Effects of 1 mg Once-Weekly Semaglutide on Functional Capacity in Patients with Type 2 Diabetes and Peripheral Artery Disease: Trial Design and Baseline Characteristics from STRIDE a 52-Week, Randomized, Double-Blind, Placebo-Controlled Trial

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Background

- People living with lower extremity **peripheral arterial disease** (**PAD**) can suffer from severe functional impairment and reduced quality of life
- People living with **type 2 diabetes** (**T2D**) are almost two times more likely to have **PAD** than those without **T2D**[1]
- There are a limited number of therapies that improve the functional capacity in people living with **PAD**[2] and **no glucose-lowering medication** has been shown to improve functional capacity in people with **PAD** and **T2D**[3-5]
- **Glucagon like peptide 1 receptor agonists** (**GLP-1 RAs**) have been shown to reduce the risk of cardiovascular events, improve glycemic control and reduce body weight in people with atherosclerotic cardiovascular disease and **T2D**

Trial design

- **STRIDE** is a randomized, double-blind, placebo-controlled, phase 3b trial, comprising a **52-week treatment phase** with a 5-week follow-up (**Figure 1**)

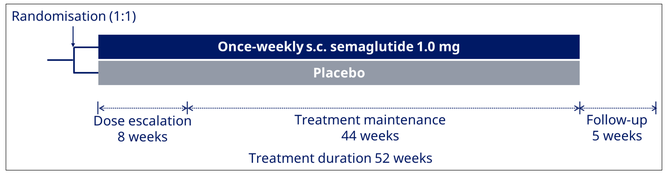

Figure 1. STRIDE trial overview with a 52-week main phase and 5-week follow-up.

- The trial is designed to evaluate 1 mg once-weekly subcutaneous semaglutide, a **GLP-1 RA**, treatment in adults (≥18 years old) with early-stage symptomatic **PAD** (**Fontaine IIa, intermittent claudication**) and **T2D**
- Participants have:
  - Been diagnosed with **T2D** ≥180 days prior to screening
  - Stable **PAD** for ≥90 days prior to screening
  - A HbA_{1c} ≤10%
  - An ABI ≤0.90 or TBI ≤0.70
  - A maximum walking distance ≤600m on a graded treadmill test
  - No other conditions limiting their walking ability
- The primary endpoint in **STRIDE** is the change in maximum walking distance at week 52 on a **constant load treadmill test** with secondary endpoints summarized in **Figure 2**

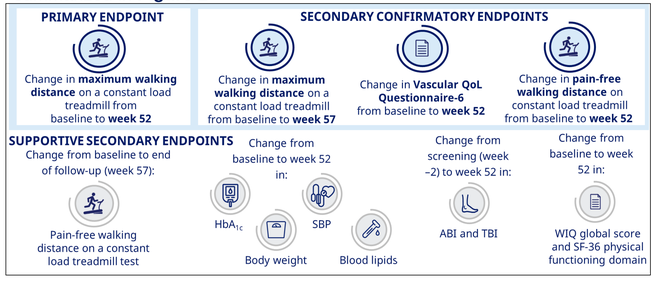

Figure 2. Summary of trial primary, secondary confirmatory and supportive secondary endpoints

References

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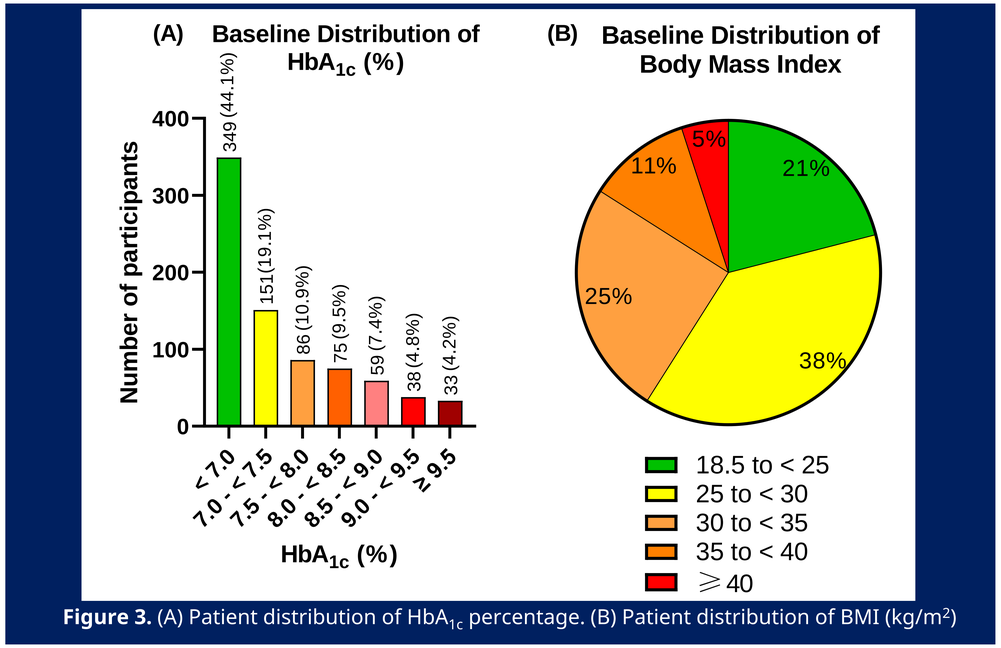

Figure 3. (A) Patient distribution of HbA_{1c} percentage. (B) Patient distribution of BMI (kg/m^2)

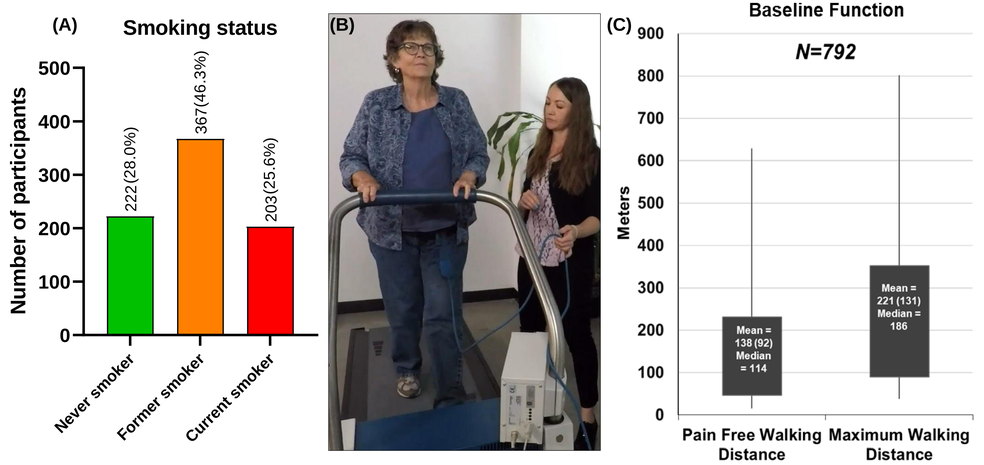

Figure 4. (A) Smoking status of participants (B) Example of constant load treadmill use (C) Baseline functional assessment in **STRIDE** Box and whisker plot illustrate the Q1;Q3 and min;max

- **STRIDE** enrolled **792 participants** who had a **median duration of T2D of 12 years** with a baseline **median HbA_{1c} %** of **7.1** and a **median BMI of 28.6 kg/m^2** with categorical data shown in **Figure 3A & B**
- Participants were predominantly ≥ 65 years (**median age: 68 years**), male (**75.4%**), weighed ≥70kg (**77.8%**) and were current/prior smokers (**71.9%**) (**Figure 4A**)
- The **functional capacity** of participants at baseline was impaired on a **constant load treadmill test** (**Figure 4B**) with the mean and median **maximum walking distance** being **221 meters** and **186 meters**, respectively (**Figure 4C**)

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Baseline characteristics and demographics

- Patients were enrolled in the **STRIDE** trial across **20** countries in North America (**N=113, 14.3%**), Europe (**N=448, 56.6%**) and Asia (**N=231, 29.2%**) (**Figure 5A**)
- The race of participants enrolled in **STRIDE** is summarized in **Figure 5B**, with the majority (**N=538, 67.9%**) being **white**

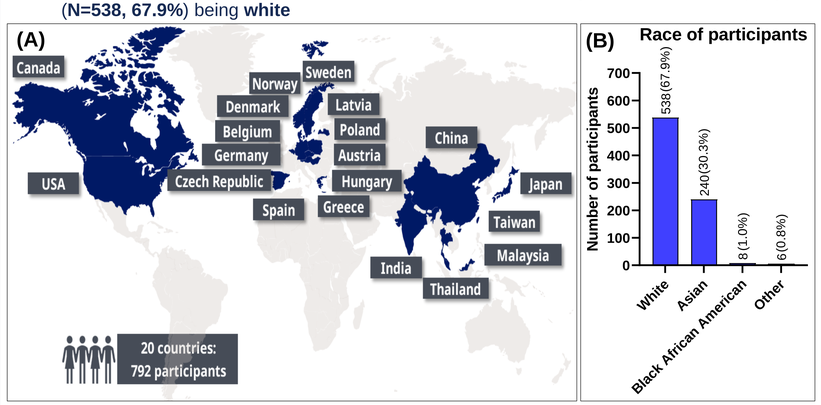

Figure 5. (A) Countries where participants were enrolled (B) Race of participants

- The majority (**85%**) of patients had an **eGFR of ≥60 mL/min/1.73m²** indicating either normal or mildly impaired kidney function
- The baseline measurements of the **median ABI** (**0.79**) and **median TBI** (**0.51**) respectively, were in the expected below normal range[6,7] (**Figure 6A & B**)

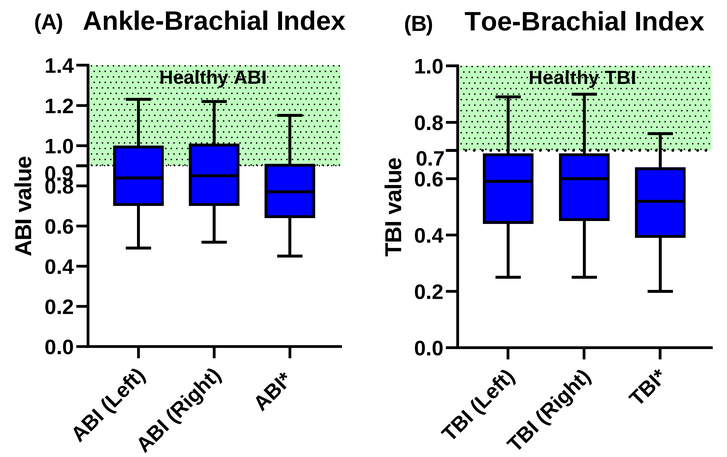

Figure 6. Baseline measurements of (A) ABI and (B) TBI. Box and whisker plots show median, Q1;Q3 and p5;p95 * Minimum value of both left and right indices respectively

Conclusions

- **STRIDE** has enrolled participants with early-stage symptomatic **PAD** (Fontaine IIa, intermittent claudication), **T2D**, **frequent risk factors** such as **older age**, **former or current smoking status** and an overweight **BMI** as well as **functional impairment**
- The **baseline characteristics,** presented here, highlight the degree of **functional impairment and risk factors** in this trial population of people with **PAD** and will enable assessment of the functional outcomes of semaglutide treatment in people with **PAD** and **T2D**

Presenting Author Conflict of interest

Dr. Bonaca is the Executive Director of CPC, a non-profit academic research organization affiliated with the University of Colorado; that receives or has received research grant/consulting funding between August 2021 and present from: Abbott Laboratories, Agios Pharmaceuticals, Inc., Alexion Pharma, Alnylam Pharmaceuticals, Inc., Amgen Inc., Angionetics, Inc., Anthos Therapeutics, ARCA Biopharma, Inc., Array BioPharma, Inc., AstraZeneca and Affiliates, Atentiv LLC, Audentes Therapeutics, Inc., Bayer and Affiliates, Beth Israel Deaconess Medical Center, Better Therapeutics, Inc., Boston Clinical Research Institute, Bristol-Meyers Squibb Company, Cambrian Biopharma, Inc., Cardiol Therapeutics Inc., CellResearch Corp., Cleerly Inc., Cook Regentec LLC, CSL Behring LLC, Eidos Therapeutics, Inc., EP Trading Co. Ltd., EPG Communication Holdings Ltd., Epizon Pharma, Inc., Esperion Therapeutics, Inc., Everly Well, Inc., Excon Consulting Pvt. Ltd., Faraday Pharmaceuticals, Inc., Foresee Pharmaceuticals Co. Ltd., Fortress Biotech, Inc., HDL Therapeutics Inc., HeartFlow Inc., Hummingbird Bioscience, Insmed Inc., Ionis Pharmaceuticals, IQVIA Inc., Janssen and Affiliates, Kowa Research Institute, Inc., Kyushu University, Lexicon Pharmaceuticals, Inc., Medimmune Ltd., Medpace, Merck & Affiliates, Nectero Medical Inc., Novartis Pharmaceuticals Corp., Novo Nordisk, Inc., Osiris Therapeutics Inc., Pfizer Inc., PhaseBio Pharmaceuticals, Inc., PPD Development, LP, Prairie Education and Research Cooperative, Prothena Biosciences Limited, Regeneron Pharmaceuticals, Inc., Regio Biosciences, Inc., Saint Luke's Hospitel of Kansas City, Sanifit Therapeutics S.A., Sanofi-Aventis Groupe, Silence Therapeutics PLC, Smith & Nephew plc, Stanford Center for Clinical Research, Stealth BioTherapeutics Inc., State of Colorado CCPD Grant, The Brigham & Women's Hospital, Inc., The Feinstein Institutes for Medical Research, Thrombosis Research Institute, University of Colorado, University of Pittsburgh, VarmX, Virta Health Corporation, Worldwide Clinical Trials Inc., WraSer, LLC, and Yale Cardiovascular Research Group. Dr. Bonaca receives support from the AHA SFRN under award numbers 18SFRN33900085 (BWH-DH SFRN Center) and 18SFRN33960262 (BWH-DH Clinical Project). Dr. Bonaca reports modest stock holdings in Medtronic and Pfizer. Dr. Bonaca receives consulting fees from Audentes.