Dolutegravir-Based Regimens Viral Load Decay at Week 4 Could Predict Sustained Viral Suppression at Week 96

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Introduction

- The medium- and long-term implications of rapid viral load early-phase decay during integrase inhibitor–based therapy are not fully understood
- The integrase inhibitor dolutegravir (DTG) plus 2 nucleoside reverse transcriptase inhibitors has been evaluated in 3 phase III studies in treatment-naive subjects
- DTG-based regimens (DBRs) achieved non-inferiority in SPRING-2 vs raltegravir (RAL)–based regimens, while superiority was achieved in SINGLE and FLAMINGO vs Atripla® and boosted darunavir (DRV/r)–based regimens, respectively[1-3]
- This analysis was conducted to assess the predictive value of rapid virological response (RVR) at Week 4 on sustained virological response (SVR) at Week 96 in naive subjects treated with DBRs

Methods

- Post hoc cross-sectional analysis of subjects enrolled in the naive DTG phase III clinical trials, SPRING-2, SINGLE, and FLAMINGO
- RVR and SVR were assessed at Weeks 4 and 96, respectively, based on HIV-1 RNA <50 as determined by FDA snapshot
- Positive (PPV) and negative (NPV) predictive values were calculated; PPV as the proportion of subjects suppressed at Week 4 who were also suppressed at Week 96, and NPV as the proportion of subjects not suppressed at Week 4 who were also not suppressed at Week 96

Results

Table 1. PPV and NPV of SVR at Week 96

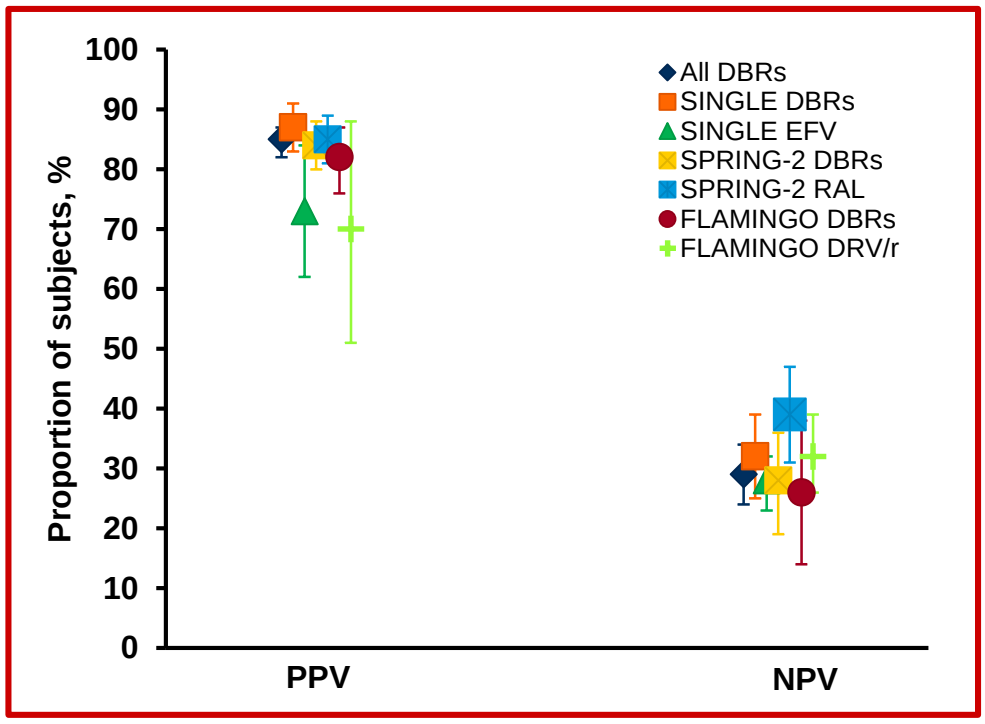
SVR at Week 96	SINGLE		SPRING-2		FLAMINGO	
	DTG (N=414)	EFV (N=419)	DTG (N=411)	RAL (N=411)	DTG (N=242)	DRV/r (N=242)
PPV (%, 95% CI)	87 (83,91)	73 (62,84)	84 (80,88)	85 (81,89)	82 (76,87)	70 (51,88)
NPV (%, 95% CI)	32 (25,39)	28 (23,32)	28 (19,36)	39 (31,47)	26 (14,38)	32 (26,39)

- A total of 2139 subjects were analysed, including those receiving DBRs and comparator arms; 1067 subjects received DTG across the 3 studies
- The analysis revealed that 70% of subjects receiving DBRs achieved RVR at Week 4, and 80% attained SVR at Week 96. The PPV and NPV of SVR in the DBR study population were 85% (95% CI: 82%-87%) and 29% (95% CI: 24%-34%), respectively (Figure 1)
- The PPV of the DBRs was numerically higher than for efavirenz (EFV) or DRV/r plus 2 nucleosides and similar to that with RAL plus 2 nucleosides (Table 1 and Figure 1)
- The NPV with RAL was numerically higher than with DBRs, reflecting that more DBR subjects without RVR ended with SVR

Discussion

- Limitations of this analysis included using a post-randomisation measure (Week 4 virological response) as a predictor, and the inclusion of an open-label randomised clinical trial, where there was potential for bias
- The PPVs for DBRs were consistent with or numerically higher than the comparators, correlating with study outcomes at Week 96, which supports the predictive value of undetectability at Week 4

Figure 1. PPV and NPV Associated With All DBR Regimens and Individual Studies



- In addition, the NPV of the DBRs was also consistently lower and/or comparable with other regimens. Raltegravir in SPRING-2 showed the numerically highest NPV. The implication of NPV in this context needs further investigation
- Overall, DBRs, in the context of the population analyzed, showed the highest level of undetectability at Week 4 that defined the PPV and NPV

Conclusions

- This analysis suggests that RVR at Week 4 with DBRs is a potential predictor of SVR at Week 96
- The NPV of RVR with DTG is numerically lower than with RAL
- Characterisation of patients who do not achieve RVR and subsequent undetectability deserves further investigation
- These data may support clinicians to further individualise therapy and monitoring

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References: 1. Raffi F, Jaeger H, Quiros-Roldan E, et al. Once-daily dolutegravir versus twice-daily raltegravir in antiretroviral-naive adults with HIV-1 infection (SPRING-2 study): 96 week results from a randomised, double-blind, non-inferiority trial. *Lancet Infect Dis*. 2013;13:927-935. **2.** Walmsley S, Baumgarten A, Berenguer J, et al. Dolutegravir plus abacavir/lamivudine for the treatment of HIV-1 infection in antiretroviral therapy-naive patients: week 96 and week 144 results from the SINGLE randomized clinical trial. *J Acquir Immune Defic Syndr*. 2015;70:515-519. **3.** Molina JM, Clotet B, van Lunzen J, et al. Once-daily dolutegravir versus darunavir plus ritonavir for treatment-naive adults with HIV-1 infection (FLAMINGO): 96 week results from a randomised, open-label, phase 3b study. *Lancet HIV*. 2015;2:e127-136.