

## PE29

### Polyvalent immune responses correlate with lower number of HIV infected CD4 T-cells in chronically infected subjects treated with autologous RNA pulsed DC therapy

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**Background:** AGS-004 immunotherapy consists of autologous DCs electroporated with autologous amplified HIV RNAs (Gag, Vpr, Rev and Nef). AGS-004 was administered every four weeks to chronic HIV patients while on standard antiretroviral therapy (ART). At week 14, after 4 administrations a 12-week analytical treatment interruption (ATI) began, during which AGS-004 dosing continued every four weeks. Thirty six participants completed ATI, 23 of whom received AGS-004. This study evaluated the impact of AGS-004 on the level of integrated HIV DNA (pDNA) in CD4 T cells and its correlation with the immune response.

**Methods:** Peripheral blood samples were collected during a clinical study at baseline, week 8 during ART treatment and week 18 and week 26 during ATI. PBMCs were isolated using Ficoll separation and CD4 T cells were isolated using negative selection with a human CD4+ T Cell Isolation kit (Miltenyi). Genomic DNA was isolated using the Genra Puregene kit (Qiagen). 15,000 genomes were used in a repetitive Alu-Gag based PCR. pDNA analysis was conducted on 35 subjects. Immunomonitoring data was available on 32 subjects. Levels of pDNA were correlated with the magnitude and quality of immune responses for 31 subjects. Immunomonitoring was conducted to determine if HIV-specific immune responses were generated. The analysis was conducted against all four or individual antigens used in AGS-004.

**Results:** There were no differences in pDNA levels in immunized versus placebo subjects (N=35). However, in an analysis of AGS-004-treated subjects (N=21), HIV pDNA levels were significantly lower in those subjects who developed multifunctional memory T cell responses (N=14) after two, five or seven doses of AGS-004 (weeks 8, 18 and 26) but not at baseline. The attenuation of pDNA levels were not associated with immune response to any individual antigen. These data taken together indicate that a polyvalent immune response directed against multiple antigens is important for the control of pDNA levels in CD4 T cells.

**Conclusions:** The results of this study provide a rationale to combine AGS-004 with ART and a latency reversing agent for the purpose of boosting the immune response to eliminate HIV reservoirs in infected individuals.