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

Richard G. Wunderink, MD[1]; Antoine Roquilly, MD, PhD[2]; Martin Croce, MD[3]; Daniel Rodriguez Gonzalez, MD[4]; Satoshi Fujimi, MD, PhD[5]; Joan R. Butterton, MD[6]; Natasha Broyde, MS[6]; Myra W. Popejoy, PharmD[6]; Jason Y. Kim, MD, MSCE[6] and Carisa S. De Anda, PharmD[6]; [1]Northwestern University Feinberg School of Medicine, Northwestern Memorial Hospital, Chicago, Illinois; [2]CHU Nantes, Nantes, Lorraine, France; [3]Regional One Health, Memphis, Tennessee; [4]Nuevo Hospital Civil de Guadalajara, Guadalajara, Jalisco, Mexico; [5]Osaka General Medical Center, Sumiyoshi-ku, Osaka, Japan; [6]Merck & Co., Inc., Kenilworth, New Jersey

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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

Jean A. van Wyk, MB,ChB[1]; Choy Y. Man, BSc[1]; Jörg Sievers, DPhil[1]; Rimgaile Urbaityte, MSc[2]; Mark Underwood, PhD[1]; Allan R. Tenorio, MD[1]; Keith Pappa, PharmD[1]; Brian Wynne, MD[1]; Kimberly Smith, MD[1] and Martin Gartland, PhD[1]; [1]ViiV Healthcare, Brentford, England, UK; [2]GlaxoSmithKline, Uxbridge, UK

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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.