



# Preliminary safety and immunogenicity of a B-subtype DNA prime/recombinant fowlpox virus boost candidate prophylactic HIV vaccine

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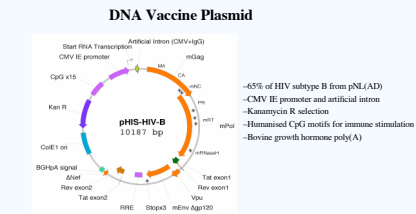
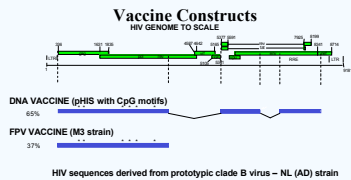
## Introduction

DNA Prime Vector Boost regimes have shown great promise in mouse models for the induction of effective CD4+ and CD8+ T cell responses which efficiently control viral load post challenge with high dose pathogenic SHV or SHV<sub>2</sub>. We tested our lead candidate for safety and immunogenicity in a Phase I clinical trial.

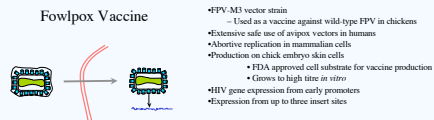
## Aim

- Primary Aim**
- Assess safety and immunogenicity of prime-boost regime (proof of principle)
- Secondary Aim**
- Better understand nature and breadth of immune responses
  - Assess risk behaviour in participants

## Method



## Method



### Clinical Trial Design

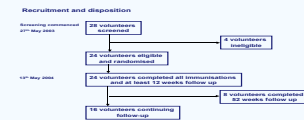
- Design**
- double blind, placebo-controlled in 24 volunteers
  - 3:1 vaccine:placebo randomisation
  - healthy adults 18-55 yrs of age at low risk of HIV-infection
  - frequent assessments for 52 weeks
  - interim analysis of data up to week 12

- Immunisation dose and schedule**
- DNA: 1mg (IM) on day 0 and week 4
  - rFPV: 5 x 10<sup>7</sup> pfu/mL (IM) on week 8
- Each immunisation approximately 1mL volume  
(DNA- dominant arm, rFPV- non-dominant arm)

- Safety measures**
- History and OE, FBC, UBC, LFT, U/A and HIV antibodies
- Immunogenicity measures**
- Primary - IFN-γ ELISPOT against HIV antigens (weeks 0, 8, 9, 12 and 24)
  - Secondary - Lymphoproliferative assay and intracellular cytokine assay (weeks 0, 9, 12 and 24)

- Primary end point: week 9**
- mean change in IFN-γ responses from freshly isolated PBMC following stimulated by gag pool 122
  - number of volunteers with positive IFN-γ responses by T cells stimulated by gag pool 122
  - Serum and PBMC repository for retrospective immunological tests (eg tetramer CTL, humoral responses)
- Multiple secondary endpoints including:**
- Change in stimulation index for lymphoproliferative responses to p24 by LPA and other HIV antigens/assay proportion of responders
  - ICCS of IFN-γ/IL-2 CD69 in response to HIV gag antigens
  - Anti-HIV gag, pol and env antibodies (ELISA and Western blot)
  - Mean change in ELISPOT HIV gag response from baseline to wk 8
  - Mean change in ELISPOT HIV gag response from wk 8 to wk 9

## Results



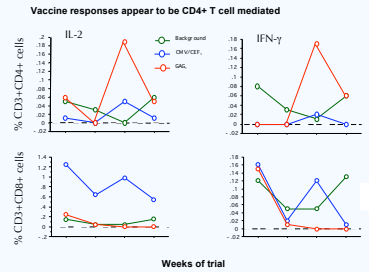
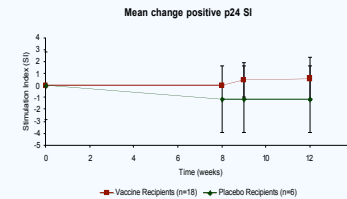
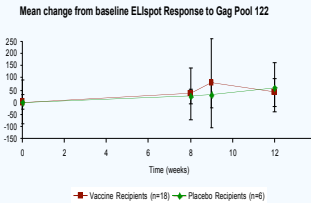
**Demographics**

	Vaccine (n=18)	Placebo (n=6)	Total (n=24)
Male (%)	14 (78)	1 (17)	15 (63)
Female (%)	4 (22)	5 (83)	9 (37)
Mean age			
years (±SD)	37.0 (11.7)	44.0 (10.8)	39.0 (11.5)
Heterosexual (%)	5 (21)	2 (8)	7 (29)

**Vaccine Placebo Total Protocol Compliance**

	Vaccine	Placebo	Total
N (%) 1 <sup>st</sup> DNA prime	18 (100)	6 (100)	24 (100)
N (%) 2 <sup>nd</sup> DNA prime	18 (100)	6 (100)	24 (100)
N (%) rFPV boost	18 (100)	6 (100)	24 (100)

- Safety**
- No serious adverse events
  - No HIV infection
  - Vaccine site reactions: no ulceration, one episode of induration, no erythema > 2.5cm
  - Local reactions: no lymphadenopathy
  - Systemic reactions: no recorded febrile episodes (one reported), no anaphylaxis
  - Clinical adverse events: several URTIs and GI upsets
  - Laboratory adverse events: no event > grade 2, increased ALT/ALP in 2 vaccine recipients, leucopenia in one vaccinee and one placebo recipient



## Conclusions

- trial successfully recruited
- data are robust and validated
- vaccine constructs (as specified) are safe and well tolerated
- no significant immune responses observed following administration
- modest and inconsistent responses observed in two subjects
- latter responses are apparently CD4+ T lymphocyte driven
- candidates warrant further investigation

## Acknowledgements

NCHECR is funded by the Australian Government Department of Health & Ageing and is affiliated with the Faculty of Medicine, The University of New South Wales.  
This project was funded by an HIVDTT Contract through the NIH Division of AIDS.  
HIV Gag and Pol Peptides were supplied by the NIH AIDS Research and Reference Reagent Program.