Getting to Zero: HIV vaccines to eliminate the pediatric HIV-1 epidemic

IMPAACT Vaccine Working Group

Overview

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Despite wide availability of ARV, pediatric HIV-1 continues to be a major public health challenge

- >200,000 children become HIV infected annually
  - 700 infants become infected with HIV-1 daily
  - High rate of acquisition in early adolescence
- Current PMTCT will not eliminate MTCT:
  - Poor maternal coverage, adherence, and acute infection
  - high rates of prematurity (PROMISE)
- PrEP and other existing prophylaxis difficult to initiate in early adolescence

Additional interventions will be required to achieve an **HIV-free generation**
Bi-modal pediatric HIV-1 epidemic

HIV-1 prevalence (%)

Age

0 1 2 3 12 13 14 15 16 17 18 19-24

Critical window to develop active immunity (10+ years)

Maternal immunization or Infant passive immunization

Passive immune protection

Passive immune protection
Opportunities for immune-based maternal/infant interventions to reduce MTCT

Modeled after the successful Hep B passive/active maternal and infant immunization strategy

1. Enhancement of protective maternal antibodies during pregnancy (CHAVI-ID)
   – *In utero*, peripartum

2. Passive antibody immunization at birth for high risk infants (VRC01/LS – P1112)
   – Peripartum, early postnatal

3. Active immunization to prevent breast milk transmission (IMPAACT 2004)
   – Late postnatal transmission, acute maternal infection during lactation
Immune-based interventions to reduce transmission in early adolescence

1. Q3 month passive antibody administration ("Depo" like approach) with potent, long-acting bnAb
   - Young women, young MSM

2. Active immunization/boosting throughout childhood to prevent breast milk and early adolescent sexual transmission (IMPAACT2004, CAP523)
Next 5 years – infant and adolescent passive antibody trials

1. Passive antibody protection against breast milk transmission (VRC01/LS)
   – PK/safety (P1112)
   – Efficacy in high transmission areas (partnership with Pepfar?)

2. Maternal immunization to enhance autologous virus neutralization
   - Clade B/C rgp120 (CERES trial – CHAVI-ID)

3. Passive antibody protection of high risk adolescents
   – PK/PD/tolerability (partnership with HVTN/PTN)
   – Efficacy (partnership with HVTN/PTN)
Next 5 years – infant active vaccination trials

• Current HIV vaccine candidates don’t elicit broad neutralization

• Novel strategies for induction of neutralizing B cell lineages – likely to need years of antibody maturation

• IMPAACT 2004
  – ALVAC/Env immunization with Sanofi/GSK products
  – Same products as HVTN 702 efficacy study
  – Immune correlates from adult efficacy study could bridge to infant indication

• Env Seq-1 (CAP 523)
  – B cell lineage design Env vaccine to initiate broad neutralizing responses
Getting to zero pediatric HIV cases

- Maternal immunization of HIV+ women
- VRC01 LS for high risk BF infants
- Universal active HIV vaccine
- Long acting bnAb for high risk adolescents
Timeline 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