Safety of 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 response in people with HIV and cancer. 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 defines safety and PD-1 receptor occupancy in blood and tissue and determines the dose used in the second part that compares Nivolumab to placebo during ART interruption.

Results: 25 PWH have enrolled, with 9 screened out (5 positive ANA, 2 positive GAD antibodies, 1 elevated LFTs, 1 elevated HIV viral load). 16 participants received 0.1 (n=6), 0.3 (n=6) or 1 (n=4) mg/kg Nivolumab. There was one possible immune related adverse event (hepatitis) at 4 weeks post-Nivolumab (ALT 135 [Grade 2] and AST 181 [Grade 3] units/L) with normal LFTs 2 weeks before and after this. Other related events related include: mild groin bruising/pain (n=16) post FNA in all cohorts and mild fatigue (n=9) in the 0.3-1 mg/kg cohorts which resolved. One unrelated serious adverse event (appendicitis) occurred and one unrelated increase in ALT (123 units/L [Grade1]) occurred 12 weeks post Nivolumab after the participant had 17 standard alcoholic drinks which resolved with decreased alcohol intake.

Conclusion: Single low dose Nivolumab at 0.1, 0.3 or 1 mg/kg with groin FNAs is safe and well tolerated. The trial will complete the 1mg/kg dosing cohort then select the dose for the second part of the trial and report HIV-specific immune responses post Nivolumab

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