Low dose Nivolumab in Adults with HIV on Antiretroviral therapy: The NIVO-LD Trial

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ABSTRACT:

Background: Programmed death (PD-1) is expressed on activated and exhausted T-cells which persist on antiretroviral therapy (ART). PD-1 blockade can reverse HIV latency and increase HIV specific T-cell responses. Single low-dose Anti-PD-1 (Nivolumab) could reduce the HIV reservoir and increase anti-HIV immunity in people with HIV (PWH), with less immune related adverse events.

Methods: NIVO-LD is a two-part trial in PWH on ART receiving a single low-dose of Nivolumab (0.1, 0.3 or 1 mg/kg) with fine needle aspirates (FNAs) of a groin lymph node before and 2 weeks after dosing. The first part of the trial (Cohort A) defines safety and PD-1 receptor occupancy in blood and tissue and determines the dose used in the second part (Cohort B) that compares Nivolumab to placebo during ART interruption.

Results: For Cohort A 26 PWH were enrolled (Median 49 yrs, 88% male), with 8 screened out. For 18 participants dosed there was one possible immune related adverse event (hepatitis) (ALT 135 [Grade 2] and AST 181 [Grade 3] units/L) which resolved. Other related events were: mild groin bruising/pain (n=16) post FNAs and mild fatigue (n=9) in the 0.3-1 mg/kg cohorts which resolved. Two unrelated increases in liver transaminases occurred after significant alcohol intake which resolved with ceasing alcohol. Median PD-1 occupancy in CD4+ / CD8+ T-cells in lymph node 2 weeks after 0.1, 0.3 and 1 mg/kg Nivolumab was 62%/62%, 91%/94% and, 81%/84% respectively. Median PD-1 occupancy in blood was similar to lymph node at 2-weeks with increasing duration of occupancy with increasing dose (median 1%, 4% and 48% at 12 weeks post 0.1, 0.3 and 1 mg/kg respectively). No changes in HIV DNA were seen from baseline to week 17.

Conclusion: Single low dose Nivolumab at 0.1, 0.3 or 1 mg/kg with groin FNAs is safe and well tolerated. PD-1 receptor occupancy was similar in blood and lymph

node and was prolonged following 1mg/kg. The second randomised part of the trial has commenced with a single 1mg/kg dose.

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