

**Therapeutic Vaccination Trial with subsequent HAART Treatment
Interruption (TI): A randomized, single blind, controlled, phase II study with
an MVA-nef vaccine in HIV-1 infected patients with CD4 cell counts $\geq 250/\mu\text{l}$**

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HIV-NEF-004

Overview

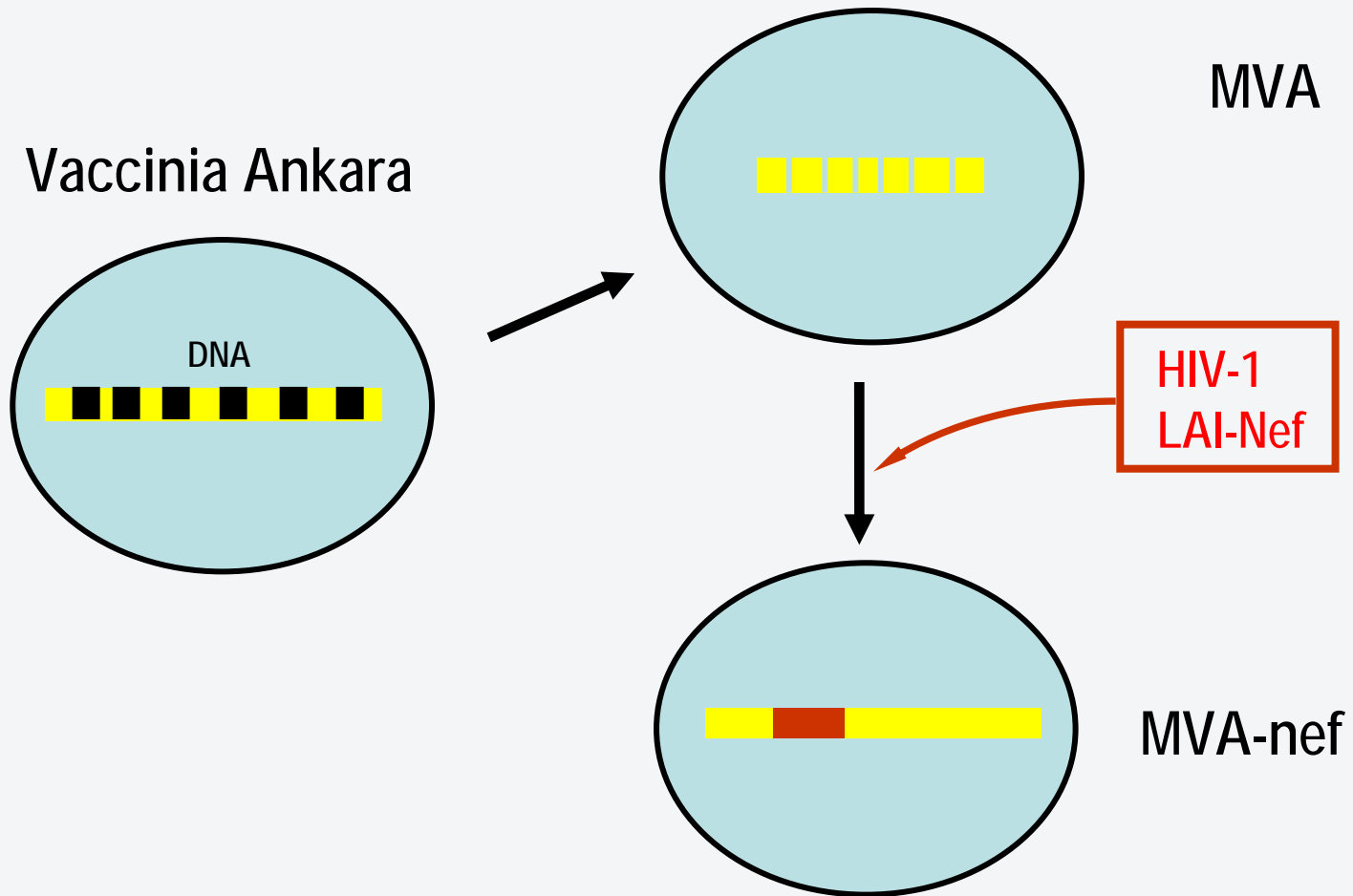
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- **Study Design**
- **Safety Data**
- **Viral Load and CD4 Cell Count after HAART
Treatment Interruption**
- **Conclusion**



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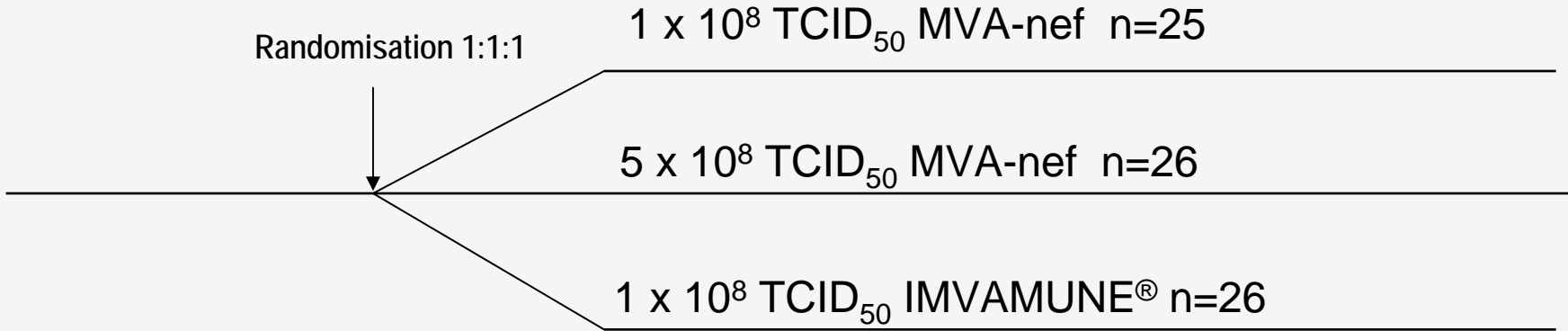
Study Vaccine MVA-nef



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Study Design

Design: 3 groups, single-blind, controlled, randomized 1:1:1
Study population: 77 HIV-infected patients, 18-60 yr, m/f, CD4 count > 250/ μ l
Vaccines: 1E8 TCID₅₀ MVA-nef vs. 5E8 TCID₅₀ MVA-nef vs. 1E8 TCID₅₀ IMVAMUNE®



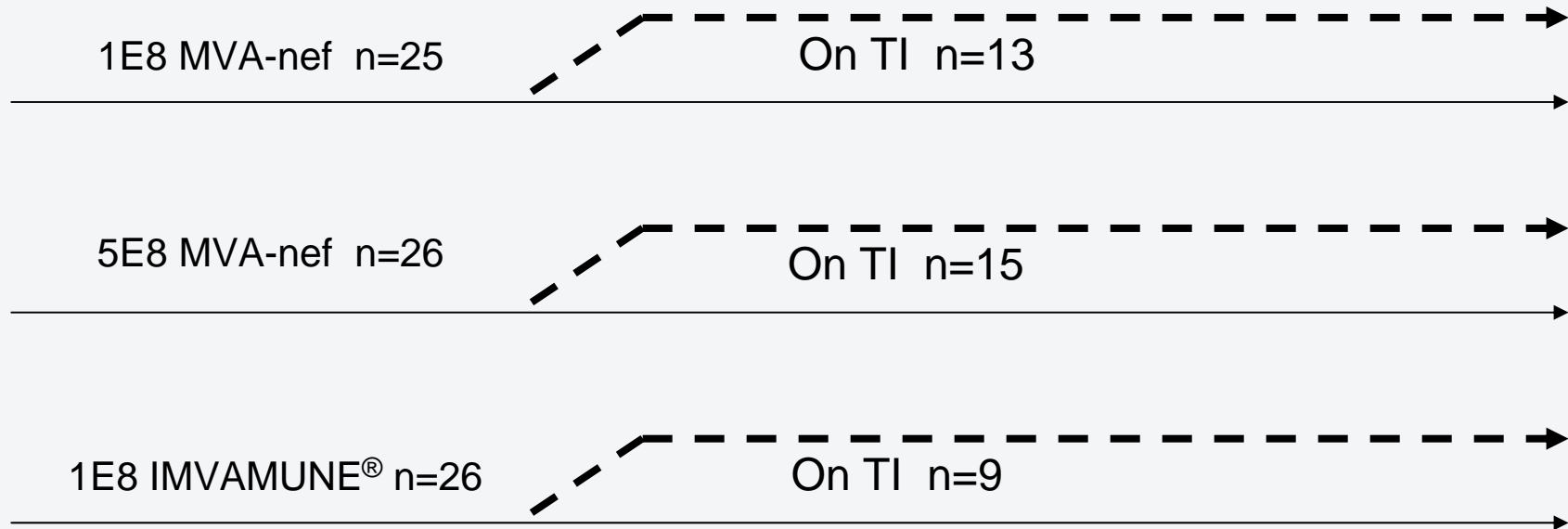
Screening	1 st Vaccination	2 nd Vaccination	3 rd Vaccination
Week -4 to -1	0 (1)	8 (9)	16 (17) (20) (52)



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Study Design – HAART Treatment Interruption (TI)



weeks 0 8 16 20 24 26 28 32 40 52

1st 2nd 3rd TI
Vaccination



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Patients participating in Treatment Interruption (TI)

Group	Patients interrupting HAART	Patients on TI at week 52	Restart of HAART
1E8 TCID₅₀ MVA-nef	13	8	5 (wk 8, 11, 12, 14, 24)
5E8 TCID₅₀ MVA-nef	15	11	4 (wk 6, 12, 14, 18)
1E8 TCID₅₀ IMVAMUNE®	9	6	3 (wk 8, 13, 24)
Total	37	25	12



Adverse Events

Systemic AE ≥ grade 3 with a relationship to vaccinations

Symptom	Low Dose 1E8 TCID ₅₀ MVA- nef (N=25)		High Dose 5E8 TCID ₅₀ MVA- nef (N=26)		Control 1E8 TCID ₅₀ IMVAMUNE® (N=26)	
	n	%	n	%	n	%
Fever	1	4.0	0	0.0	1	3.8
Headache	2	8.0	3	11.5	1	3.8
Myalgia	0	0.0	3	11.5	0	0.0
Fatigue	2	8.0	6	23.1	2	7.7
Exhaustion	0	0.0	1	3.8	0	0.0
Swelling right arm	0	0.0	0	0.0	1	3.8

N=Number of subjects, n=Number of subjects fulfilling criteria, %=n/N

Grade 3 = unable to perform daily activities

Grade 3 Fever ≥ 39°C



Adverse Events

Local adverse reactions \geq grade 3

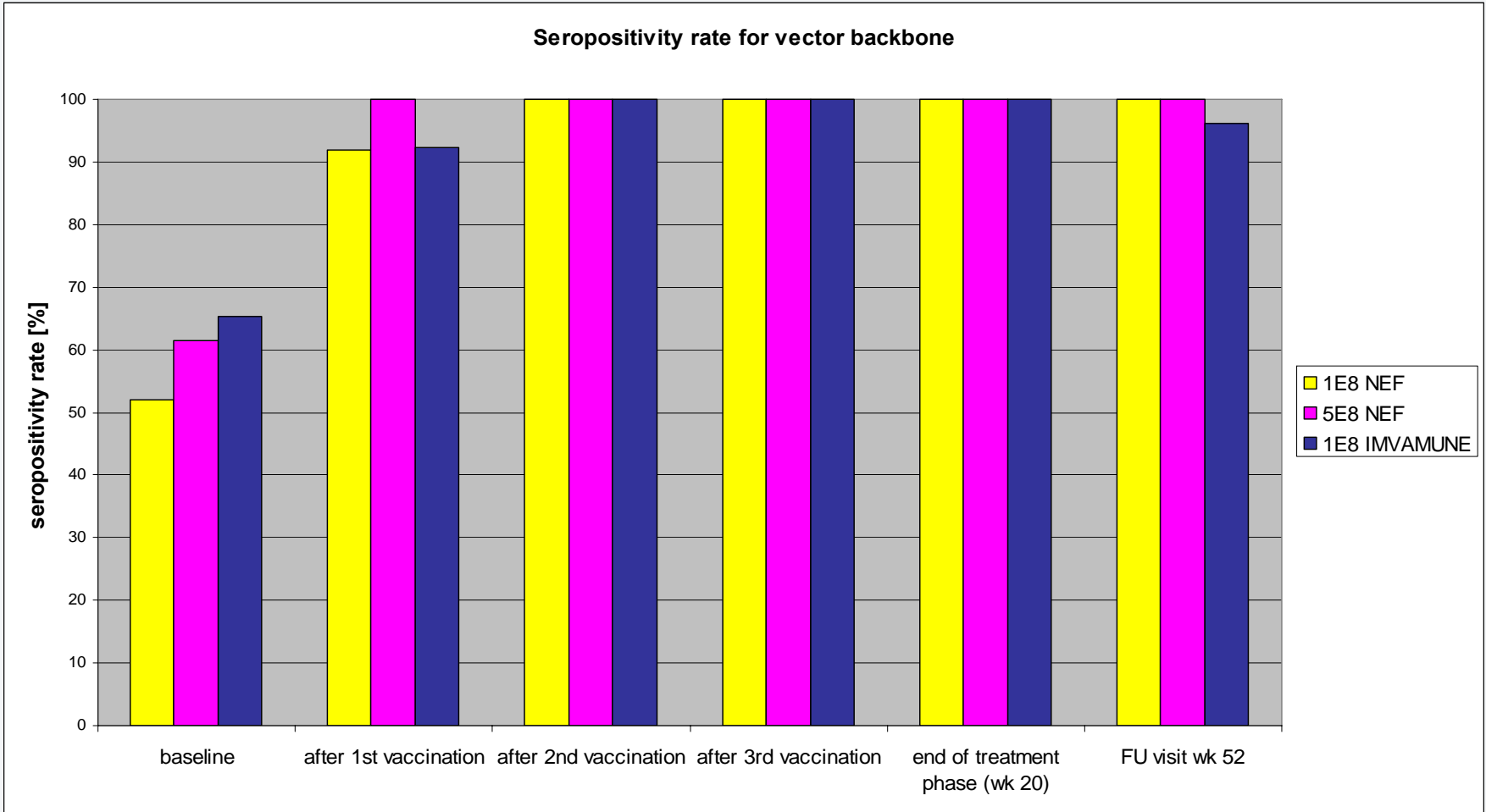
Symptom (at injection site)		Low Dose 1E8 TCID ₅₀ MVA- nef (N=25)		High Dose 5E8 TCID ₅₀ MVA-nef (N=26)		Control 1E8 TCID ₅₀ IMVAMUNE® (N=26)	
		n	%	n	%	n	%
Pain	\geq grade 3	2	8.0	3	11.5	0	0.0
Erythema	\geq 100mm	4	16.0	6	23.1	7	26.9
Swelling	\geq 100mm	1	4.0	3	11.4	2	7.7
Induration	\geq 100mm	0	0.0	2	7.7	0	0.0
Pruritus	\geq grade 3	0	0.0	0	0.0	1	3.8

N=Number of subjects, n=Number of subjects fulfilling criteria, %=n/N



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Immunogenicity – Vector backbone seropositivity rate



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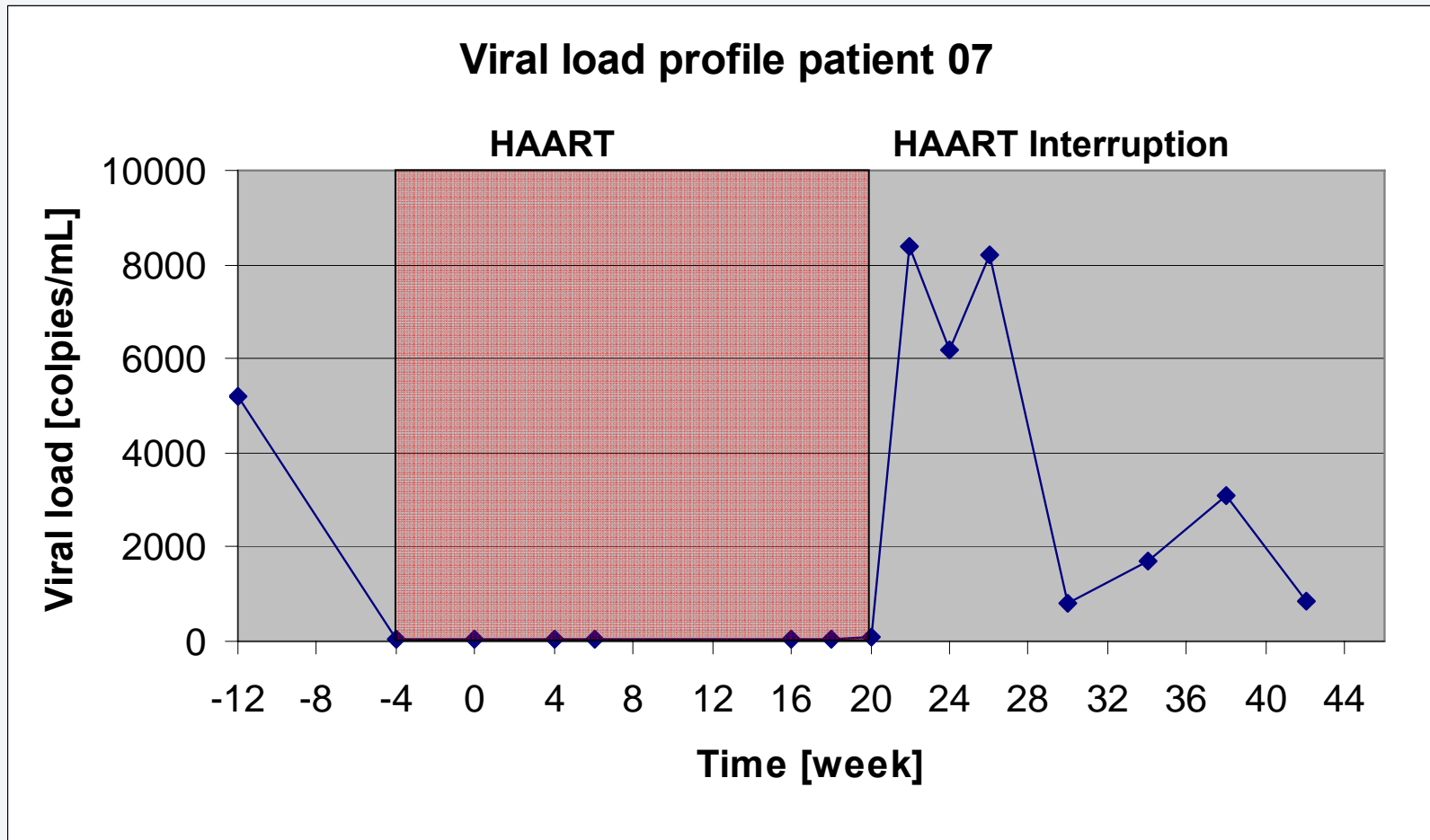
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Previous Study HIV-NEF-002

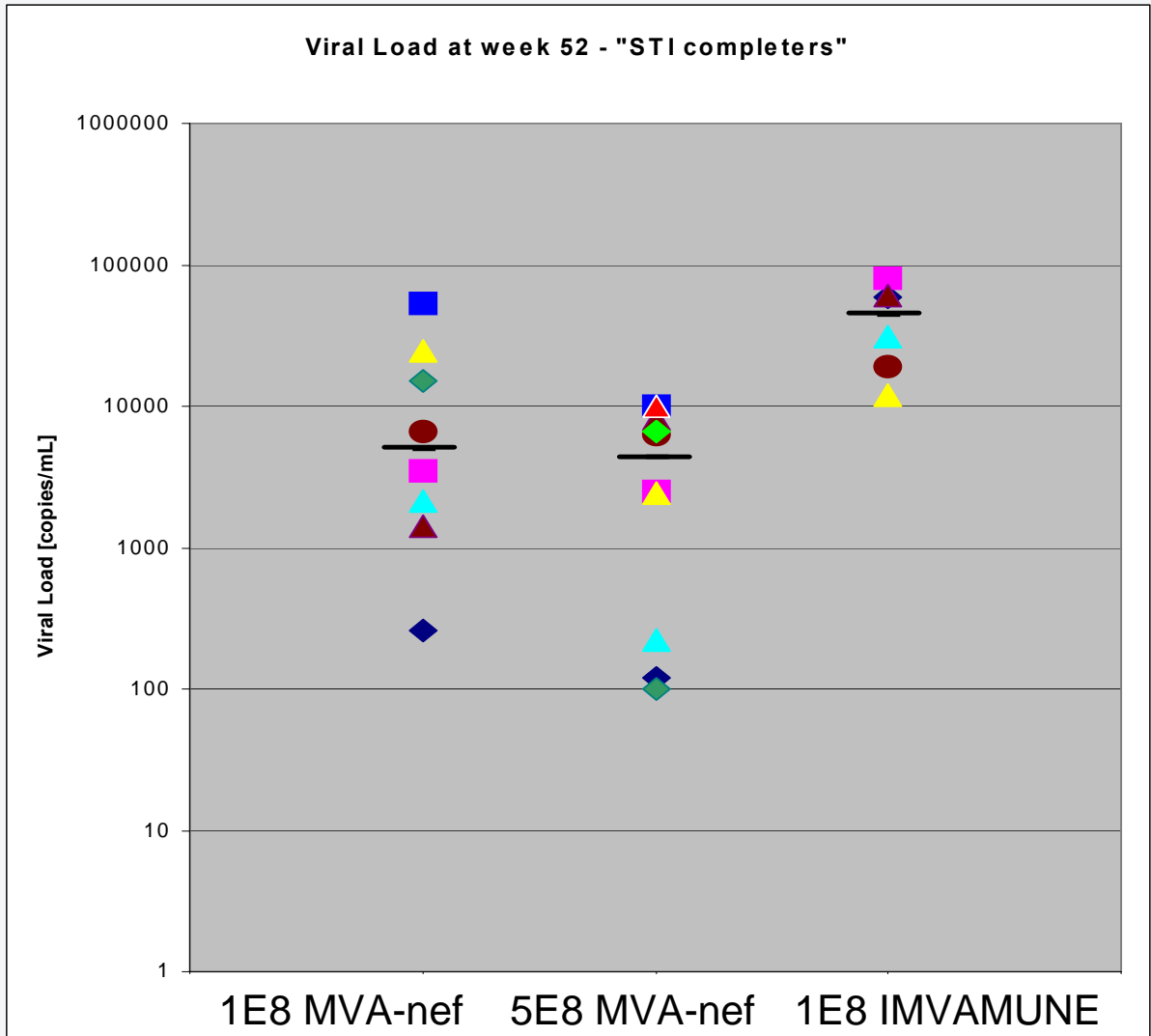
Viral Load Profile after HAART Interruption (wk 20)



Historical viral load: 5200 copies / mL



Median and individual viral load values at study week 52 of patients interrupting HAART

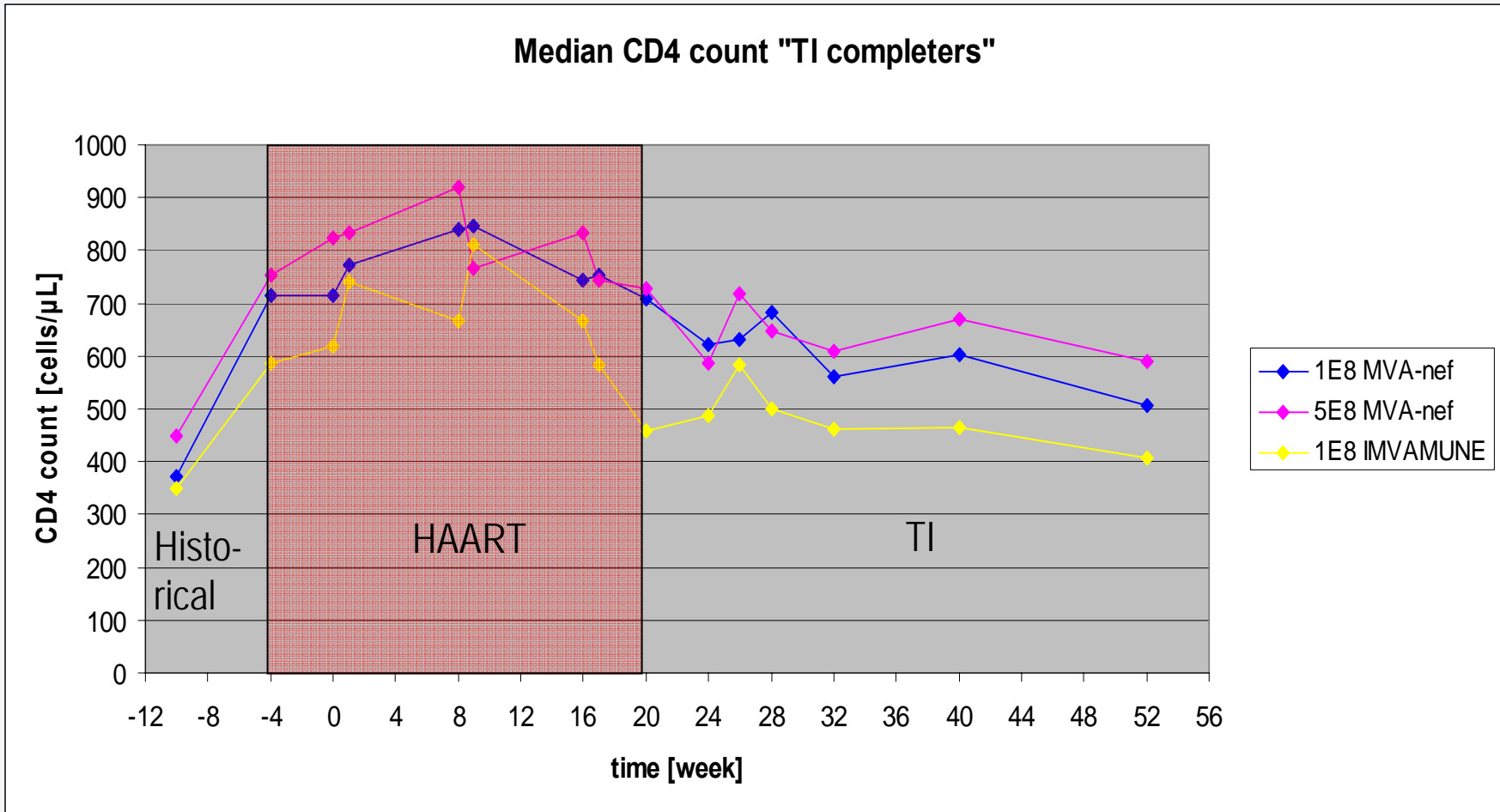


The black bars indicate the median viral load levels



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Median CD4 count of TI-completers



Conclusions

MVA-nef and IMVAMUNE® are safe in HIV-1 infected patients on HAART

Seroconversion rate regarding the vector backbone was 100% after the 2nd vaccination with IMVAMUNE® as well as with MVA-nef

Viral loads of all patients who restarted HAART were back below detection limit

After TI high dose MVA-nef vaccination resulted in better viral load control than IMVAMUNE® vaccination

Long-term follow-up of TI-participants will have to show the clinical relevance of the observed effects.



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