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LATE BREAKER ORAL ABSTRACTS

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Enrichment of the HIV reservoir in CD32+ CD4 T cells occurs early and is closely associated with immune checkpoint receptor expression

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Background: CD32 has been identified as a marker of a substantially enriched HIV reservoir. Here, we explore the relationship of CD32 expression on CD4 T cells with other correlates of reservoir size including time to viral rebound after treatment interruption.
Methods: CD32 expression was measured by flow cytometry on PBMCs (n = 39) and tonsillar tissue (n = 1) from individuals who initiated ART during primary HIV infection (PHI), and uninfected controls (n = 10). Co-expression with immune checkpoint receptors (ICRs), lineage, memory and T follicular helper (Tfh) markers was measured. HIV DNA was quantified in bulk and sorted CD32+ and CD32– populations.
Results: One-year post-ART initiation, the frequency of CD32+ CD4 T cells was 1.5% (range 0.2–6.4), and did not differ from controls. CD32+ CD4 T cells were found predominantly within differentiated memory subsets (transitional, effector memory and T_{EMRA}) compared with CD32- CD4 T cells (all $p < 0.001$) for HIV+ (n = 20) and controls. CD32+ CD4 T cells were highly enriched for HIV DNA compared with CD32– cells (average 103-fold, n = 6, p = 0.03), although CD32 percentage did not correlate with reservoir size (n = 29). In a subset of individuals (n = 19) who interrupted ART after 48 weeks, CD32+ CD4% did not predict viral load rebound, although all three individuals with persistently undetectable viraemia had CD32+ CD4% below the median.
CD32+ CD4 T cells from blood had higher expression of PD-1, Tim-3 and TIGIT (all $p < 0.0001$) and a higher density of CD2 (p = 0.001) than CD32- cells in HIV+ participants (n = 20) and controls. Tonsil CD32+ CD4 T cells (n = 1) showed a similar pattern of memory distribution and ICR expression as the periphery. Although tonsillar CD32+ CD4 T cells had higher individual expression of Bcl-6, ICOS and CXCR5 than CD32- cells, the co-expression pattern was not consistent with a Tfh phenotype.
Conclusions: We confirm the role of CD32 as a marker of the HIV reservoir, and show that this may occur early during PHI on more differentiated CD4 T cells and is highly co-expressed with ICRs. That expression is similar between HIV+ and HIV– individuals and suggests that preferential infection or survival of CD32+ cells, rather than CD32 up-regulation, is responsible for the observed enrichment.

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A Phase 3 randomized controlled clinical trial of bictegravir in a fixed dose combination, B/F/TAF, vs ABC/DTG/3TC in treatment-naive adults at Week 48

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Background: Integrase strand transfer inhibitors (INSTIs) are recommended as first-line antiretroviral therapy in combination with 2 nucleoside reverse transcriptase inhibitors. Bictegravir (B), a novel, potent INSTI with a high in vitro barrier to resistance and low potential for drug interactions, has been coformulated with emtricitabine (F) and tenofovir alafenamide (TAF) as a fixed-dose combination (B/F/TAF). We report results from a blinded Phase 3 study comparing B/F/TAF to coformulated abacavir, dolutegravir and lamivudine (ABC/DTG/3TC).
Methods: HIV-infected, treatment-naive, HLA-B*5701-negative, HBV-uninfected adults with estimated glomerular filtration rate (eGFR) ≥50 mL/min were randomized 1:1 to receive blinded treatment with fixed-dose combination B/F/TAF (50/200/25mg) or ABC/DTG/3TC (600/50/300mg) with matching placebos once daily. The primary endpoint was proportion of participants with HIV-1 RNA (VL) <50 c/mL at W48 (FDA snapshot). Noninferiority was assessed through 95.002% confidence intervals (CI) (12% margin). Secondary endpoints were safety (adverse events (AEs) and laboratory abnormalities) and pre-defined analyses of changes from baseline in bone mineral density (BMD) and measures of renal function, including eGFR and proteinuria.
Results: 629 participants were randomized and treated (314 B/F/TAF, 315 ABC/DTG/3TC): 10% women, 36% Black, 16% VL >100,000 c/mL, 11% CD4 <200 cells/mL. Median baseline characteristics: age 32 yrs, CD4 count 444 cells/μL and VL 4.47 log10 c/mL. At W48, B/F/TAF was non-inferior to ABC/DTG/3TC, with 92.4% on B/F/TAF and 93.0% on ABC/DTG/3TC achieving HIV-1 RNA <50 c/mL (difference −0.6%; 95.002% CI −4.8% to 3.6%, p = 0.78). No resistance mutations emerged in either group. Comparing B/F/TAF to ABC/DTG/3TC throughout, the most common AEs were diarrhoea (13%, 13%), headache (11%, 14%) and nausea (10%, 23%). Few participants (0 vs. 4 (1%)) had any AEs leading to premature study drug discontinuation. At W48, mean percentage changes from baseline in BMD were −0.83% versus −0.60% (p = 0.39) (lumbar spine) and −0.78% versus −1.02% (p = 0.23) (total hip). No differences between treatments were noted in changes from baseline for eGFR and proteinuria at W48.

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