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Session: 184. Late Breaker Oral Abstract Session 2
Friday, October 4, 2019: 1:55 PM

Background. Integrase strand transfer inhibitor (INSTI)-based antiretroviral therapy (ART) has been implicated in greater weight gain than other regimens among people with HIV, but there is little evidence about its role in serious clinical outcomes proximal to weight gain. We therefore examined the impact of initial ART regimen class/drug on incident diabetes mellitus (DM) in a large North American HIV cohort.

Methods. Treatment-naive adults (218 years) initiating INSTI-, protease inhibitor (PI)-, or non-nucleoside reverse transcriptase inhibitor (NNRTI)-based ART from January 2007 to December 2016 in the North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD) were included. Individuals were followed until January 2007 to December 2016 in the North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD) were included. Individuals were followed until randomized, multicenter, double-blind, placebo-controlled efficacy trial of a prime-boost regimen or two doses of placebo, with 202 and 199 in the respective arms included in the analysis. We evaluated a recombinant chimpanzee adenovirus 35 vector vaccine prime followed by a recombinant modified vaccinia Ankara boost, both encoding nonstructural proteins of HCV. HCV-uninfected adults 18–45 years old at risk for HCV infection due to injection drug use were randomized to receive the prime-boost regimen or placebo at Days 0 and 56. Treatment participants were monitored for vaccine reactogenicity, adverse events, and HCV viremia. Vaccine safety, immuno- nogenicity, and efficacy against progression to chronic HCV infection were assessed.

Results. A total of 455 subjects received the prime-boost regimen or two doses of placebo, with 202 and 199 in the respective arms included in the analysis. We evaluated a recombinant chimpanzee adenovirus 35 vector vaccine prime followed by a recombinant modified vaccinia Ankara boost, both encoding nonstructural proteins of HCV. HCV-uninfected adults 18–45 years old at risk for HCV infection due to injection drug use were randomized to receive the prime-boost regimen or placebo at Days 0 and 56. Treatment participants were monitored for vaccine reactogenicity, adverse events, and HCV viremia. Vaccine safety, immuno- nogenicity, and efficacy against progression to chronic HCV infection were assessed.

Conclusion. A randomized, placebo-controlled, Phase II/III trial of a prime-boost vaccine to prevent chronic HCV infection was completed in an at-risk population, demonstrating the feasibility of conducting rigorous vaccine research in people who inject drugs. The regimen elicited robust immune responses without evidence safety concerns, but did not provide protection against chronic HCV infection.

Abstracts. OFID 2019:6 (Suppl 2) • S973

Disclosures. Kaseem Bourgi, MD, Gilead Sciences (Grant/Research Support), Joseph J. Eron, MD, Gilead Sciences (Consultant, Grant/Research Support), Janssen (Grant/Research Support), Merck (Consultant), ViV Healthcare (Consultant, Grant/ Research Support), M. John Gill, MB, ChB, MSc, Gilead (Board Member), Merck (Board Member), Viro (Board Member), Michael Silverberg, PhD, MPH, Gilead (Grant/Research Support). Other Authors: No reported disclosures.

LB10. A Randomized, Double-Blind, Placebo-Controlled Efficacy Trial of a Vaccine to Prevent Chronic Hepatitis C Virus Infection in an at-Risk Population
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Session: 184. Late Breaker Oral Abstract Session 2
Friday, October 4, 2019: 2:05 PM

Background. The development of a safe and effective vaccine to prevent chronic hepatitis C virus (HCV) infection is a critical component of elimination efforts, providing the rationale for the first HCV vaccine efficacy trial.

Methods. In a randomized, double-blind, placebo-controlled efficacy trial (NCT01436357), we evaluated a recombinant chimpanzee adenovirus 35 vector vaccine prime followed by a recombinant modified vaccinia Ankara boost, both encoding nonstructural proteins of HCV. HCV-uninfected adults 18–45 years old at risk for HCV infection due to injection drug use were randomized to receive the prime-boost regimen or placebo at Days 0 and 56. Treatment participants were monitored for vaccine reactogenicity, adverse events, and HCV viremia. Vaccine safety, immunogenicity, and efficacy against progression to chronic HCV infection were assessed.

Results. A total of 455 subjects received the prime-boost regimen or two doses of placebo, with 202 and 199 in the respective arms included in the analysis. We evaluated a recombinant chimpanzee adenovirus 35 vector vaccine prime followed by a recombinant modified vaccinia Ankara boost, both encoding nonstructural proteins of HCV. HCV-uninfected adults 18–45 years old at risk for HCV infection due to injection drug use were randomized to receive the prime-boost regimen or placebo at Days 0 and 56. Treatment participants were monitored for vaccine reactogenicity, adverse events, and HCV viremia. Vaccine safety, immuno- nogenicity, and efficacy against progression to chronic HCV infection were assessed.

Conclusion. A randomized, placebo-controlled, Phase II/III trial of a prime-boost vaccine to prevent chronic HCV infection was completed in an at-risk population, demonstrating the feasibility of conducting rigorous vaccine research in people who inject drugs. The regimen elicited robust immune responses without evidence safety concerns, but did not provide protection against chronic HCV infection.

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LB11. A Single Dose of the MVA-BN Smallpox Vaccine Induces an Early Protective Antibody Response Similar to a Traditional Replicating Vaccine and Is Suitable for Emergency Scenarios
Jane Macclennan, BSc MRPharms1; Heinz Weidenthaler, MD2; Phillip Pittman, MD3; Darya Schmidt, PhD4; Paul Chaplin, PhD5;2 Bavarian Nordic, Martinsried, Bayern, Germany;3 USAMRIID, Fort Detrick, Maryland

Session: 184. Late Breaker Oral Abstract Session 2
Friday, October 4, 2019: 2:15 PM

Background. Smallpox remains a high-priority threat due to its potential for re-emergence through events including bioterrorism and spontaneous mutation. While traditional replicating smallpox vaccines such as ACAM2000 are associated with serious side effects, the non-replicating MVA BN smallpox vaccine was developed as a safer alternative.

Methods. This phase 3 non-inferiority study compared indicators of efficacy between the MVA-BN smallpox vaccine and ACAM2000. The co-primary endpoints were (1) to compare vaccine-induced serum neutralizing antibodies (geometric mean titer [GMT]) at pre-defined Peak Visits, as measured by plaque reduction neutralization test (PRNT) and (2) to assess the attenuation of ACAM2000-induced takes following MVA-BN administration by measuring maximum lesion area (MLA). Early neutralizing antibody GMTs at Day 14, a timepoint considered protective for traditional replicating smallpox vaccines, were also compared following single doses of either vaccine.

Results. A total of 440 subjects were evenly randomized to receive either 2 doses of MVA-BN followed by 1 dose of ACAM2000 at 4 week intervals (Group 1) or a single dose
of ACAM2000 (Group 2). Peak neutralizing antibody GMTs were significantly higher following 2 MVA-BN doses (153.5) compared with ACAM2000 (79.3), with a ratio of 1.935 (95% CI: 1.562, 2.397). At Day 14, neutralizing antibody GMTs were equal following a single dose of either MVA BN or ACAM2000 (16.2, ratio of 0.997; 95% CI: 0.738, 1.348), with similar seroconversion rates (90.4% vs. 91.8%, respectively). The median MLA induced by ACAM2000 was significantly reduced when subjects received prior MVA BN in Group 1 (0 mm) compared with Group 2 (76.0 mm²), suggesting protection against orthopoxvi- rus. MVA BN was well tolerated, demonstrating a better safety profile than ACAM2000.

Conclusion. Two doses of MVA BN induce significantly higher peak neutralizing antibody responses compared with ACAM2000. A single dose induces an early neutralizing antibody response equal to ACAM2000 at Day 14, demonstrating the suitability of MVA BN in both pre- and post-outbreak scenarios. This study was partly funded by BARDA under contract HHS0100200700034C.

Disclosures. Samuel Engerix-B®, Engerix-B® in key subgroups. No safety signals were observed; solicited and unsolicited adverse events were consistent across the vaccine groups. There were no differences in any HAI antibody titer outcome between children receiving the two vaccines. Overall, the cohort had HAI titers at levels sufficient to be considered seropositive at baseline. Those unvaccinated in the preceding season had higher seroconversion rates than those vaccinated in both seasons.

Of 1,607 randomized subjects, 42.3% were from United States, 41.6% EU, and 16.1% Canada. Males (38.5%) and females (61.5%) were enrolled to 18–44 (18.6%), 45–64 (44.6%), and ≥65 year (36.8%) age groups. Both co-primary endpoints were met. In the non-inferiority analysis, SPR in Sci-B-Vac™ recipients aged 21 years was 91.4% vs. 76.5% for Engerix-B®; SPR difference: 14.9%; 95% confidence interval (CI) [11.2%, 18.6%]. Superiority analysis showed that SPR in Sci-B-Vac™ recipients aged 21 years was 89.4% vs. 71.1% for Engerix-B®; SPR difference: 18.3% (95% CI [12.2%, 20.7%] (figure). Significantly higher SPR for Sci-B-Vac™ vs. Engerix-B® was noted in subgroups (gender, BMI, diabetes, smoking and particularly age—SPR difference for 45–64 (14.7% [9.8–18.9%]) and 21–65 (18.9% [11.6–26.1%]) years). No major safety signals were observed; solicited and unsolicited adverse events were consistent with the known vaccine safety profiles.

Conclusion. Sci-B-Vac™ met immunogenicity endpoints for non-inferiority in adults aged ≥21 years and (2) superiority in adults aged 45–64 years, compared with the monovalent vaccine, Engerix-B®. Sci-B-Vac™ SPV was higher compared with Engerix-B® in key subgroups. No safety signals were observed and safety and tolerability were consistent with the known profile of Sci-B-Vac™.

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LB14. Cerebrospinal Fluid Profiling of the Human Host Response Reveals Species-Specific Enterovirus Biosignatures in Acute Flaccid Myelitis Cases Francisco Diaz-Mitoma, MD, PhD, Francisco Brigs, MD, PhD, Yale Samuels, BS, PhD, Manfred Grubb, PhD, Asmeeta Achari, MS, BS, Guixia Yu, BS, Steve Miller, MD, PhD, Scot Federman, BA, Shaun Arevelo, BS, Hannah Sample, BS, Kelsey Zorn, MHS, BA, Kathleen Harrigan, PhD, MPH, RN, Samuel Dominguez, MD, PhD, Samuel Dominguez, MD, PhD, Carol Glaser, MD, DVM, Debra Wadford, PhD, Kevin Messacar, MD, Kevin Messacar, MD, Michael Wilson, MD, Charles Chiu, MD, PhD, Charles Chiu, MD, PhD, University of California, San Francisco, San Francisco, California.

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