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Oral presentation

OA05-06 LB. First-in-human Phase 1 safety and immunigenicity of an adenovirus serotype 26 HIV-1 vaccine vector

LR Baden*[1], R Dolin[2], KL O'Brien[3], P Abbink[3], A La Porte[3], MS Seaman[3], E Choi[1], R Tucker[1], M Weitjens[2], MG Pau[2], J Goudsmit[2] and DH Barouch[3]

Address: [1]Brigham and Women's Hospital, Boston, MA, USA, [2]Crucell, Leiden, Netherlands and [3]Beth Israel Deaconess Medical Center, Boston, USA

* Corresponding author

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Background

Adenovirus serotype 26 (Ad26) is a rare Ad serotype that differs substantially from Ad5 in terms of baseline seroprevalence, receptor usage, tropism, innate immune profile, adaptive immune phenotype, and protective efficacy in the SIV/macaque model. Here we report the initial safety and immunogenicity assessment of a prototype Ad26 vector in humans.

Methods

Ad26 expressing the VRC EnvA test antigen was manufactured by Crucell. 36 Ad26 seronegative, healthy subjects were enrolled in a randomized, double-blinded, placebo-controlled, dose-escalation phase 1 study. Groups of 12 subjects received doses of 109, 1010, or 1011 vp of the Ad26-EnvA vector (N=10/group) or placebo (N=2/group) at weeks 0, 4, and 24. We performed a pre-specified blinded immunogenicity analysis after the first two immunizations. Validated IFN-gamma ELISPOT assays were performed with positivity criteria of >55 SFC/106 PBMC and >4-fold background.

Results

26/36 subjects were female, and 70/72 vaccinations were administered. Some reactogenicity was observed after the initial immunization in the highest dose group but typically resolved within 24 h. No vaccine-associated AEs or SAEs occurred. In all three dose groups, 2 subjects/group exhibited no detectable vector- or insert-specific immune responses at any timepoint, whereas 10 subjects/group developed positive Ad26 NAb titers, EnvA-specific ELISA titers, and EnvA-specific ELISPOT responses following vaccination. In the 109 vp dose group, the median ELISA titer was 1000 (IQR 300-3,000) and the median ELISPOT response was 381 SFC/106 PBMC (IQR 125-545) at week 8. In the 1011 vp dose group, the median ELISA titer was 5,477 (IQR 3,000-10,000) and the median ELISPOT response was 365 SFC/106 PBMC (IQR 85-715) at week 8.

Conclusion

The Ad26 vector is safe and immunogenic in humans at all three doses. Ad26 is therefore a promising new vector for further clinical studies to evaluate novel inserts such as mosaic HIV-1 Gag, Pol, Env antigens.