGFR and had a median UP/C of 1.2 g/g (median urinary protein excretion of 1.8 g/day )
- Sparsentan, as a novel DEARA and a non-immunosuppressing agent, is being examined as a new therapeutic in this disease with an unmet need for novel therapies

**1.** Le W, et al. *Nephrol Dial Transplant*. 2012;27:1479-1485.

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