

Induction maintenance does it matter?

Charles Boucher

Erasmus Medical center

Erasmus University

Rotterdam, the Netherlands

Disclaimer

- All “expert” based opinion
- Don't try this at home

HIV therapy

- Paradox of drug development and approval
- Regimens are developed and evaluated in drug naïve individuals for first line in trials typically lasting for 48 weeks
- Once approved, these regimens can and are prescribed in individuals who are suppressed for decades to follow

HIV therapy

- Initially we used low genetic barrier drugs in double and then triple combinations
- These regimens barely did the job
- Indeed some of these (triple) regimens failed because of increased viral variability when HIV RNA plasma levels were high and resistance escaped was observed?

HIV therapy

- Drug development eg boosting for PI and second generation drugs with higher genetic barrier were developed
- Despite these improvements we continue to use triple combinations in first line
- Rational for first line (induction), but not necessarily required for patient who have been suppressed for a prolonged time

Long term suppressed patients

- The amount of replicating virus is zero or close to zero.
- The variability of the viral population is (strongly) reduced
- Therefore , the genetic barrier required for a drug regimen may be reduced

Implications

- In long term suppressed individuals the requirements for a regimen to *keep* someone suppressed differs from *getting* someone suppressed.
- This opens the door to re-evaluate the concept of induction maintenance approaches

Definitions

The definition “reduction maintenance” today is going from three to two drugs

However some drugs (boosted PI) have a very genetic barrier, they are sufficient active on their own.

Reduction from three to two drugs (inc boosted PI) is considered “maintenance” but in reality should be renamed two drugs HAART.

Same may apply for DTG+rilpivirine

Conclusion

Based on virological principals one can question whether the same regimens that are needed to *get* someone suppressed are needed to *keep* somebody suppressed.

Regimens consisting of one or two high genetic barrier drugs may be sufficient to keep someone suppressed, but here the definition “maintenance” may not apply

Clinical trials evaluating two drugs HAART regimens are on their way