Figure 1: Structure of the Full-length Single Chain (FLSC) Vaccine.
The fusion of HIV-1 to CD4+ cells results in post-binding intermediates that involves gp120 and the CD4 receptor. The FLSC chimeric protein vaccine is a single-chain polypeptide molecule that replicates the structural, functional, and antigenic properties of this gp120-CD4 complex intermediate. Fouts TR, et al. J. Virol 2000; 74(24):11427-36.

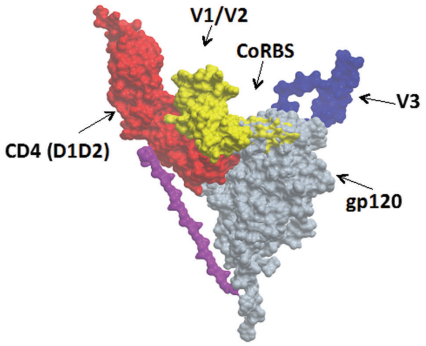
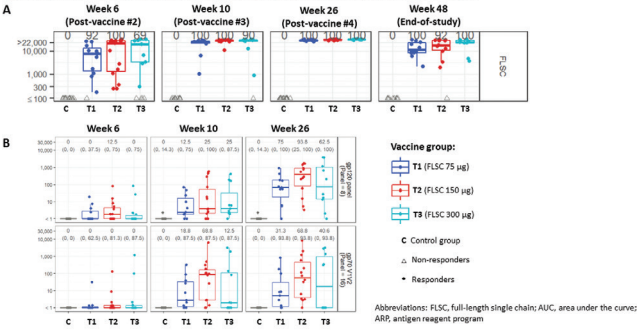


Figure 2: Immunogenicity Results
A. Binding IgG antibody response magnitude for FLSC antigen and time points, colored by group, showing durability of antibody response. B. Magnitude-breath AUC of the gp120 and gp70 V1V2.AFR breath panel by group and time points. The response rate (%) for each group and antigen is displayed.



Binding Antibody Multiplex Array (BAMA) data provided by G. Tomaras et al, Duke Human Vaccine Institute.
Statistical analyses provided by E. Chung et al, Statistical Center for HIV/AIDS Research and Prevention (SCHARP), Fred Hutchison Cancer Research Center

Disclosures. **All Authors:** No reported Disclosures.

2839. Efficacy, Pharmacokinetics (PK), and Safety Profile of Suvratoxumab (MEDI4893), a Staphylococcus aureus Alpha Toxin (AT)-Neutralizing Human Monoclonal Antibody in Mechanically Ventilated Patients in Intensive Care Units; Results of the Phase 2 SAATELLITE Study Conducted by the Public-Private COMBACTE Consortium

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Background. *Staphylococcus aureus* (SA) pneumonia imposes significant morbidity and mortality in mechanically ventilated, intensive care unit (MV ICU) patients despite best clinical care. We assessed efficacy, PK, AT-neutralizing antibodies (AT NAbs), and safety of suvratoxumab (suvra) in MV ICU subjects in the placebo-controlled, randomized Phase 2 SAATELLITE study (NCT02296320; EudraCT 2014-001097-34).

Methods. Subjects with PCR-confirmed SA colonization of the lower respiratory tract were randomized to either a single intravenous infusion of 5,000 mg suvra (n = 96) or placebo (n = 100) and followed for 190 days post dose. Efficacy endpoints were Endpoint Adjudication Committee-determined relative risk reduction (RRR) of SA pneumonia incidence in suvra vs. placebo recipients within 30 days post dose (primary endpoint, tested at 2-sided $\alpha = 0.1$), incidence of all-cause pneumonia, and all-cause pneumonia or death. Serum suvra PK and levels of AT NAbs were measured through 90 days post dose and analyzed for statistical correlation. Treatment-emergent adverse events (TEAEs) and serious AEs (SAEs) were assessed through 190 days post dose.

Results. Baseline characteristics were similar between groups. Suvra provided 31.9% RRR in incidence of SA pneumonia vs. placebo (17.7% vs. 26%; $P = 0.166$), 30% RRR ($P = 0.146$) in incidence of all-cause pneumonia, and 23% RRR ($P = 0.164$) in incidence of all-cause pneumonia or death. Suvra reduced mean hospital stay and ICU duration by 3.0 and 2.4 days, resp. vs. placebo. Mean serum ± SD suvra level was 296 ± 131 µg/mL at 30 days post dose. Serum AT Nab ± SD levels reached 156.03 ± 72.48 IU/mL at 2 days post dose, declining slowly to 33.74 ± 16.04 IU/mL by 90 days post dose. AT NAbs correlated with PK ($r^2 = 0.7$), thereby confirming functional activity of suvra over time. Proportion of subjects with TEAEs or SAEs was similar between groups: ≥1 TEAE (93.8% suvra; 93.0% placebo); ≥1 serious; and/or ≥grade 3 severity SAE (66.7% suvra; 58.0% placebo).

Conclusion. A single intravenous dose of suvra produced a trend toward reduced incidence of SA pneumonia, health resource savings, sustained functional exposure in serum, and an acceptable safety profile. These results support continued development of suvra in MV ICU patients.

Disclosures. **All Authors:** No reported Disclosures.

2840. Long-term Efficacy, Safety, and Durability of CAB and RPV as Two Drug Oral Maintenance Therapy: LATTE Week 312 Results

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Background. Cabotegravir (CAB), an INI, is under development in both oral and long-acting (LA) injectable formulations. LATTE (NCT01641809) was designed to select a daily oral dose of CAB and evaluate a two-drug ART regimen with rilpivirine (RPV), as suppressive maintenance therapy. Results enabled the LATTE-2 (NCT02120352) study to evaluate CAB LA + RPV LA dosed once every 1 or 2 months.

Methods. Phase 2b, multicentre, partially blinded dose-ranging study in ART-naïve HIV infected adults, randomized 1:1:1:1 to the induction regimen of once-daily oral CAB 10, 30, or 60 mg or efavirenz (EFV) 600 mg with TDF/FTC or ABC/3TC through W24. CAB patients with VL <50 c/mL immediately prior to W24 discontinued NRTIs and began RPV 25 mg as a two-drug oral maintenance regimen through W96. No change was made to the EFV arm. After W96, at the start of the open-label (OL) phase, all patients randomized to CAB were given the option to continue and switch to the sponsor-selected dose of oral CAB 30 mg. EFV patients completed the study at W96. The OL phase was completed at W312 (288 weeks on CAB + RPV). Successful CAB + RPV patients transitioned to the POLAR study (NCT03639311).

Results. A total of 243 patients were randomized and initiated treatment (ITT-E). Of those randomized to CAB (n = 181), 160 patients began CAB + RPV (W24) and 138 continued into OL phase (W96). One hundred and ten patients successfully completed the study (W312). Among patients who began CAB + RPV at W24, 66% maintained <50 c/mL, 9% had HIV-1 RNA ≥ 50 c/mL, and 25% were categorized as "No Virologic Data" by Snapshot at W312 (ITT-ME). There were 11 protocol-defined virologic failures (PDVF) on CAB; only 2 occurring after W144. Six patients developed treatment emergent (TE) resistance to one or both agents during the study; of which 4 patients developed TE major INI resistance mutations, 3 after W96. The median increase in CD4+ cell count from Baseline was 393 cells/mm^3 (−174 to 1118). During the maintenance and OL phases, 4% of CAB patients reported drug-related AEs ≥ Grade 2; SAEs occurred in 9% of CAB patients (none drug related); 3% of CAB patients withdrew due to AEs. 43% of CAB patients who entered maintenance phase reported TE lab abnormalities ≥ Grade 3.

Conclusion. As maintenance therapy in virologically suppressed patients, the 2DR CAB + RPV provided durable viral suppression through W312. Through 7 years of study, CAB + RPV continues to be generally safe and well tolerated.

Study Outcomes at Week 312

Week 312 Outcomes (ITT-ME Population)	CAB 10 mg N=52 n (%)	CAB 30 mg N=53 n (%)	CAB 60 mg N=55 n (%)	CAB Subtotal N=160 n (%)
Virologic Success (HIV-1 RNA < 50 c/mL)	**31 (60)**	**31 (58)**	**43 (78)**	**105 (66)**
Virologic Failure (HIV-1 RNA ≥ 50 c/mL)	**7 (13)**	**5 (9)**	**3 (5)**	**15 (9)**
Data in window not below threshold	0	1 (2)	0	1 (<1)
Discontinued for lack of efficacy	3 (6)	1 (2)	0	4 (3)
Discontinued for other reason while not below threshold	4 (8)	1 (2)	3 (5)	8 (5)
Prior change in ART	0	2 (4)	0	2 (1)
No Virologic Data	**14 (27)**	**17 (32)**	**9 (16)**	**40 (25)**
Discontinued due to AE or Death	4 (8)	2 (4)	2 (4)	8 (5)
Discontinued for Other Reasons	10 (19)	14 (26)	7 (13)	31 (19)
Missing data during window but on study	0	1 (2)	0	1 (<1)
Protocol Defined Virologic Failure (ITT-E Population)	**CAB 10 mg N=60 n (%)**	**CAB 30 mg N=60 n (%)**	**CAB 60 mg N=61 n (%)**	**CAB Subtotal N=181 n (%)**
PDVF	6 (10)	3 (5)	2 (3)	11 (6)

Adverse Events Through Week 312

Maintenance Safety Population	CAB 10 mg N=52 n (%)	CAB 30 mg N=53 n (%)	CAB 60 mg N=55 n (%)	CAB Subtotal N=160 n (%)
Grade 2-4 Drug Related Events (>3% in any arm)	**1 (2)**	**3 (6)**	**3 (5)**	**7 (4)**
Depression	**0**	**0**	**2 (4)**	**2 (1)**
Serious AEs	**5 (10)**	**5 (9)**	**5 (9)**	**15 (9)**
AEs Leading to Withdrawal	**1 (2)**	**2 (4)**	**1 (2)**	**4 (3)**
Electrocardiogram abnormal	1 (2)	0	0	1 (<1)
Acute hepatitis C	0	1 (2)	0	1 (<1)
Burkitt's lymphoma	0)	1 (2)	0	1 (<1)
Anxiety disorder	0	0	1 (2)	1 (<1)
Treatment Emergent Laboratory Abnormalities (Grade 3-4)	**24 (46)**	**16 (30)**	**29 (53)**	**69 (43)**
Alanine Aminotransferase (ALT)	1 (2)	2 (4)	0	3 (2)
Creatine Kinase (CK)	9 (17)	8 (15)	9 (16)	26 (16)
Lipase	7 (13)	1 (2)	8 (15)	16 (10)
Total Neutrophils	2 (4)	1 (2)	4 (7)	7 (4)

Disclosures. **All Authors:** No reported Disclosures.

2841. A Phase 3, Randomized, Double-Blind Study Comparing Tedizolid Phosphate (TZD) and Linezolid (LZD) for Treatment of Ventilated Gram-Positive (G+) Nosocomial Pneumonia

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Background. Hospital-acquired pneumonia (HAP) and ventilator-associated pneumonia (VAP) are frequently caused by G+ cocci; TZD has potent *in vitro* activity against these pathogens, including methicillin-resistant *Staphylococcus aureus* (MRSA). The VITAL study compared the efficacy and safety of TZD vs. LZD for the treatment of ventilated patients with G+ HAP/VAP.

Methods. Randomized, double-blind, double-dummy, global, phase 3 study in mechanically ventilated adult patients with presumed G+ HAP/VAP (clinicaltrials.gov NCT02019420). Patients were stratified by region, age, and trauma/nontrauma, then randomized 1:1 to intravenous (IV) TZD 200 mg once daily for 7 days or IV LZD 600 mg every 12 h for 10 d (patients with concurrent G+ bacteremia received 14 d of treatment). The primary efficacy endpoint was day 28 all-cause mortality (ACM) in the intent to treat (ITT) population (all randomized patients; noninferiority [NI] margin, 10%). Secondary endpoints included investigator-assessed clinical response at test of cure (TOC; NI margin, 12.5%).

Results. In total, 726 patients were randomized (TZD n = 366; LZD n = 360). Baseline characteristics were well balanced between arms. TZD was noninferior to LZD for day 28 ACM in the ITT (table). Noninferiority was not demonstrated for TZD vs. LZD for investigator-assessed clinical success at TOC in the ITT. Stratification factors, analysis population, baseline clinical/laboratory signs of HAP/VAP, G+ only vs. mixed G+/gram-negative (G–) HAP/VAP, adjunctive G– therapy, MRSA vs. methicillin-susceptible *S. aureus*, and HAP vs. VAP were evaluated, and no single factor accounted for the observed imbalance in clinical response between treatment arms. Greater than 90% of patients experienced treatment-emergent adverse events (TEAEs). Anemia, hypokalemia, and diarrhea were the most frequently reported (TEAEs) in both arms. Types and incidence rates of TEAEs overall, and of drug-related TEAEs specifically, were comparable between TZD and LZD.

Conclusion. TZD was noninferior to LZD for day 28 ACM in the treatment of ventilated G+ HAP/VAP. However, TZD was not noninferior to LZD based on the investigator-assessed clinical response at TOC. Both drugs were similarly well tolerated and TEAEs were well balanced between groups, with no new safety signals identified.

Table. Efficacy outcomes

Outcome	Analysis Set	TZD	LZD	Difference, % (95% CI)[a]
Day 28 ACM, n (%)	ITT[b], n	366	360	
		103 (28.1)	95 (26.4)	−1.8 (−8.2, 4.7)
Clinical cure at TOC, n (%)	ITT, n	366	360	
		206 (56.3)	230 (63.9)	−7.6 (−14.7, −0.5)
	CE, n	267	243	
		143 (53.6)	146 (60.1)	−6.5 (−15.1, 2.1)

ACM, all-cause mortality; CE, clinically evaluable; CI, confidence interval; ITT, intent-to-treat; LZD, linezolid; TOC, test of cure; TZD, tedizolid phosphate.

[a]The differences (TZD minus LZD) in the clinical success rates and 95% CIs were calculated using the method of Miettinen and Nurminen without stratification.

[b]Primary efficacy outcome.

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2842. Durable Efficacy of Two-Drug Regimen (2DR) of Dolutegravir (DTG) plus Lamivudine (3TC) in Antiretroviral Treatment-Naïve Adults with HIV-1 Infection at 96 Weeks: Subgroup Analyses in the GEMINI Studies

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Background. At Weeks 48 and 96 in the GEMINI-1 and GEMINI-2 studies (Clinicaltrials.gov: NCT02831673 and NCT02831764), the 2DR of DTG+3TC was noninferior to the three-drug regimen of DTG + tenofovir/emtricitabine (TDF/FTC) in achieving plasma HIV-1 RNA < 50 c/mL in treatment-naïve adults.

Methods. GEMINI-1 and 2 are identical, global, double-blind, multicenter Phase III studies. Participants with screening HIV-1 RNA ≤ 500.00 c/mL were randomized to once-daily DTG+3TC or DTG+TDF/FTC, stratified by plasma HIV-1 RNA and CD4+ cell count. The primary endpoint was the proportion of participants with plasma HIV-1 RNA < 50 c/mL at Week 48 (Snapshot algorithm). We present a secondary endpoint analysis of efficacy at Week 96 by baseline disease and demographic characteristics. For the overall population, estimates and confidence intervals were based on a stratified analysis using Cochran–Mantel–Haenszel weights.

Results. In total, 714 and 719 adults were randomized and treated in GEMINI-1 and -2, respectively. Based on a 10% noninferiority margin, DTG+3TC was noninferior to DTG+TDF/FTC at Week 96 in both GEMINI-1 and -2 and in the pooled analysis. Response rates across baseline HIV-1 RNA subgroups were high and similar in both arms in the pooled analysis, including in participants with baseline HIV-1 RNA >100,000 c/mL (Table 1). Results were also generally consistent regardless of age, gender, or race. In the CD4+ ≤ 200 cells/mm^3 subgroup, response rates were lower in the DTG+3TC group compared with DTG+TDF/FTC; most reasons for nonresponse were unrelated to virologic efficacy or treatment regimen. Across both studies, 11 participants on DTG+3TC and 7 on DTG+TDF/FTC met protocol-defined virologic withdrawal criteria through Week 96; none had treatment emergent integrase-strand-transfer-inhibitor or NRTI resistance mutations.

Conclusion. In GEMINI-1 and 2, DTG+3TC was noninferior to DTG+TDF/FTC in treatment-naïve adults at Week 96, demonstrating durable efficacy. The results of subgroup analyses of efficacy at Week 96 were generally consistent with overall study results, and further demonstrate that DTG+3TC is an effective initial treatment for HIV-infected patients across a spectrum of disease characteristics and patient populations. The studies are ongoing.

Table 1. Proportion of participants with plasma HIV-1 RNA < 50 c/mL at Week 96: Snapshot Analysis by subgroups – ITT-E population

		POOLED GEMINI-1&2	
		DTG+3TC n/N (%)	DTG+TDF/FTC n/N (%)
Overall Population		616/716 (86)	642/717 (90)
Adjusted difference (95% CI)		-3.4 (-6.7, 0.0)	
Age (years)	< 35	361/420 (86)	369/408 (90)
	35 - < 50	200/231 (87)	203/229 (89)
	≥ 50	55/65 (85)	70/80 (88)
Gender	Female	93/113 (82)	85/ 98 (87)
	Male	523/603 (87)	557/619 (90)
Race	White	426/480 (89)	451/497 (91)
	African Heritage	71/97 (73)	64/76 (84)
	Asian	59/71 (83)	65/72 (90)
	Other	60/68 (88)	62/72 (86)
Baseline HIV-1 RNA (c/mL)	≤ 100,000	499/576 (87)	510/564 (90)
	> 100,000	117/140 (84)	132/153 (86)
Baseline CD4+ (cells/mm^3)	≤ 200	43/63 (68)	48/55 (87)
	> 200	573/653 (88)	594/662 (90)

Disclosures. **All Authors:** No reported Disclosures.