PHASE IIB EFFICACY TRIAL OF MOSAIC HIV-1 VACCINE REGIMEN IN AFRICAN WOMEN: IMBOKODO

Abstract Body

Imbokodo is the first trial evaluating clinical efficacy of a heterologous HIV-1 vaccine regimen consisting of an Ad26 vector (Ad26.Mos4.HIV) expressing mosaic Gag/Pol/Env antigens for broad HIV-1 clade coverage, and an aluminum-adjuvanted clade C gp140. This trial, conducted in women at high risk for HIV-1 in sub-Saharan Africa, is supported by preclinical and early phase clinical trials demonstrating safety and immunogenicity.

We enrolled 18-35 year-old women in a randomized, double-blind, placebo-controlled, phase 2b efficacy trial in Malawi, Mozambique, South Africa, Zambia, and Zimbabwe. Women were randomized 1:1 to a heterologous prime and boost vaccine regimen or placebo administered at Months 0 and 3 (Ad26.Mos4.HIV) and Months 6 and 12 (Ad26.Mos4.HIV+clade C gp140). Pre-exposure prophylaxis was available at no charge. Primary vaccine efficacy (VE) was evaluated from Month 7 to 24 (VE[7-24]) in the per-protocol (PP) cohort. Continuation of the trial was to occur if the lower bound of the 95% confidence interval (CI) for VE(7-24) was >0%. Adverse events (AEs) were collected post each vaccination. Serious AEs and AEs of special interest (AESIs) were collected throughout the trial.

A total of 2637 women (1323 placebo, 1314 vaccine), with a median age of 23 years, were enrolled at 23 sites. Baseline characteristics were similar across arms with ~3% detectable intracellular tenofovir disoproxil fumarate levels. HIV-1 incidence between Month 7 and 24 in the PP cohort was 4.3 per 100 person-years in the placebo arm versus 3.6 in the vaccine arm (Figure). VE(7-24) was 25.2% (95% CI: –10.5% to 49.4%). The vaccine was well tolerated with mild local reactogenicity (mild/moderate pain/tenderness: 23% placebo, 50%

vaccine). Mild/moderate systemic symptoms were reported by 56% and 66% in the placebo and vaccine arms, respectively. No vaccine-related serious AEs or AESIs were reported.

HIV-1 incidence was high in this trial. Unfortunately, this vaccine regimen, although safe, did not provide statistically significant protection against HIV-1 infection in young women and, therefore, the trial was discontinued. An ongoing phase 3 trial (Mosaico) is evaluating the efficacy of an HIV-1 vaccine regimen with a modified boost (Ad26/bivalent gp140) in MSM and transgender individuals in the Americas and Europe. Biomedical interventions are urgently required to reduce the impact of HIV-1 in women in Africa.

AUTHORS

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