Tebipenem has *in vitro* activity against select multidrug-resistant Gram-negative pathogens, including fluoroquinolone-resistant and extended-spectrum ß-lactamase (ESBL)-producing Enterobacterales. TBP-PI-HBr is being developed in the United States as the first oral carbapenem for treatment of cUTI and AP.

Methods. ADAPT-PO was a global, double-blind, Phase 3 study to evaluate the efficacy and safety of oral TBP-PI-HBr vs. IV ertapenem in hospitalized adult patients with cUTI or AP. The primary endpoint was overall response (composite clinical cure and microbiologic eradication) at the test-of-cure (TOC) visit (Day 19 ± 2) in the micro-ITT population. Patients (N=1372) were randomized 1:1 to receive TBP-PI-HBr 600 mg PO q8h plus placebo IV q24h or ertapenem 1 g IV q24h plus oral placebo q8h for 7–10 days (or up to 14 days in patients with bacteremia).

Results. Oral TBP-PI-HBr met the primary objective of non-inferiority compared with IV ertapenem with an overall response rate of 58.8% (264/449) vs. 61.6% (258/419), respectively (treatment difference -3.3%; 95% CI: -9.7, 3.2; -12.5% NI margin). Clinical cure rates at TOC were > 93% in both treatment groups. Microbiological response rates for target uropathogens were comparable across treatment groups.

TBP-PI-HBr was well tolerated. Treatment-emergent adverse events (TEAEs) were observed in 25.7% TBP-PI-HBr and 25.6% ertapenem patients. Most TEAEs were mild; premature discontinuation of study drug was uncommon (< 1%). The most frequent TEAEs were diarrhea (5.0%) and headache (3.8%). No *C. difficile*-associated TEAEs were observed in the TBP-PI-HBr group; 3 cases occurred in the ertapenem group. Serious adverse events were infrequent (1.3% vs. 1.7%), with no deaths.

Conclusion. Results from this pivotal Phase 3 study provide the first head-to-head demonstration of non-inferiority of an oral (TBP-PI-HBr) antibacterial agent to an IV (ertapenem) agent in patients with cUTI and AP, with a comparable tolerability profile. If approved in the U.S., TBP-PI-HBr would provide a new oral therapeutic option — and the first oral carbapenem — for patients with serious Gram-negative infections.

Disclosures. **Lori A. Muir, n/a**, **Spero Therapeutics** (Employee)**Spero Therapeutics** (Employee, Shareholder) **Susannah M. Walpole, PhD**, **Spero Therapeutics, Inc.** (Employee) **Hanna Kwak, n/a**, **Spero Therapeutics** (Employee) **Anne-Marie Phelan, n/a**, **Spero Therapeutics** (Employee)**Spero Therapeutics** (Employee, Shareholder) **Gary E. Moore, BS/MS**, **Spero Therapeutics** (Consultant) **Akash Jain, PhD**, **Spero Therapeutics** (Employee) **Tim Keutzer, BA**, **Spero Therapeutics, Inc** (Employee) **Aaron Dane, MSc**, **Da Volterra** (Consultant)**Spero theraputics** (Consultant) **Aaron Dane, MSc**, **Spero theraputics** (Consultant) **David Melnick, MD**, **Spero Therapeutics** (Employee)**Spero Therapeutics** (Employee) **Angela K. Talley, MD**, **Spero Therapeutics** (Employee, Shareholder)

LB-4. Cefepime-Enmetazobactam Demonstrates Superiority to Piperacillin-Tazobactam in a Subgroup of Patients with Complicated Urinary Tract Infections/Acute Pyelonephritis Caused by Extended Spectrum β-Lactamase-Producing Enterobacterales

Adam Belley, PHD[1]; Philip Barth, MD[2]; Shikhar Kashyap, n/a[2]; Omar Lahlou, PhD[2]; Paola Motta, PhD[2]; Philipp Knechtle, PhD[3]; Patrick Velicitat, MD[2]; [1]Allecra Therapeutics, Beaconsfield, QC, Canada; [2]Allecra Therapeutics SAS, St. Louis, Alsace, France; [3]discoveric bio beta Ltd, Pfaeffikon, Zurich, Switzerland

Session: LB1. Late Breaking Abstracts
Saturday, October 24, 2020: 10:20 AM

Background. There is a critical need for carbapenem-sparing therapies for infections caused by extended spectrum β-lactamase (ESBL)-producing *Enterobacterales*. Enmetazobactam is a novel ESBL inhibitor combined with the cephalosporin cefepime. Treatment outcomes of cefepime-enmetazobactam (FPE) versus piperacillin-tazobactam (PTZ) were assessed in subgroups of patients with ESBL-producing baseline uropathogens (ESBL-BU) in the ALLIUM phase 3 trial of complicated urinary tract infections (cUTI)/acute pyelonephritis (AP).

Methods. 1034 cUTI/AP patients randomized 1:1 in a double-blind, multicenter trial received either 2 g cefepime/0.5 g enmetazobactam or 4 g piperacillin/0.5 g tazobactam q8h by 2h infusion for 7 to 14 days. *Enterobacterales* with MICs ≥1 µg/ml to ceftazidime, ceftriaxone, cefepime, meropenem, or FPE were genotyped for β-lactamases. In addition to the primary analysis (by stratified Newcombe) of overall success (combination of clinical cure and microbiological eradication) in the microbiological modified intent to treat population (mMITT) at test-of-cure (TOC), subgroup analyses were performed on patients with ESBL-BU non-resistant to FPE (MIC≤8 µg/ml) and PTZ (MIC≤64 µg/ml) and a subgroup (mMITT+R) that also included the ESBL-BU resistant to either agent (FPE MIC ≥16 µg/ml or PTZ MIC≥128 µg/ml).

Results. In mMITT, FPE (273/345, 79.1%) demonstrated superiority to PTZ (196/333, 58.9%) at TOC (difference, 21.2%; 95% CI: 14.3, 27.9). The prevalence rate of ESBL-BU was 20.9% (142/678), with 99.3% (141/142) expressing a CTX-M-type (-1, -3, -9, -14, -15, -27, -55, -91, -169) and 3.5% (5/142) co-expressing AmpC (CMY-2/-59). FPE (56/76, 73.7%) demonstrated superiority to PTZ (34/66, 51.5%) in this subgroup at TOC (difference 30.2%; 95% CI: 13.4, 45.1; Table). In mMITT+R, the ESBL-BU prevalence rate was 22.3% (172/771), with 6.4% (11/172) co-expressing AmpC (CMY-2/-4/-59/-99), 4.7% (8/172) co-expressing a metallo-β-lactamase (VIM-1, NDM-1), and 2.3% (4/172) co-expressing OXA-48. Superiority of FPE (67/91, 73.6%) compared to PTZ (41/81, 50.6%) was also observed at TOC despite inclusion of ESBL-BU resistant to either agent (difference 30.0%; 95% CI: 14.9, 43.3).

Table

Treatment arm/β-lactamase genotype[1]	Overall response[2]					
	Success		Failure		Indeterminate	
	N	%	N	%	N	%
mMITT, ESBL-producing subgroup (N=142)						
Cefepime-enmetazobactam (N=76)	56	73.7	16	21.1	4	5.3
ESBL	54	-	15	-	3	-
ESBL+AmpC	2	-	1	-	1	-
Piperacillin-tazobactam (N=66)	34	51.5	31	47.0	1	1.5
ESBL	33	-	31	-	1	-
ESBL+AmpC	1	-	0	-	0	-
Treatment difference[3]: 30.2% (95% CI: 13.4, 45.1)						
mMITT+R[4], ESBL-producing subgroup (N=172)						
Cefepime-enmetazobactam (N=91)	67	73.6	20	22.0	4	4.4
ESBL	61	-	18	-	3	-
ESBL+AmpC	3	-	1	-	1	-
ESBL+AmpC+MBL	1	-	1	-	0	-
ESBL+MBL	1	-	0	-	0	-
ESBL+OXA	1	-	0	-	0	-
Piperacillin-tazobactam (N=81)	41	50.6	35	43.2	5	6.2
ESBL	37	-	33	-	3	-
ESBL+AmpC	1	-	0	-	0	-
ESBL+AmpC+MBL	1	-	0	-	0	-
ESBL+MBL	1	-	2	-	1	-
ESBL+OXA	1	-	0	-	1	-
Treatment difference: 30.0% (95% CI: 14.9, 43.3)						

[1]ESBL genotypes could also co-express SHV or TEM original-spectrum β-lactamases.
[2]Success is defined as clinical cure or improvement and microbiological eradication.
[3]Treatment differences in overall success rate between the two treatment arms were calculated and the 95% CI (2-sided) was computed based on the stratified Newcombe method.
[4]mMITT+R includes patients within the mMITT population with baseline pathogens also resistant to either cefepime-enmetazobactam (≥16 µg/ml) or piperacillin-tazobactam (≥128 µg/ml).

Conclusion. FPE may represent a new empiric carbapenem-sparing option in settings where ESBL are endemic.

Disclosures. **Adam Belley, PHD**, **Allecra Therapeutics SAS** (Consultant) **Philip Barth, MD**, **Allecra Therapeutics SAS** (Consultant) **Shikhar Kashyap, n/a**, **Allecra Therapeutics SAS** (Consultant)**Allecra Therapeutics SAS** (Consultant) **Omar Lahlou, PhD**, **Allecra Therapeutics SAS** (Employee) **Paola Motta, PhD**, **Allecra Therapeutics SAS** (Employee) **Patrick Velicitat, MD**, **Allecra Therapeutics SAS** (Employee)

LB-5. DAV132 Protects Intestinal Microbiota of Patients Treated with Quinolones, a European Phase II Randomized Controlled Trial (SHIELD)

Annie Ducher, MD[1]; Maria J.G.T. Vehreschild, n/a[2]; Maria J.G.T. Vehreschild, n/a[2]; Thomas J. Louie, MD[3]; Oliver A. Cornely, MD[4]; Céline Féger, PhD[1]; Aaron Dane, MSc[5]; Aaron Dane, MSc[5]; Marina Varastet, PhD[1]; Jean de Gunzburg, PhD[1]; Antoine Andremont, PhD[6]; France Mentré, MD[7]; [1]Da Volterra, Paris, France, Paris, Ile-de-France, France; [2]University of Cologne, Faculty of Medicine and University Hospital of Cologne, Cologne, Niedersachsen, Germany; [3]Cumming School of Medicine, University of Calgary, Calgary, Canada, Calgary, Alberta, Canada; [4]University of Cologne, Faculty of Medicine, Department I of Internal Medicine; Cologne Excellence Cluster on Cellular Stress Responses in Aging-Associated Diseases (CECAD); Clinical Trials Centre Cologne (ZKS Köln), Cologne, Germany, Cologne, Nordrhein-Westfalen, Germany; [5]DaneStat Consulting, Macclesfield, Cheshire, England, United Kingdom; [6]Da Volterra, Paris, France & 6. Paris University, IAME, INSERM U1137, Paris, France, Paris, Ile-de-France, France; [7]Paris University, IAME, INSERM U1137, Paris, France, Paris, Ile-de-France, France

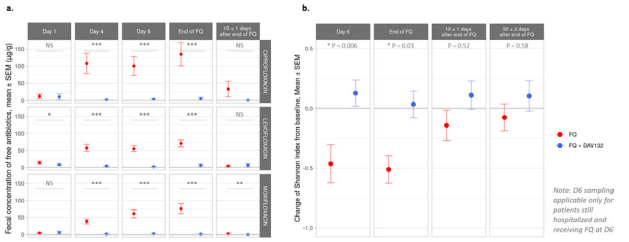
Session: LB1. Late Breaking Abstracts
Saturday, October 24, 2020: 10:30 AM

Background. Antibiotics elicit intestinal dysbiosis with short and long-term deleterious effects. A colon-targeted adsorbent, DAV132, prevents dysbiosis in healthy humans and may protect antibiotic-treated patients.

Methods. Hospitalized patients receiving oral/iv fluoroquinolones (FQ) for the treatment of or prophylaxis of febrile neutropenia were randomized to receive DAV132 (7.5g tid orally), or not, during FQ receipt and followed up 51d. Plasma FQ levels were assessed at D4 (LC-MS/MS). Feces were collected during and up to 30d after FQ receipt for assessment of free fecal FQ levels (LC-MS/MS), gut microbiome α/β diversity (16S rRNA), resistance to colonization by *C. difficile* (Cd; *ex-vivo* proliferation). Relatedness of adverse events (AEs) to drugs was adjudicated by blinded independent experts.

Results. 243 patients from 23 sites, median age 71y, ≥1 chronic comorbidity 95%, received levofloxacin (43%), ciprofloxacin (40%) or moxifloxacin (18%) for (79% iv). During receipt, fecal FQ levels were lowered by >97% with DAV132 vs. No DAV132 (p< 0.0001), whilst plasma levels did not change significantly. Microbiome diversity was significantly protected with DAV132 using all metrics, e.g. the change from D1 of Shannon index at End-of-FQ (difference of means at End-of-FQ 0.42, 95% CI: 0.085; 0.752). The proportions of patients with DAV132- and/or FQ-related AEs (primary endpoint) did not differ significantly (14.8 vs. 10.8%, difference of proportions: 3.9%; 95% CI: -4.7; 12.6). No Cd infection occurred. Resistance to colonization by Cd was reduced in stools of patients receiving FQ only, but was maintained in those of patients who also received DAV132 (p=0.035). The acquisition of fecal carriage of vancomycin-resistant *enterococci* (VRE) was reduced with DAV132 (p=0.019).

Figure 1: a. Free fluoroquinolones fecal concentration (mean ± SEM, µg/g) over time per FQ treatment group; b. Change of Shannon Index from baseline (mean ± SEM) over time



Conclusion. DAV132 was well tolerated in elderly hospitalized patients with comorbidities. It neither altered antibiotic plasma levels nor elicited changes in concomitant drugs regimens. Intestinal microbiota diversity was protected and resistance to colonization by Cd was preserved. DAV132 is a promising, novel product to prevent antibiotic-induced intestinal dysbiosis.

Disclosures. **Annie Ducher, MD**, **Da Volterra** (Employee, Shareholder) **Maria J.G.T. Vehreschild, n/a**, **3M** (Grant/Research Support)**Astellas Pharma** (Grant/Research Support)**Astellas Pharma** (Consultant)**Astellas Pharma** (Speaker's Bureau)**Basilea** (Speaker's Bureau)**Berlin Chemie** (Consultant)**Da Volterra** (Grant/Research Support)**Da Volterra** (Grant/Research Support)**Gilead** (Grant/Research Support)**Gilead** (Speaker's Bureau)**Merck/MSD** (Speaker's Bureau)**Merck/MSD** (Grant/Research Support)**MSD/Merck** (Consultant)**Organobalance** (Grant/Research Support)**Organobalance** (Speaker's Bureau)**Pfizer** (Speaker's Bureau)**Seres Therapeutics** (Grant/Research Support) **Thomas J. Louie, MD**, **Da Volterra** (Consultant) **Oliver A. Cornely, MD**, **Actelion** (Consultant, Grant/Research Support, Speaker's Bureau)**Al Jazeera Pharmaceuticals** (Consultant)**Allecra Therapeutics** (Consultant, Grant/Research Support, Speaker's Bureau)**Amplyx** (Consultant, Grant/Research Support, Speaker's Bureau)**Astellas** (Consultant, Grant/Research Support, Speaker's Bureau)**Basilea** (Consultant, Grant/Research Support, Speaker's Bureau)**Biosys UK Limited** (Consultant, Grant/Research Support, Speaker's Bureau)**Cidara** (Consultant, Grant/Research Support, Speaker's Bureau)**Da Volterra** (Consultant, Grant/Research Support, Speaker's Bureau)**Entasis** (Consultant, Grant/Research Support, Speaker's Bureau)**European Commission** (Grant/Research Support)**F2G** (Consultant, Grant/Research Support, Speaker's Bureau)**German Federal Ministry of Research andEducation** (Grant/Research Support)**Gilead** (Consultant, Grant/Research Support, Speaker's Bureau)**Grupo Biotoscana** (Consultant, Grant/Research Support, Speaker's Bureau)**Janssen Pharmaceuticals** (Consultant, Grant/Research Support, Speaker's Bureau)**Matinas** (Consultant, Grant/Research Support, Speaker's Bureau)**MedicinesCompany** (Consultant, Grant/Research Support, Speaker's Bureau)**MedPace** (Consultant, Grant/Research Support, Speaker's Bureau)**Melinta Therapeutics** (Consultant, Grant/Research Support, Speaker's Bureau)**Menarini Ricerche** (Consultant, Grant/Research Support, Speaker's Bureau)**Merck/MSD** (Consultant, Grant/Research Support, Speaker's Bureau)**Mylan Pharmaceuticals** (Consultant)**Nabriva** (Consultant)**Noxxon** (Consultant)**Octapharma** (Consultant, Grant/Research Support, Speaker's Bureau)**Paratek Pharmaceuticals** (Consultant, Grant/Research Support, Speaker's Bureau)**Pfizer** (Consultant, Grant/Research Support, Speaker's Bureau)**PSI** (Consultant, Grant/Research Support, Speaker's Bureau)**Roche Diagnostics** (Consultant)**Scynexis** (Consultant, Grant/Research Support, Speaker's Bureau)**Shionogi** (Consultant) **Céline Féger, PhD**, **Da Volterra** (Consultant) **Aaron Dane, MSc**, **Da Volterra** (Consultant)**Spero theraputics** (Consultant) **Aaron Dane, MSc**, **Spero theraputics** (Consultant) **Marina Varastet, PhD**, **Da Volterra** (Employee) **Jean de Gunzburg, PhD**, **Da Volterra** (Board Member, Consultant, Shareholder) **Antoine Andremont, PhD**, **Bioaster** (Consultant)**Da Volterra** (Board Member, Consultant, Shareholder) **France Mentré, MD**, **Da Volterra** (Consultant)

LB-6. Increased Diagnoses of Acute HIV Infection through Routine ED Screening and Rapid Linkage to Care and initiation of HAART During the COVID-19 Pandemic

Kimberly Stanford, MD[1]; Jessica Schmitt, LCSW[2]; Michelle M. Taylor, LCSW[3]; Dylan Eller, MPH[1]; Eleanor Friedman, PhD[2]; Moira McNulty, MD, MS[1]; Jessica Ridway, MD, MS[1]; Aniruddha Hazra, MD[1]; Moore Michelle, RN, APN[1]; Kathleen Beavis, MD[1]; [1]University of Chicago, Chicago, Illinois; [2]University of Chicago Medicine, Chicago, IL; [3]UCM, Chicago, Illinois

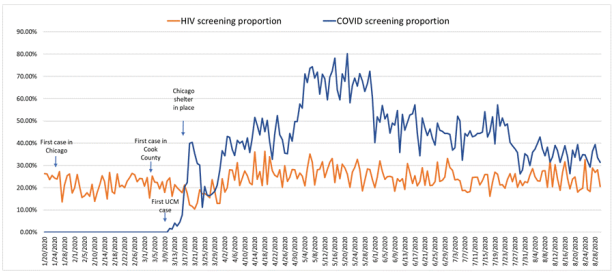
Session: LB1. Late Breaking Abstracts
Saturday, October 24, 2020: 10:40 AM

Background. The COVID-19 pandemic has negatively impacted routine HIV screening in healthcare settings. This has serious implications, especially for patients with acute HIV infection (AHI) presenting with symptoms suggesting COVID-19 infection. This is a high priority population for rapid linkage to care (LTC) and initiation of HAART.

Methods. We reviewed data from our eXpanded HIV Testing and LTC (X-TLC) Program, a collaboration effort between 13 healthcare centers on the South and West Sides of Chicago. Since 2016, most sites had 4th or 5th generation HIV Ag/Ab testing available.

Results. Most sites experienced reductions in HIV screens during the COVID-19 pandemic. Advanced planning by our ED incorporated blood draws for HIV screens as part of COVID-19 evaluations. UCM performed 19,111 HIV screens (11,133 in the ED) between 1/1/20 and 8/17/20, along with 100,635 COVID PCRs (14,754 in ED) between 3/17/20 and 8/17/20. Nine patients were diagnosed with AHI after the first case of COVID-19 in Chicago (1/24/20), and 7 were diagnosed after the first case of community transmission in Cook County (3/8/20). All cases of AHI were diagnosed in the ED. The rate of AHI was significantly higher in 2020 versus the prior 4 years (14.4 vs 6.8 per year, $p < 0.05$). AHI patients comprised 25.7 % (9/35) of all new diagnoses, the highest percent ever. There were 7 men (6 identified as MSM) and 2 cis-gender women, median age of 25 years (21 to 28 years). The median viral load was 6 million (115,000 to > 6 million) copies/mL. Eight of 9 patients presented with an illness indistinguishable from COVID-19, including 1co-infected patient. All were LTC and started on HAART from time of PCR result within a median of 1 day (0–38), but 3 days (range 1–41) from sample collection as a result of delayed reflex PCR confirmatory testing due to high demands on lab personnel and scarcity of reagents due to COVID-19 PCR volumes (since resolved).

HIV Screening and COVID-19 Testing in the ED During COVID-19



Conclusion. Continued HIV screening in our ED during the COVID-19 pandemic identified an increased number of patients with AHI. These individuals may be more likely to present for care due to fear of COVID-19 infection. We achieved rapid LTC and initiation of HAART without any incremental increases in resources. All HIV screening programs should incorporate blood-based HIV screening into their COVID-19 testing programs.

Disclosures. **Moira McNulty, MD, MS**, **Gilead Sciences** (Grant/Research Support)

LB-7. Weight Change in Suppressed People with HIV (PWH) Switched from Either Tenofovir Disoproxil Fumarate (TDF) or Abacavir (ABC) to Tenofovir Alafenamide (TAF)

Paul Sax, MD[1]; Keri N. Althoff, PhD, MPH[2]; Keri N. Althoff, PhD, MPH[2]; Todd T. Brown, MD, PhD[3]; Janna Radtchenko, MBA[4]; Helena Diaz Cuervo, PhD[5]; Helena Diaz Cuervo, PhD[5]; Moti Ramgopal, MD FIDSA[6]; Steven Santiago, MD[7]; Graeme Moyle, MD[8]; Karam Mounzer, MD[9]; Richard Elion, MD[10]; [1]Brigham and Women's Hospital, Harvard Medical School, Boston, MA; [2]Johns Hopkins University, Baltimore, Maryland; [3]Johns Hopkins, Baltimore, Maryland; [4]Trio Health, Louisville, Colorado; [5]Gilead Sciences, Madrid, Madrid, Spain; [6]Midway Specialty Care Centers, Fort Pierce, Florida; [7]CareResource, Miami, Florida; [8]Chelsea & Westminster Hospital, London, England, United Kingdom; [9]Philadelphia FIGHT, Philadelphia, PA; [10]George Washington University School of Medicine, Washington, DC

Session: LB1. Late Breaking Abstracts
Saturday, October 24, 2020: 10:50 AM

Background. Weight gain in PWH occurred in both naïve and switch studies and is linked to use of integrase inhibitors (INSTIs) with varying associations with nucleoside reverse transcriptase inhibitors (NRTIs). One hypothesis is that gain associated with TAF when switching from TDF is a result of cessation of TDF-induced weight suppression.

Methods. The study evaluated weight change in suppressed PWH on INSTI+NRTIs switched from ABC or TDF to TAF. Eligible pts had HIV, were ≥ 18 yrs at index (date of switch), treatment-experienced with known prior regimen, suppressed at index (-12 to +1 mo) and 1 yr, ≥ 6 mo pre-index history, with weight measures at index and 1 yr, no current or pre-index use of protease inhibitor or non-nucleoside reverse transcriptase inhibitor. Univariate comparisons were performed using X^2 for categorical and t-test for continuous variables; negative binomial model with log link function evaluated risk of gain ≥ 3% of body weight between groups accounting for age, gender, race, body mass index (BMI), CD4. Linear mixed effects model was used to estimate mean weight at index and 1 yr post switch.

Results. Of 970 pts, 828 (85%) switched from TDF to TAF and 142 (15%) from ABC to TAF. Groups were balanced by race, gender, index BMI [Table 1]. Figures 1a-b describe pre- and post-switch INSTI use. At 1 yr, mean unadjusted weight change was 1.4 kg in TDF and 0.2 in ABC group p=0.039. TDF to TAF had higher proportion of PWH with gain ≥ 3% vs ABC to TAF (40% vs 27% p=0.003); differences in gain ≥ 5% and ≥ 10% were not statistically significant (26% vs 22% p=0.323 and 10% vs 6% p=0.220). Pts who gained ≥ 3% were younger, with greater proportion of females, non-obese, with 1 prior regimen, and prior elvitegravir (EVG) use. In adjusted analysis TDF to TAF had higher risk of gain ≥ 3% vs ABC to TAF [Figure 2]. In sensitivity analysis accounting for EVG or dolutegravir (DTG) use, TDF to TAF also had higher risk of ≥ 3% gain vs ABC to TAF: adjusted risk ratio (aRR)= 1.38 [1.01–1.89] and aRR= 1.42 [1.02–1.97].