Molecular Characterisation of HIV Acquisition Events in the PARTNER Study

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on behalf of the PARTNER Study Group
The PARTNER Study

- Prospective observational study of the risk of HIV transmission among serodifferent couples reporting unprotected sex while the positive partner was on ART
- 75 sites in 14 European countries
- PARTNER 1 (2010-2014) recruited and followed up heterosexual couples (n=548) and MSM couples
- PARTNER 2 extension (to 2018) recruited and followed up MSM couples only (= 972 MSM couples in total)
The PARTNER Study: Main Analysis

Incidence rate of HIV transmission

<table>
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<tr>
<th>Number of phylogenetically linked HIV infections that occurred during eligible couple-years of follow-up</th>
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<td>Eligible couple-years of follow-up*</td>
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*Follow-up periods eligible for inclusion if couples had sexual intercourse without condoms and without PEP or PrEP and the HIV-positive partner had a viral load <200 copies/ml at the most recent visit (within the past year)
HIV Acquisitions in PARTNER

- **22 HIV acquisitions** in participating couples
  - 11 in PARTNER 1 (10 MSM, 1 heterosexual)
  - 11 in PARTNER 2 (all MSM)
  - 16/22 events (15 MSM, 1 heterosexual) during eligible follow-up
  - 6/22 events (all MSM) outside eligible follow-up
    - Reasons for non-eligibility of follow-up period: no data on sexual behaviour (n=3), no condomless sex (n=1), PEP use (n=1), no viral load measurement in the HIV-positive partner (n=1)
Aim of this Study

- To obtain a detailed molecular characterisation of HIV acquisition events
  - Include events that occurred during or outside eligible follow-up
  - Use sensitive techniques to characterise the viral strains*
  - Perform anonymised phylogenetic analysis** to determine linkage between viral sequences of putative source and putative recipient

*Work supported by a BHIVA Research Award

**Maximum-likelihood and Bayesian Markov Chain Monte-Carlo inferences
Study Design

When a HIV-negative partner was found to have become HIV-positive, a venous blood sample was taken from both partners to determine the genetic relatedness of the respective HIV sequences.

- Partner on suppressive ART
- Newly positive partner

HIV-1 DNA from PBMC

HIV-1 RNA from plasma
Sequencing - Conventional

- Population (Sanger) sequencing of pol and env
  - 22/22 (100%) couples for pol and 18/22 (87%) couples for env
- 22/22 HIV-positive partners had subtype B
- 9/22 (41%) newly HIV-positive partners had non-B infections
  - A1, C, G, CRF02_AG, CRF20_BG, CRF29_BF, CRF60_BC, CRF14_BG

No linkage in any of the 22 couples
Median pairwise genetic distance between PARTNER sequences consistently >0.040

*Pol* = median 0.069 (IQR 0.057–0.076)

*Env* = median 0.14 (IQR 0.125–0.169).
Sequencing - Deep

- Illumina MiSeq
- Plasma virus from 8 HIV acquisition events
  - 6 in eligible and 2 in non-eligible follow-up
- ~1,000bp pol amplicon (codons 14 to 345 of RT)
- Virus variants of putative recipient detected with sensitivity ≥1%
- Haplotypes analysed phylogenetically for relatedness to the PBMC sequence of the putative source

No linkage in any of the 8 couples
Putative transmitter’s sequences
Viral haplotypes
Control sequences
Conclusions

- Using both conventional and sensitive sequencing methodologies, and including HIV acquisition events occurring in non-eligible periods, there was no evidence of within-couple transmissions in PARTNER.
Thank you

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