SWITCHING TO DTG/3TC IS NON-INFERIOR TO CONTINUING CURRENT ANTIRETROVIRAL REGIMEN AT WEEK 48: SALSA SUBGROUP ANALYSES

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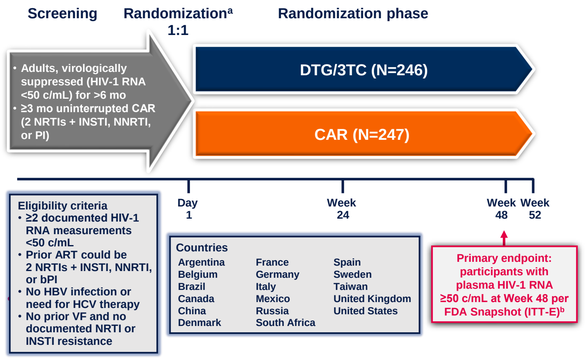
Introduction

- Investigations into the use of 2-drug regimens (2DRs) have been ongoing as a means for reducing the number of antiretroviral agents taken by individuals with HIV-1 who need lifelong ART[1]
- Durable, non-inferior efficacy of the 2DR DTG/3TC has been observed in phase 3 clinical trials in treatment-naive individuals (compared with DTG + TDF/FTC in the GEMINI-1 and -2 studies for 3 years)[2-4] and treatment-experienced individuals (compared with continuing TAF-based regimens in the TANGO study for 3 years and any current antiretroviral regimen [CAR] in the SALSA study for 1 year)[5-7]
- Evidence from the GEMINI, TANGO, and SALSA studies also supports the good safety and tolerability of DTG/3TC for up to 3 years[4,6,7]
- Analyses from the GEMINI and TANGO studies have demonstrated non-inferior efficacy and similar rates of AEs across demographic and baseline characteristics subgroups, consistent with findings from the overall population[8,9]
- Here, we report efficacy and safety in the SALSA study by demographic characteristics, baseline third agent class, and disease characteristics at Week 48

Methods

- SALSA is a phase 3, randomized, controlled, open-label study of participants with HIV-1 RNA <50 c/mL for >6 months on a stable 3- or 4-drug regimen for ≥3 months, without prior virologic failure or NRTI or DTG resistance-associated mutations (Figure 1)

Figure 1. Study Design



[a]Stratified by baseline third agent class (PI, INSTI, or NNRTI). [b]5% non-inferiority margin.

- The primary endpoint was the proportion of participants with plasma HIV-1 RNA ≥50 c/mL at Week 48 (Snapshot algorithm, intention-to-treat–exposed [ITT-E] population, 5% non-inferiority margin)

Results

Participants

- 493 participants were randomized to switch to DTG/3TC FDC (n=246) or continue CAR (n=247)
- Demographics and baseline characteristics were similar between treatment groups (Table 1)
  - The most commonly used third agents at screening were EFV (31%) and DTG (17%)

Table 1. Demographics and Baseline Characteristics: ITT-E Population

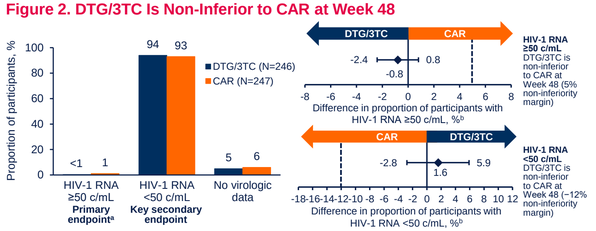
Parameter	DTG/3TC (N=246)	CAR (N=247)
Age		
Median (range), y	45 (22-74)	45 (23-83)
Age ≥50 y, n (%)	98 (40)	95 (38)
Female, n (%)	108 (44)	84 (34)
Race, n (%)		
White	149 (61)	144 (58)
African American/African heritage	45 (18)	48 (19)
Asian	31 (13)	39 (16)
Other	21 (9)	16 (6)
CD4+ cell count, median (range), cells/mm^3	675 (154-2089)	668 (94-1954)
CD4+ cell count, cells/mm^3, n (%)		
<500	60 (24)	63 (26)
≥500	185 (75)	184 (74)
Duration of ART before Day 1, median (range), mo	63 (4-240)	71 (12-253)
Baseline third agent class, n (%)		
NNRTI	123 (50)	124 (50)
INSTI	98 (40)	98 (40)
PI	25 (10)	25 (10)
NRTIs received at screening in >30% of participants		
FTC	149 (61)	156 (63)
TDF[a]	109 (44)	109 (44)
3TC	96 (39)	89 (36)
TAF	83 (34)	91 (37)
Historical genotypic resistance results available at screening, n (%)	100 (41)	99 (40)
Weight, median (range), kg	73 (43-154)	75 (36-160)
BMI, median (range), kg/m^2	25 (18-51)	26 (14-69)

[a]Includes tenofovir disoproxil succinate (DTG/3TC, n=1; CAR, n=3).

Virologic Outcomes

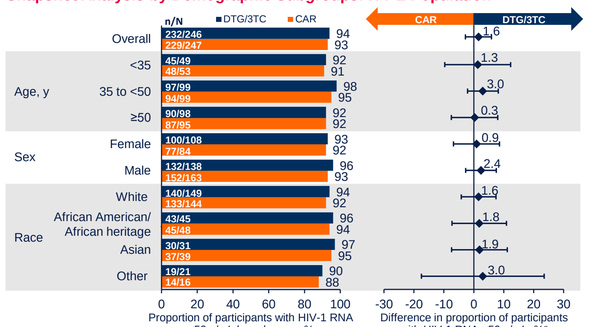
- DTG/3TC was non-inferior to continuing CAR at Week 48 using Snapshot virologic failure (DTG/3TC, 0.4%; CAR, 1.2%; adjusted treatment difference, −0.8%; 95% CI, −2.4% to 0.8%)
- DTG/3TC was non-inferior to continuing CAR at Week 48 using Snapshot virologic response (DTG/3TC, 94.3%; CAR, 92.7%; adjusted treatment difference, 1.6%; 95% CI, −2.8% to 5.9%; Figure 2)
- No confirmed virologic withdrawals or observed resistance occurred in either group
- Snapshot virologic response rates between treatment groups were generally consistent with the overall analysis across demographic subgroups (Figure 3) and across baseline regimen third agent class and disease characteristics subgroups (Figure 4)

Figure 2. DTG/3TC Is Non-Inferior to CAR at Week 48



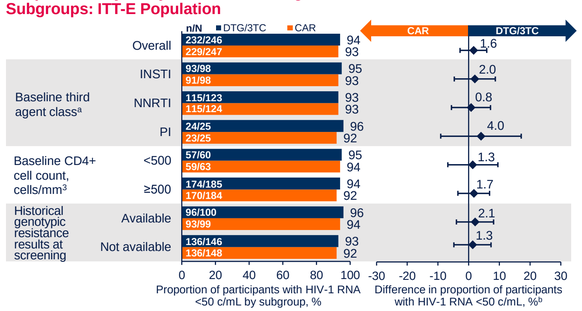
[a]Primary endpoint (Snapshot virologic non-response, ITT-E). [b]Based on Cochran-Mantel-Haenszel stratified analysis (DTG/3TC − CAR) adjusting for baseline third agent class.

Figure 3. Proportion of Participants With HIV-1 RNA <50 c/mL at Week 48: Snapshot Analysis by Demographic Subgroups: ITT-E Population



[a]Adjusted difference (95% CI) for overall population (DTG/3TC − CAR) based on Cochran-Mantel-Haenszel stratified analysis adjusting for baseline third agent class; unadjusted difference for subgroups calculated by proportion on DTG/3TC − proportion on CAR.

Figure 4. Proportion of Participants With HIV-1 RNA <50 c/mL at Week 48: Snapshot Analysis by Baseline Third Agent Class and Disease Characteristics Subgroups: ITT-E Population



[a]Study population was stratified by baseline third agent class (PI, INSTI, or NNRTI). [b]Adjusted difference (95% CI) for overall population (DTG/3TC − CAR) based on Cochran-Mantel-Haenszel stratified analysis adjusting for baseline third agent class; unadjusted difference for subgroups calculated by proportion on DTG/3TC − proportion on CAR.

Safety

- Overall incidence of any AEs was comparable between the DTG/3TC and CAR groups through Week 48 (Table 2)
  - Frequency of drug-related AEs was higher in the DTG/3TC group compared with the CAR group through Week 48, with more comparable rates observed post–Week 24
  - Few drug-related AEs leading to study withdrawal were observed in both treatment groups

Table 2. Summary of AEs Through Week 48: Safety Population

	Day 1 to Week 48		Week 24 to Week 48	
Parameter, n (%)	DTG/3TC (N=246)	CAR (N=247)	DTG/3TC (N=236)	CAR (N=242)
Any AE	180 (73)	172 (70)	110 (47)	100 (41)
Drug-related AEs[a]	48 (20)	16 (6)	11 (5)	4 (2)
AEs leading to study withdrawal	5 (2)	3 (1)	1 (<1)	2 (<1)
Drug-related AEs leading to study withdrawal	4 (2)	1 (<1)	0	1 (<1)
Any SAE	7 (3)	16 (6)	3 (1)	7 (3)
Drug-related SAEs	0	0	0	0

[a]Drug-related AEs occurring in ≥3% of participants in either group (DTG/3TC, n [%] vs CAR, n [%]): weight increased (14 [6] vs 0 [0]), insomnia (7 [3] vs 1 [<1]), and dizziness (7 [3] vs 0 [0]).

- Safety across subgroups was generally consistent with the overall analysis and similar between treatment groups (Table 3)

Table 3. Frequency of All AEs by Subgroup Through Week 48: Safety Population

		DTG/3TC		CAR	
Variable	Subgroup	n/N	%	n/N	%
Overall	—	180/246	73	172/247	70
Age	<35	37/49	76	36/53	68
	35 to <50	67/99	68	69/99	70
	≥50	76/98	78	67/95	71
Sex	Female	77/108	71	60/84	71
	Male	103/138	75	112/163	69
Race	White	103/149	69	97/144	67
	African American/ African heritage	36/45	80	38/48	79
	Asian	23/31	74	27/39	69
	Other	18/21	86	10/16	63
Baseline third agent class	INSTI	71/98	72	70/98	71
	NNRTI	93/123	76	85/124	69
	PI	16/25	64	17/25	68
Baseline CD4+ cell count, cells/mm^3	<500	45/60	75	42/63	67
	≥500	87/123	71	134/185	72
Historical genotypic resistance results at screening	Available	75/100	75	73/99	74
	Not available	105/146	72	99/148	67

Conclusions

- Switching to DTG/3TC FDC in virologically suppressed adults was non-inferior to CAR at Week 48 in the overall population; results by demographics, baseline third agent class, and disease characteristics subgroups were consistent with the overall analysis
  - Diverse demographic groups, including individuals who are female, aged ≥50 years, or identifying as Asian, African American, or of African heritage, were included
- DTG/3TC FDC was generally well tolerated through Week 48 in the primary analysis, with frequencies of AEs in the overall population consistent with those in the subgroup analysis
- Results from this subgroup analysis of the SALSA study further support DTG/3TC FDC as a robust switch option for virologically suppressed adults with HIV-1 regardless of baseline demographics, third agent class, or disease characteristics

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