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1581. Weight and Metabolic Changes with Long-Acting Lenacapavir in a Combination Regimen in Treatment-Naïve People with HIV-1 at Week 80
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Background. Lenacapavir (LEN) is a highly potent, long-acting, first-in-class inhibitor of HIV-1 capsid protein approved for the treatment of HIV-1 infection in adults with multidrug resistance in combination with other antiretrovirals. CALIBRATE is an ongoing phase 2 study in people with HIV-1 (PWH) who are newly initiating treatment. At Week 80 (W80), subcutaneous (SC) and oral LEN, in combination with other antiretrovirals, maintained high rates of virologic suppression. In PWH initiating treatment, weight increases associated with a return to health effect have been observed. This analysis examined weight and metabolic changes to the W80 timepoint.

Methods. Participants were randomized (2:2:2:1) to 1 of 4 treatment groups (TG). TG1 and TG2 both received SC LEN (927 mg) every 6 months + oral once daily (QD) emtricitabine/tenofovir alafenamide (F/TAF) for 28 weeks, after which virologically suppressed participants continued a 2-drug maintenance regimen: SC LEN (927 mg) with oral QD TAF (TG1) or oral QD bictegravir (BIC) (TG2). TG3 received oral QD LEN + F/TAF, and TG4 received oral QD BIC/F/TAF throughout. The metabolic profile of LEN was assessed from baseline to W28 and after initiating the 2-drug maintenance regimen to W80. Due to the small sample size, no statistical testing was performed.

Results. 182 participants (7% female, 52% Black) were randomized and dosed (n=52, 53, 52, 25 in TG1 to TG4, respectively). Baseline median age was 29 years; 15% had baseline viral load >100,000 c/mL. Baseline median weight and body mass index (BMI) were 78.2 kg and 25.8 kg/m², respectively. Weight, BMI, and fasting lipid profiles for each treatment group through W80 are presented (Table).

Table. Weight, BMI and fasting lipids at baseline through to W80*

Endpoint	Week	TG1 SC LEN + F/TAF n=52		TG2 SC LEN + BIC n=53		TG3 Oral LEN + F/TAF n=52		TG4 BIC/F/TAF n=25	
		Mean	n	Mean	n	Mean	n	Mean	n
Weight (kg)	Baseline	82.4	52	80.5	53	80.4	52	88.1	25
	W8	85.3	49	83.2	51	84.1	50	89.8	25
	W24	85.9	49	84.3	47	85.0	48	91.7	23
	W80	86.7	48	84.8	42	85.2	46	92.5	24
BMI (kg/m ²)	Baseline	27.3	52	26.2	53	26.8	52	27.1	25
	W8	28.3	49	27.1	51	27.8	50	27.7	25
	W24	28.6	49	27.4	47	28.1	48	28.0	23
	W80	28.8	48	27.5	42	28.2	46	28.7	24
Total cholesterol (mg/dL)	Baseline	164	28	157	23	170	22	165	9
LDL cholesterol (mg/dL)	Baseline	102	28	91	23	105	22	100	9
W80	100	28	101	20	109	24	97	18	
Triglycerides (mg/dL)	Baseline	108	28	113	23	117	22	102	9
W80	109	28	137	20	120	24	101	18	
HDL cholesterol (mg/dL)	Baseline	41	28	42	23	41	22	45	9
W80	46	28	44	20	46	24	51	18	
Total cholesterol to HDL ratio	Baseline	4.1	28	4.1	23	4.4	22	3.8	9
W80	4.0	28	4.2	20	4.3	24	3.6	18	
Fasting lipid abnormalities from baseline through to W80 - Grade 3 or 4									
		n	n	n	n	n	n	n	n
Total cholesterol		2	1	2	1	0	0	0	0
LDL cholesterol		2	1	2	1	4	3	0	0
Triglycerides		0	0	8	4	0	0	4	1

*Only values obtained at a fasting state were analyzed. BIC, bictegravir; BMI, body mass index; F, emtricitabine; LEN, lenacapavir; SC, subcutaneous; TG, treatment group; W, week

Conclusion. In this phase 2 study of treatment-naïve PWH, treatment regimens that included SC or oral LEN in combination with other antiretroviral agents led to expected weight gain and increase in BMI, consistent with the return to health phenomenon, and were not associated with clinically relevant increases in lipids.

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