An Approach to Improve Diversity and Inclusion in Clinical Trials: The DEFINE Trial (D/C/F/TAF Evaluated as a Fixed Dose Combination Regimen in Participants Switching from an Integrase Inhibitor who have Experienced Rapid Weight Gain)

Keith Dunn,[1] Richard Bruce Simonson,[1] Rachel Rogers,[1] Purnima Kassam,[1] Donghan Luo,[2] Amanda Gibson,[1] David Anderson,[1]
[1]Janssen Scientific Affairs, LLC, Titusville, NJ, USA; [2]Janssen Research & Development, LLC, Titusville, NJ, USA

Background: Weight gain following initiation of integrase inhibitor (INI)-based regimens has been observed in people living with HIV and appears to disproportionately affect women and Black/African American patients. Currently, it is unknown whether weight gain can be attenuated or reversed by switching off an INI-based regimen. In the US, women and Black/African Americans are often under-represented in HIV clinical trials. The purpose of this presentation is to highlight the unique design of DEFINE, a trial currently in progress, as an approach to improve diversity and inclusion in clinical trials and address this current data gap.

Methods: DEFINE is an ongoing prospective, randomized, open-label, 48 week, Phase 4 study evaluating the tolerability of switching to darunavir/cobicistat/emtricitabine/tenofovir alafenamide (D/C/F/TAF) compared to continuing an INI + tenofovir alafenamide/emtricitabine (TAF/FTC) regimen in virologically suppressed adults living with HIV who have experienced rapid and significant weight gain, defined as $\geq$10% increase within a 12 month time-period. To ensure representation of a diverse patient population, specific actions with regards to site selection and enrollment requirements were implemented. For example, site feasibility questionnaires asked investigators if they would be willing to participate in the study if required to enroll one Black/African American patient for every two non-Black/African American patients. Similar questions regarding gender enrollment were also included. Sites unwilling or unable to meet these criteria received low or no consideration for selection. As another example, the Interactive Web Response System was built to monitor diversity demographics at each site, and lock sites from screening new patients if their enrolled subject demographics drop below 30% female and/or 30% Black/African American participants. The primary objective of the study is to assess the percent change in body weight at Week 24 from baseline when switching to D/C/F/TAF compared to continuing the INI + TAF/FTC regimen in virologically suppressed patients. Additional key outcomes include assessment of body composition, efficacy, safety, resistance, and patient reported outcomes.

Results: Between October 2019 and July 2020, 52 potential study sites completed feasibility questionnaires. Of the 52 sites, 9 (17%) were placed on hold or were declined due to expected low enrollment of either female or Black/African American patients. A total of 30 sites were selected across 27 cities and 17 states in the US. As of November 2020, 38% of screened patients were female and 44% were Black/African American, and projected enrollment timelines remain on track.

Conclusions: The clinical trial design and operational processes in the DEFINE trial may be used as a model for future studies to ensure diversity among participants. Importantly, this model also demonstrated that enrolling a diverse population could be achieved without compromising enrollment timelines. The DEFINE study will represent the first randomized controlled trial switching patients from an INI-based regimen to D/C/F/TAF, and results from this study may provide insight on managing patients who rapidly gain weight on an INI-based regimen.