seropositive cohorts, proportion of subjects who reported injection site AEs was higher in V160 recipients than placebo controls. Proportion of subjects who reported systemic AEs was comparable across V160 doses/formulations and placebo. In the CMV seronegative cohort, immune responses increased with incremental dosing. More importantly, recipients of V160 from several dose levels mounted NAB and CMI responses at 1 month post dose 3 (PD3) that were comparable to baseline levels measured in seropositive subjects.

Conclusion. V160 had acceptable safety profile across all dose levels and formulations studied; Vaccine was immunogenic and elicited NAB and CMI responses at 1 month PD3 that were comparable to natural CMV seropositive controls. Vaccine was well tolerated in all groups. AEs were managed in the study with no SAEs reported.

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1022. Establishing Models of Herpes Simplex Virus Type 2 Superinfection of Herpes Simplex Virus Type 1 Seropositive Mice to Test The Efficacy of a Novel Vaccine
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Background. Multiple subunit vaccines that elicit neutralizing antibodies (nAbs) against the immunodominant HSV-2 glycoproteins D and/or B (gD and gB) were advanced into the clinic after demonstrating protection against disease in animal models. However, although the vaccines elicited nAbs in seronegative and boosted nAbs titers in HSV-1–seropositive (HSV-1+1) participants, clinical trials examining gD vaccination for HSV-2 infection suggested that nAbs alone are not sufficient. The results also indicate that current animal models are not predictive of clinical trial outcomes. We recently engineered a candidate single cycle virus strain deleted in gD (ΔgD-2) and showed that it elicited high titer non-neutralizing Abs that provide complete protection against HSV-1 or HSV-2. The Abs passively protect naive mice and activate the Fc receptor to induce antibody-dependent cell mediated cytotoxicity (ADCC). We hypothesize that ΔgD-2 will protect HSV-1+1 individuals from HSV-2 because it elicits a different type of immune response. To test this hypothesis, we established a model of HSV-2 superinfection in HSV-1+1 mice.

Methods. We infected mice by corneal scarification with serial dilutions of a clinical strain of HSV-1 (Bx'1.1) to identify a sublethal dose associated with seroconversion. We then superinfected mice on the skin with HSV-2 and monitored for disease. The presence of virus in dorsal root ganglia (DRG), the site of HSV latency, was determined.

Results. Corneal infection with 10^4 PFU of HSV-1 resulted in disease in 18/29 (62%) mice and 13/18 survived. Seroconversion was documented in 9/13 survivors. Survivors were superinfected 2 weeks post-recovery with HSV-2. All of the mice developed signs of disease, but only 2/9 who were HSV-1+1 died compared with 4/4 seronegative mice (P = 0.02, Fisher exact test). HSV-2 DNA was detected in the DRG of all 12/13 mice.

Conclusion. Sublethal HSV-1 corneal disease provides partial protection against HSV-2 superinfection and provides a model to test vaccine efficacy. We speculate that superinfection boosts preexisting nAb titers, a response consistent with immune repertoire freeze, but that ΔgD-2, because it elicits ADCC Abs, will overcome repertoire freeze and provide greater protection against HSV-2 superinfection.

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1023. Sustained Lesion and Shedding Rate Reductions in Genital Herpes Patients 24 Months after Immunization with GEN-003, a Genital Herpes Immunotherapy
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Background. Herpes simplex viruses (HSVs) are the main cause of genital ulcers worldwide. GEN-003 is an investigational genital herpes immunotherapy composed of HSV-2 antigens gD2DTMR and ICP4.2, and the saponin-based adjuvant Matrix-M2 (MM2). In a Phase 2 dose-ranging study (GEN-003-002), 3 doses of GEN-003 reduced HSV-2 lesion rate (percent of days with genital lesions) and anogenital HSV-2 shedding rate (percent of days with detectable virus). The antiviral effect of GEN-003 persisted to 12 months after the 3-dose vaccination regimen. We report here the results of an extension study to evaluate efficacy and immunogenicity of GEN-003 post 24 months post-vaccination.

Methods. GEN-003-002 subjects who received at least 1 dose of GEN-003 (dose groups: 30 or 60 µg of antigens combined with 25, 50 or 75 µg of MM2) were eligible to enroll in the extension study. At 24 months post-vaccination, anogenital swabs were collected twice daily for 28 days for HSV-2 DNA detection by quantitative PCR. During this period, subjects also reported genital herpes lesion data via a daily reporting tool. Blood samples were collected at the end of the swab collection period to evaluate humoral and cellular immune responses. HSV-2 immunoglobulin G (IgG) was measured by ELISA, and HSV-2 neutralizing antibodies were measured by a colometric assay. Cellular responses were evaluated in peripheral blood mononuclear cells using an interferon-γ/granzyme B Fluorosspot assay.

Results. 140 subjects were enrolled. At 24 months, those in the two best-performing groups (N = 003-002b) were comparable to natural CMV seropositive controls. HSV-2 DNA was undetected in 120/140 subjects, and HSV-2 neutralizing antibodies were measured by a colometric assay. Cellular responses were evaluated in peripheral blood mononuclear cells using an interferon-γ/granzyme B Fluorosspot assay.

Conclusion. GEN-003 induces reductions in HSV-2 shedding and genital herpes lesion rates that persist to 24 months following treatment. Humoral immune responses to GEN-003 are maintained at 24 months after immunization.

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1024. Estimating the Health and Economic Impact of Universal Varicella Vaccination in Jordan
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Background. To evaluate the impact of adding universal varicella vaccination (UVV) to the existing childhood vaccination programme in Jordan, and identify the most cost-effective strategy.

Methods. A dynamic transmission model of varicella infection was calibrated to available varicella seroprevalence data within the region and validated against local epidemiological data. Local direct and indirect costs and healthcare utilization data were used. We considered the health and economic impact of one dose UVV administered concurrently with MMR at 12 months of age with 95% coverage, and two dose strategies with short (6 month) and long (4 year) intervals between First and Second dose. We took the societal perspective (direct and indirect costs) and discounted costs and QALYs by 3%/year to assess cost-effectiveness.

Results. The model estimated the current burden of varicella at 172,000 cases/year, an incidence rate of 2,200/100,000 persons. In the 5th/25th year after vaccination, all strategies substantially reduced total varicella incidence by 89.5%/96.6% (1 dose), 92.3%/98.0% (2 dose short), and 90.5%/98.3% (2 dose long), compared with no vaccine (Figure 1). In the absence of vaccination, an estimated 47.89 M ($28.81 M direct, $19.08 indirect) was spent annually on varicella treatment. The average annual total treatment costs over 25 years from the societal perspective were $4,011 (1 dose), $3,341 (2 dose short), and $3,435 (2 dose long). Considering a willingness to pay (WTP) threshold of $3,600 USD / QALY and the societal perspective, the 1 dose program was the most cost-effective with cost savings of $83.40 USD and health gain of 4.12 x 10^{-1} QALYs per person. 2 dose programs are similarly cost-saving and highly effective compared with a scenario of no vaccination; however, moving incrementally from a 1 dose strategy, incremental cost-effectiveness ratios (ICERS) were $6.9M/QALY (short vs. 1 dose) and $13.5M/QALY (long vs. short), both well as above the WTP threshold. All strategies reached.

Conclusion. One or two dose UVV in Jordan will significantly reduce varicella disease burden and is cost saving relative to no vaccine over 25 years.