Poster #SAT-219

# Immunoglobulin A Nephropathy (IgAN) Patient Baseline Characteristics in Asian Versus Non-Asian Regions in the Sparsentan PROTECT Study

**Muh Geot Wong[1], Jonathan Barratt[2], Radko Komers[3], Alex Mercer[4], Brad Rovin[5], on behalf of the DUPLEX and PROTECT Steering Committee**

[1]Department of Renal Medicine, Concord Repatriation General Hospital, Concord, NSW, Australia and Concord Clinical School, University of Sydney, Concord, NSW, Australia; [2]Department of Cardiovascular Sciences, University of Leicester General Hospital, Leicester, UK; [3]Travere Therapeutics, Inc., San Diego, CA, USA; [4]JAMCO Pharma Consulting, Stockholm, Sweden; [5]Division of Nephrology, Ohio State University Wexner Medical Center, Columbus, Ohio, USA

*Contact information:*
*Medinfo@Travere.com*

**Presented at the World Congress of Nephrology 2023;**
**March 30 to April 2, 2023; Bangkok, Thailand**

**To obtain a PDF of this presentation:**

No personal information is stored.

TRAVERE™ THERAPEUTICS

# DISCLOSURES

- **MGW:** Received honorarium for scientific presentation from Amgen, AstraZeneca, Baxter, CSL Behring, Dimerix, Eledon, George Clinical, Horizon, and Travere Therapeutics, Inc
- **JB:** Has received research grants from Argenx, Calliditas Therapeutics, Chinook Therapeutics, Galapagos NV, GlaxoSmithKline, Novartis, and Travere Therapeutics, Inc. and is medical/scientific advisor to Alnylam Pharmaceuticals, Argenx, Astellas Pharma, BioCryst Pharmaceuticals, Calliditas Therapeutics, Chinook Therapeutics, Dimerix, Galapagos NV, Novartis, Omeros, Travere Therapeutics, Inc., UCB, Vera Therapeutics and Visterra
- **RK:** Employee and stockholder, Travere Therapeutics, Inc.
- **AM:** Consultant to Travere Therapeutics, Inc. through contract with JAMCO Pharma Consulting AB
- **BR:** Is a consultant to Calliditas, Omeros, Novartis, Travere Therapeutics, Inc., and Vera

# Background

- IgAN is a heterogenous disease
- Retrospective data indicate differences in clinical risk factors and IgAN disease progression when comparing individuals of Pacific Asian vs non-Pacific Asian origin,[1] raising the possibility of differences in IgAN according to race or geographic region
- Recent randomized controlled trials in IgAN, including STOP-IgAN[2] and TESTING,[3] have enrolled a relatively homogenous population of patients according to race
- Sparsentan is a novel, non-immunosuppressive, single molecule, dual endothelin angiotensin receptor antagonist (DEARA) with high selectivity for the endothelin type A receptor ($ET_AR$) and the angiotensin II subtype 1 receptor ($AT_1R$)[4]
- In the randomized controlled phase 2 DUET trial, sparsentan significantly reduced proteinuria compared with the ARB irbesartan in patients with focal segmental glomerulosclerosis[5]
- The ongoing PROTECT trial is evaluating the long-term antiproteinuric and nephroprotective efficacy and safety of sparsentan versus the active control irbesartan in 404 adults with IgAN
- Here, we report the blinded and aggregated baseline characteristics of patients with IgAN enrolled in the phase 3 PROTECT trial according to geographic region and racial background

ARB, angiotensin receptor blocker; IgAN, Immunoglobulin A nephropathy.

1. Barbour SJ, et al. *Kidney Int*. 2013;84(5):1017-24. 2. Rauen T et al. *N Engl J Med*. 2015;373:2225-36.
3. Wong MG, et al. *Am J Nephrol.* 2021;52:827-36. 4.Trachtman H, et al. *Drugs of the Future*. 2020;45:79.
5. Trachtman H, et al. *J Am Soc Nephrol*. 2018;29(11):2745-54.

METHODS

# Study Design

- PROTECT is an ongoing, global, Phase 3, multicenter, randomized, double-blind, parallel-group, active controlled study of sparsentan vs irbesartan in patients with biopsy-proven IgAN with overt proteinuria despite maximal ACEi/ARB therapy
- Double-blind period of 114 weeks followed by an open-label extension of up to 156 weeks
- Patients were randomized 1:1 to sparsentan (2-week titration to target dose of 400 mg/day) or irbesartan (2-week titration to target dose of 300 mg/day), stratified by screening eGFR and urine protein excretion values
- The primary efficacy endpoint is the change from baseline in urine protein/creatinine ratio (UP/C) based on a 24-hour urine sample at Week 36
- Key secondary efficacy endpoints include chronic eGFR slope over 1 and 2 years (6-58 weeks and 6-110 weeks, respectively) and total eGFR slope over the full double-blind treatment period of 110 weeks

METHODS

# Eligibility Criteria

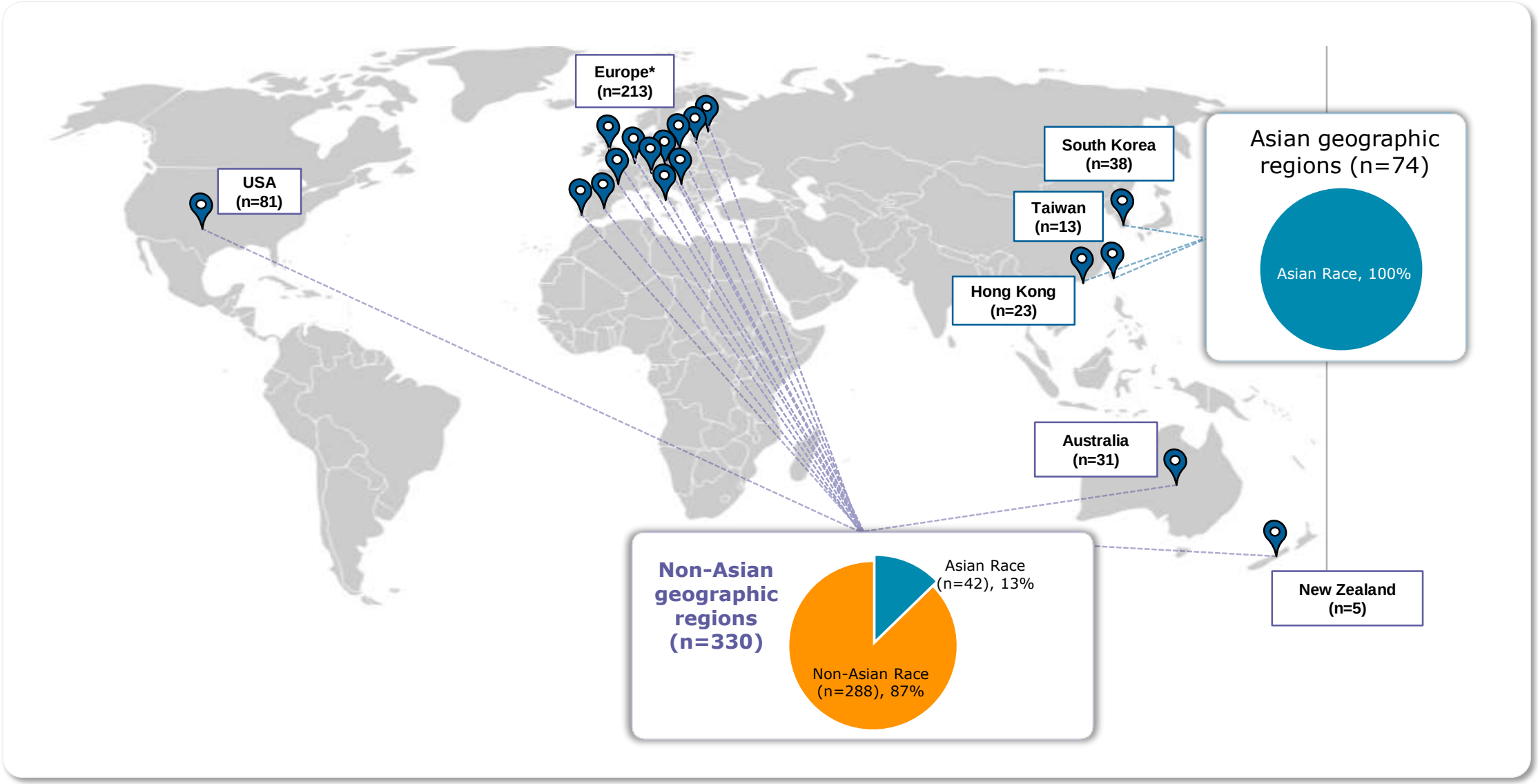
- Key inclusion criteria:
  - Male or female aged ≥18 years
  - Biopsy-proven IgAN
  - At screening: urine protein excretion value ≥1 g/day; eGFR ≥30 mL/min/1.73 m2; systolic blood pressure ≤150 mmHg; diastolic blood pressure ≤100 mmHg
  - On a maximized stable dose of ACEi and/or ARB for ≥12 weeks prior to screening that is both the patient's maximum tolerated dose AND ≥50% the maximum labeled dose
- Key exclusion criteria:
  - Secondary IgAN or IgA vasculitis
  - Cellular glomerular crescents present in >25% of glomeruli on kidney biopsy within 6 months prior to screening
  - A cause of CKD in addition to IgAN
  - Systemic immunosuppressive medications (including corticosteroids) for >2 weeks within 3 months prior to screening
  - Significant cerebrovascular, cardiovascular, or hepatic conditions

METHODS

# Analysis

- This report descriptively summarizes the blinded and aggregated baseline characteristics of patients enrolled in the PROTECT trial from Asian and non-Asian regions
- The primary analysis population includes patients who were randomized in PROTECT and received at least 1 dose of assigned treatment

# Figure 1. Enrollment in the PROTECT Study by Geographic Region and Asian vs Non-Asian Race




Includes patients who were randomized and received ≥1 dose of study drug in PROTECT.
*Countries with enrollment in Europe include Belgium (n=12), Croatia (n=11), Czech Republic (n=13), Estonia (n=7), France (n=13), Germany (n=16), Italy (n=26), Lithuania (n=11), Poland (n=13), Portugal (n=12), Spain (n=30), and UK (n=49).

RESULTS

# Table 1. Baseline Demographic Characteristics and Relevant Medical History by Asian and Non-Asian Race Within Geographic Regions

| Characteristic | Asian Geographic Regions | Non-Asian Geographic Regions | | |
|---|---|---|---|---|
| | Asian Race (n=74) | Overall (n=330) | Asian Race (n=42) | Non-Asian Race (n=288) |
| Age at informed consent, years, median (IQR) | 49 (40-56) | 46 (36-56) | 46 (38-57) | 46 (36-56) |
| Sex, n (%) | | | | |
| Male | 43 (58) | 239 (72) | 20 (48) | 219 (76) |
| Female | 31 (42) | 91 (28) | 22 (52) | 69 (24) |
| Age at IgAN diagnosis, years, median (IQR)* | 42 (33-51) | 38 (29-49) | 37 (31-46) | 38 (29-49) |
| Time from initial kidney biopsy to informed consent, years, median (IQR)† | 3.0 (1.0-9.0) | 4.0 (1.0-10.0) | 4.5 (2.0-9.0) | 4.0 (1.0-10.0) |
| History of diabetes, n (%) | 8 (11) | 35 (11) | 6 (14) | 29 (10) |
| History of hypertension, n (%) | 43 (58) | 266 (81) | 26 (62) | 240 (83) |
| Blood pressure, mmHg, mean ± SD | | | | |
| Systolic | 124 ± 14 | 130 ± 13 | 125 ± 10 | 131 ± 13 |
| Diastolic | 80 ± 11 | 83 ± 11 | 81 ± 9 | 83 ± 11 |
| BMI, kg/m$^2$, mean ± SD | 27 ± 5 | 29 ± 6 | 28 ± 5 | 29 ± 6 |

Asian geographic regions include Hong Kong, Taiwan, and South Korea. Non-Asian geographic regions include all other countries. For patients who selected multiple races, if one of the races was Asian, the patient was included as Asian. All patients enrolled from Asian regions were of Asian race.
BMI, body mass index; IgAN, immunoglobulin A nephropathy; IQR, interquartile range.
*Age at IgAN diagnosis is derived based on the year of IgAN diagnosis and year of birth.
†Time from initial biopsy is derived based on the year of the initial kidney biopsy and year of signed informed consent.

# Table 2. Laboratory Values at Baseline by Asian and Non-Asian Race Within Geographic Regions

| Characteristic | Asian Geographic Regions | Non-Asian Geographic Regions | | |
|---|---|---|---|---|
| | Asian Race (n=74) | Overall (n=330) | Asian Race (n=42) | Non-Asian Race (n=288) |
| UP/C, g/g, median (IQR) | 1.4 (0.9-1.9) | 1.2 (0.8-1.8) | 1.3 (0.9-2.1) | 1.2 (0.8-1.8) |
| Urinary protein excretion, g/day, median (IQR) | 1.7 (1.2-2.5) | 1.8 (1.3-2.8) | 1.7 (1.2-2.4) | 1.8 (1.3-2.9) |
| Nephrotic range proteinuria (>3.5 g/day), n (%) | 8 (11) | 41 (12) | 4 (10) | 37 (13) |
| UA/C, g/g, median (IQR) | 1.2 (0.8-1.6) | 1.0 (0.7-1.5) | 1.0 (0.7-1.7) | 1.0 (0.7-1.4) |
| Urinary albumin excretion, mg/day, median (IQR) | 1465 (1087-2195) | 1499 (1057-2288) | 1485 (1034-1834) | 1508 (1059-2376) |
| eGFR* | | | | |
| Mean ± SD | 59 ± 24 | 56 ± 24 | 58 ± 24 | 56 ± 24 |
| Median (IQR) | 52 (41-73) | 50 (38-70) | 51 (38-72) | 50 (38-70) |
| eGFR,* n (%) | | | | |
| ≥90 | 12 (16) | 39 (12) | 6 (14) | 33 (11) |
| ≥60 to <90 | 16 (22) | 81 (25) | 11 (26) | 70 (24) |
| ≥45 to <60 | 19 (26) | 75 (23) | 8 (19) | 67 (23) |
| ≥30 to <45 | 25 (34) | 117 (35) | 15 (36) | 102 (35) |
| ≥15 to <30 | 2 (3) | 18 (5) | 2 (5) | 16 (6) |
| Hemoglobin, g/L, mean ± SD | 134 ± 15 | 140 ± 16 | 134 ± 14 | 141 ± 16 |

A central laboratory was used for all laboratory testing analyses. Asian geographic regions include Hong Kong, Taiwan, and South Korea. Non-Asian geographic regions include all other countries. For patients who selected multiple races, if one of the races was Asian, the patient was included as Asian.
eGFR, estimated glomerular filtration rate in ml/min/1.73 $m^2$; IQR, interquartile range; SD, standard deviation; UA/C, urine albumin/creatinine ratio; UP/C, urine protein/creatinine ratio.
eGFR was determined using the Chronic Kidney Disease Epidemiology (CKD-EPI) formula.

# Table 2. Laboratory Values at Baseline by Asian and Non-Asian Race Within Geographic Regions (cont.)

| Characteristic | Asian Geographic Regions | Non-Asian Geographic Regions | | |
|---|---|---|---|---|
| | Asian Race (n=74) | Overall (n=330) | Asian Race (n=42) | Non-Asian Race (n=288) |
| Plasma lipid profile, mmol/L, mean ± SD | | | | |
| Total cholesterol | 4.6 ± 1.0 | 5.0 ± 1.1 | 5.1 ± 1.2 | 5.0 ± 1.1 |
| HDL cholesterol | 1.3 ± 0.4 | 1.3 ± 0.4 | 1.3 ± 0.4 | 1.3 ± 0.4 |
| LDL cholesterol | 2.4 ± 0.8 | 2.9 ± 1.0 | 3.0 ± 1.0 | 2.9 ± 1.1 |
| Triglycerides | 1.9 ± 1.0 | 1.9 ± 1.1 | 2.1 ± 1.1 | 1.9 ± 1.1 |
| Serum albumin | | | | |
| Mean ± SD | 41 ± 5 | 42 ± 4 | 41 ± 4 | 42 ± 3 |
| Median (IQR) | 42 (38-44) | 42 (40-44) | 42 (40-44) | 42 (40-44) |
| Serum potassium, mmol/L, mean ± SD | 4.7 ± 0.4 | 4.6 ± 0.4 | 4.4 ± 0.5 | 4.7 ± 0.4 |
| Serum creatinine, µmol/L, mean ± SD | 126 ± 42 | 138 ± 46 | 128 ± 45 | 140 ± 46 |
| Serum cystatin C, mg/L, mean ± SD | 1.4 ± 0.4 | 1.5 ± 0.4 | 1.5 ± 0.4 | 1.5 ± 0.4 |
| Hematuria/microscopic hematuria, n (%) | 38 (51) | 187 (57) | 19 (45) | 168 (58) |
| Urine sodium, mEq/L, mean ± SD[†] | 79 ± 28 | 80 ± 33 | 69 ± 25 | 82 ± 33 |

A central laboratory was used for all laboratory testing analyses. Asian geographic regions include Hong Kong, Taiwan, and South Korea. Non-Asian geographic regions include all other countries. For patients who selected multiple races, if one of the races was Asian, the patient was included as Asian.
HDL, high-density lipoprotein; IQR, interquartile range; LDL, low-density lipoprotein; SD, standard deviation.
[†]The assessment of macroscopic hematuria was not possible due to the use of a central laboratory, resulting in an unreliable analysis of macrohematuria due to the transport time and analysis delays.

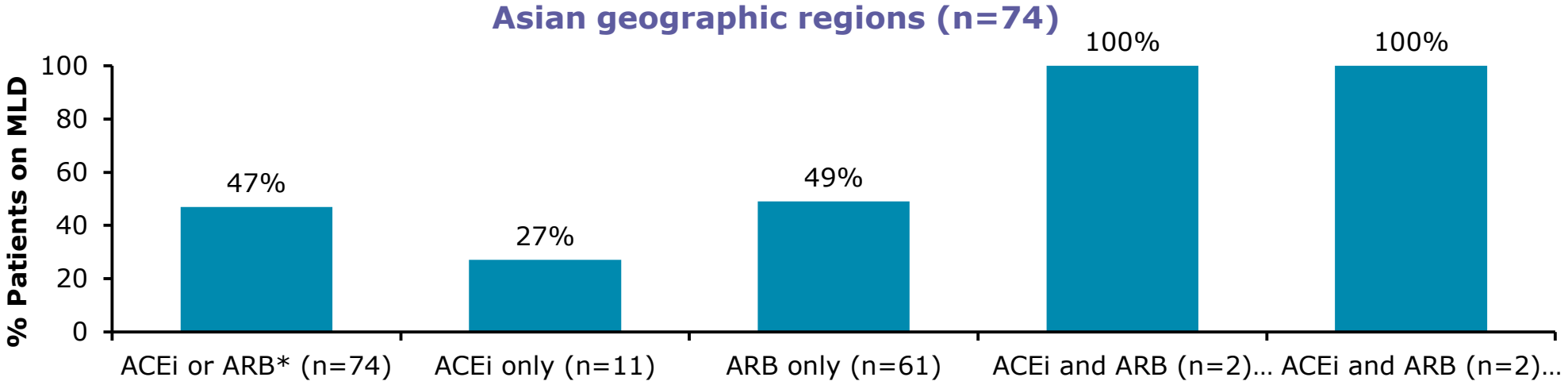
RESULTS

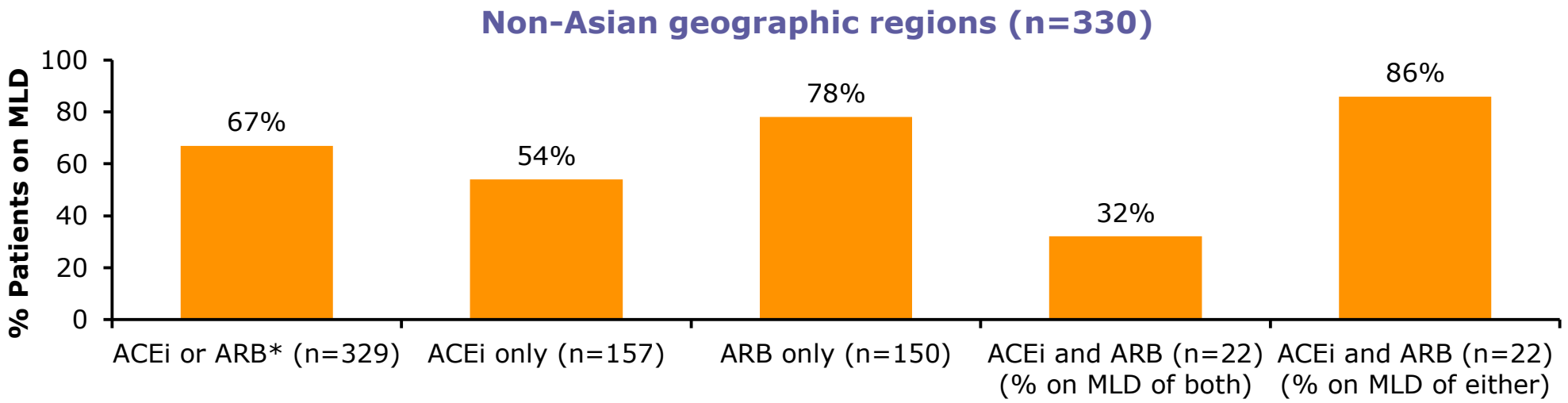
# Table 3. Medications at Screening and Baseline by Asian and Non-Asian Race Within Geographic Regions

| Characteristic | Asian Geographic Regions | Non-Asian Geographic Regions | | |
|---|---|---|---|---|
| | Asian Race (n=74) | Overall (n=330) | Asian Race (n=42) | Non-Asian Race (n=288) |
| ACEi and ARB treatment at screening, n (%)* | | | | |
| Any RAASi | 74 (100) | 329 (100) | 42 (100) | 287 (100) |
| ACEi only | 11 (15) | 157 (48) | 17 (40) | 140 (49) |
| ARB only | 61 (82) | 150 (45) | 23 (55) | 127 (44) |
| ACEi and ARB | 2 (3) | 22 (7) | 2 (5) | 20 (7) |
| MLD of ACEi or ARB† | 35 (47) | 221 (67) | 29 (69) | 192 (67) |
| Baseline medication use, n (%)‡ | | | | |
| Antihypertensive medications§ | 27 (36) | 147 (45) | 14 (33) | 133 (46) |
| Diuretics | 5 (7) | 57 (17) | 5 (12) | 52 (18) |
| Beta-blockers | 9 (12) | 46 (14) | 5 (12) | 41 (14) |
| Alpha-blockers | 5 (7) | 17 (5) | 0 | 17 (6) |
| Calcium channel blockers | 20 (27) | 89 (27) | 10 (24) | 79 (27) |
| Other | 1 (1) | 22 (7) | 1 (2) | 21 (7) |
| Lipid-lowering medications | 50 (68) | 173 (52) | 24 (57) | 149 (52) |

Asian geographic regions include Hong Kong, Taiwan, and South Korea. Non-Asian geographic regions include all other countries. For patients who selected multiple races, if one of the races was Asian, the patient was included as Asian.
ACEi, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; MLD, maximum labeled dose; RAASi, renin-angiotensin-aldosterone system inhibitors.
*ACEi and ARB treatment at screening; RAASi were prohibited during the study.
†Calculated as the percentage of patients on MLD of ACEi or ARB among those who received any RAASi at screening.
‡Baseline medications were started prior to randomization (Day 1) and continued after the initial dose of study medication.
§Antihypertensive medications exclude ACEis, ARBs, aldosterone blockers, and aliskiren.

# Figure 2. Maximum Labelled Dose of ACEi/ARB at Baseline




For patients with more than 1 record of MLD percentage and for patients taking both ACEi and ARB treatment, the highest percentage MLD was included.
N's below each bar represent the denominator (number of patients on stated RAASi at screening).
*Calculated as the percentage of patients on MLD of ACEi or ARB among those who received any RAASi (ACEi only, ARB only, or ACEi and ARB) at screening.
ACEi, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; MLD, maximum labeled dose.

# CONCLUSIONS

- The population enrolled in the PROTECT trial from Asian regions included more females, a lower percentage of patients with a history of hypertension and baseline hypertensive medication use, and were less likely to be on MLD of RAASi compared with patients enrolled from non-Asian regions
- Key measures of kidney function, proteinuria, and eGFR were similar at baseline when comparing Asian and non-Asian patients in PROTECT
- The PROTECT trial recruited participants from varied geographic regions and racial backgrounds, which will enable characterization of the treatment effect of sparsentan in these diverse patient populations

# ACKNOWLEDGMENTS


- The study was sponsored by Travere Therapeutics, Inc. (San Diego, CA). Medical writing assistance was provided by Julia Burke, PhD of MedVal Scientific Information Services, LLC (Princeton, NJ), and was funded by Travere Therapeutics, Inc.