The quest for a prophylactic HIV vaccine continues: results from a phase I trial using novel routes of DNA vaccination in HIV uninfected volunteers

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Background

- As the HIV epidemic continues to expand, it is widely accepted a preventative HIV vaccine is a vital public health priority
- DNA vaccines are being increasingly utilized based on several advantages over other vaccines including rapid manufacture, cost effectiveness and lack of concerns associated with the administration of infectious agents
- Limitations to DNA vaccination are related to inefficient uptake of DNA into cells and rapid degradation, thus ineffective antigen presentation
- Ongoing efforts investigating DNA vaccine delivery are therefore of great interest in an effort to improve immunogenicity and these include cutaneous routes
- Previous studies have shown a dose sparing effect of intradermal (ID) vaccination, where only 10-20% of a conventional intramuscular dose (IM) is needed to be adequately immunogenic
- Transcutaneous (TC) vaccine delivery, is ‘needle-free’ and in a recent Phase I clinical trial using an influenza/tetanus vaccine, this method favoured the development of CD8+ T cell responses, a potentially crucial killing mechanism in HIV. This method has never been utilised in a DNA preventative HIV vaccine trial
- Physical methods of delivering DNA such as in vivo electroporation (EP) have been shown to enhance DNA immunogenicity in early clinical trials
- In this Phase I RCT we report on the safety and immunogenicity of a GTU® MultiHIV B clade DNA vaccine in HIV uninfected participants administered via the 3 different routes described above

Methods

- 30 HIV uninfected participants deemed eligible according to strict criteria, were randomised to receive GTU® MultiHIV Clade B DNA vaccine at weeks 0/4/12 by 1 of 3 routes: IM=ID+IM, IM=TC+IM
- Participants were assessed for local and systemic reactogenicity and adverse events
- T cell responses to vaccine encoded peptides (rev, tat, nef, gag, CTL coded for by pol and env genes) made were measured by IFN-γ ELISPOT and intracellular cytokine staining (ICS)
- An exploratory end point to assess CD8+ T cell function was conducted using a viral inhibition assay (VIA)

Recruitment and participant flow

- 59 participants were screened with 30 deemed eligible according to inclusion/exclusion criteria. The table below shows the demographics of enrolled participants (Table 1)
- 3 participants did not complete all vaccine visits, but remained in follow up: In the ID+IM group the participant moved away before trial completion. In the TC+IM group the participant chose to not have the final vaccine due to ongoing hypopigmentation over the vaccine site, and in the EP+IM group the participant chose not to continue with vaccinations due to pain linked to the EP procedure

Results

3. Viral inhibition assay (VIA)

- A viral inhibition assay was used to measure the in vitro ability of CD8+ cells to inhibit HIV replication based on a previously published assay and using a panel of 6 viruses (Table 2)
- All groups showed viral inhibitory activity to at least one virus at the primary end point, in 2/9, 4/9 and 5/7 participants across groups ID+IM, TC+IM, EP+IM respectively.
- The greatest number of participants with detectable HIV-specific CD8+ cells capable of inhibiting any virus was in the EP+IM group (71% participants) and to the greatest number of viruses in the panel (4/6), with the greatest cross clade inhibition (Figs 5A and 5B).

Conclusions

- The GTU® MultiHIV B clade DNA vaccine was safe and well tolerated across all routes of vaccine administration and showed the greatest cellular immunogenicity when administered IM with EP
- The use of EP induced the greatest and broadest CD8+ viral inhibitory activity, although all groups also showed inhibition
- Importantly and in line with other clinical trials using EP, participants found the procedure to be tolerable and acceptable
- It is important to place this predominantly T cell based DNA vaccine in the context of wider clinical trials assessing combined T cell responses, in the ultimate goal of developing a robust HIV preventative vaccine

References: