Table1

	Overall	Non-Massive Weight Gain	Massive Weight Gain*	Bivariate OR (95% CI)	Bivariate p-value	Multivariate OR (95% CI)	Multivariate p-value
	266	213	53				
Age (median, IQR)	36 (29 – 45)	37 (30 -44)	35 (28 – 46)	1.0 (0.7 – 1.3)	0.95		
Female (n,%)	25 (9%)	17 (8%)	8 (15%)	2.0 (0.8 – 5.0)	0.12	1.7 (0.6 – 4.8)	0.35
Black (n,%)	38 (14%)	31 (15%)	7 (13%)	0.9 (0.3 – 2.2)	0.70		
Hispanic (n,%)	114 (43%)	92 (43%)	22 (42%)	0.9 (0.5 – 1.8)	0.76		
White (n,%)	106 (40%)	84 (39%)	22 (42%)	-	-		
Baseline CD4 (cells/ul) (median, IQR)	288 (157 – 435)	319 (199 – 441)	88 (31 – 284)	0.6** (0.5 – 0.8)	<0.0001	0.8** (0.6 – 0.9)	0.01
Baseline HIV Viral Load (cps/ml) (median, IQR)	63369 (23952 – 154283)	52864 (19008 – 108764)	168000 (88128 – 494432)	3.9**(2.2 –6.7)	<0.0001	3.9**(2.2 – 6.7)	0.002
Weight at baseline (lbs) (median, IQR)	163 (142-182)	167 (147-185)	145 (132-161)				
% Weight Gain at 2 years (median, IQR)	4.0 (-1.1 – 11.6)	2.0 (-1.9 – 6.5)	20.6 (16.7 – 33.6)				
Baseline BMI (kg/m²) (median, IQR)	23.7 (21.4 – 27.0)	23.9 (22.0 – 27.6)	22.6 (20.7 – 25.0)	0.9 (0.8 – 1.0)	0.007	0.9 (0.9 – 1.0)	0.19
Regimen							
INSTI (n,%)	94 (35%)	78 (37%)	16 (30%)	0.4 (0.2 – 1.0)	0.26	0.7 (0.3 – 1.9)	0.97
NNRTI (n,%)	112 (42%)	94 (44%)	18 (34%)	0.4 (0.2 – 0.9)	0.14	0.6 (0.2 – 1.3)	0.23
PI (n,%)	60 (23%)	41 (19%)	19 (36%)	-	-		
NRTI							
ABC (n,%)	27 (10%)	21 (10%)	6 (11%)	1.2 (0.4 – 3.1)	0.80		
TAF (n,%)	43 (16%)	34 (16%)	9 (17%)	1.1 (0.5 – 2.5)	0.98		
TDF (n,%)	196 (74%)	158 (74%)	38 (72%)	-	-		

* Massive weight gain defined as the top 20% of weight gainers at two years measured by percent gain compared to baseline; **OR reported per 100 cells/ul CD4 count increase and 1 log viral load increase. IQR, interquartile range; lbs, pounds; BMI, body mass index; INSTI, integrase strand transfer inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; ABC, abacavir; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate, OR, odds ratio

Conclusion. In this real-world dataset, drug class or specific NRTI use was not associated with massive weight gain which was primarily dependent on baseline CD4 count and HIV viral load. There was a moderate correlation between early weight gain and massive weight gain at 2 years which can help with patient counseling and interventions aimed at slowing weight gain in this population.

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

73. Interim Resistance Analysis of Long-Acting Lenacapavir in Treatment-Naïve People with HIV at 28 Weeks

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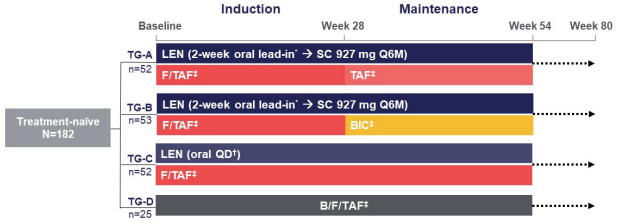
Session: O-16. HIV Treatment

Background. Lenacapavir (LEN) is a first-in-class HIV-1 capsid (CA) inhibitor in clinical development for treatment and prevention of HIV-1 infection. CALIBRATE is an ongoing, phase 2 clinical study evaluating subcutaneous (SC) or oral LEN, in combination with other antiretrovirals, in treatment-naïve people with HIV-1. High rates of virologic success (HIV-1 RNA < 50 copies/mL) were achieved with LEN-based regimens by FDA Snapshot analysis at Week 28. Here, we present interim resistance analyses through Week 28.

Methods. Participants were randomized (2:2:2:1) to treatment groups (TG) (Figure): SC LEN + oral daily emtricitabine/tenofovir alafenamide (F/TAF); at Week 28, participants switch F/TAF to oral TAF (TG-A) or bictegravir (B, BIC) (TG-B); oral daily LEN + F/TAF (TG-C), or oral daily B/F/TAF (TG-D). Genotypic analyses (population sequencing) of HIV-1 reverse transcriptase and integrase, and genotypic (deep sequencing)/phenotypic analyses for CA were performed at screening; genotypic and phenotypic analyses were conducted at confirmed virologic failure.

Figure. CALIBRATE Study Design



*LEN 2-week oral lead-In: oral 600 mg on Day 1 and 2, 300 mg on Day 8 (followed by SC LEN 927 mg on Day 15)

†Oral 600 mg on Day 1 and 2, followed by 50 mg QD

‡F/TAF, TAF, BIC, B/F/TAF are administered as oral QD

Results. 182 participants were randomized and dosed in TG-A to D (n=52, 53, 52, 25). Most participants had subtype B HIV-1 (92.9%). Sequence analysis of baseline samples found 65% of amino acid residues were conserved with < 1% variation across CA overall, and 55% of residues were fully conserved. No mutations were detected at 6 positions in CA associated with reduced susceptibility to LEN in vitro; residues were fully conserved at 5 positions (L56, M66, Q67, K70, N74), and < 2% variation was observed at 1 position (T107). Three participants met the criteria for resistance analysis: 2 participants resuppressed to < 50 copies/mL while continuing treatment. One participant on SC LEN + F/TAF developed emergent resistance to LEN (Q67H+K70R) and emtricitabine (M184M/I), followed by resuppression after starting dolutegravir, zidovudine + lamivudine, tenofovir disoproxil fumarate.

Conclusion. Emergent resistance to LEN was uncommon in treatment-naïve participants receiving SC or oral LEN (0.6%, 1/157). These interim resistance findings support the ongoing evaluation of LEN for treatment and prevention of HIV.

Disclosures. **Laurie VanderVeen, PhD**, **Gilead Sciences** (Employee, Shareholder) **Nicolas Margot, MA**, **Gilead Sciences** (Employee, Shareholder) **Vidula Naik, MSc**, **Gilead Sciences** (Employee, Shareholder) **Silvia Chang, Masters**, **Gilead Sciences, Inc** (Employee, Shareholder) **Ross Martin, PhD**, **Gilead Sciences, Inc** (Employee, Shareholder) **Hadas Dvory-Sobol, PhD**, **Gilead Sciences** (Employee, Shareholder) **Martin Rhee, MD**, **Gilead Sciences** (Employee, Shareholder) **Christian Callebaut, PhD**, **Gilead Sciences** (Employee, Shareholder)

74. Maternal Dolutegravir (DTG) Use During Pregnancy and Birth Outcomes: The Antiretroviral Pregnancy Registry (APR)

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Session: O-16. HIV Treatment

Background. The APR is prospective exposure-registration cohort study, monitoring for early warning signals of major teratogenic effects of antiretrovirals (ARV) used during pregnancy. This analysis aimed to assess maternal demographics, pregnancy and neonatal outcomes including birth defects among infants with periconception and prenatal exposure to DTG using APR data.

Methods. Descriptive analysis with frequency tabulation of pregnancy and neonatal outcomes is reported. Periconception is defined as any exposure within two weeks prior to or through 28 days after conception.

Results. There were 1010 prospectively reported pregnancies with exposure to DTG through 31January2021, with 526 periconception exposures, 105 exposed later during 1st trimester, 260 during 2nd trimester and 119 during 3rd trimester. Maternal median age at conception was 30 years and 77.0% of pregnancies were reported from the United States. At the time of reporting, 46.6% had CD4 count ≥500 cells/μL, 31.8% had 200-499 cells/μL, 12.5% had < 200 cells/μL and 9.1% unknown.

The 1010 DTG exposed pregnancies resulted in 1036 outcomes: 956 (92.3%) live births (26 twin pairs), 12 (1.2%) stillbirths, 28 (2.7%) induced abortions, and 38 (3.7%) spontaneous abortions. Among live births, 39 (4.1%) reported birth defects. For 1st trimester exposures, overall defect prevalence was 3.3% (19/576, 95% CI:2.0-5.1) and for 2nd/3rd trimester exposures defect prevalence was 5.3% (20/380, 95% CI:3.2-8.0). One neural tube defect (NTD) case of anencephaly with periconception DTG exposure was reported.

Among the 873 singleton, live births without birth defects, 92 (10.5%) were preterm (< 37 weeks of gestation); 103 (11.8%) had low birth weight (lbw) < 2500 grams including 22 (2.5%) < 1500 (very lbw) grams.

Table 1. Birth Defect Outcomes of Pregnant Women Exposed to DTG Prospective Registry Cases with Follow-up Closed through 31 January 2021

	Total Outcomes N	Live Births	Defect* Cases	CNS Defect (1,2)	NTD Cases (1)	Encephalocele (2)
Any InSTI Exposure [3]	2435	2243	77	7	1	0
Periconception	1402	1244	38	4	1	0
Later First Trimester	206	195	5	1	0	0
Second/Third Trimester	821	800	34	2	0	0
Any Dolutegravir Exposure [3]	1036	956	39	5	1	0
Periconception	539	475	16	2	1	0
Later First Trimester	107	101	3	1	0	0
Second/Third Trimester	390	380	20	2	0	0

Note: ART = antiretroviral therapy; CNS = central nervous system; NTD = neural tube defect.
Note: Periconception is defined as any exposure 2 weeks prior to conception through 28 days gestational age; Later First Trimester is defined as any exposure in the first trimester that begins after 28 days gestational age.
[1] NTD cases are a subset of CNS defects and are counted in both columns.
[2] Encephalocele cases are a subset of CNS defects and are counted in both columns.
[3] Includes cases with missing trimester of exposure.
* Comparators for population expected rate of defects (2.72 - 4.17/ 100 live births from MACDP and TBDR respectively).
MACDP =Metropolitan Atlanta Congenital Defects Program; TBDR=Texas Birth Defects Registry

Table 2. Neonatal Outcomes (among Singleton, Live Births without Birth Defects) Prospective Registry Cases with Follow-up Closed through 31 January 2021

Neonatal Outcomes	Overall DTG Exposed	Earliest exposure to DTG - Periconception	Earliest exposure to DTG - Later 1st Trimester	Earliest exposure to DTG - 2nd/3rd Trimester
Total Outcomes, N	873	436	94	343
Gestational Age*				
>= 37 weeks	778 (89.1%)	387 (88.8%)	80 (85.1%)	311 (90.7%)
< 37 weeks (Preterm)	92 (10.5%)	48 (11.0%)	14 (14.9%)	30(8.7%)
Missing	3 (0.3%)	1 (0.2%)	0	2 (0.6%)
Birth Weight*				
>= 2500 grams	750 (85.9%)	368 (84.4%)	83 (88.3%)	299 (87.2%)
< 2500 grams (LBW)	103 (11.8%)	55 (12.6%)	11 (11.7%)	37 (10.8%)
< 1500 grams (very LBW)	22 (2.5%)	14 (3.2%)	3 (3.2%)	5 (1.5%)
Missing	20 (2.3%)	13 (3.0%)	0	7 (2.0%)

DTG = Dolutegravir; LBW = Low Birth Weight.
*Among singleton, live births without birth defects.
Note: Periconception is defined as any exposure 2 weeks prior to conception through 28 days gestational age; Later First Trimester is defined as any exposure in the first trimester that begins after 28 days gestational age; Second Trimester begins at 14 weeks gestational age and Third Trimester begins at 28 weeks gestational age.

Conclusion. APR data do not demonstrate an increased risk of overall birth defects with DTG use above the population expected rate of defects (2.72 to 4.17 per 100 live births from Metropolitan Atlanta Congenital Defects Program [MACDP] and Texas Birth Defects Registry [TBDR] respectively). The number of periconception exposure outcomes is not yet sufficient to evaluate potential association of DTG with NTD. The Registry continues to closely monitor birth defects, including NTDs in pregnancies exposed to DTG and other integrase inhibitors.

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