IMPAAACT 2004 Infant Vaccine Study

Overview

**Rationale:** ~250,000 infants still become HIV-1 infected annually, despite expanded ARV use

**Proposed Approach:** Phase 1 safety/immunogenicity trial in an African infant cohort
  - expected initiation date: March 2017
  - primary immunogenicity results available: Nov 2018
**Rationale**

- Efficacy in infants can be demonstrated with only **short lived protection (~1 year)**
  - RV144 was 60% efficacious in 1st year

- Infants make vaccine-elicited IgG responses that are higher magnitude than RV144 vaccinees and of long duration
  - 22 fold higher V1V2 IgG response in Chiron 230 Env/MF59 immunized infants compared to RV144 vaccinees
  - 56% of infants still had responses detectable at 2 years
    (Fouda et al, JID, 2014)

- Infants make no IgA responses to pox/protein immunization

- Newborns have minimal exposure to environmental/microbiota antigens

- Infant immunization could be boosted in adolescence for broad, mature Ab responses prior to sexual debut
The infant immune system is a distinct immune “landscape” for HIV-1 Env vaccination

Adult vaccine-elicited responses will not predict infant vaccine-elicited responses
HIV-infected infants can rapidly develop broad neutralizing responses

• Early development of cross-clade tier 2 neutralizing responses in 2/3’s of HIV-infected infants
  • Goo and Overbaugh et al, Nat Med 2014
  • Overbaugh et al and Goulder et al, CROI 2016

• May be mediated by less mutated broadly neutralizing antibodies (bnAbs) compared to adult bnAbs
  • Overbaugh at al CROI 2016
Prior infant vaccine safety data

• 3 clinical trials of neonatal immunization with ALVAC/Env product have been safe
  • Env/MF59 in PACTG 230 Chiron trial
  • ALVAC/Env in PACTG 326
  • ALVAC in HPTN 027 (African infants)

• MF59 also used in infant influenza vaccine trials

• Plan to monitor response to EPI vaccines in HIV-1 vaccinees
IMPAACT 2004 Vaccine Product/Dose

- ALVAC: vCP2438
  - Sanofi Pasteur

- Bivalent rgp120: TV1/1086C
  - Novartis/GSK
  - 15mcg/dose
    - Selected dose based on Chiron/MF59 dose escalation study

- Env stability testing post dilution completed by Duke QA unit

Week 24 gp120 IgG responses
Placebo Groups will be combined for statistical analysis.

Follow all groups for two years
Follow vaccine groups for four years (durability)
Potential long term follow up/boosting in adolescence for vaccine group(s)
Primary Objectives

1. Assess the safety of three candidate infant HIV vaccine regimens:
   • a gp120-only regimen, a conventional prime-boost regimen, and an accelerated prime-boost regimen

2. Determine which of the three regimens induces an early (10 week) V1V2-specific IgG response > than maternally-acquired V1V2-specific IgG levels among placebo recipients
   • Durability of response through breastfeeding period is a key secondary aim
IMPAAACT2004 Protocol update

• Completed DAIDS PSRC and regulatory review
• HVTN 702 efficacy trial passed Go-No Go and regulatory reviews, plans to initiate study in Nov 2016
• Awaiting approval for vaccine products from the P5 committee,
• Planning for IMPAAACT2004 South African MCC regulatory review submission in Nov 2016 for review in Jan 2017
• Expect completion of regulatory and IRB approvals in March 2017
• HVTN 107 adult safety data needed for co-administration group – planned to begin in Jan 2017
Timelines of maternal/infant vaccine clinical studies

- P1112 – passive VRC01 PK/safety
- IMPAACT 2004 – infant Env vaccine safety/immunogenicity
- CERES trial – maternal Env vaccine safety/immunogenicity in HIV+ women
- CAP 523 EnvSeq-1 immunization in infants