M. John Gill, MB, ChB, MSc[8]; Mari Kitahata, MD, MPH[9]; Sonia Napravnik, PhD, MPH[7]; Michael Silverberg, PhD, MPH[10]; Angel M. Mayor, MD[11]; Amanda Willig, PhD, RD[12]; Amanda Willig, PhD, RD[12]; Michelle Floris-Moore, MD[7]; Timothy Sterling, MD[1]; John R. Koethe, MD[1]; John R. Koethe, MD[1]; [1]Vanderbilt University Medical Center, Nashville, Tennessee,; [2]University of Texas Health Science Center at Houston, Houston, Texas,; [3]Indiana University School of Medicine, Indianapolis, Indiana,; [4]Kaiser Permanente Mid-Atlantic States, Rockville, Maryland,; [5]Johns Hopkins University, Baltimore, Maryland,; [6]McGill University Health Centre, Montreal, Quebec, Canada,; [7]University of North Carolina at Chapel Hill, Chapel Hill, North Carolina,; [8]University of Calgary, Calgary, Alberta, Canada,; [9]University of Washington, Seattle, Washington,; [10]Kaiser Permanente Northern California, Oakland, California,; [11]Universidad Central del Caribe, Carolina, Not Applicable, Puerto Rico, [12]University of Alabama at Birmingham, Birmingham, Alabama

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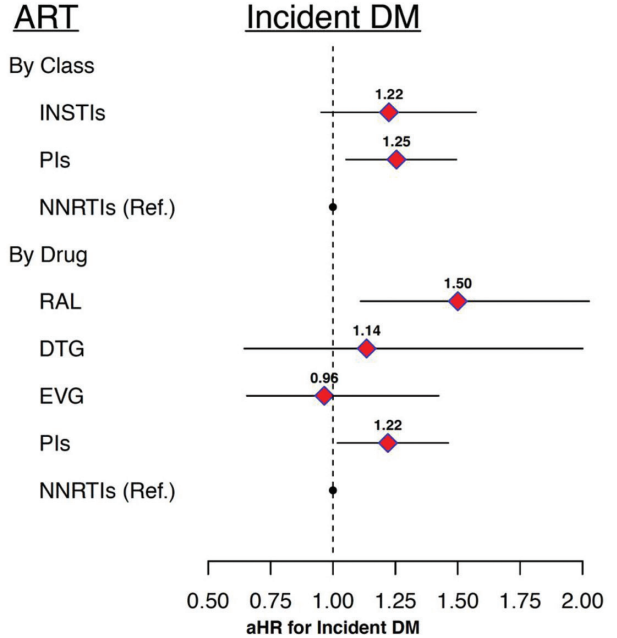
Background. Integrase strand transfer inhibitor (INSTI)-based antiretroviral therapy (ART) has been implicated in greater weight gain than other regimens among people with HIV, but there is little evidence about its role in serious clinical outcomes proximal to weight gain. We therefore examined the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

Methods. Treatment-naïve adults (≥18 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 date of incident DM (HgA1c >6.5%, diabetes-specific medication, DM diagnosis along with diabetes-related medication, or random glucose measure ≥200 mg/dL), virologic failure, regimen core switch, cohort close (through December 2016), death date, or loss to follow-up (≥12 months with no contact before cohort close). Cox regression stratified by site and adjusting for age, sex, race, HIV transmission risk, year of ART initiation, and baseline weight, $CD4^+$ cell count, and HIV-1 RNA yielded adjusted hazard ratios (HR) and 95% confidence intervals (CI) for incident DM by ART class and INSTI drug.

Results. Among 21,516 eligible ART initiators, 10,553 (49%) started NNRTIs, 6,677 (31%) PIs, and 4,286 (20%) INSTIs, with median follow-up of 3.0, 2.4, and 1.6 years, respectively. Among INSTI initiators, 21% started dolutegravir (DTG), 28% raltegravir (RAL), and 51% elvitegravir (EVG). Overall, 669 (3%) developed DM. Patients differed by all characteristics except baseline body mass index and HIV-1 RNA. Those starting INSTIs vs. NNRTIs had increased risk of incident DM (HR = 1.22; CI: 0.95–1.57) similar in magnitude as for PI vs. NNRTI initiators (HR = 1.25; CI: 1.05–1.49) (figure). Among INSTIs, starting RAL- vs. NNRTI-based ART was associated with a 50% increased risk of DM (HR = 1.50, CI: 1.11–2.03).

Conclusion. Initiating ART with INSTI- or PI- vs. NNRTI-based regimens may confer increased risk of incident DM, though risk is heterogeneous among INSTIs. Further research is needed to determine whether this elevated risk can be attributed to weight gain.

Figure. Adjusted hazard ratios (aHR) and 95% confidence intervals for the association between antiretroviral therapy (ART) regimen classes and drugs and incident diabetes mellitus (DM).



- INSTI: integrase strand transfer inhibitor; PI: protease inhibitor; NNRTI: non-nucleoside reverse transcriptase inhibitor; RAL: raltegravir; DTG: dolutegravir; EVG: elvitegravir
- Continuous covariates were modeled using restricted cubic splines with 5 knots to relax linearity assumptions, missing data were multiply imputed, and Cox models were stratified by site.

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LB10. A Randomized, Double-Blind, Placebo-Controlled Efficacy Trial of a Vaccine to Prevent Chronic Hepatitis C Virus Infection in an at-Risk Population

Andrea L. Cox, MD, PhD[1]; Kimberly Page, PhD[2]; Michael Melia, MD[1]; Rebecca Veenhuis, PhD[1]; Guido Massaccesi, BS[1]; William Osburn, PhD[1]; Katherine Wagner, MPH[3]; Linda Giudice, MD, PhD[4]; Ellen Stein, MPH[4]; Alice K. Asher, PhD[4]; Ventzislav Vassilev, PhD[5]; Lan Lin, MD[5]; Alfredo Nicosia, PhD[6]; Stefania Capone, BS[6]; Elisa Scarselli, PhD[6]; Antonella Folgori, PhD[6]; Richard Gorman, MD[7]; Soju Chang, MD[7]; Peter Wolff, MHA[7]; T. Jake Liang, MD[8]; Marc Ghany, MD[8]; Michael Wierzbicki, PhD[9]; Paula Lum, MD, MPH[4]; [1]Johns Hopkins University, Baltimore, Maryland,; [2]University of New Mexico, Albuquerque, New Mexico,; [3]The University of New Mexico, Albuquerque, New Mexico,; [4]The University of California, San Francisco, San Francicso, California,; [5]GlaxoSmithKline Vaccines, Wavre, Brussels Hoofdstedelijk Gewest, Belgium,; [6]ReiThera, srl, Rome, Piemonte, Italy,; [7]The National Institute of Allergy and Infectious Diseases, Rockville, Maryland,; [8]The National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, Maryland,; [9]The Emmes Company, Rockville, Maryland

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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, multicenter, double-blind, placebo-controlled efficacy trial (NCT01436357), we evaluated a recombinant chimpanzee adenovirus 3 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. Trial 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 groups included in the according-to-protocol efficacy cohort. Overall incidence of infection was 14.1 infections per 100 person-years. There were no differences in development of chronic infection between vaccine and placebo arms, with 14 chronically infected subjects in each group. Specifically, the vaccine efficacy in preventing chronic infection was −0.53 (95% confidence interval [CI], −2.5 to 0.34). Of vaccinated subjects, 78% generated T-cell responses to ≥1 vaccine-encoded HCV antigens. The vaccine was generally safe and well tolerated with no serious vaccine-related adverse events. There were more solicited reports of adverse events after either injection in the vaccine group (81%) than in the placebo group (59%), with the difference mainly due to injection-site reactions. Serious adverse events and deaths occurred with similar frequencies in the two groups.

Conclusion. A randomized, placebo controlled, Phase I/II 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 evident safety concerns, but did not provide protection against chronic HCV infection.

Disclosures. Ventzislav Vassilev, PhD, GlaxoSmithKlein Vaccines (Employee), Lan Lin, MD, GlaxoSmithKlein Vaccines (Employee), Alfredo Nicosia, PhD, ReiThera (Employee, Shareholder), Antonella Folgori, PhD, ReiThera (Employee), ReiThera (Employee, Shareholder. **Other Authors:** No reported disclosures.

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 Maclennan, BSc MRPharmS[1]; Heinz Weidenthaler, MD[1]; Phillip Pittman, MD[2]; Darja Schmidt, PhD[1]; Paul Chaplin, PhD[1]; [1]Bavarian Nordic, Martinsried, Bayern, Germany,; [2]USAMRIID, Fort Detrick, Maryland

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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 predefined Peak Visits, as measured by plaque reduction neutralization tests (PRNT) and (2) to assess the attenuation of ACAM2000-induced takes after 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