HIV viral load decay after initiation of HAART: is “time to undetectability” a valuable clinical parameter?

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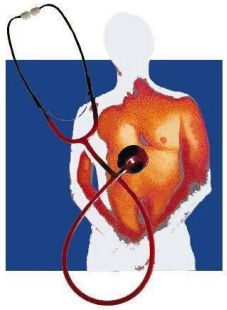


Goals of HAART

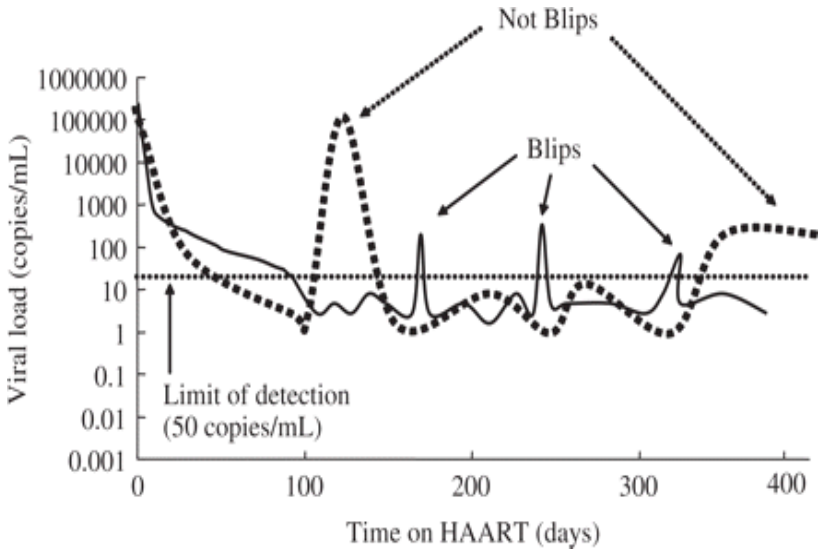
1) to obtain an undetectable viral load as soon as possible
   - within 6 months
   - if > 6 months = “primary virological failure”

2) to maintain “undetectability” as long as possible

→ if not maintained:

- **“secondary virological failure”**
  -2 consecutive measurements above limit of detection

- **“blip”**
  -isolated detectability of < 1000 cop/ml
  -significance?



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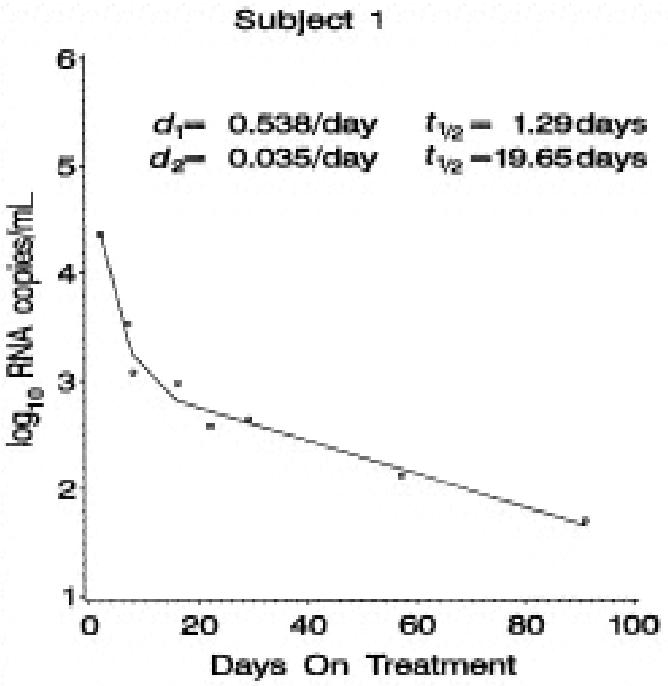
Viral dynamics after initiation of HAART



$$V(t) = P_1 e_1^{-d_1 t} + P_2 e^{-d_2 t}, \; t \geq t_c$$

- from initiation of HAART to undetectability
- bi-exponential slope
- significance:
  - understanding of pathogenesis
  - effects of antiretroviral therapy
- not used in clinical practice
- → *'time to undetectability' (TTU)* ?

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Hypothesis

- longer TTU → less powerful control of viral replication?
  - higher risk of blips?
  - higher risk of virological failure?
  - less thorough immune recovery?

- are other baseline parameters predictive of the late effects of HAART?
  - $CD4^+$ T-cell count
  - viral load

Materials & Methods

- retrospective analysis
- patients seen at the Aids Reference Centre UZ Brussels
- selection criteria
  - first HAART, for at least 2 years
  - known combination of at least 3 antiretroviral drugs
  - no primary virological failure
- periodic analysis of VL and $CD4^+$ T-cell count from 0 – 96 weeks
  - calculation of ‘TTU’ (days)
  - occurrence of ‘blips’ and ‘secondary virological failure’
- statistical analysis by SPSS

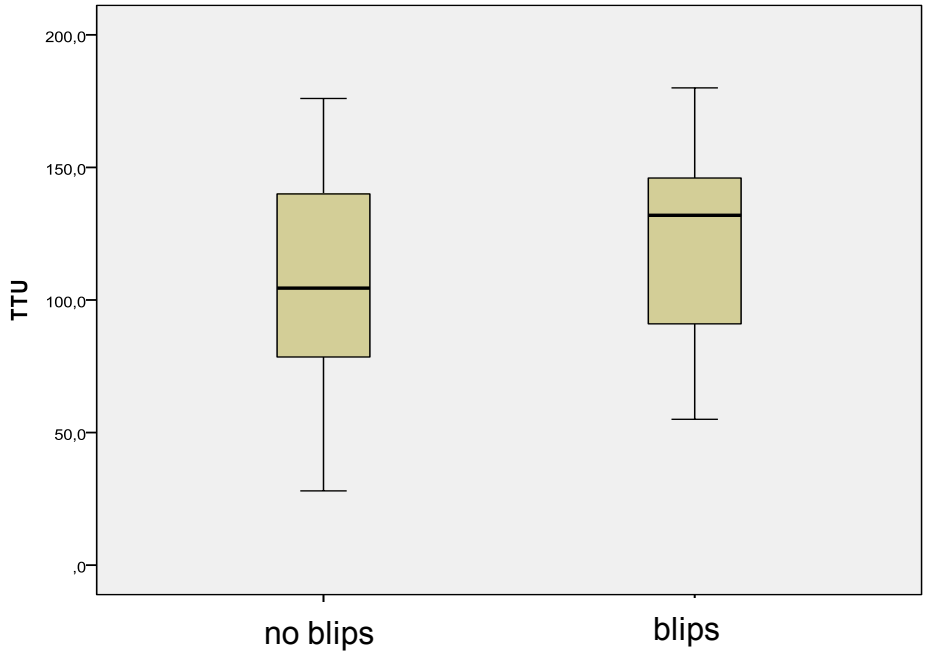
Results (1)

- 133 patients, initiating HAART between 1998-2007

- patients' characteristics:
  - mean age: 45 years
  - man/woman: 1.7 / 1
  - 21 patients with blips
  - 19 patients with secondary virological failure
  - mean TTU: 107,7 days
  - mean $CD4^+$ T-cell count at initiation of HAART: 188,2 /mm^3
  - range viral load at initiation of HAART: from 1880 to >50.000 cop/ml

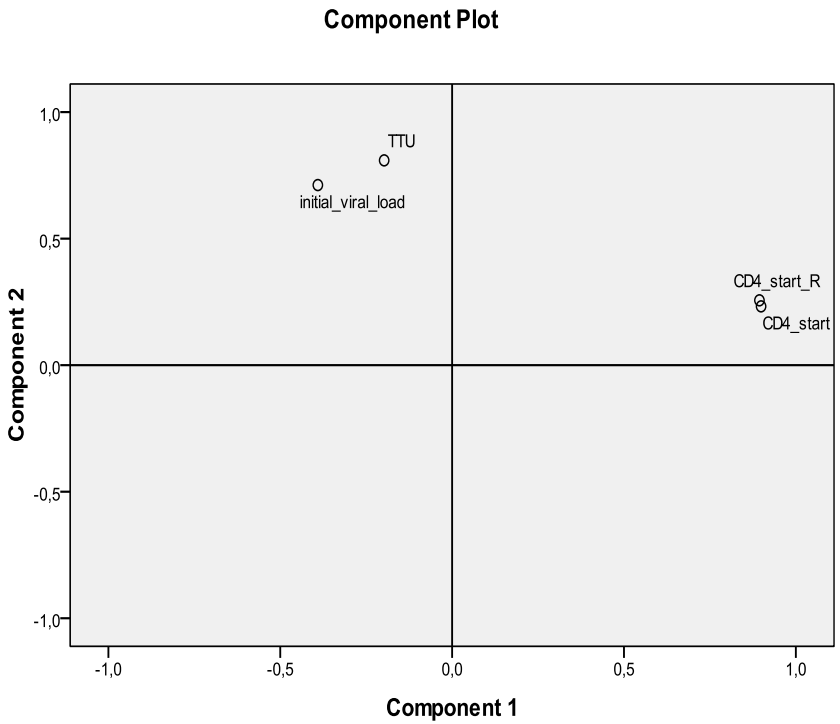
Results (2)

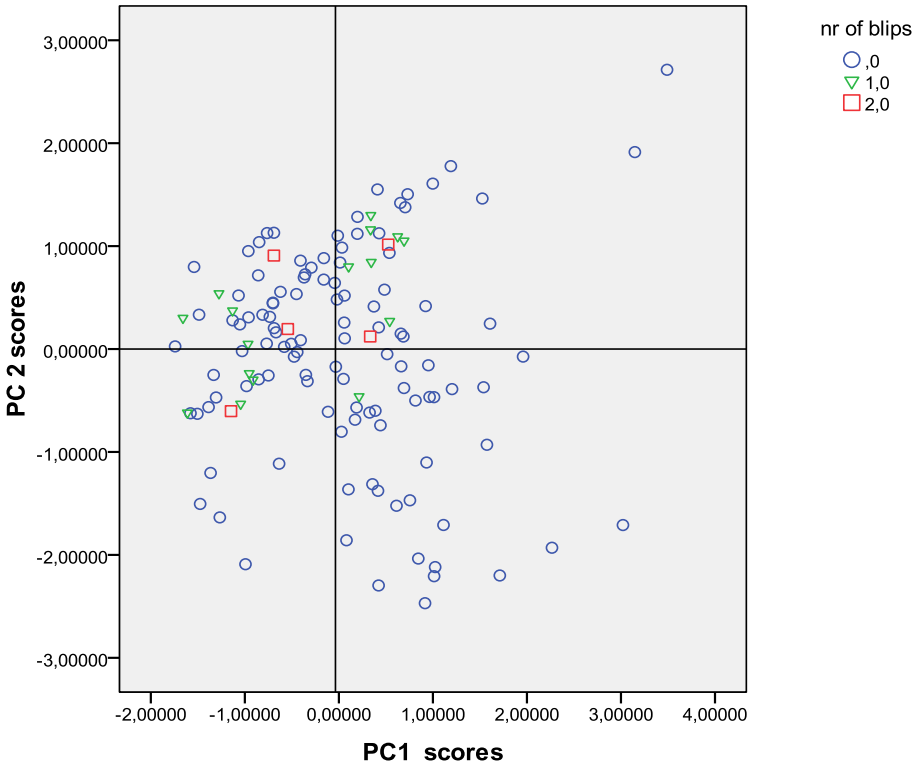
- ***is TTU predictive of the occurrence of blips?***



- **Student t-test:** p= 0,126
- patients with blips have on average longer TTU
- however this difference is not significant

Results (3)





- **PCA:** if blips occur, then predominantly in patients with longer TTU

→ occurrence of blips related to TTU ?

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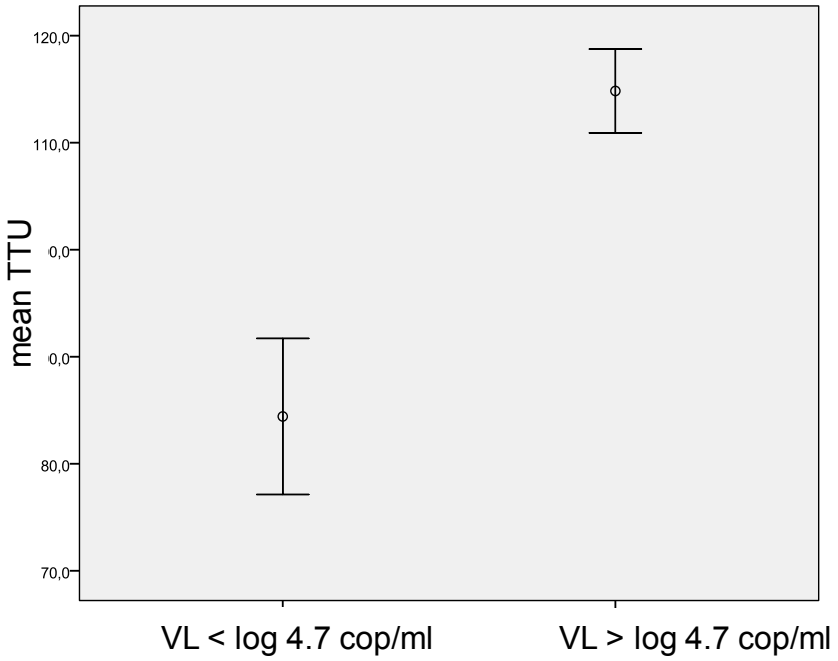
Results (4)

- ***is TTU predictive of the occurrence of virological failure?***
  - **Pearson correlation**: p= 0,944
  - confirmed by **PCA**
  - patients with longer TTU have no higher risk on virological failure

- ***is TTU predictive of the increase in $CD4^+$ T-cell count after initiation of HAART?***
  - significant **Spearman correlation** after 3 and 12 months, but not after 6, 9 and 24 months
  - significance?
  - relevance is low as mainly long-term immune recovery is important

Results (5)

- ***is there a relation between the viral load at initiation of HAART and the TTU?***
  - **Spearman correlation**: p < 0,01
  - patients with higher VL have longer TTU
  - explanation:
    - more viral particles to be cleared?
    - more advanced disease is less sensitive to antiretroviral therapy?

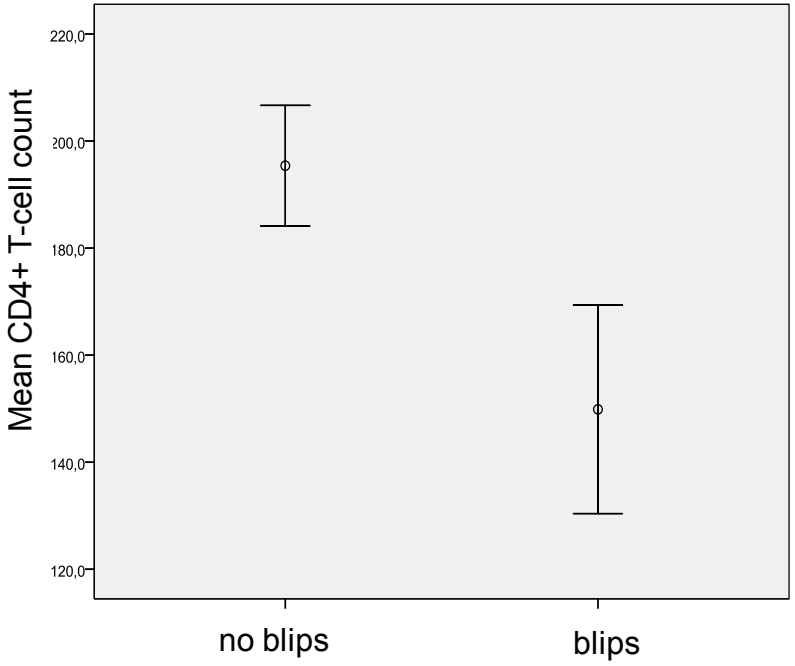


Results (6)

- ***are there other baseline parameters predictive of blips?***

  - viral load at initiation of HAART
    - **Kendall's tau-b:** p= 0,002
    - patients with higher initial VL have higher risk of blips

  - $CD4^+$ T-cell count at initiation of HAART
    - **Student t-test:** p= 0,051
    - patients with blips have on average lower CD4+ T-cell counts at initiation of HAART



Results (7)

- ***is the occurrence of blips predictive of the occurrence of virological failure?***
  - X^2-test: p= 0,308
  - blips are not related to a higher risk of virological failure
  - this result confims earlier studies

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Conclusions

- patients with a longer TTU may have a higher risk of blips
- blips do not increase the risk of secondary virological failure, although they might reflect a phase of less well controlled viral replication
- if initial viral load is high, TTU might be longer and the risk of blips is higher
- if initial $CD4^+$ T-cell count is low, the risk of blips is higher

  $\rightarrow$ emphasis on optimal adherence in patients with high VL/low $CD4^+$

- patients with a longer TTU do not have a higher risk of secondary virological failure and TTU does not seem to influence immune recovery
- a slow but steady viral response in the first 6 months after initiation of HAART is not a reason for intensification of therapy

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