

## **Preliminary Analysis of FIT Protocol # C060401:**

### **Safety, Immunogenicity and Efficacy of GTU<sup>®</sup>- MultiHIV B Clade DNA Vaccine, a Randomized Placebo-Controlled Phase II Trial in Untreated HIV- infected Individuals.**

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# Background

- The HIV epidemic and burden of disease in South Africa is substantial
  - 5.5 million people are infected with HIV
  - Nationally 29.1% of antenatal clinic attendees are HIV positive
- Majority of HIV vaccines being tested globally are preventative
- Therapeutic HIV vaccines in HIV infected individuals may modify the course of infection and progression to AIDS by maintaining
  - Low viral loads
  - High CD4 cell counts
- Chronically infected individuals that are not eligible for ARV's
  - Public sector access in South Africa CD4 cut-off is < 200 cells/mm<sup>3</sup>

# Vaccine Candidates

## First Generation Vector

### GTU®-MultiHIV B

- Contains regulatory & structural genes from Han-2 isolate
- Evaluated in Phase IIA therapeutic clinical study in South Africa

## Second Generation Vector

### Auxo-GTU®-MultiHIV A,B,C,FGH

- Contains regulatory & structural genes from A, B, C consensus and FGH ancestor sequences
- Preclinical data in NHP [R Le Grande, OA04-03]
- To be used in 2008 Phase I/II study

Rev

Nef

Tat

CTL(pol+env)

opt p17/24

# Protocol Outline

- Study design
  - Randomised, single-blinded, placebo-controlled
- Sample size
  - 40 on active vaccine candidate and 20 on placebo
- Route of administration
  - IM (1mg) and ID (0.5mg) via Biojector
- Immunization schedule
  - 0, 1, 3 months followed by 2 boosts at 19 and 20 months
- Study population
  - Healthy HIV subtype C infected, 18-40yrs, CD4 > 350 cells/mm<sup>3</sup>, viral load > 50 copies/ml, no AIDS defining illness and no history of HAART therapy
- Primary endpoints:
  - Safety: post each injection and SAE
  - Immunogenicity: IFN- $\gamma$  ELISPOT, Nef and Gag antibodies, cross-clade IFN- $\gamma$  ELISPOT and IL-2 ICS
    - Positive responses defined as  $\geq 55$  SFC/10<sup>6</sup> PBMC and  $\geq 4$ -fold over media control
- Secondary endpoint:
  - Clinical effects: CD4, CD3, CD8 and viral load
- Study Duration
  - Q1/2006-Q1/2009



# Enrollment Characteristics Participants

	Mean	Range
<b>Age</b> (yrs)	29	20 - 40
<b>Viral load</b> copies/mL	41,077	366,00 –55,000
<b>CD4</b> cells/mm <sup>3</sup>	560	987 - 360

- Female:Male 4:1
- Reasons for screening failure
  - Low CD4 (25.7%)
  - Other medical (22.9%)
  - HBsAg +ve (14.3%)
  - Other non medical (17.1%)
  - Pregnancy (11.4%)
  - Psychiatric (8.6%)

# Safety: Local Reactogenicity

\*occurred at least once after immunisations 1, 2 or 3

Treatment arm	FIT ID		Placebo ID		FIT IM		Placebo IM	
	Imm	>30min	Imm	>30min	Imm	>30min	Imm	>30min
Bleeding	52	0	30	0	10	0	10	0
Itching	14	10	10	0	0	0	0	0
Bruising	0	0	0	0	0	0	0	0
Haematoma	0	0	0	0	0	0	0	0
Persistent redness	0	5	0	10	0	0	0	0
Persistent oedema	67	62	60	20	5	0	0	0
Induration	19	24	10	10	0	5	0	0
Others	5	5	10	0	5	10	0	30
<b>Any symptom</b>	<b>76</b>	<b>67</b>	<b>80</b>	<b>20</b>	<b>14</b>	<b>14</b>	<b>10</b>	<b>30</b>

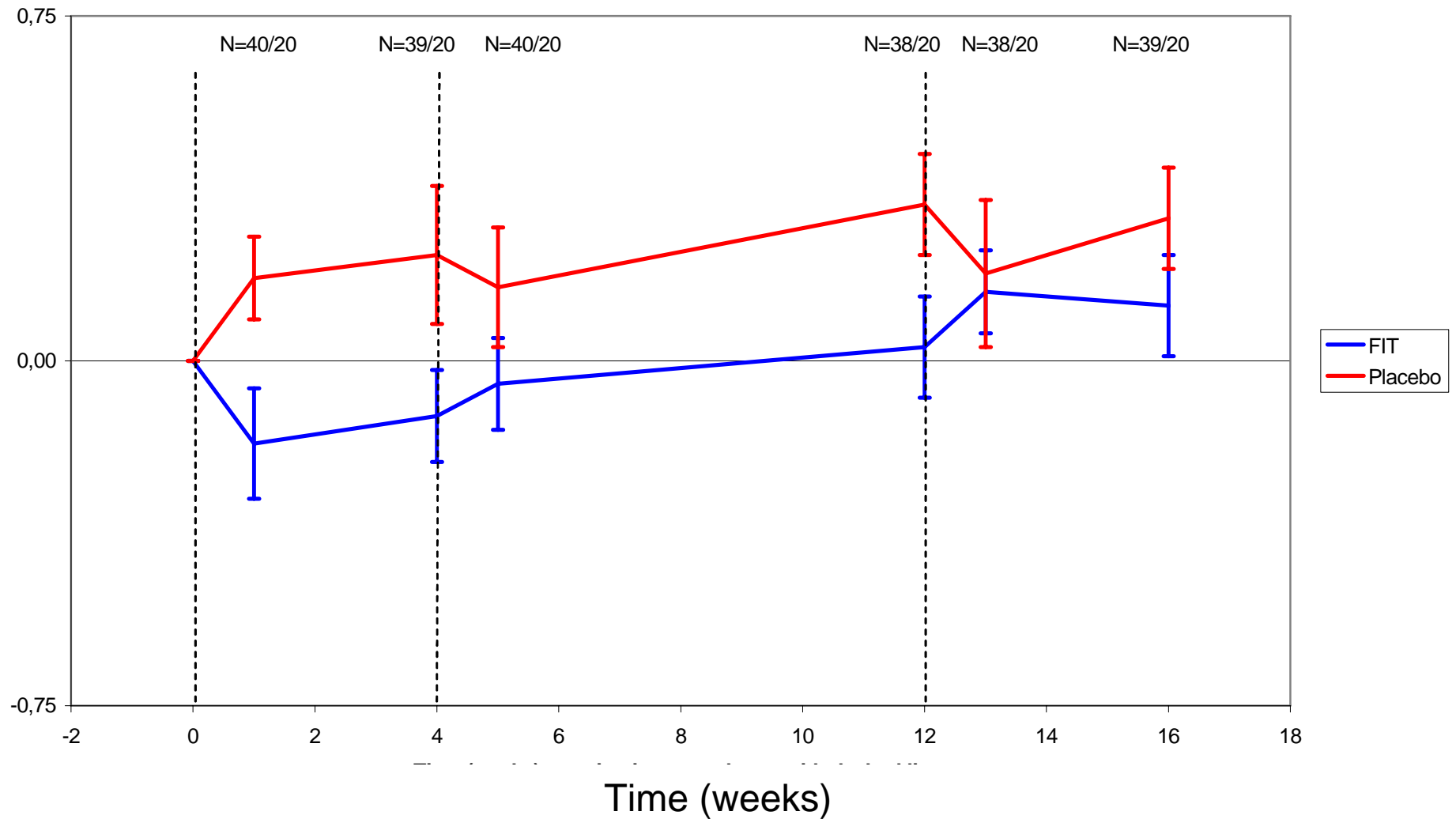
Abbreviations: Imm: immediate; >30min: after 30 minutes

# Most common AE's After Vaccination

\*occurred in > 5% of all participants

Event	FIT (ID + IM) (N = 40)	Placebo (ID + IM) (N = 20)
Lymphadenopathy	12 (30%)	11 (55%)
Upper respiratory tract infection	9 (23%)	6 (30%)
Headache	7 (18%)	4 (20%)
Diarrhoea	5 (13%)	0 (0%)
Rash	3 (8%)	2 (10%)
Vaginal candidiasis	3 (8%)	2 (10%)
Eczema	0 (%)	2 (10%)

## Clinical Impact: Log Viral Load Mean Change from Baseline



\*FIT vs. Placebo P 0.007

## Vaccine Responders

Reduction in log viral load >0.5  
log-unit at least once between  
week 1 and 16

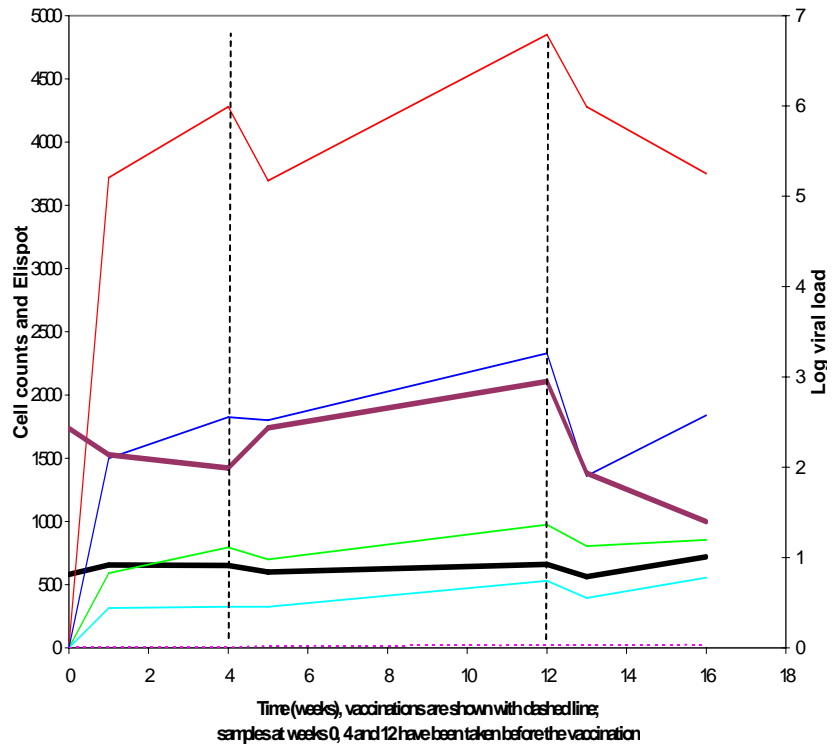
	FIT		Placebo	
	N	%	N	%
ID	12	60	2	20
IM	11	55	4	40
<b>Total</b>	<b>23</b>	<b>58</b>	<b>6</b>	<b>30</b>

Reduction in log viral load >1  
log-unit at least once between  
week 1 and 16

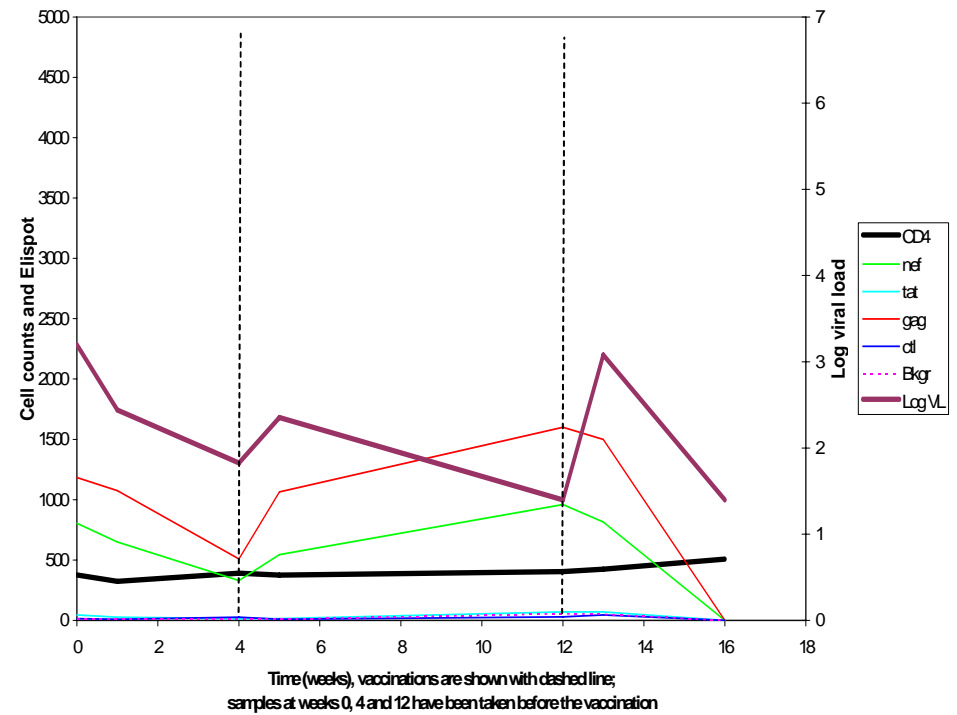
	FIT		Placebo	
	N	%	N	%
ID	4	20	1	10
IM	3	15	0	0
<b>Total</b>	<b>7</b>	<b>18</b>	<b>1</b>	<b>5</b>

# CD4 and ELISPOT Effects in Responders

Subject 233 (FTID)



Subject 212 (FTIM)



# Preliminary Conclusions

- Safe and well tolerated
  - Limited local reactogenicity
- Clinically
  - Statistically significant difference in log viral load between treatment groups (IM and ID) and placebo
  - CD4 counts remain stable
- Immunological
  - ELISPOT responses to most vaccine antigens (Gag, Nef, CTL epitopes)
  - ID group responses are better than the IM responses
- Continued follow up
  - Clinical effect
    - Decline in viral load and maintenance in CD4 counts
  - Boosts

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