Safety and Efficacy of Dolutegravir in Treatment-Naive Patients 50 Years and Over: Subgroup Analysis of 48-Week Results From SPRING-2, SINGLE, FLAMINGO, and ARIA

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Abstract

Background: Due to benefits of antiretroviral treatment (ART) the HIV population is aging. This analysis presents the safety and efficacy of dolutegravir-based regimens (DBRs) in these phase III/IIIb studies by age group.

Methods: Data from the 4 studies were collated and examined. In SPRING-2, FLAMINGO, SINGLE, and ARIA, subjects assigned to DBRs were evaluated by age subgroup: under 50 years or older. Adverse events (AEs), response rates (by FDA snapshot), comorbidities, and comedications were summarised in each group.

Results: 1315 subjects were identified; 1157 <50 (18-49) years versus 158 ≥50 (50-79) years. The high efficacy and low AE rates were consistent across both ≥50 and <50 subgroups. Grade 2 to 4 nervous system and psychiatric AEs were uncommon. The rate of AEs leading to discontinuation remained low in subjects taking DBRs.

Conclusion: Analysis of these studies shows DTG once daily to be an effective and well-tolerated treatment option in older patients ≥50 years, which is consistent with overall study results and in the majority patient group <50 years.

Introduction

- Dolutegravir (DTG)-based regimens (DBRs) have been well tolerated in ART-naive adult studies and have shown superior efficacy versus darunavir/ritonavir (DRV/r) + 2 NRTIs (FLAMINGO); the fixed-dose combination tenofovir/emtricitabine/efavirenz (SINGLE); atazanavir/ritonavir (ATZ/r) + tenofovir/emtricitabine (TDF/FTC; ARIA women-only study) and noninferior efficacy versus raltegravir (RAL) + 2 NRTIs (SPRING-2). This analysis presents the pooled safety and efficacy of DBRs in these phase III/IIIb studies by age group <50 and ≥50 years old.

Methods

- Data from SINGLE, SPRING-2, FLAMINGO, and ARIA were reviewed. Subjects assigned to DBRs were pooled and evaluated by age subgroup; those under 50 years and those 50 years or older.
- In SPRING-2 and FLAMINGO, investigators were allowed to select NRTIs abacavir/lamivudine (ABC/3TC) or TDF/FTC, while in SINGLE and ARIA, TDF/FTC with efavirenz (single tablet) and ATV/r (respectively) were compared to DTG with ABC/3TC.
- Comorbidities and comedications at baseline along with adverse events (AEs) and response rates (by FDA snapshot) were summarised in each group.
- Response rates (by FDA snapshot) at 48 weeks and AEs were summarized in subgroups: age < versus ≥50 years).

Results

- Baseline demographic and disease characteristics are shown in Table 1.
- The ≥50 age group showed a trend toward a greater number of comorbidities and comedications than those <50.
- DTG efficacy rates at 48 weeks remained high across both age groups (Figure 1).
- Approximately 30% of patients in both groups reported psychiatric disorders at baseline, with a slightly higher trend toward nervous system disorders in the older age group (Table 2).
- Safety summaries showed comparable grade 2 to 4 drug-related AEs across subgroups and low rates of AEs leading to withdrawals across all DTG subgroups (Table 3).

Table 1. Baseline demographics and disease characteristics

	DTG-based regimens (pooled)	
	<50 years (N=1157)	≥50 years (N=158)
Age, mean (range)	34.3 (18-49)	55.5 (50-79)
Female, n (%)	344 (30)	65 (41)
Non-white, n (%)	344 (30)	52 (33)
RNA viral load >100,000 (copies/mL), n (%)	321 (28)	57 (36)
CD4 counts (cells/mm^3), n (%)		
<50	30 (3)	4 (3)
50 to <200	137 (12)	28 (18)
200 to <350	390 (34)	56 (35)
350 to <500	350 (30)	43 (27)
≥500	250 (22)	27 (17)
Patients with comorbidities, n (%)	648 (56)	108 (68)
Patients with ≥2 comorbidities	369 (32)	73 (46)
Patients on comedications, n (%)	1024 (89)	152 (96)
Comedications per patient, mean (SD)	7.2 (6)	9.8 (8)

Data pooled from all patients receiving dolutegravir in the SPRING-2, SINGLE, FLAMINGO, and ARIA studies.

Table 2. Top 5 medical classifications of reported baseline comorbidities

	DTG-based regimens (pooled)		
n (%)	<50 years (N=1157)	≥50 years (N=158)	Total (N=1315)
Psychiatric disorders	350 (30)	53 (34)	403 (31)
Gastrointestinal disorders	267 (23)	39 (25)	306 (23)
Nervous system disorders	209 (18)	38 (24)	247 (19)
Cardiac disorders	132 (11)	55 (35)	187 (14)
Metabolism and nutrition disorders	100 (9)	40 (25)	140 (11)

Data pooled from all patients receiving dolutegravir in the SPRING-2, SINGLE, FLAMINGO, and ARIA studies.

Figure 1. Pooled virologic efficacy and CD4+ cell counts by age group in subjects receiving dolutegravir-based regimens through 48 weeks

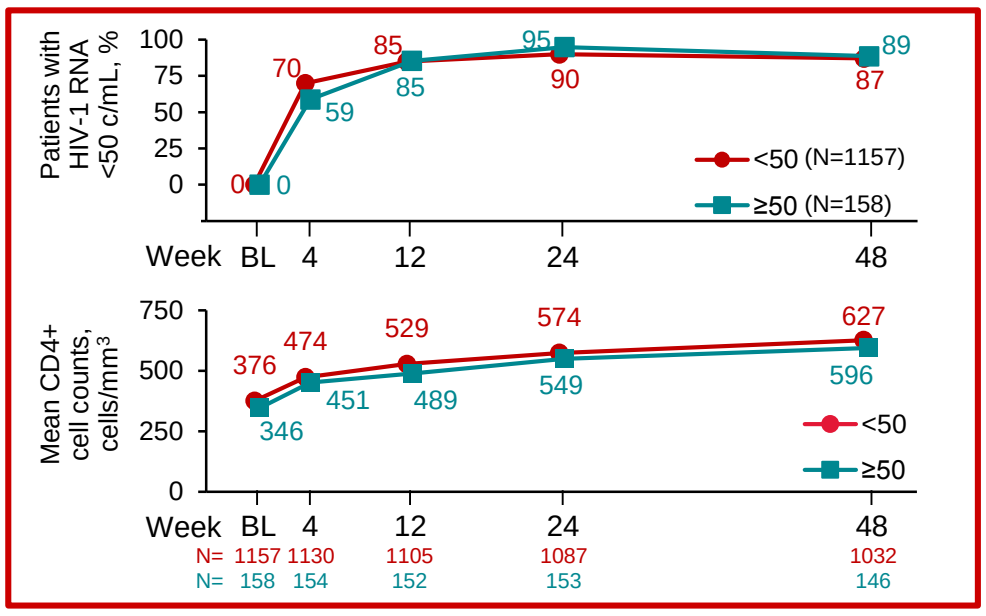

Table 3. Most frequently reported drug-related adverse events

	DTG-based regimens (pooled)		
n (%)	<50 years (N=1157)	≥50 years (N=158)	Total (N=1315)
Grade 2-4 drug-related AEs[a]	123 (11)	16 (10)	139 (11)
Gastrointestinal	41 (4)	7 (4)	48 (4)
Psychiatric	35 (3)	5 (3)	40 (3)
Nervous system	27 (2)	1 (<1)	28 (2)
General and administration site[b]	13 (1)	5 (3)	18 (1)
Discontinuations due to AEs	32 (3)	2 (1)	34 (3)

Data pooled from all patients receiving dolutegravir in the SPRING-2, SINGLE, FLAMINGO, and ARIA studies. [a]All other AE types were reported in <1% of patients in each group. AE, adverse event. [b]Includes fatigue, asthenia, chills, and malaise.

Discussion

- In the UK, due to individuals aging on antiretroviral therapy (ART) and a growing number of individuals aged 50 or over diagnosed with HIV, approximately 1 in 3 patients accessing HIV care is over 50 years of age.
- This population may be more difficult to treat because they are likely to be on other comedications and diagnosed with other comorbidities.
- Although the numbers are small, this pooled analysis of DTG randomized, controlled, naive studies suggests that its superior efficacy and tolerability is comparable in age groups above and below 50 years.

Conclusions

- In the 4 treatment-naive clinical trials, DTG once daily was seen to be a consistently effective and well-tolerated treatment option across age group above and below 50 years.

Acknowledgments

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