Mini Oral# MO254

Baseline Characteristics of Patients Enrolled in the Ongoing Phase 3 Randomized, Double-Blind, Active-Control Trial of Sparsentan for the Treatment of Focal Segmental Glomerulosclerosis (DUPLEX)

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TRAVERE THERAPEUTICS

- FSGS often follows a progressive course to chronic kidney failure[1] and has a profound negative impact on patient QOL and long-term survival[2-4]
- Sparsentan is a novel single molecule Dual Endothelin Angiotensin Receptor Antagonist (DEARA) being investigated for the treatment of FSGS[5]
- The ongoing Phase 3 DUPLEX study is examining the long-term antiproteinuric and nephroprotective efficacy and safety of sparsentan compared with an active control, the ARB irbesartan, in adults and pediatric patients with FSGS

Objective

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

1. Korbet SM. *J Am Soc Nephrol*. 2012;23:1769-1776. **2.** Gipson DS, et al. *Kidney Int*. 2011;79:678-685. **3.** Abdel-Kader K, et al. *Clin J Am Soc Nephrol*. 2009;4:1057-1064. **4.** Troost JP, et al. *Am J Kidney Dis*. 2021;77:216-225. **5.** Komers R, et al. *Kidney Int Rep*. 2020;5:494-502.
ARB, angiotensin receptor blockers; FSGS, focal segmental glomerulosclerosis; QOL, quality of life.

METHODS

DUPLEX Study Design

- Ongoing, global, Phase 3, multicenter, randomized, double-blind, parallel-group, active controlled study (the final patient visit in the double-blind period is anticipated early 2023; EudraCT number: 2016-005141-23; US ClinicalTrials.gov identifier: NCT03493685)
- Double-blind period of 112 weeks followed by open-label extension up to 156 weeks
- Primary efficacy endpoint is the slope of eGFR over ~2 years of randomized treatment
- Surrogate efficacy endpoint is the proportion of patients achieving UP/C ≤1.5 g/g and a >40% reduction from baseline of the double-blind period in UP/C at Week 36
- Patients receiving RAASi underwent a 2-week washout prior to randomization
- Patients were randomized 1:1 to sparsentan (2-week titration to the target dose 800 mg/day) or irbesartan (2-week titration to the target dose 300 mg/day) stratified by screening eGFR and UP/C[1]

Patient Key Inclusion and Exclusion Criteria

- Male or female aged 8-75 years (US/UK) or 18-75 years (outside US/UK) weighing ≥20 kg; biopsy-proven FSGS lesion or documentation of a genetic mutation in a podocyte protein associated with FSGS; at screening: UP/C ≥1.5 g/g, eGFR ≥30 mL/min/1.73m^2
- Patients with a known secondary cause of FSGS were excluded

1. Target dose for patients weighing 20 kg-≤50 kg at screening is sparsentan 400 mg/day and irbesartan 150 mg/day.

RESULTS

Baseline Characteristics of Patients Enrolled in DUPLEX

	Patients[a] (N=371)
Age at informed consent, years, median (IQR)	42 (27.0, 56.0)
Age group 9 years to <18 years, n (%)	35 (9.4)
Female, n (%)	171 (46)
Race, n (%)	
White	276 (74)
Asian	50 (13)
Black or African American	29 (8)
Other	22 (6)
Not Hispanic or Latino, n (%)	281 (76)
Documented history of nephrotic syndrome, n (%)	112 (30.2)
History of hypertension, n (%)	238 (64.2)
Systolic / diastolic blood pressure, mmHg, mean±SD	131.9±14.9 / 83.8±10.5
BMI, kg/m², mean±SD	27.7±5.9
Serum creatinine, µmol/L, mean±SD	124.5±49.3
Serum albumin, g/L, mean±SD/median (IQR)	34.9±7.4 / 36.0 (30.0, 40.0)

	Patients[a] (N=371)
UP/C, g/g, median (IQR)	3.0 (2.2, 4.6)
Nephrotic range UP/C, n (%)	
>3.5 g/g in adults (age ≥18 years)	124 (36.9)
>2.0 g/g in pediatrics (age <18 years)	34 (97.1)
eGFR, mL/min/1.73m², mean±SD/median (IQR)	63.8±30.3 / 55.0 (41.0, 80.0)
eGFR, mL/min/1.73m², n (%)	
≥90	70 (18.9)
≥60 - <90	98 (26.4)
≥45 - <60	79 (21.3)
≥30 - <45	101 (27.2)
≥15 - <30	23 (6.2)
Pre-treatment RAASi use, n (%)	271 (73)
Baseline medication use, n (%)	
Non-RAASi antihypertensive medications	222 (60)
Lipid-lowering medications	217 (58)
Diuretics	133 (36)
Immunosuppressive agents	92 (25)

[a]The interim analysis set included all patients who were randomized and received at least one dose of double-blind study medication.

CONCLUSIONS

- DUPLEX is the largest randomized controlled trial to date in FSGS
- The DUPLEX trial enrolled patients with FSGS (excluding patients with a known secondary cause of FSGS) at risk of progression to chronic kidney failure despite prior treatment[1]
- At baseline, the patients enrolled in DUPLEX had a similar proportion of patients with chronic kidney disease stages 1 to 4

1. Troost JP, et al. *Am J Kidney Dis*. 2021;77:216-225.

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- Disclosures
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  - JR: Consultant to and Research Grants from Travere Therapeutics, Inc.,
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