STRIIVING: Switching to Abacavir/Dolutegravir/Lamivudine Fixed Dose Combination (ABC/DTG/3TC FDC) From a PI, NNRTI, or INI-Based Regimen Maintains HIV Suppression at Week 48

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J Lake,[1] B Trottier,[2] J Garcia-Diaz,[3] H Edelstein,[4] P Kumar,[5] UF Bredeek,[6] M Loutfy,[7] C Brennan,[8] J Koteff,[8] B Wynne,[9] J Hopking,[10] M Aboud[11]

[1]University of California, Los Angeles, CA, USA; [2]Clinique Médicale l'Actuel, Montreal, Quebec, Canada; [3]Ochsner Clinic Foundation, New Orleans, LA, USA; [4]Highland Hospital, Alameda Health System, Oakland, CA, USA; [5]Georgetown University, Washington DC, USA; [6]Metropolis Medical, San Francisco, CA, USA; [7]Maple Leaf Research, Toronto, Ontario, Canada; [8]ViiV Healthcare, Research Triangle Park, NC, USA; [9]ViiV Healthcare, Collegeville, PA, USA; [10]GlaxoSmithKline, London, United Kingdom; [11]ViiV Healthcare, London, United Kingdom

Introduction

- Abacavir 600 mg/dolutegravir 50 mg/lamivudine 300 mg (ABC/DTG/3TC) fixed-dose combination (Triumeq®) is a complete regimen built around DTG, an unboosted integrase transfer inhibitor with a high barrier to resistance
  - First approval of ABC/DTG/3TC: August 2014 in North America
- The STRIIVING study (ClinicalTrials.gov, NCT02105987) was conducted to evaluate the efficacy, safety, tolerability, and treatment satisfaction of switching to ABC/DTG/3TC in subjects with HIV who are stable and suppressed on a variety of antiretroviral therapy (ART) regimens
- The 24-week primary endpoint results, which demonstrated noninferiority of switching to ABC/DTG/3TC compared with continuing current antiretroviral therapy, were reported previously[1]
- Here we report the efficacy and safety results for patients treated with ABC/DTG/3TC in the early-switch arm after 48 weeks and after 24 weeks for patients in the late-switch arm

Methods

- The STRIIVING study was a 48-week, phase IIIb, randomized, open-label, active-controlled, multicenter, parallel-group, noninferiority study conducted at 96 sites in the United States, Puerto Rico, and Canada
- Eligibility criteria: ≥18 years of age, HIV-1–positive status, stable ART regimen (ART with 2 NRTIs plus either a PI, NNRTI, or INI) ≥6 months with virological suppression (HIV-1 RNA <50 c/mL), and negative status for the *HLA-B*5701* allele
- At baseline, subjects were randomized to receive ABC/DTG/3TC (early switch) or continue on current ART (late switch) from Day 1 to Week 24
  - At Week 24, subjects in the late-switch group switched from current ART to ABC/DTG/3TC; subjects in the early-switch group remained on ABC/DTG/3TC
- The primary endpoint for the STRIIVING study was the proportion of subjects with plasma HIV-1 RNA <50 c/mL at Week 24 using the Snapshot (missing, switch, or discontinuation=failure) algorithm
  - Noninferiority margin was set at 10%

Results

Study Population

- Of 841 subjects screened, 553 were randomly assigned (1:1) to receive ABC/DTG/3TC in the early-switch group (n=275) or continue on current ART in the late-switch group (n=278; Figure 1)
- In the early-switch group, 4% of subjects discontinued taking ABC/DTG/3TC between Day 1 and Week 24 due to adverse events (AEs), but no additional subjects discontinued after Week 24
  - 2% of late-switch subjects discontinued ABC/DTG/3TC between Week 24 and Week 48
- 245 of 278 patients (88%) completed the first 24 weeks on current ART; 244 switched to ABC/DTG/3TC at Week 24

Figure 1. Subject Disposition Through 48 Weeks

Screened (N=841)

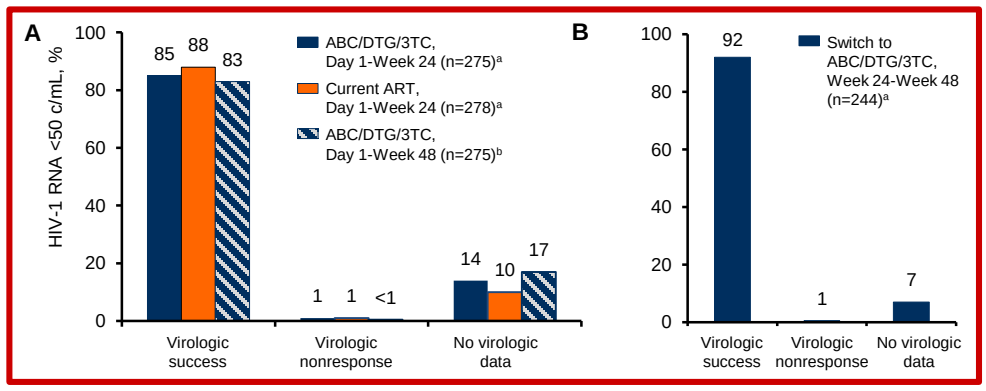
Early-switch group			Late-switch group	
Day 1-Week 24 ABC/DTG/3TC (n=275)	Day 1-Week 48 ABC/DTG/3TC (n=275)		Day 1-Week 24 current ART (n=278)	Week 24-Week 48 ABC/DTG/3TC (n=244)
239 (87%)	**230 (84%)**	**Completed**	**245 (88%)**	**230 (94%)**
36 (13%)	**45 (16%)**	**Withdrawn**	**33 (12%)**	**14 (6%)**
10 (4%)	10 (4%)	Adverse event	0	4 (2%)
0	0	Lack of efficacy (virologic failure)	0	0
15 (5%)	15 (5%)	Protocol deviation	17 (6%)	1 (<1%)
0	0	Stopping criteria met	0	1 (<1%)
3 (1%)	8 (3%)	Lost to follow-up	3 (1%)	3 (1%)
4 (1%)	5 (2%)	Investigator discretion	3 (1%)	0
4 (1%)	6 (2%)	Withdrew consent	10 (4%)	5 (2%)

ART, antiretroviral therapy.

Efficacy

- Through week 24, 85% of subjects were suppressed on ABC/DTG/3TC compared with 88% on current ART (treatment difference -3.4%; 95% CI, -9.1% to 2.3%; Figure 2)
  - 83% of subjects in the early-switch group were suppressed on ABC/DTG/3TC through Week 48
- From Week 24 to Week 48 in the late-switch arm, 92% of subjects who switched to ABC/DTG/3TC were suppressed

Figure 2. (A) Virologic Outcomes in Subjects Assigned to the Early-Switch Group or to Continue on Current ART; (B) Virologic Outcomes in Subjects Who Switched to ABC/DTG/3TC at Week 24



ART, antiretroviral therapy; ITT-e, intent-to-treat exposed. [a]ITT-e analysis. [b]Includes 10 patients who were originally considered to have virologic nonresponse in the ITT-E analysis but were found to have received commercial ABC/DTG/3TC (Triumeq®) instead of study drug.

- Through Week 24, 10 subjects (4%) in the early-switch group had no virologic data due to discontinuation related to AEs or death
  - Weeks 24 to 48, no additional subjects discontinued due to AEs or death
- After switching to ABC/DTG/3TC at Week 24, 4 subjects (2%) in the late-switch group had no virologic data due to discontinuation related to AEs or death
- 4 patients had HIV-1 RNA >50 c/mL at the Week 48 Snapshot (3 in the early-switch group and 1 in the late-switch group); all 4 subsequently resuppressed to <50 c/mL
- No patients met protocol-defined virologic failure

Safety

- At Week 48, 206 AEs (75%) were reported by early-switch subjects, 180 (65%) of which occurred between Day 1 and Week 24 (Table)
  - 60 AEs (22%) at Week 48 were drug related; 57 (21%) occurred between Day 1 and Week 24

Table. Adverse Events

	Early Switch		Late Switch
	ABC/DTG/3TC Day 1 to Wk 24 N=275 n (%)	ABC/DTG/3TC Day 1 to Wk 48 N=275 n (%)	ABC/DTG/3TC Wk 24 to Wk 48 N=244 n (%)
Any AE	180 (65)	206 (75)	146 (60)
Common AEs (occurring ≥5% of subjects in either arm)			
Nausea	27 (10)	28 (10)	15 (6)
URTI	20 (7)	35 (13)	22 (9)
Diarrhea	20 (7)	20 (7)	9 (4)
Fatigue	19 (7)	22 (8)	6 (2)
Headache	13 (5)	17 (6)	10 (4)
Cough	14 (5)	17 (6)	6 (2)
Insomnia	10 (4)	14 (5)	9 (4)
Nasopharyngitis	10 (4)	13 (5)	6 (2)
Any drug-related event (occurring ≥2% of subjects in either arm)	57 (21)	60 (22)	32 (13)
Any serious AE[a]	6 (2)	9 (3)	6 (2)
Any fatal event[a]	1 (<1)	1 (<1)	1 (<1)
Discontinuations due to AE or death	10 (4)	10 (4)	4 (2)

AE, adverse event; URTI, upper respiratory tract infection. [a]No serious or fatal AEs were considered drug related.

Conclusions

- Efficacy
  - The virologic response rate was maintained through 48 weeks in the early-switch group
  - In the late-switch group, virologic suppression was observed in 92% of subjects on ABC/DTG/3TC (24 weeks postswitch)
  - There were no protocol-defined virologic failures in the study
- Tolerability
  - There were no further discontinuations due to AEs in the early-switch arm after Week 24
  - Low rate of discontinuations in the late-switch arm (2%)
- Summary
  - Data through 48 weeks support switching to ABC/DTG/3TC once daily for subjects with HIV-1 on stable suppressive ART

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Reference: 1. Trottier B, Lake J, Logue K, et al. Switching to abacavir/dolutegravir/lamivudine fixed dose combination (ABC/DTG/3TC FDC) from a PI, INI or NNRTI based regimen maintains HIV suppression. Presented at: 55th Annual Interscience Conference on Antimicrobial Agents & Chemotherapy; September 18-21, 2015; San Diego, CA.