Acceptability of Rilpivirine LA (RPV LA): Long-Acting Injectable Pre-Exposure Prophylaxis (PrEP) in HPTN 076

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BACKGROUND

Continuing high HIV incidence rates coupled with low adherence to HIV prevention agents (daily oral and topical) in clinical trials among African women underscores the need for more acceptable and easier to use HIV prevention. Strong global demand for injectable contraception suggests that new, long-acting, injectable HIV pre-exposure prophylaxis (PrEP) formulations could meet this need.1

HPTN 076, a phase II, double-blind, 2:1 randomized trial, compared the safety, tolerability, acceptability and PK of 1200mg RPV LA (placebo, P) among low-risk, sexually active, HIV-uninfected women in the United States (US), South Africa and Zimbabwe.

The results of the safety and pharmacokinetics of RPV LA through Week 76 are presented in the IAS 2017 Poster# MOLBPEC32. The results of the safety and pharmacokinetics of RPV LA through Week 76 are presented in the IAS 2017 Poster# MOLBPEC32.

METHODS

Four sites participated in HPTN 076: Emunnusen CRIS in Cape Town, South Africa; Spinhus CRIS in Harare, Zimbabwe; Bronx Prevention Center CRS in Bronx, New York; and Rutgers, New Jersey Medical School CRS in Newark, New Jersey.

After a four-week oral run-in phase, participants were administered an injectable product, either RPV LA or placebo, on six occasions, eight weeks apart. Participants received two 3 mL intramuscular (IM) injections on each occasion - one injection in each buttock.

We compared the acceptability of injectable study product (RPV LA) attributes versus placebo injection, preference and future interest in injectable PrEP by site (African versus US) and arm (RPV LA versus placebo) via quantitative surveys administered at baseline (Week 0) and first (Week 4), second (Week 6) and sixth (Week 44) injection visits.

Between Weeks 44 and 76, three Focus Group Discussions (FGDs) were conducted with participants from all four sites who had completed their sixth injection visit (N=27).

RESULTS

The study enrolled 136 (100 African, 36 US) participants with a median age of 31 years [IQR 25-38]. Baseline, US

At baseline, more than half (57%) of the participants in the African sites and 47% of those in the US sites reported having ever used injectable contraception and about half (53%) in both the African and the US sites reported currently using injectable contraception.

PREFERENCES FOR PREVENTION

The vast majority of participants at all sites preferred using the long-acting injectable and interest increased in both locations over the course of the study. (Figure 1)

Some US participants reported preference for daily oral pills at baseline and 28 weeks (25%) and some preferred a topical method at either baseline or 28 weeks, but preference for other methods was very low at all African sites.

PERCEIVED NEED

At baseline, most participants did something to reduce their risk of HIV – including having sex with only one partner (74%), reports were significantly higher in Africa versus the US at 83% vs 50%, p<0.0005) and condom use (24%) – although only 31% said that they always used condoms. More participants from the African sites were very worried about HIV at US sites (34% versus 11%, p<0.01).

PERCEIVED NEED (CONTINUED)

At exit, FGD participants continued to describe varying levels of perceived risk about HIV in Cape Town, participants felt that communities were less concerned about acquiring HIV than in the past, whereas in Harare, both knowledge and perceived risk were described as having increased. US participants believed the risk was high, but that people tended to be careless.

“People are not frightened by it (HIV) because even if you are sitting and talking, a person will say yes, I don’t care about that HIV. We will just have it; we will just go to the clinic and take our pills. It’s not a dog’s disease, it’s everyone’s disease.” FGD Participant, Cape Town.

“IT is a big concern, and I am actually afraid of the young people, because they are a little careless right now on a whole. I think they don’t know enough about HIV and they are a part of that young people. I am not giving it much importance, as they should. They are not recognizing how serious this disease is.” FGD Participant, US.

Acceptability of Injectable Attributes

Most participants (>75%) rated injectable attributes (number, location and frequency) as very acceptable.

“I want it if (injectable) because we do not trust how our medical counsellors, themselves, they will else. Also, men do not agree to use condoms so I will know that once I have my injection, I will be alright.” FGD Participant, Zimbabwe.

While few reported rash or other side effects, 61%-67% reported pain with injection, with non-significant differences over time and between arms.

In FGDs, participants described initial fear of the injectable and variable experiences with pain over time. A US participant admitted.

“Getting the shots was my way. Everything else was fine with the staff, everything. The atmosphere was just calm and welcoming. But I learnt several months in and two years ago you could not even take a battery and try to draw and play until my mother got me.”

A participant from Cape Town suggested that the pain experienced during her first injection almost prevented her from continuing:

“For me I felt like not coming back again. When I had my first injection my bull was paining the whole week and also I thought to myself I’m not going to come back.”

EASE OF USE

Some appreciated that the injection was easy and private and there was not a need to take daily pills.

“Like what has been mentioned by others who shared before, the injection is go good and different from pills. With the pills, you may have a journey and forget them at home, but with the injection, once you are injected that it, and you will know it lasts 2 months and you will go again after 2 months. So I find it less.”

FGD Participant, Zimbabwe.

“If you are in a situation where you cannot use condom, or in a situation where you forget. You have your shot and you are good, you don’t have to worry about it. If like, condon, nothing.”

FGD Participant, US.

RECOMMENDED CHANGES TO INJECTABLE

About half (48%) of participants recommended no changes to the injectable. The most frequently (16%) endorsed change related to having only one injection, even if the injection contained a larger volume. Less than 10% suggested that the duration of protection increase. And, in the placebo arm about 17% suggested that the injection should be in the arm (instead of buttck). This was endorsed much less frequently (8% but not significant) in the RPV LA arm.

In FGDs, some African participants were confused about why they received two injections rather than one; for instance, one participant thought she received one shot with water only and one with the product and several participants thought there were two injections because there were two different drugs. They therefore suggested that the injections be combined and only one shot be given.

FIGURE 3: Recommendations for Injectable Changes, Week 28

STUDY BURDEN

At exit (N=112) 10% (10%) participated that both the time required overall for the study and the time spent waiting for study visits was too long. In the majority (N=17, 10%) felt the time was acceptable or “just right.” Only 17 (4.3%) said they ever experienced any problems or concerns related to the study; however in the FGD, participants raised concerns about some of the study visit procedures. Some participants were not comfortable with the collection of vaginal and rectal fluids and this was made worse when these procedures were done by male staff, most from African sites.

Most (N=91, 83%) said that the money paid for participation was adequate; about 16% (N=21) said it was too little. More than two-thirds of participants (N=110, 92%) said they would participate in similar research in the future.

DISCUSSIONS & CONCLUSION

Almost half of African and one-quarter of US participants perceived moderate to high risk of acquiring HIV and reported low levels of consistent condom use. In this context, a long-acting injectable PrEP product was seen as highly acceptable and preferable to other new prevention products.

Most aspects of the injectable were highly acceptable, although about two-thirds of participants experienced some injection site pain. Most recommendations for improving acceptability were related to reducing injection pain.

Although HPTN is not planning further studies of RPV LA, two phase III trials of a different long-acting injectable PrEP product, delivered in a single injection, are being planned (HPTN 084) or are in the field (HPTN 085).

REFERENCES


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HPTN 076 Study Abbreviations: The trial regulatory sponsor, PATH Drug Solutions, as well as B&I Melinda Gates Foundation and Janssen Pharmaceuticals.

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