Background

Various anti-HIV immunotherapy strategies have been associated with ART-free control in non-human primates.1-3

We sought to determine whether a combination of such strategies was safe and could avert virologic control in people with HIV (PWH) after ART discontinuation.

Methods

We performed a single-arm proof-of-concept study to evaluate the efficacy of a combination approach involving (1) Gag conserved element (CE)-targeted DNA+IL-12 prime/MVA boost vaccination, followed by (2) a combination of two broadly neutralizing antibodies (bNAbs; 10-1074, VRC07-523LS) and a TLR-9 agonist (leftolimod) and then (3) two bNAbs given at the time of ATI.

Results

Two participants experienced ALT elevations (Grade 3 and Grade 4) that were considered possibly related to the treatment regimen but ultimately attributed to external causes.

7/10 exhibited atypical rebound dynamics characterized by non-exponential growth and/or oscillations; 5/10 had set points < 1000 copies/mL and 7/10 < 5000 copies/mL (Fig 2).

Viral rebound occurred on average 15 weeks after ART interruption (Fig 3). Median ATI length was 37 weeks.

One individual did not rebound (18 months off ART), with low levels of non-intact provirus in gut tissue and intermittent detection below the quantification limit of HIV DNA and RNA in PBMCs during the ATI.

Higher bNAb exposure (AUC) was associated with a later time to rebound (p=0.054 and p=0.052 for 10-1074 and VRC07-523LS, respectively), but bNAb levels at rebound were highly variable across participants (1.3-38.3 mcg/mL for 10-1074, 0.2-57.9 mcg/mL for VRC07-523LS).

The vaccine regimen increased the magnitude of IFNγ CE-specific CD4+ and CD8+ T cell responses in all 10 participants between pre-vaccination and 2-weeks post-boost (Fig 4; median CD4: 0.030% vs 0.341% [p=0.002]; CD8: 0.026% vs 0.158% [p=0.002]).

Phenotypic susceptibility to both 10-1074 and VRC07-523LS declined over time (Fig 5).

Neither antibody levels nor associated susceptibility could completely explain the different post-ART set points between the three non-controllers and the 7 with set points < 5000 copies/mL, suggesting the involvement of other factors.

Conclusions

Seven of ten individuals exhibited evidence of at least partial virologic control post-ART.

Treatment-mediated virologic and immunologic factors may have contributed to this outcome.

Ongoing work is evaluating changes in the characteristics of the reservoir and T cell responses prior to and during the ATI, including assessment of the vaccinal effect.

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