

# HIV

- PrEP
- Neue Medikamente
- Elite Controller behandeln?
- Heilung möglich?

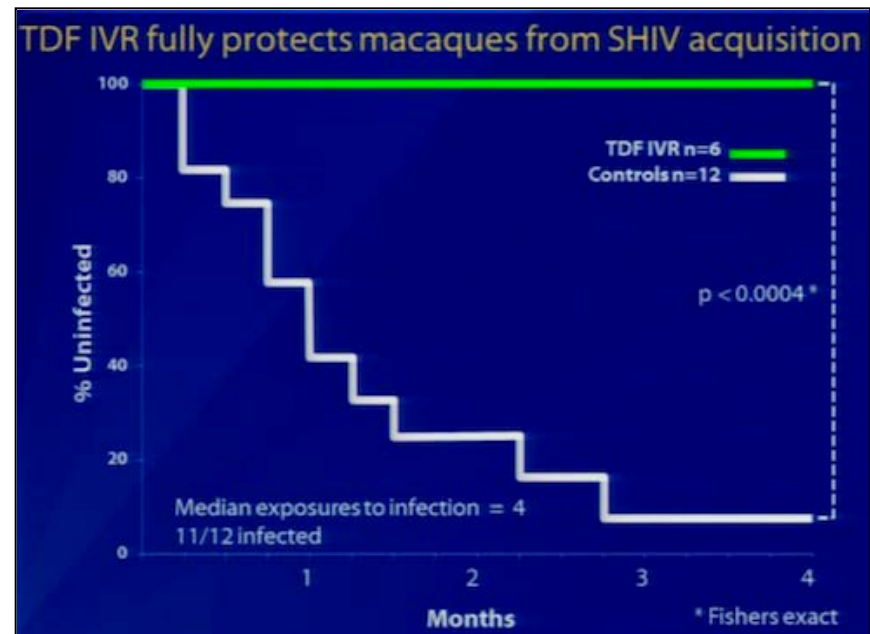


Pietro Vernazza und St. Galler Team

# Vaginalring: Das Kondom für die Frau?



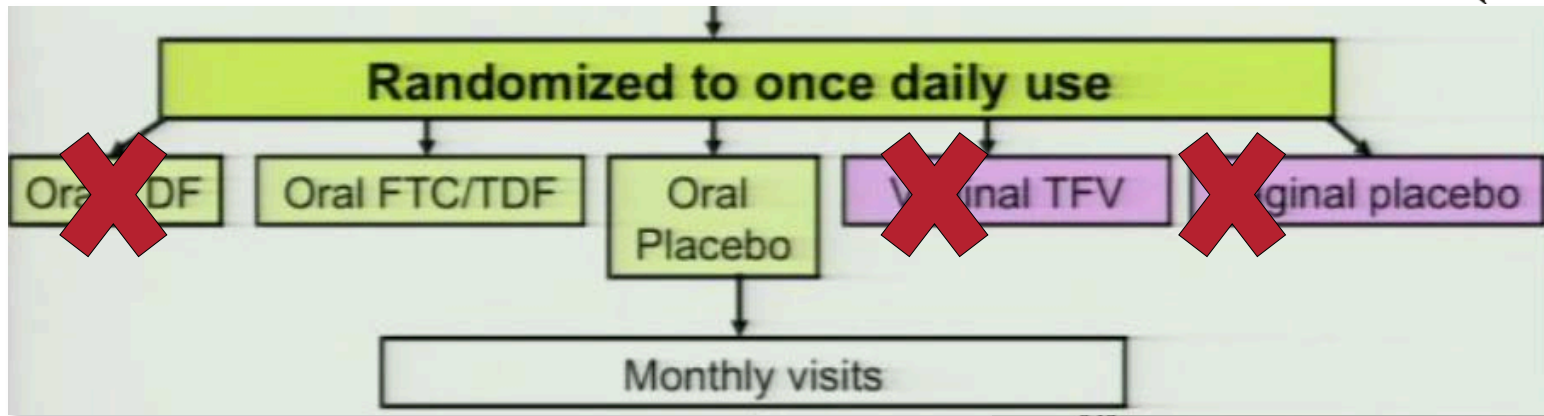
- Polyurethan-Ring mit TFV Reservoir
- Abgabe TFV im flüssigen Milieu: 2.7mg/d; 28d
- TFV wird in Lymphocyten aufgenommen
- Makakken-Modell
  - Ring 4 Wochen
  - 16 Challenges
- Wirksamkeit: Infekt
  - 0/ 6 TFV-Vag-Ring
  - 11/12 Placebo



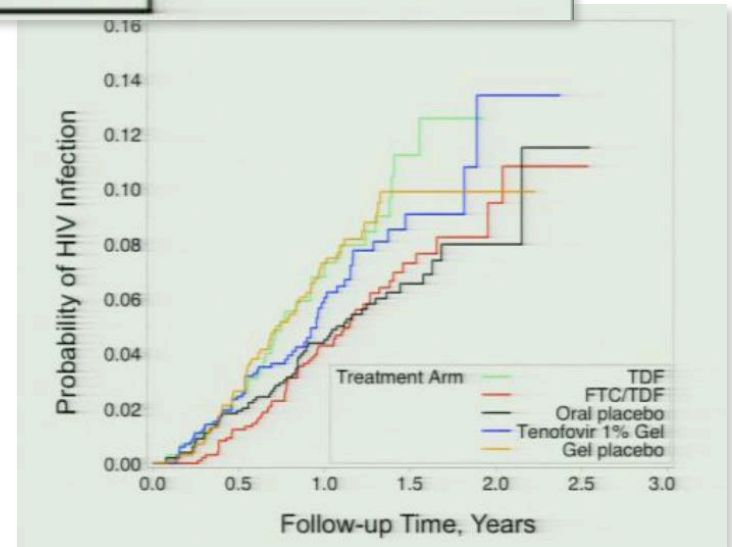


# VOICE: Endlich Resultate aus TDF/FTC

- TDF Vaginal-Gel, RCT, >5000 Frauen



- Adherence (return): 87-94%
- 312 SC (Inzidenz 5.7%)
- Problem: <40% TDF i. Pla
  - Besser bei Alter >25J,
  - Verheiratet

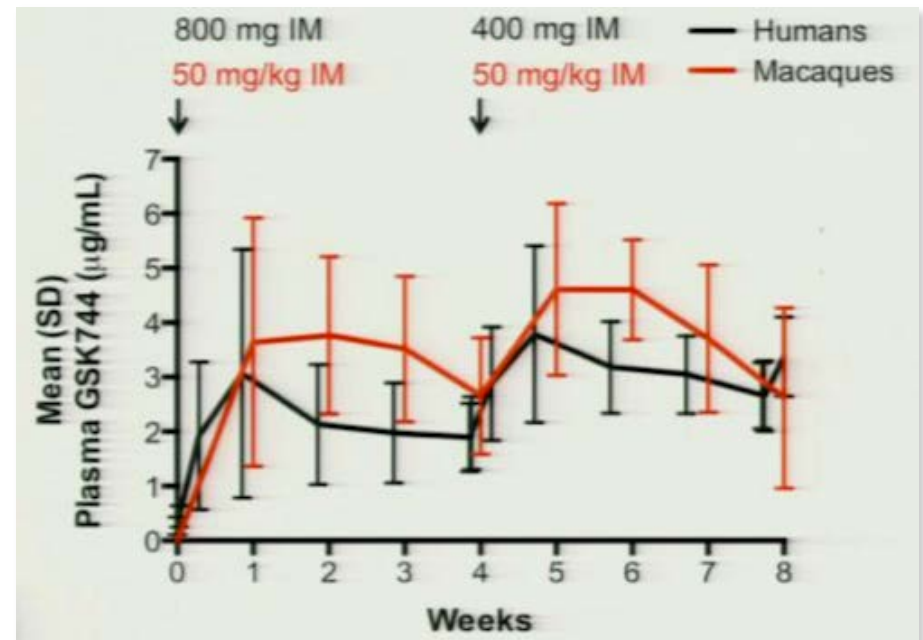
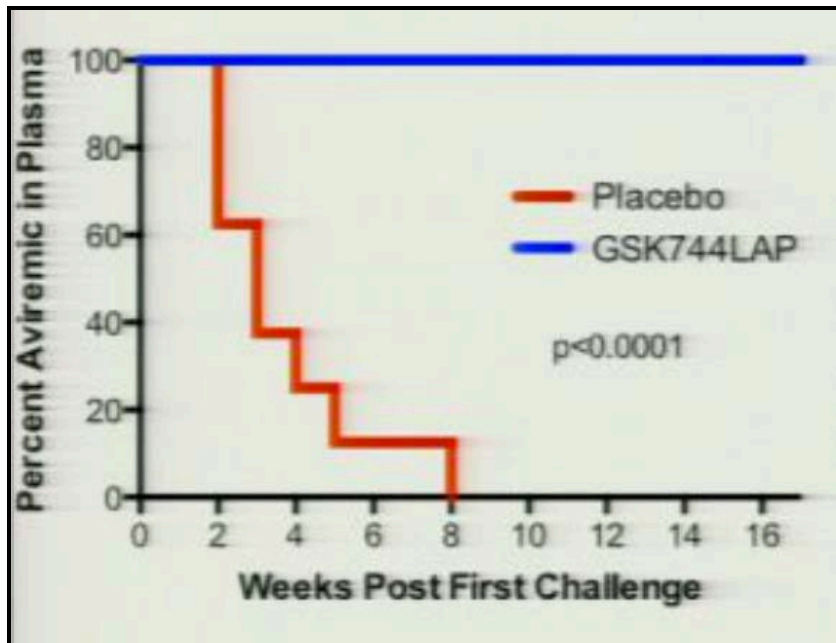


## Hauptproblem Adherence

# Neue Applikationsformen für PrEP



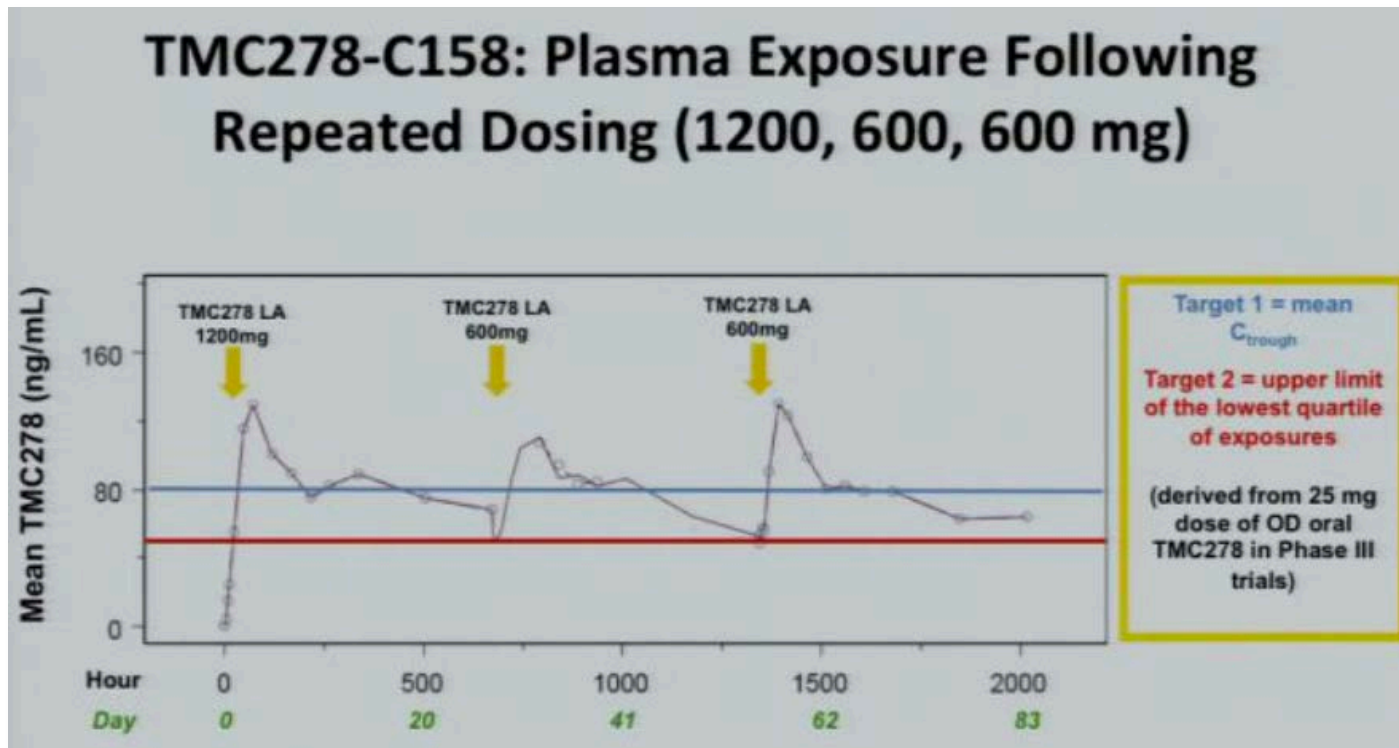
- GSK-744: LA-INI: 800mg >12 Wo / IC<sub>90</sub>
- PrEP im Makakkenmodell: 50mg im. W0/4
- 8 rektale Challengedosen (1/wo)





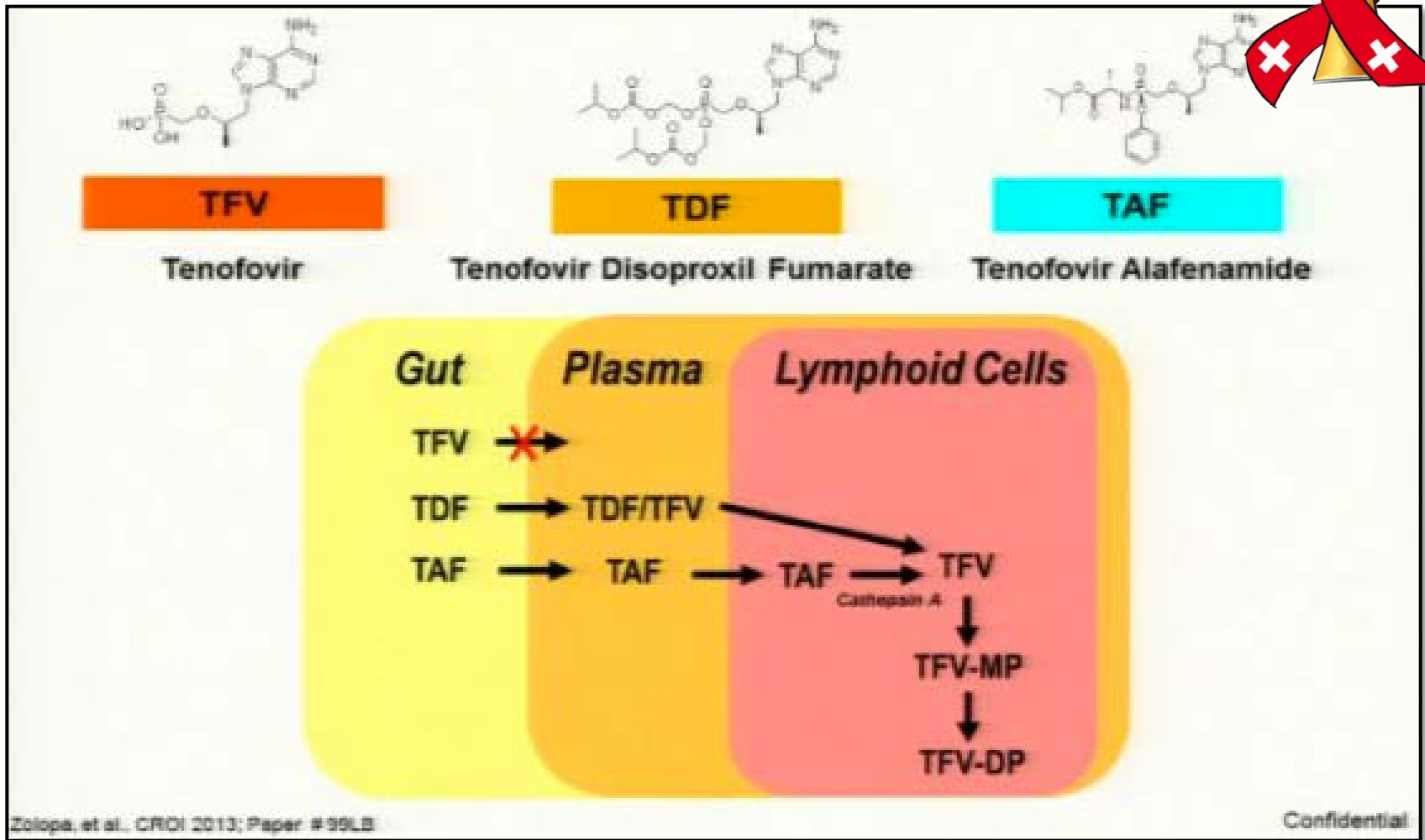
## Weitere Kandidaten... (Gulick, #122)

- Ibalizumab: mAB bindet an CD4, blockiert Entry
  - Monatliche Injektion möglich
- TMC-278-C158: LA-Rilpivirine

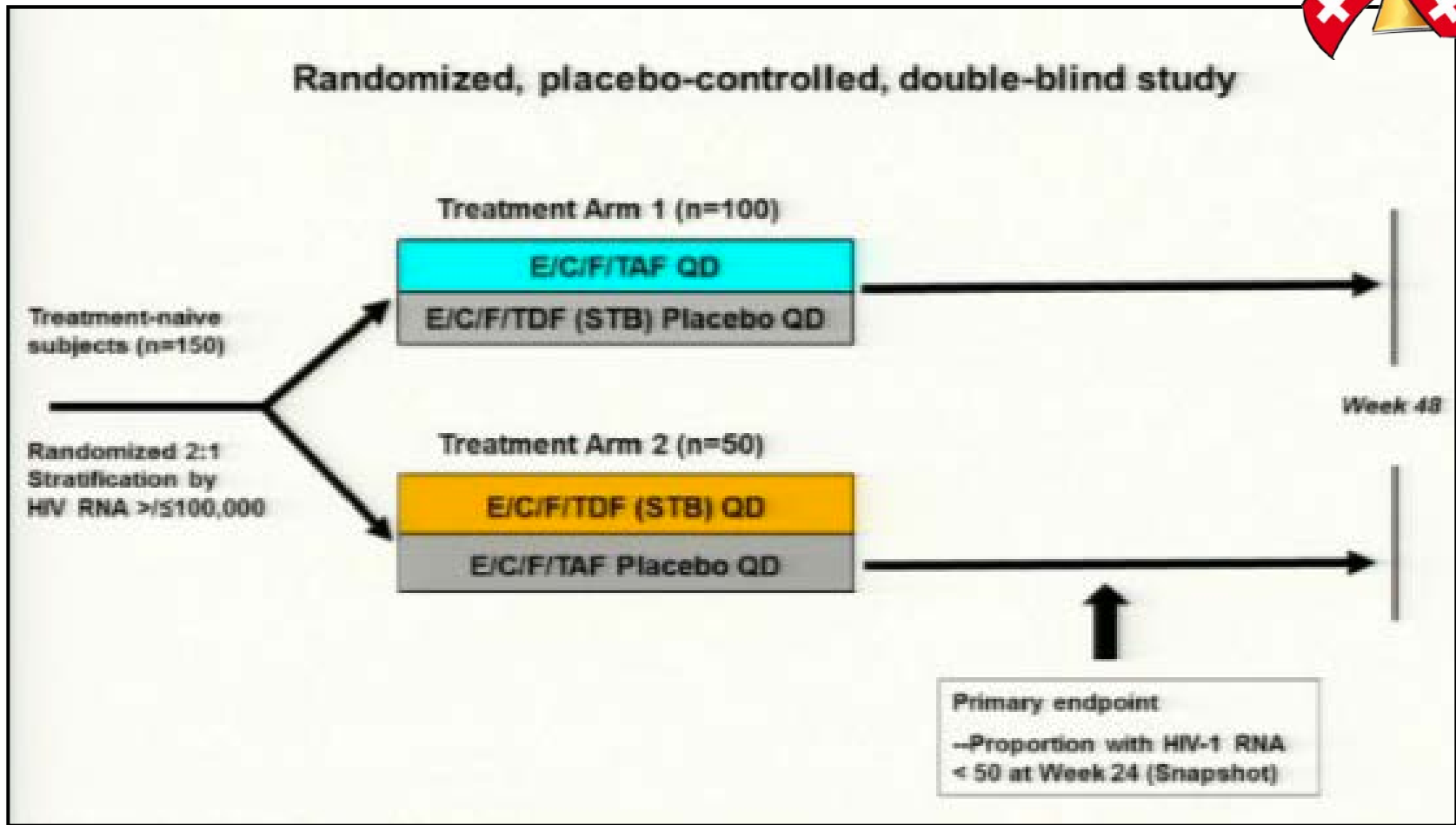


Reduziertes Potential für Nephrotoxizität

# Tenofovir Alafenamide (TAF)



# Head-to-head Vergleich TDF/TAF

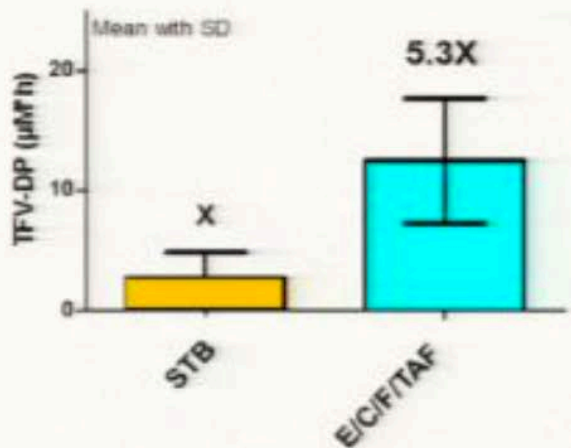




# Intrazelluläre Akkumulation



PBMC TFV-DP AUC<sub>0-24h</sub> at Week 4 or 8



- E/C/F/TAF
- PBMC TFV-DP exposure was 5.3-fold higher (90% CI: 2.9 to 9.6)
  - Plasma TFV exposure (AUC<sub>12h</sub>) was 91% lower

Plasma TFV PK Mean (%CV)	E/C/F/TAF (n=19)	STB (n=7)
C <sub>trough</sub> (ng/ml)	11.4 (17.9)	82.8 (26.6)
AUC <sub>12h</sub> (ng·hr/ml)	326.2 (14.8)	3795.2 (21.9)

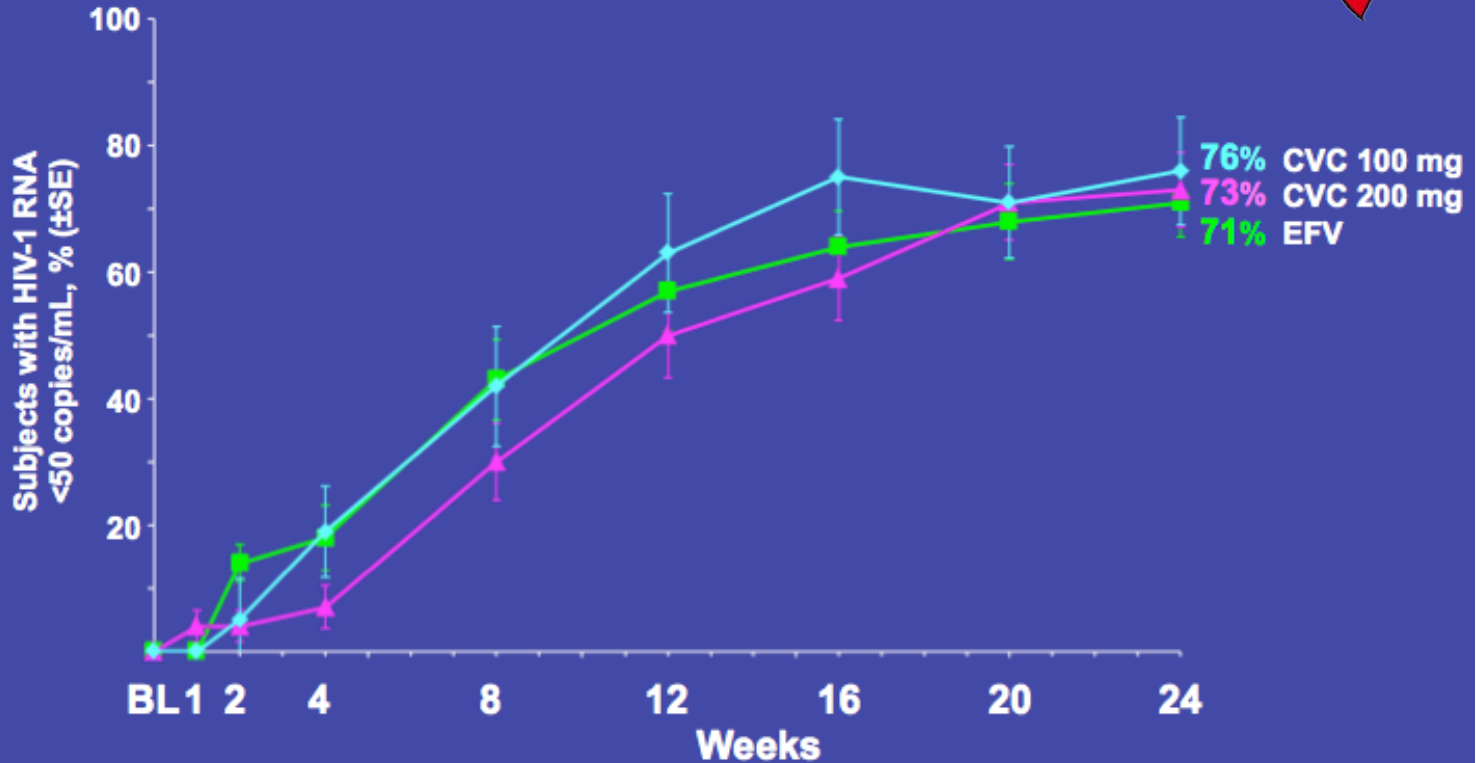


Ein neuer CCR5 & CCR2 Antagonist

# Cenicriviroc – Phase IIb Studie



## HIV-1 RNA <50 copies/mL (ITT-FDA Snapshot)



CVC 100 mg (N=59)	◆	0	3	11	25	37	44	42	45
CVC 200 mg (N=56)	▲	2	2	4	17	28	33	40	41
EFV (N=28)	■	0	4	5	12	16	18	19	20

## Ein neuer CCR5 & CCR2 Antagonist

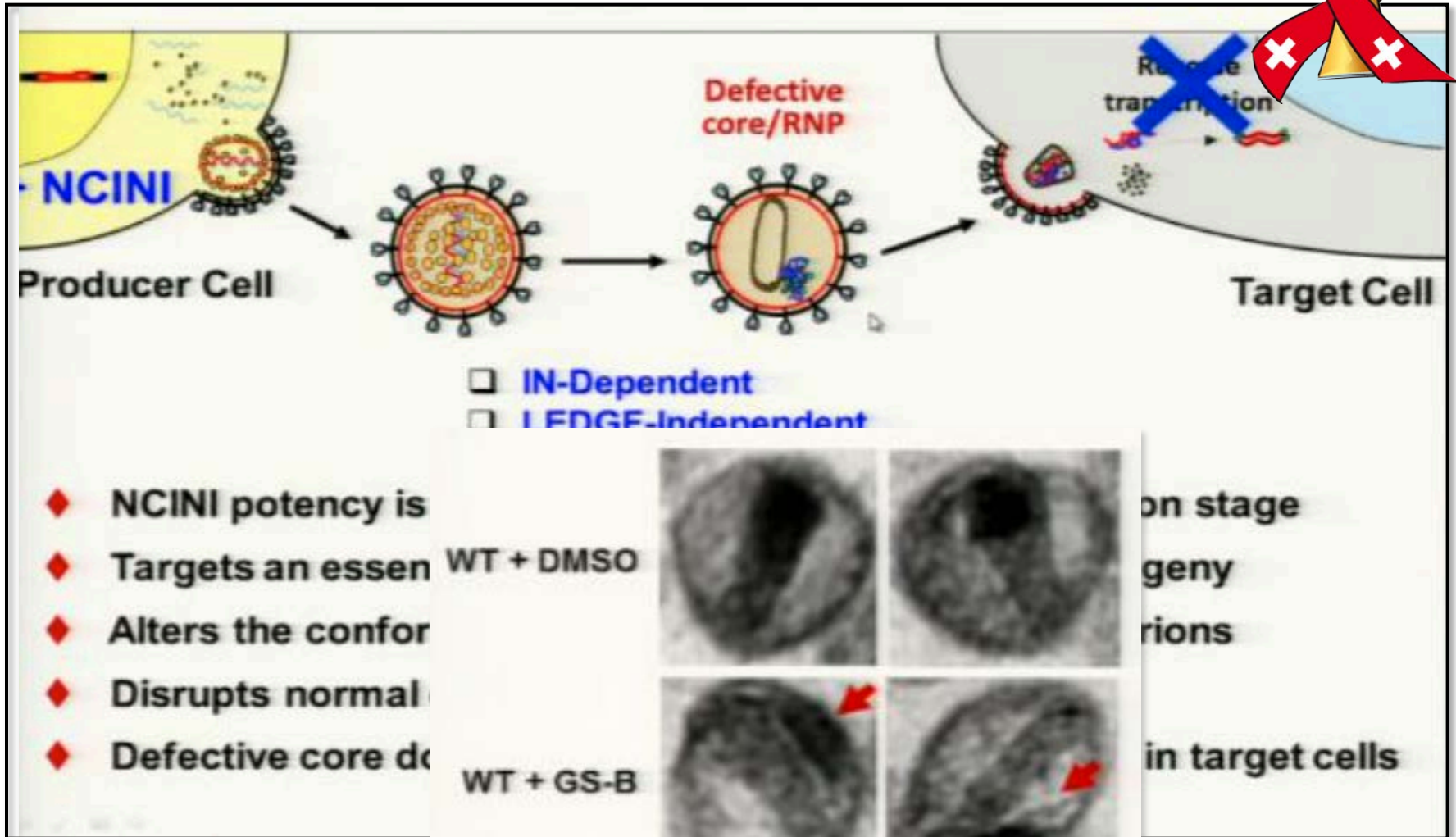
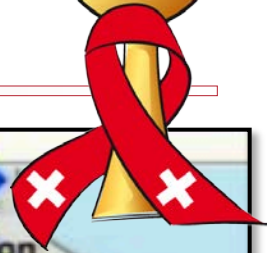
# Cenicriviroc – Phase IIb Studie



Nebenwirkungen: Grad 2 oder schwerer

Adverse events <sup>a</sup> (incidence $\geq 5\%$ )	CVC 100 mg (N=58)	CVC 200 mg (N=57)	EFV (N=28)
<b>Any Grade <math>\geq 2</math> AE</b>	<b>9%</b>	<b>9%</b>	<b>32%</b>
Nausea	0%	4%	7%
Abnormal dreams	2%	0%	11%
Rash events	2%	0%	7%
Insomnia	0%	0%	7%

# New target – new drugs

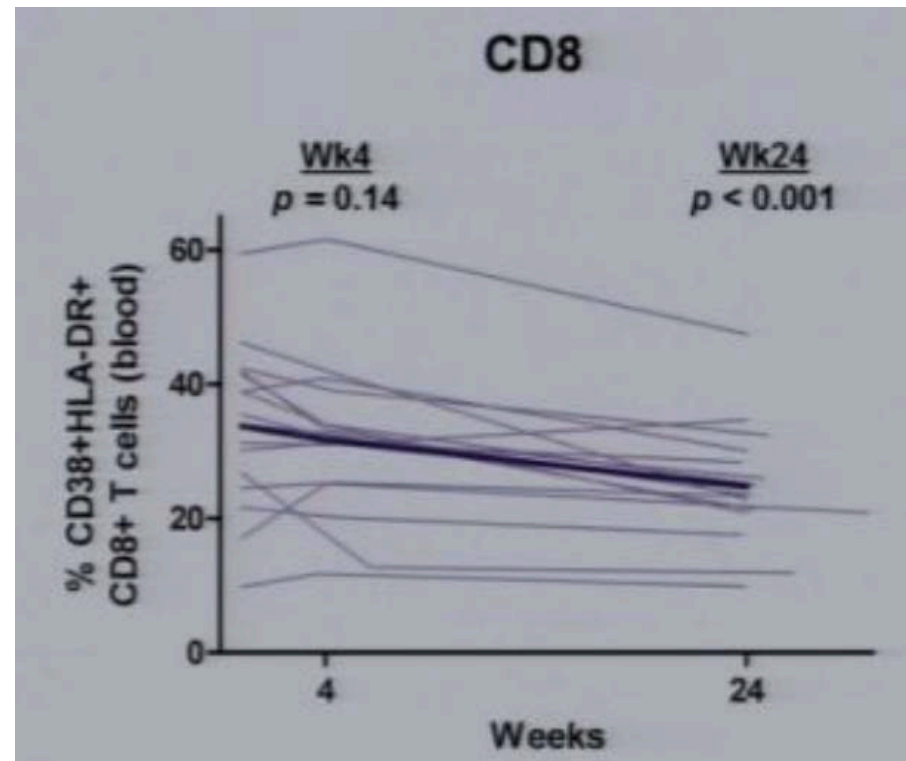
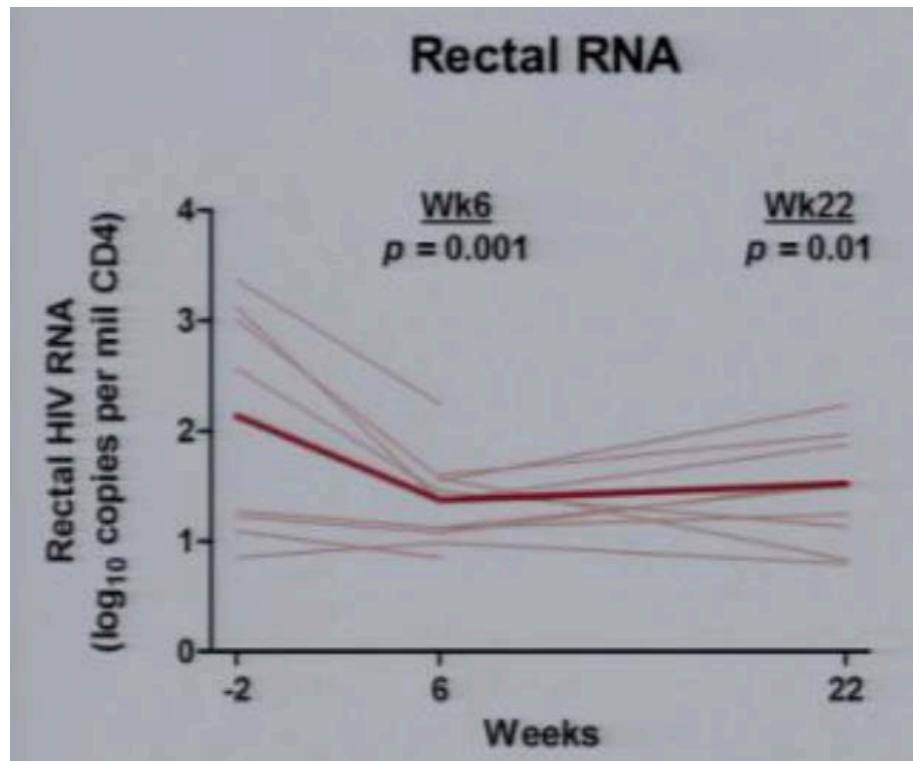


# Behandlung von (Elite-) Controllern ?

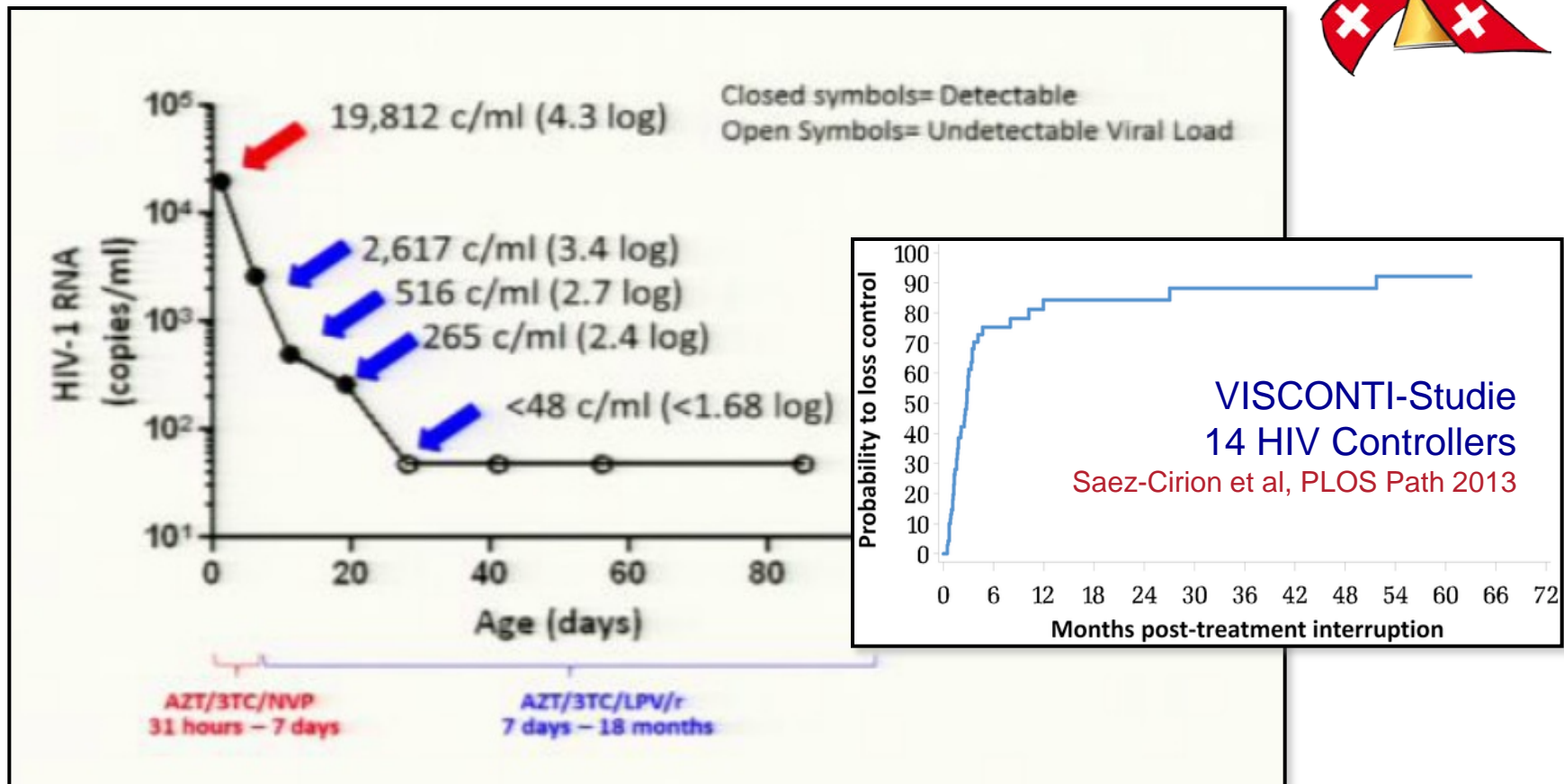


- ↘ HIV-RNA im Plasma (ultrasensitiv)
- ↘ Rektaler HIV-RNA
- ↘ aktivierte CD8
- ⊖ HIV-DNA (Blut/Rektum), ⊖ Effekt auf aktivierte CD4

**N=16** (4 Elite)



# Geheiltes Kind – gute PR-Arbeit !



Abstract 48LB