

Indicators of Therapeutic Vaccine Effect using GTU-MultiHIV B clade DNA in Treatment-Naïve Subtype C HIV-1 Infected Subjects

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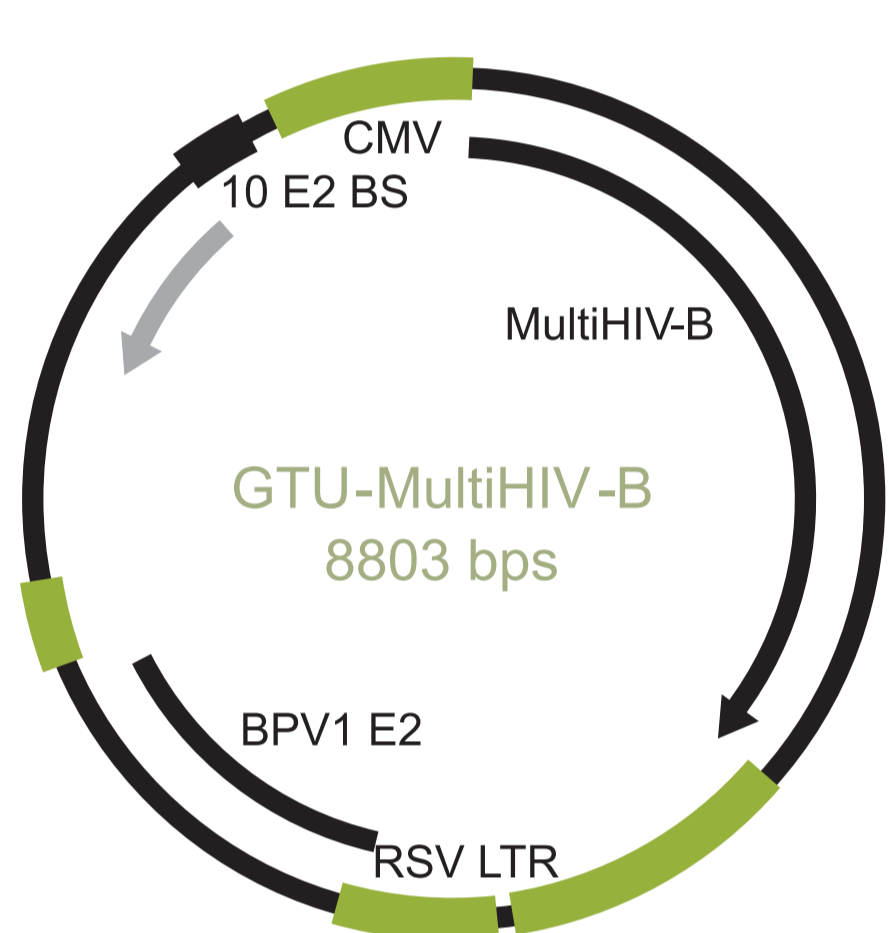
FIT Biotech: Addressing an urgent need for therapeutic HIV vaccines

- 5.7 million people (3.2 million of which are women) are infected with HIV in South Africa
- The National Antiretroviral (ARV) Programme in South Africa has initiated ARV's in over 500,000 people since 2004
- But ARV delivery is limited because of; -High costs of ARV's
 - Overburdening of the health services due to
 - shortages of qualified staff and
 - limited laboratory capacity for diagnostic and follow up testing
- Therapeutic HIV Vaccines may be advantageous in resource constrained settings because they may potentially;
 - Reduce the burden of ARV delivery on existing health services
 - Decrease the occurrence of side-effects in people on multiple ARV's
 - Decrease the number and therefore the costs of ARV's required for maintenance therapy

Why therapeutic HIV vaccines are important

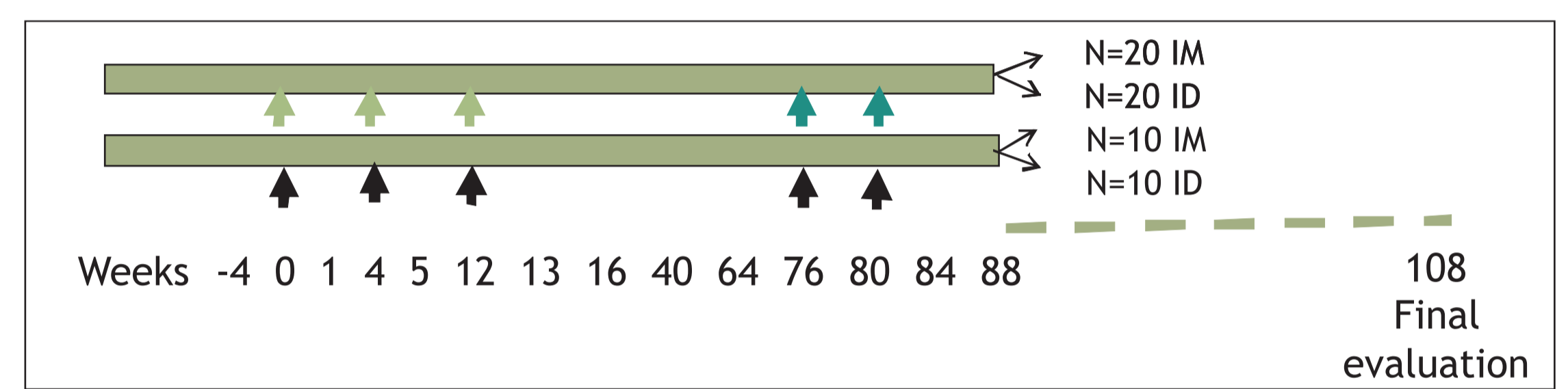
- Globally research is focused on preventative HIV vaccines
- Preventative HIV vaccines do not address the needs of people already infected with HIV
- An effective therapeutic HIV vaccine may
 - Lower plasma viral load, decreasing the likelihood of sexual and mother-to-child transmission of HIV
 - Restore functional CD4 cells delaying the development of opportunistic infections with AIDS
 - Enable earlier therapeutic intervention in HIV infected individuals
 - Provide immunological support for HIV infected people already on ARV's
 - Be the most cost-effective solution to controlling HIV in resource constrained countries where ARV access is limited

FIT Biotech's novel therapeutic HIV vaccine (GTU-MultiHIV-B)



- GTU DNA technology is unique because it allows;
 - Long-term expression of a gene of interest
 - Less DNA needed per immunisation
 - E2 BPV segregation/partitioning function
 - Versatility
- Potential applications include:
 - Other infectious diseases eg TB vaccines
 - Oncology
 - Gene therapy

Study Design Trial: A randomized Phase IIA placebo-controlled trial with GTU-MultiHIV-B (FIT-06)



Primary endpoints : safety & immunogenicity
Secondary endpoints : pVL, CD4 cell counts
Mean enrollment characteristics :
- Age 29 yrs (range: 18 -40 yrs).
- Plasma viral load > 38000 copies/mL
- CD4 cells/μl > 500
- Subtype C infected
- Untreated volunteers

■ Treatment -naïve
▲ FIT-06 IM (1mg), ID (0.5 mg)
▲ FIT-06 IM (2mg), ID(1mg)
▲ Placebo IM & ID

Statistical methods used for clinical data analysis

- Intention-to-treat (ITT) analysis
 - Includes all randomized patients who did not discontinue before week 5 due to SAE's (N=60)
- Repeated measures analysis of covariance (RMANCOVA)
 - Characterizes changes from baseline in viral load log (copies/mL) and CD4/CD8 cell counts (cells/μl)
 - Baseline values were used as a covariate

Results from the Phase IIA GTU-MultiHIV B (FIT-06) trial

- Table 1** demonstrates that immunization with FIT Biotech's GTU-MultiHIV B therapeutic HIV vaccine decreases plasma viral load compared to placebo
- The greatest decrease in plasma viral load is demonstrated after intramuscular (IM) delivery of the FIT Biotech's GTU-MultiHIV B vaccine as shown in **Figure 2**
- Figure 3** demonstrates that this beneficial effect on plasma viral is enhanced in those volunteers with favorable HLA alleles (HLA B*5073)
- Immunization with FIT Biotech's GTU-MultiHIV B therapeutic HIV positively impacts CD4 and CD8 cell numbers and function
 - This is observed by the increase in antigen (Ag) specific CD4 cells as shown in **Figure 4** and the
 - Increase in TNFα secreting CD4 and CD8 cells shown in **Figure 1**
- FIT Biotech's GTU-MultiHIV B therapeutic HIV vaccine improves the functional profile of both CD4 and CD8 T cells in vaccinees

Table 1: Overall average change in plasma viral load and CD4 cell counts (108 weeks).

Average Change in Plasma Viral Load

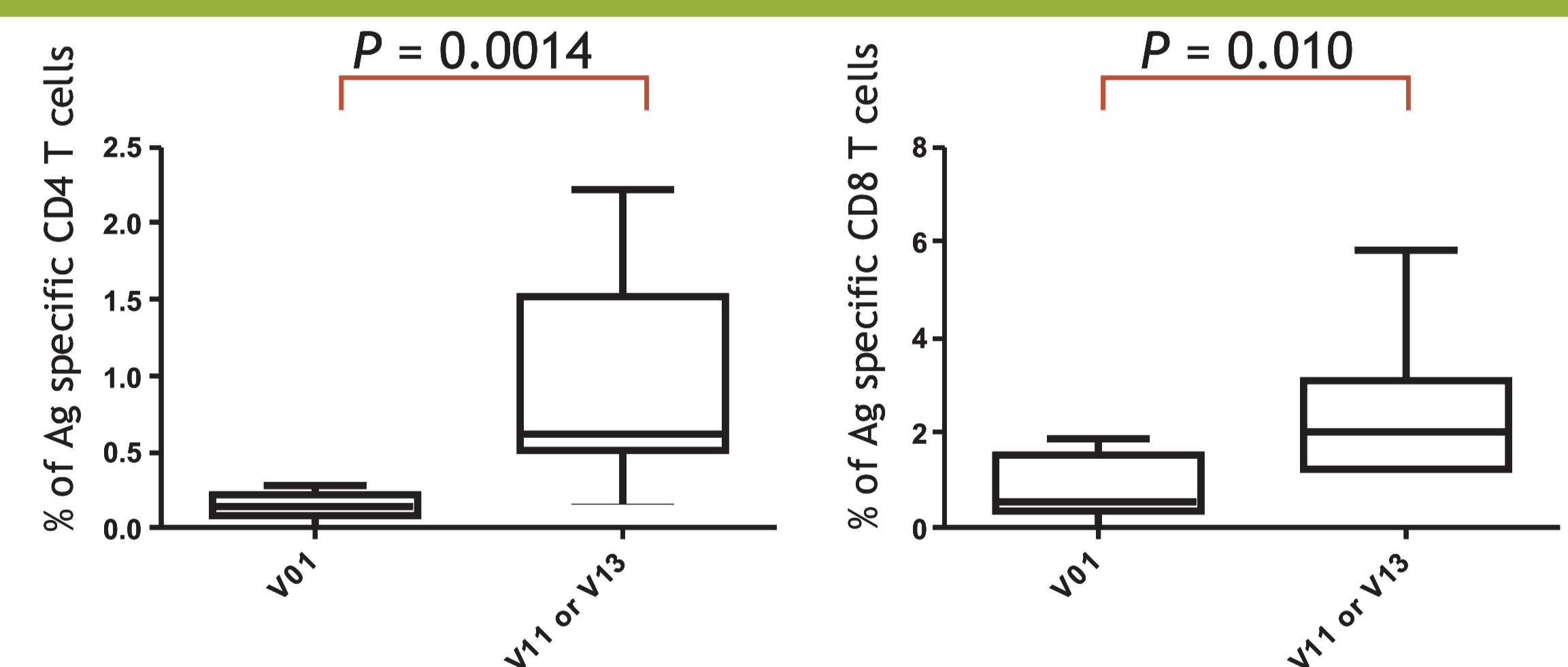
Comparison	Estimate log(VL)	P-value
FIT vs. Placebo	-0.31	0.012
ID: FIT vs. Placebo	-0.16	0.257
IM: FIT vs. Placebo	-0.47	0.001

Average Change in CD4 Cell Counts

Comparison	Estimate (cells/μL)	P-value
FIT vs. Placebo	+45	0.068
ID: FIT vs. Placebo	+18	0.514
IM: FIT vs. Placebo	+72	0.013

ID=Intradermal IM=Intramuscular

Figure 1: HIV specific CD4 and CD8 T-cell responses increase following vaccination



Additional Relevant Data:

- Responses to Gag-B and/or Gag-C at V11 (week 76) and/or V13 (week 84) were observed:
 - CD4 response observed in 83% of participants
 - CD8 response observed in 67% of participants
 - CD4 and CD8 response observed in 55% of participants
- An increase of antigen-specific CD4 and CD8 T cells secreting TNFα was observed

Figure 2: IM immunization with GTU-MultiHIV-B preserves virological control

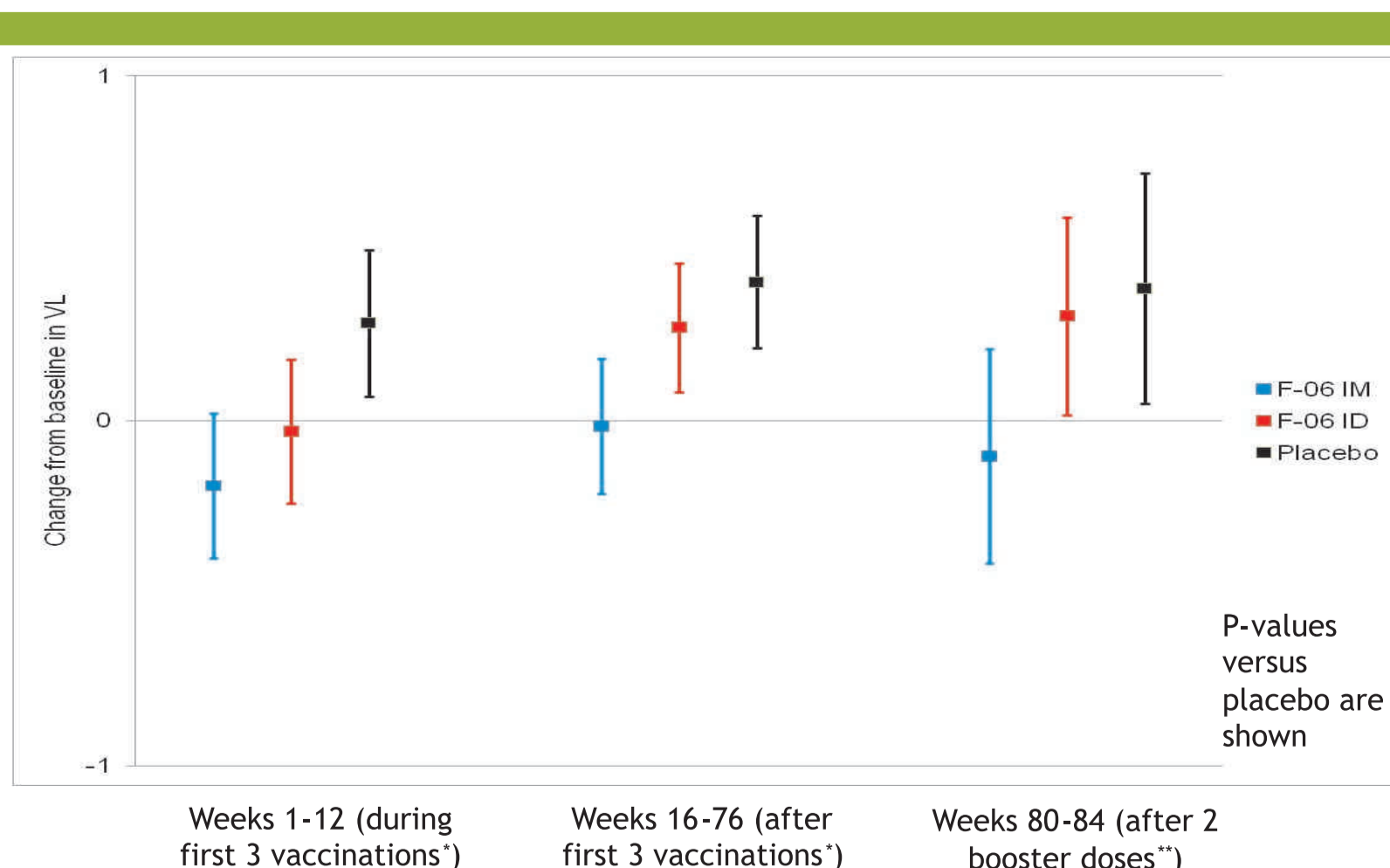


Figure 3: IM & ID immunizations with GTU-MultiHIV-B preserve virological control in subjects with favorable HLA alleles

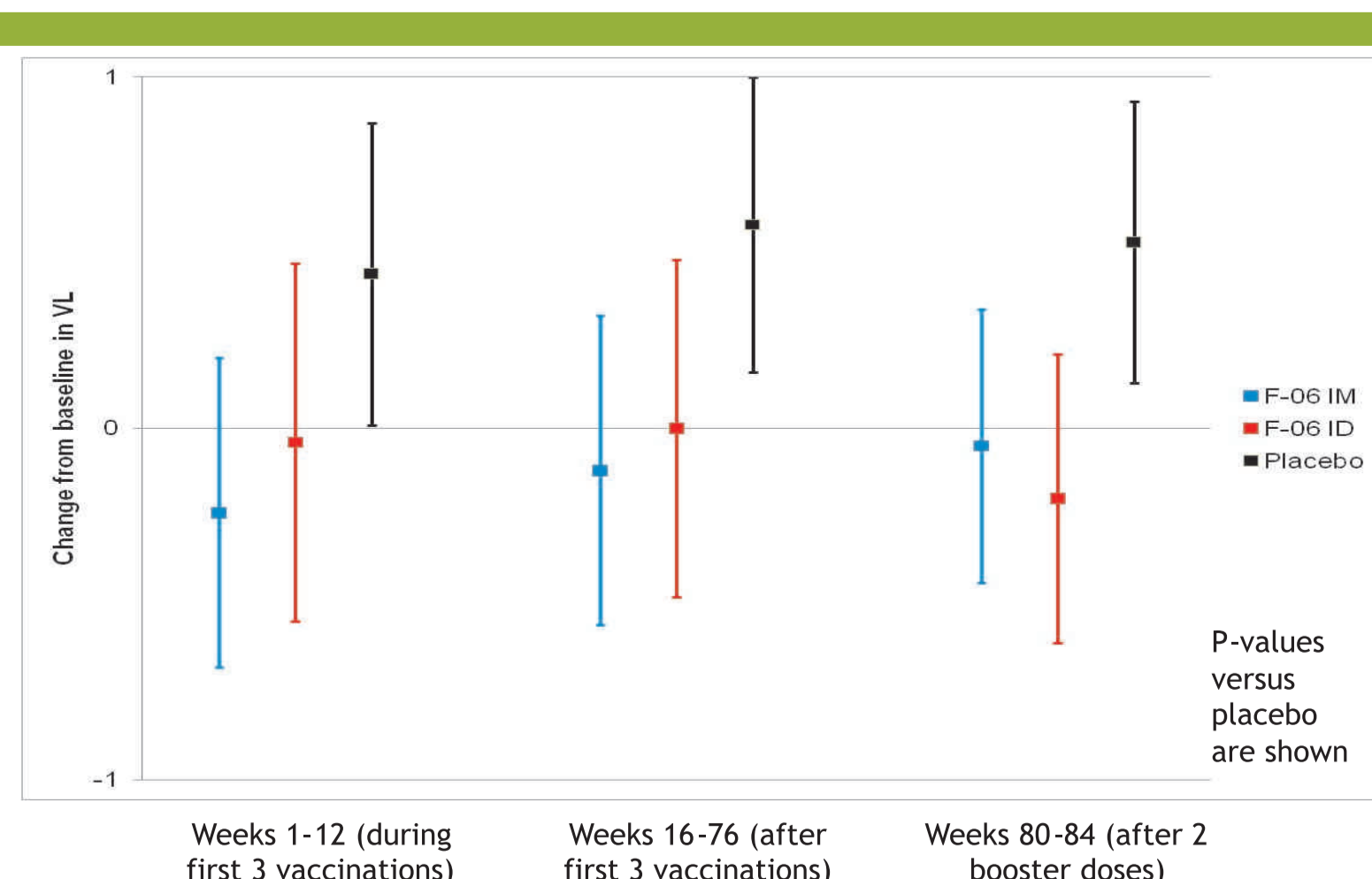
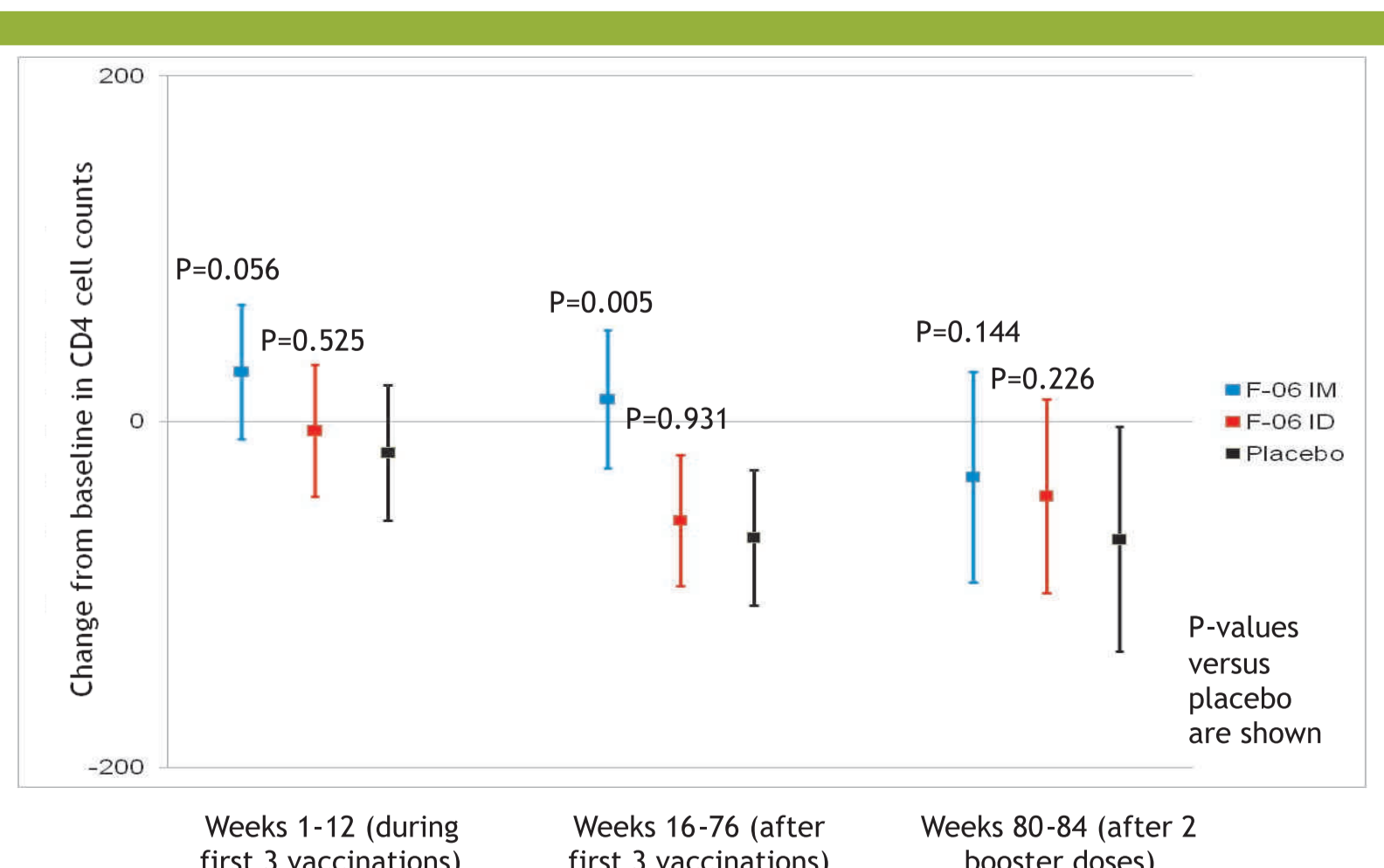


Figure 4: IM immunization with GTU-MultiHIV-B preserves CD4 cell counts



Conclusions

- FIT Biotech has developed a novel class of DNA vaccines with superior properties
- When compared to placebo, IM immunization with FIT Biotech's vaccine had an impact of more than 0.5 log on HIV viremia for at least two years
- A relative increase in CD4 cell numbers was observed
- Immunization with FIT's Vaccine resulted in significant CD4+ and CD8+ T-cell function
- Enhanced effects were observed in subjects with favorable HLA alleles
- This is the first immune-based intervention to affect viremia in HIV infected, untreated volunteers
- These results provide the basis for further development of promising immunotherapies for HIV infection