Continuously Alternating Therapy (CAT)

- A New Option in Salvage Therapy?

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What options do we have in salvage therapy?

Goals of salvage therapy:

- slow the progression of viral damage
- maintain a clinically stable patient
- bridge the time until new drugs are available

Possible strategies:

- interrupting therapy
- Continuing therapy

interrupting therapy

- Switches virus to wild type and increases virological response to subsequent therapy regimen
- Reduces toxicity
- Decreases risk of viral evolution

Continuing therapy

- Slows immunological deterioration
- preserves a less fit virus

VerhofstedeC. et al, AIDS 1999
Miller V. et al, AIDS 2000
Deeks et al, N Engl J Med 2001

background

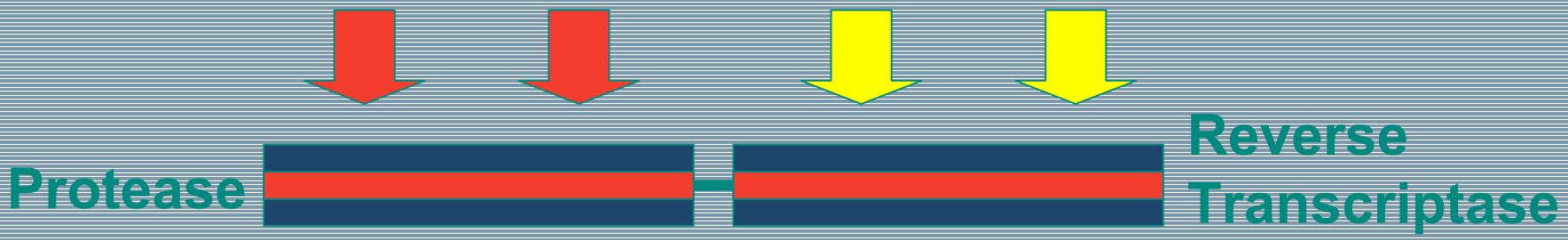
- **Is it possible to combine the benefits of treatment interruption with the benefits of continuous treatment?**

- **Can we select a susceptible virus without the risks of a interrupting therapy ?**

background

- **Can two alternatingly administered therapy regimen, each targeting one viral enzyme only, raise viral susceptibility to a subsequent cycle?**

hypothesis



design

- One armed, prospective, open label pilot study
- 2 regimens:
  - regimen 1: >3 drugs targeting the RT-Gene
  - regimen 2: 2 drugs targeting the Protease-Gene
- Drugs were chosen according to tolerability and side effects
- Regular switches between regimens every 4 weeks

inclusion criteria

- Susceptibility to less than 3 currently available antiretroviral drugs
- Documented resistance to substances from at least 2 different classes
- Viral load at BL >5000 cop/ml

endpoints

Primary endpoints:

- VL at week 24 , 48
- CD4+ T cell count at week 24, 48

  as compared to baseline

Secondary endpoints:

- Changes in resistance pattern at the end of each cycle
- Opportunistic infections

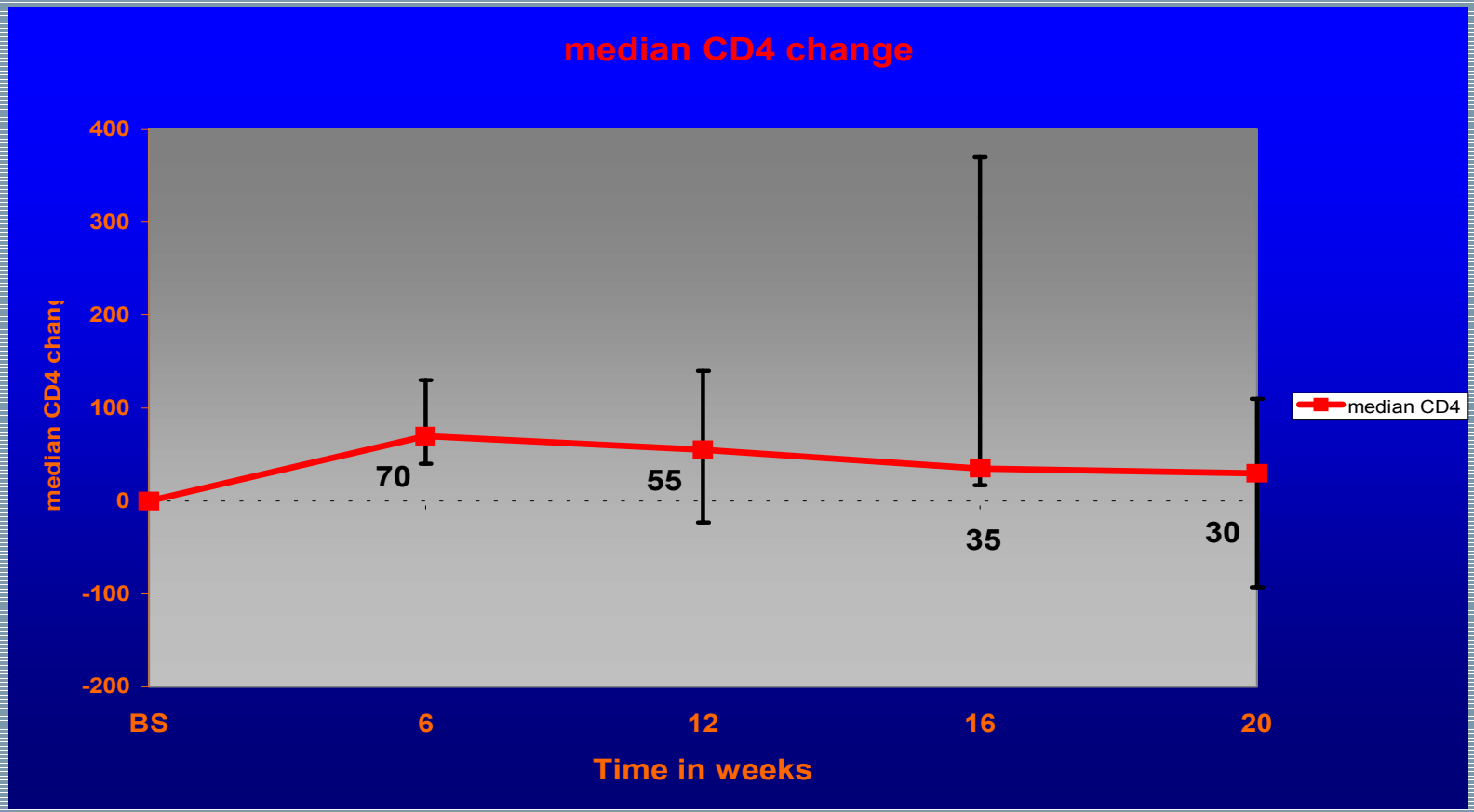
study population

Median age:	**44 yrs (36; 53)**	
Sex:	**Male (100%)**	
Median CD4 count:	**100/µl (9; 363)**	
Median VL :	**5,04 log (3,98; 5,88)**	
Number of patients:	**BL:**	**n=7**
	week 6:	**n=7**
	week 20:	**n=4**

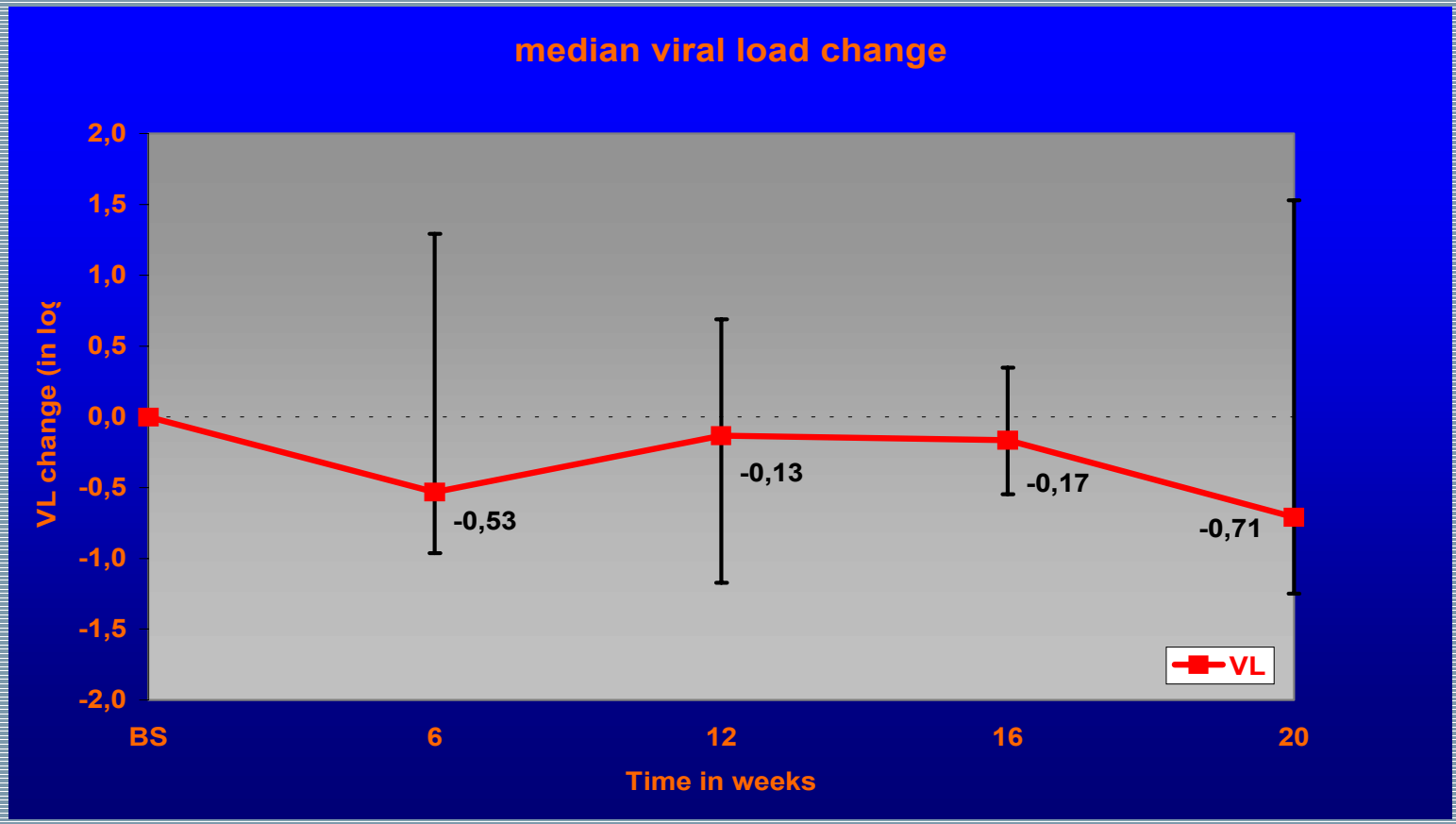
Mean numbers of mutations:

Protease gene:	**6**
RT gene:	**8**

median CD4 change at week 6/12/16/20



median VL change at week 6/12/16/20



results

- 5/7 patients kept immunologically and clinically stable

- 2/7 patients had clinical progression:
  - 1 pt died on MAI infection at week 11
  - 1 pt aquired a bacterial pneumonia at week 20

conclusions

- At present, there is no convincing evidence that a continuously alternating therapy leads to more susceptibility for the interrupted drug

- A continuously alternating therapy is able to keep a patient with MDR clinically and immunologically stable over a period of more then 20 weeks

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the patients