Unmasking and tracking Tuberculosis risk during HIV acquisition and antiretroviral therapy

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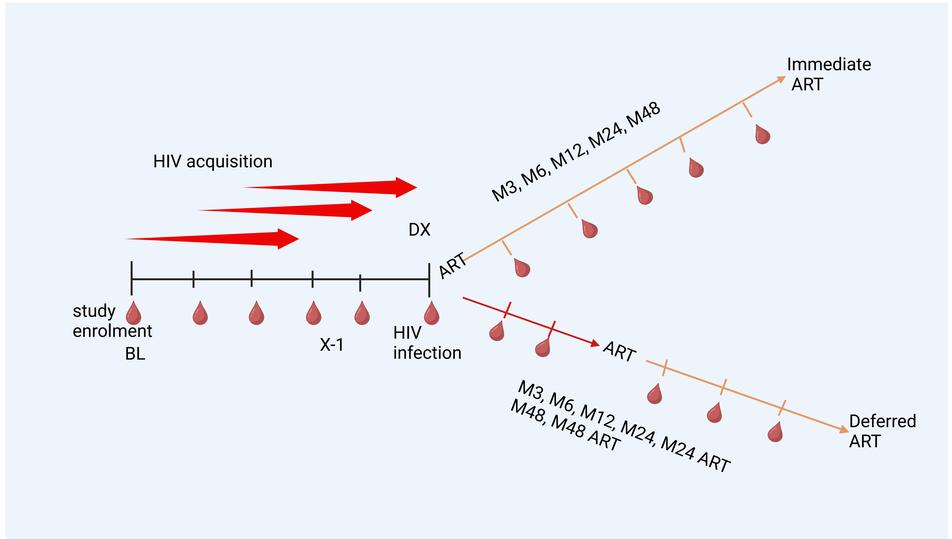
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INTRODUCTION

Risk of progression from *Mycobacterium (Mtb)* infection to active TB disease is estimated to be up to 20x higher in PLWH, with fatality rates 16 - 35%

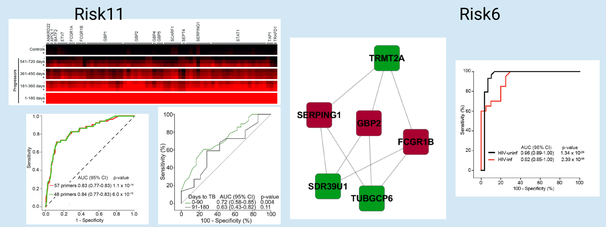
How does HIV infection and antiretroviral therapy change TB risk?

Determine TB risk using published transcriptomic signatures of TB risk

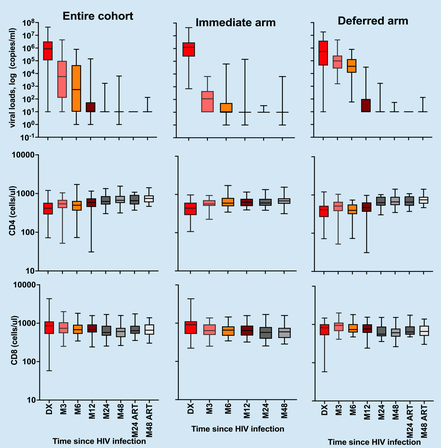


Study design: A study MSM and transgender women, designed to understand risks associated with HIV acquisition and how timing of ART modulates HIV infection. Participants were followed up from enrolment and screened monthly for HIV infection. If HIV positive they were randomized to either receive ART immediately (within 120 days of a positive result, Immediate ART) or after 120 days (Deferred ART). RNAlater was collected monthly before HIV acquisition and at several interval whilst on ART. For our study, we selected RNAlater collected at study enrolment (BL), last sample collected before HIV diagnosis (X-1), immediately after HIV diagnosis (DX) and several timepoints after HIV diagnosis up to 48 months after ART.

TB risk signatures and participant characteristics

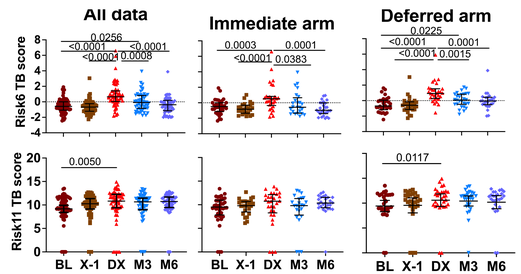


TB risk signatures were developed in South African TB progressors. We previously evaluated these signatures in persons living with HIV and showed that these signatures could both predict and differentiate active TB disease from other TB states (references: Darboe et al., 2019, Penn-Nicholson et al., 2020).



Clinical characteristics of study participants: A decrease in viral loads was observed in the study cohort, whilst the CD4 counts increased steadily over time. All participants were assigned males at birth. Of the 88 participants in our cohort, 49 received deferred ART. 81% of the cohort wee of mixed ancestry, 14% were White, 3% were indigenous and 2% were Asians. The median age of participants was 25 (18 - 52) at study enrolment.

TB risk changes in the first 6 months after HIV diagnosis



Changes in transcriptomic TB risk scores in the first 6 months is dependent on the Risk signature tested. Signature scores decrease in the deferred arm before ART (all timepoints shown here are before ART in the deferred arm). Risk6 scores were calculated by subtracting the geometric mean of the downregulated genes from the geometric mean of the upregulated genes. Risk11 scores were calculated using the geometric mean of the genes.

Preliminary findings

We show here that there is a potential use of TB risk signatures as determinants of individual risk in PLWH.

Viremia decreased in the deferred arm before treatment start

There was a weak association between viremia and Risk6 scores(r=0.39, p<0.0001) but not Risk11 scores (r=0.06, p=0.47)

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