



Therapeutic vaccines against HIV and AIDS

Anne-Marte Bakken Kran
Dep. of Infectious Diseases
Ullevål University Hospital

HIV/AIDS

- 40 mill people infected, 2.5 mill children
- 5 mill new HIV-infections in 2003
- 14 000 new infections every day
- HIV-vaccine research USA: 700 mill USD

HAART

Highly Active Antiretroviral Therapy



- Highly effective



- Availability
- Cost
- Toxicity
- Resistance
- Eradication (not completely)
- Impaired HIV-specific immunity

Therapeutic vaccines against HIV and AIDS

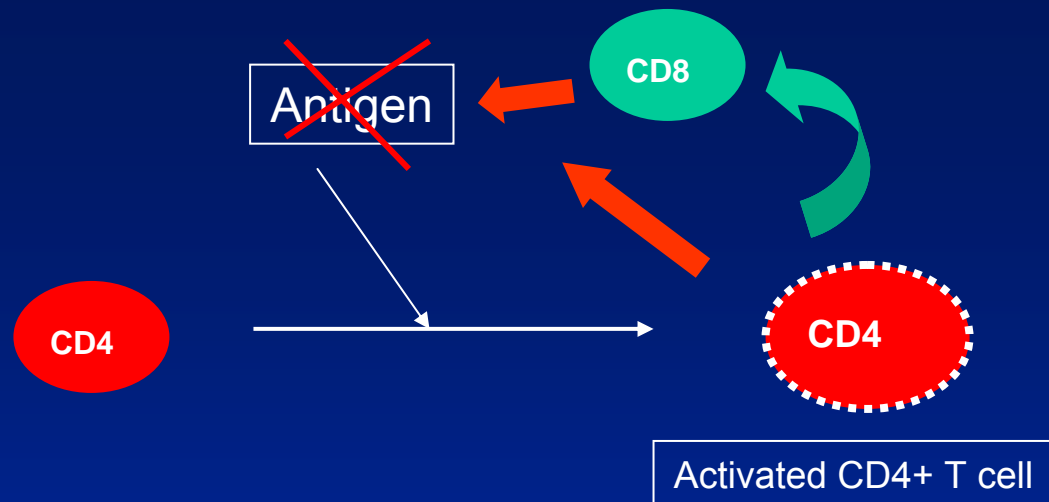
- HIV-vaccines today
- HIV immunology
- Clinical trials at Ullevål University Hospital
- Challenges ahead

Vaccines

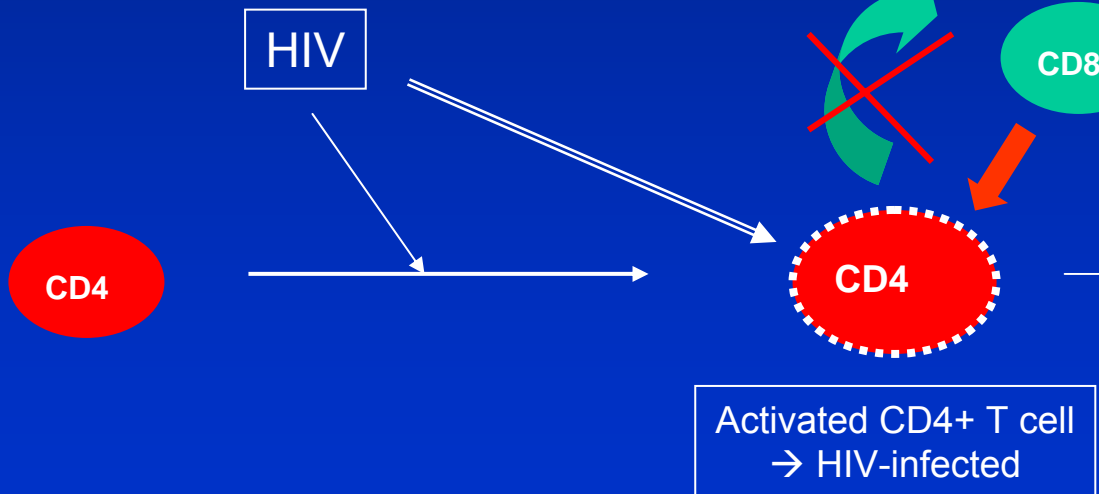
- Humoral responses
- Cellular immune responses

HIV vaccines

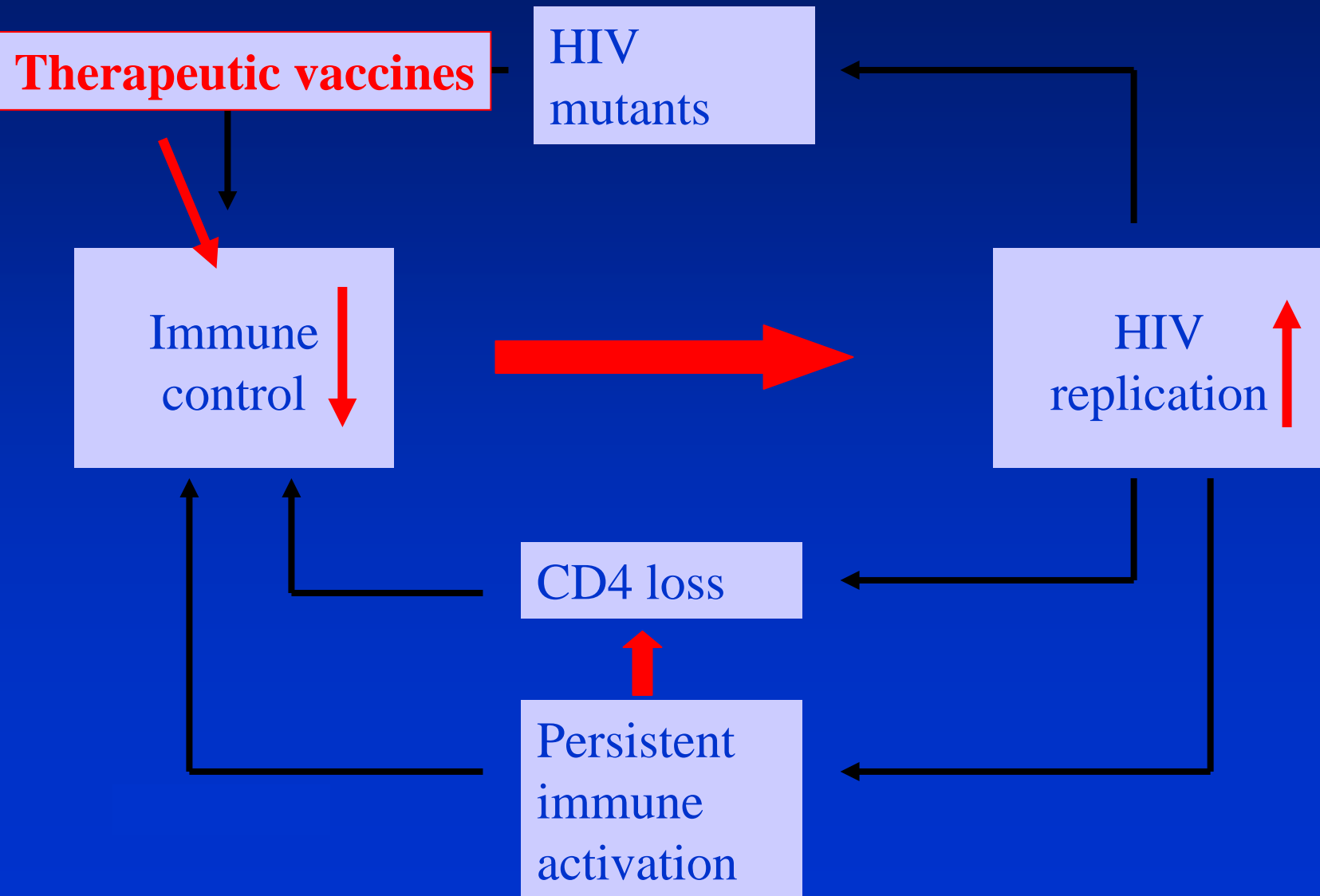
- Preventive
 - Neutralizing antibodies + Cellular immune responses
- Therapeutic
 - Cellular immune responses



Impaired CD8 function



Viscious circles in chronic HIV



Current HIV vaccines

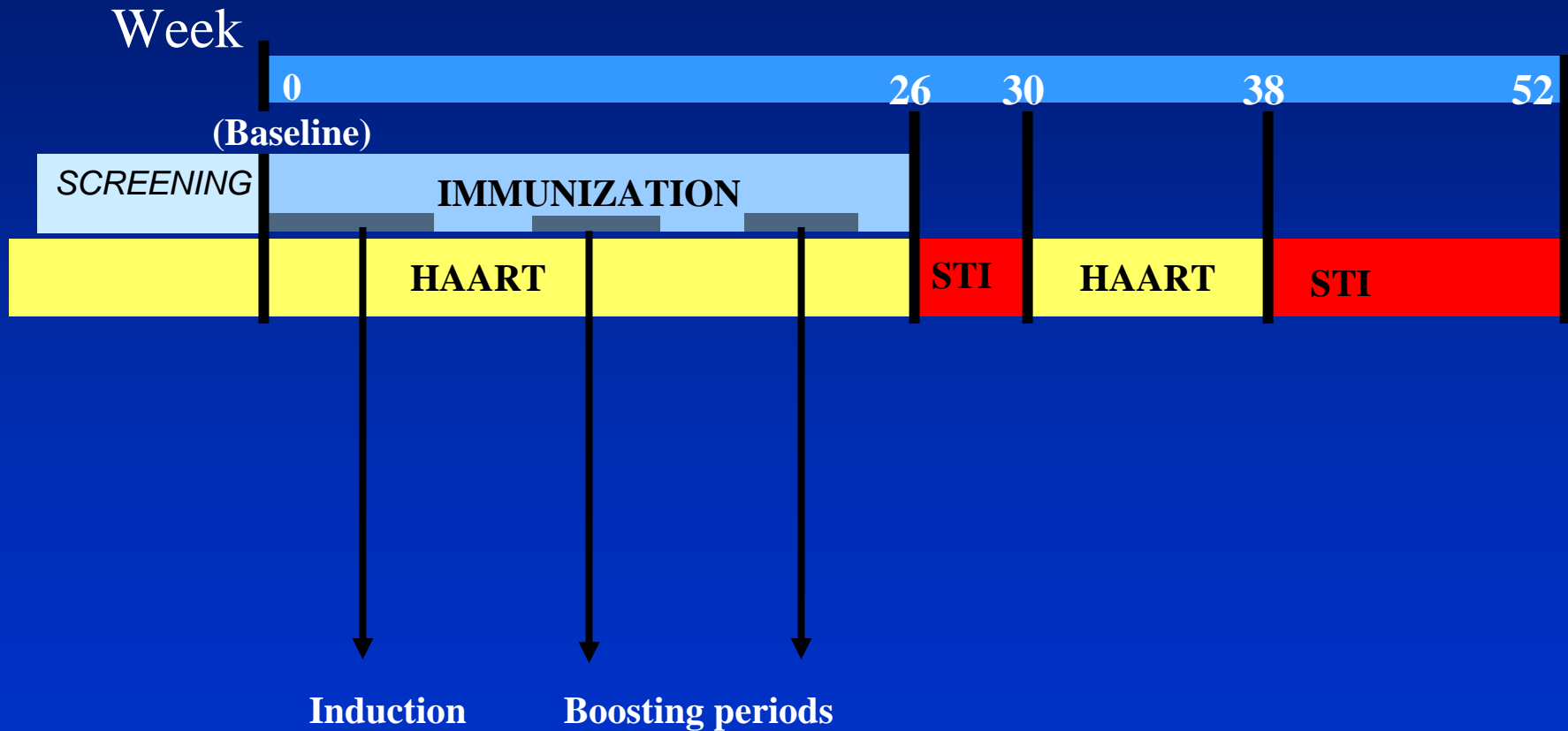
- Vectors expressing different HIV-proteins
 - » (canarypox, vaccinia, adenovirus, MVA)
- DNA vaccines
- Lipopeptides
- Peptides
- Peptide-pulsed autologous dendritic cells
- Combinations (prime-boost regimens)

Therapeutic HIV vaccine trials at Ullevål University hospital

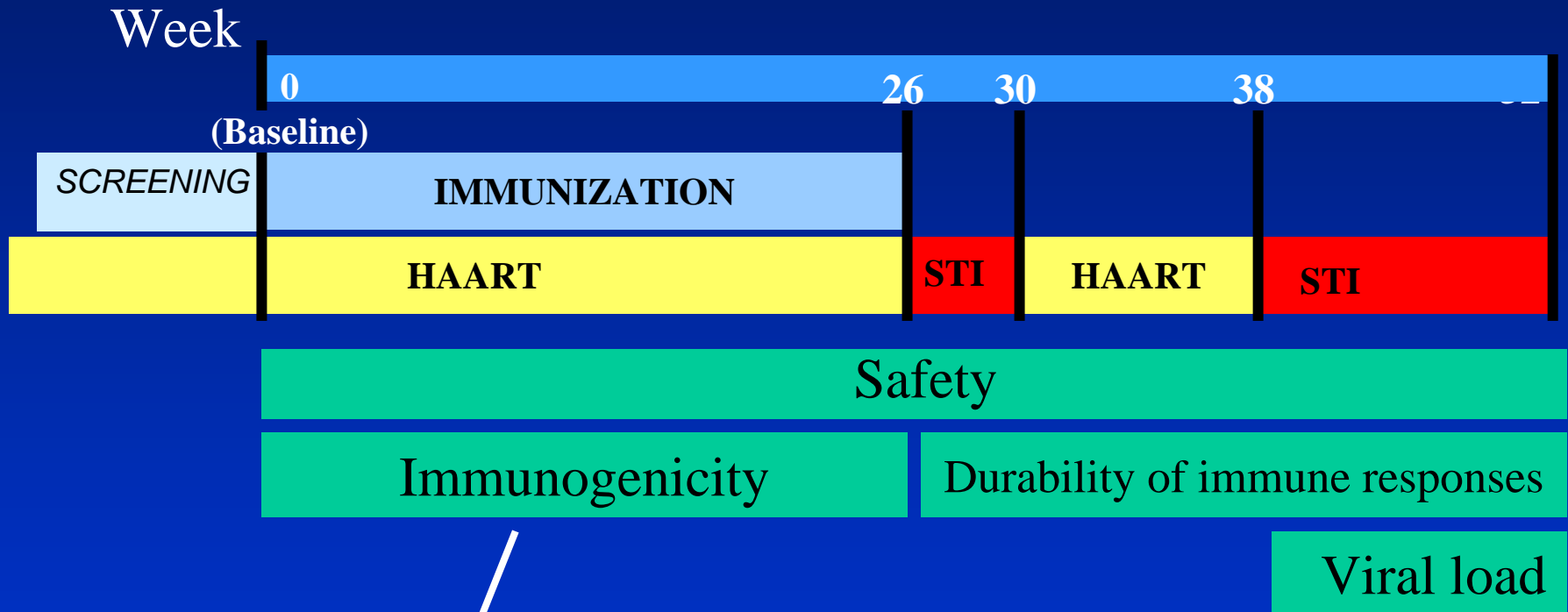
- Vacc-4x (Phase II) (n=40)
 - Modified p24 peptider (20-27 mers)
 - Healthy non-AIDS HIV+ on effective HAART
 - Two dose groups

- Vacc-5q (Phase I) (n=20)
 - Modified HIV peptides (p24, p17, tat)
 - Patients on / off HAART

Immunization schedule Vacc-4x



Immunization schedule

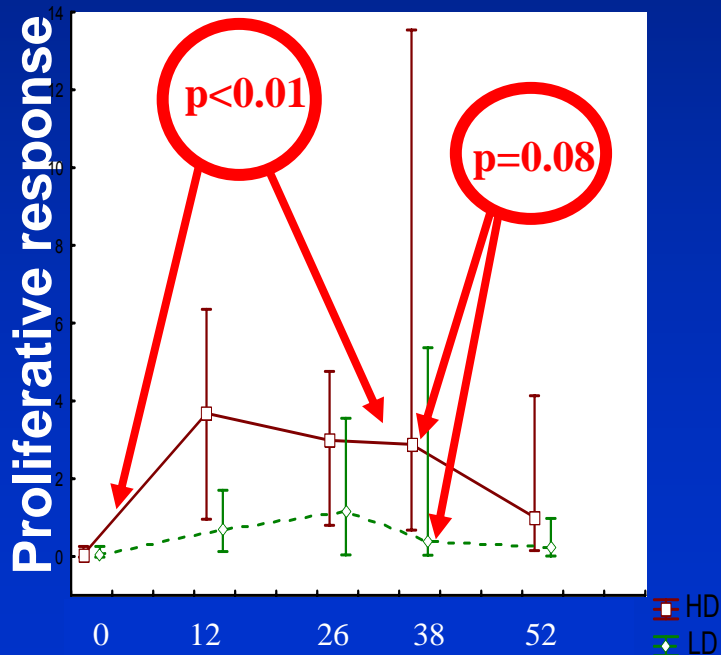


In vivo: DTH skin tests

In vitro: Activation (IFN- γ)/ T cell proliferation

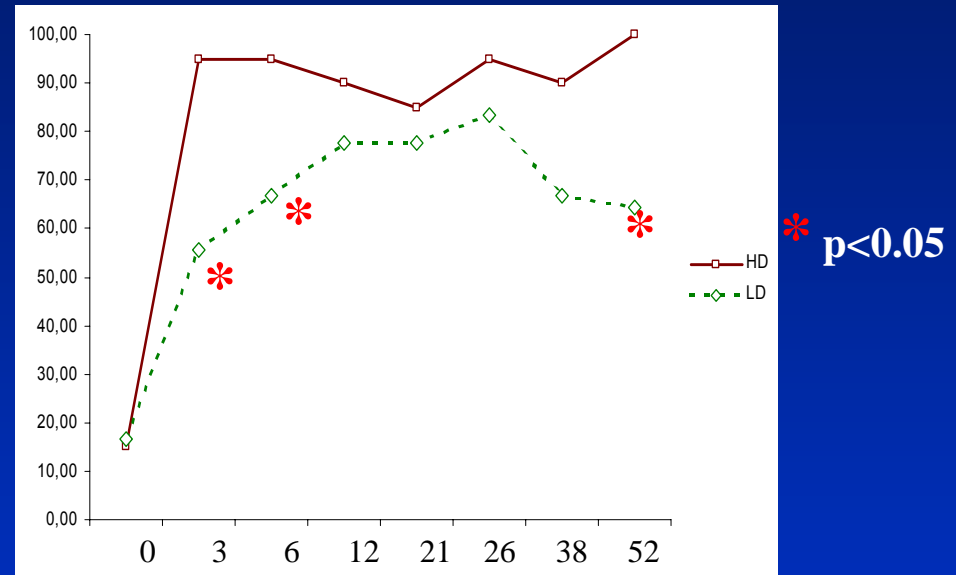
Immunogenicity

- New immune-responses induced



A-M B.Kran 08.10.04

% Positive DTH reactions

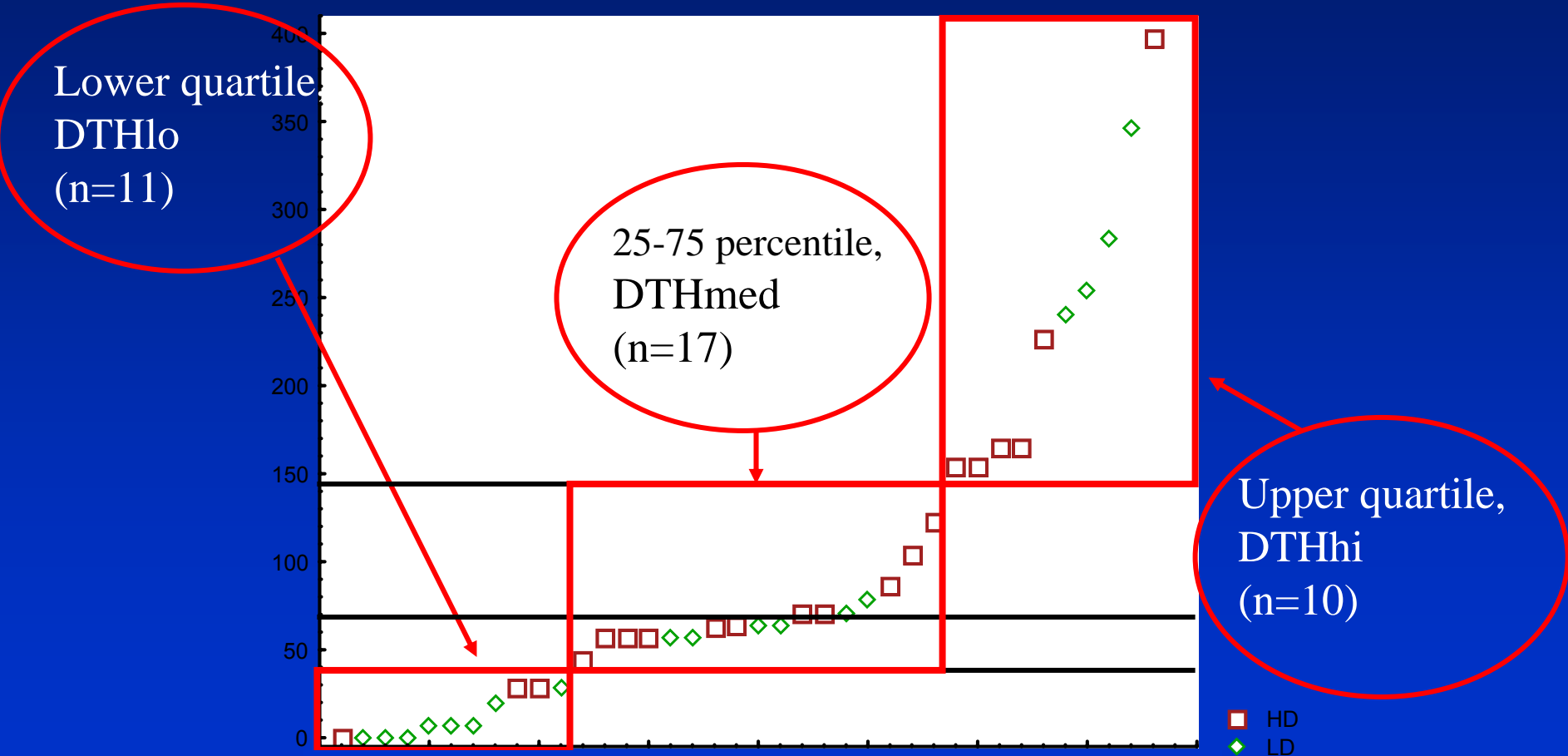


- Dose-dependent differences

Vacc-4x: Primary end-points

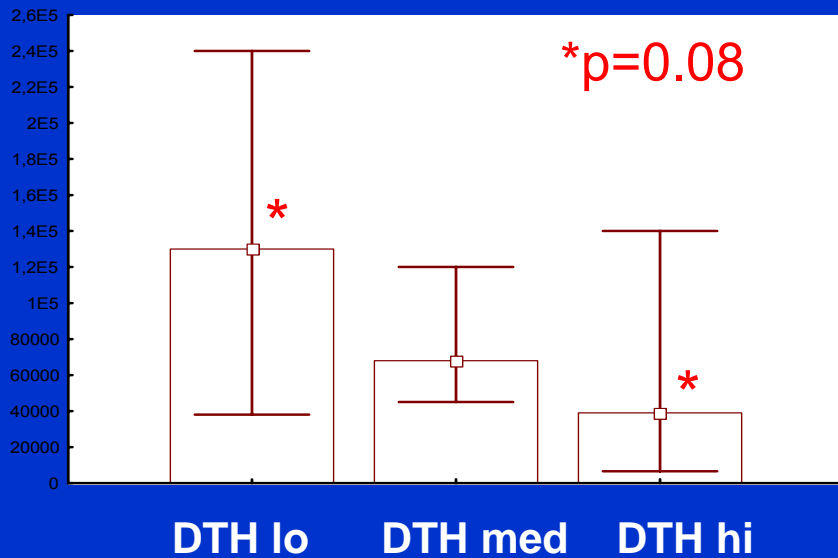
- Good safety
- Highly immunogenic (~90%)
- High-dose "advantage"

DTH week 38

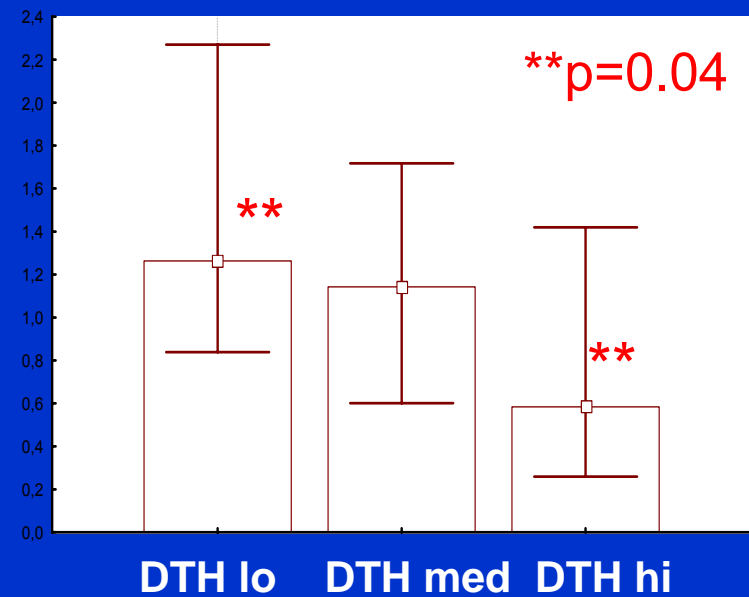


Differences in HIV-RNA

HIV RNA week 52



HIV RNA w52/preHAART RNA



Characteristics of Vacc-4x high-responders

- Nadir CD4
- Time from seroconversion
- Time on HAART
- PreHAART HIV-RNA, CD4- and CD8-counts
- Pre-study HIV-RNA, CD4- and CD8-counts
- Baseline DTH
- Baseline p24-reactivity

No differences between
- DTHhi
- DTHmed
- DTHlo

Conclusions Vacc-4x trial

- **Safe and immunogenic**
- **First clinical trial suggesting associations between induced immune responses and improved viral control**
- **Clinical benefit (?)**

Challenges

- High genetic variability (host and virus)
- Rapid mutations
- Integration into host cell genome/infection of memory T cells and APC
- Insufficient pool of memory T-cells
- Lack of good animal model
- Protective immune response unknown
- ? Correlates of efficacy and protection

Acknowledgements

Ullevål University Hospital:

- * **Dag Kvale**
- * Mette Sannes
- * Malin Jørgensen
- Johan N. Bruun
- Karin Stuedahl

Rikshospitalet University Hospital:

Inger Nina Farstad
Espen Ø. Kvale

- * Bionor Immuno:
Birger Sørensen
Maja A. Sommerfelt
Jørgen Nyhus

Mericon A/S:
Ingebjørg Baksaas