HPTN 076: TMC278 LA Safe, Tolerable and Acceptable for HIV Pre-Exposure Prophylaxis

Linda-Gail Bekker,* Sue Li,† Elizabeth Tolley,* Mark Mazikazi,* Nyaradzo Mgodzi,* Jessica Justman,* Shobha Swaminathan,* Adelaysi Adeleye,* Jennifer Fallon,* Neilupama Sistera

BACKGROUND

• Adherence to daily pre-exposure prophylaxis (PEP), in either oral or topical gel formulation, is a difficult goal for many and underscores the need for alternative strategies.

• Long acting injectable PEP is one such alternative strategy. Given the popularity of long acting contraceptives among women, the combination of effective, long acting injectable PEP with an effective injectable contraceptive is a promising way to prevent both pregnancy and HIV infection.

• HPTN 076 evaluated safety and acceptability of the long acting injectable form of rilpivirine (TMC278 LA) from Janssen Pharmaceuticals, Belgium.

METHODS

• HPTN 076 was a phase 1, double-blind, 2:1 randomized trial, comparing the safety, efficacy and tolerability of TMC278 LA for PEP in late sexually active HIV-uninfected women.

• Four sites participated in HPTN 076: Emavundleni CRS in Cape Town, South Africa; Spilhaus CRS in Harare, Zimbabwe; Bronx Prevention Center CRS in Bronx, NY; and Rutgers, New Jersey Medical School CRS in Newark, NJ.

• Injectable product, either TMC278 LA or placebo, was administered on six occasions, eight weeks apart: study Weeks 0, 2, 28, 36, 44 and 52. Participants received product at each time point in two, 2mL, nonabsorbable (silicone base) needles. One injection was given in each buttock. All study subjects were randomized to Phase 1, Week 12, before the last injection visit.

• Prior to injections, participants were given 26 doses of daily oral product, either placebo or 25mg rilpivirine (RPV). Participants were observed taking the oral product up to six times in clinic. The remaining doses were self-administered during study Weeks 0 – 4 (Oral Run-in Phase).

• Participants presenting with Grade 2 or greater RELATED Adverse Events (AEs) during the Oral Run-in phase did not progress to the Injection Phase. On a case by case basis, participants with Grade 3 or 4 UNRELATED AEs were permitted to move into the Injection Phase.

• In general, study product was ceased during the Injection Phase using the same criteria. Product was re-started in specific instances after review and consent from the study clinician.

RESULTS

• RPV drug concentrations were determined via a validated liquid chromatographic tandem mass spectrometric (LC-MS/MS) method with a lower limit of quantification of 1 ng/mL.

• Participants identified one or more attributes of injectable prevention they liked and disliked at baseline. Participants’ in all active arms liked that the injectable was:

  - Easier to use (>80%)
  - Term protection (>73%)
  - Acceptability did not differ by arm. At the last injection visit 68% of women participating in the Injection Phase. Product was administered at each time point in two, 2mL, nonabsorbable (silicone base) needles.

CONCLUSIONS

• The lower quartile RPV concentrations were consistently above the PA Trough at all times through eight weeks post injection.

• TMC278 LA injections administered every eight weeks in this clinical trial cohort of African and Asian women were safe, acceptable, and acceptable.

• Data from this study support further development of injectable agents for PEP.

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