A5353: A pilot study of dolutegravir (DTG) + lamivudine (3TC) for initial treatment of HIV-1-infected participants with HIV-1 RNA <500,000 copies/mL

**Background**

LPV/r = 3TC was introduced to LPV/r + SMX in SABERL1, but LPV/r has shortcomings.

- Strengths of dolutegravir (DTG) + lamivudine (3TC)
  - The potent, well-tolerated drug
  - Robust resistance profile of DTG – Low resistance barrier of 3TC
  - Could save $550 million to > $3 billion in ART costs in the US over 5 years2

**Objective**

- Efficacy in compartments (genital, CNS) and pregnancy
- Efficacy at baseline VL > 100,000 copies/mL (cpm)
- Baseline HIV-1 RNA <100,000 copies/mL
- None emergence of RT, INI, major protease resistance mutations
- No emergence of minor protease variants

**Data Management**

- 83% of patients were genotyped successfully
- 96% [91%, 99%]

**Sample Size**

- Participants with VL ≥1000 and <100,000 copies/mL
- 3 patients met PDVF, one of whom had emergent R263RK mixture and M184V

**Protocol-Defined Virologic Failure (PDVF) Definition**

- Confirmed VL > 400 cpm at week 16 or 20
- Loss to follow-up, pregnancy

**Participant Disposition Up to Week 24**

- 96% [91%, 99%]

**Adverse Events**

- No severe adverse events
- Most events were possibly/probably treatment-related
- Palpitations

**Conclusions**

- In this pilot study, DTG+3TC demonstrated potent virologic efficacy with a study entry VL up to 500,000 copies/mL.
- Virologic failure was uncommon and associated with suboptimal adherence
- 3 patients met PDVF, one of whom had emergent R263KR mixture and M184V
- Future work in A533:
  - Investigate baseline and on-treatment RT and INI minority variants in the participants with virologic failure and a matched control group
  - Perform phenotyping on the participant with emergent R263KR mixture
- Analysis of pharmacokinetic interactions

- Two large randomized studies (GEMINI-1 and GEMINI-2) are underway and will provide more data on the resistance barrier of DTG+3TC

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