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?
Viral dynamics after initiation of HAART

- from initiation of HAART to undetectability
- bi-exponential slope
- significance:
  - understanding of pathogenesis
  - effects of antiretroviral therapy
- not used in clinical practice

\[ V(t) = P_1 e^{-d_1 t} + P_2 e^{-d_2 t}, \quad t \geq t_0 \]

→ ‘time to undetectability’ (TTU)?
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 /mm³
  - range viral load at initiation of HAART: from 1880 to >50,000 cop/ml
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?
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?
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
is the occurrence of blips predictive of the occurrence of virological failure?

- $\chi^2$-test: $p = 0.308$
- blips are not related to a higher risk of virological failure
- this result confirms earlier studies
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
  → 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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