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O425 Efficacy and safety of maraviroc in treatment-experienced (TE) patients infected with R5 HIV-1: 96-week combined analysis of the MOTIVATE 1 and 2 studies

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Purpose of the study

MOTIVATE 1 and 2 are randomized, double-blind, placebo (PBO)-controlled Phase III studies assessing the efficacy and safety of maraviroc (MVC) in TE patients with R5 HIV-1. In both studies, MVC (QD/BID) + optimized background therapy (OBT) demonstrated significantly greater virological and immunological efficacy and a similar safety profile compared with PBO+OBT at weeks 24 and 48 [1].

Methods

1,076 patients with triple drug-class experience and/or triple-class resistance, R5 virus (Trofile™), and HIV-1 RNA ≥5,000 copies/mL were randomized 1:2:2 to PBO, MVC QD or BID. All patients received OBT (3–6 antiretrovirals +/- low-dose ritonavir; darunavir/r not permitted due lack of PK data). The study was unblinded after week 48 (primary end-point). Patients in both MVC arms who had not experienced treatment failure through week 48 were rolled over to open-label MVC BID, but are referred to below by their baseline (BL) randomization assignment. The PBO arm contains patients who were virologically suppressed at week 48 and remained on OBT through week 96. After week 48, substitutions in OBT were allowed in all arms.

Summary of results

More patients in the MVC arms maintained HIV-1 suppression (to <400 and <50 copies/mL) through week 96 than those in the PBO arm. Fewer patients in the MVC arms experienced virologic failure between week 48 and 96 compared with the PBO arm. Incidence of SAEs, Category C events and malignancies were similar among treatment arms even when unadjusted for exposure, which was significantly greater in each of the MVC arms compared with the PBO arm. See table in Figure 1.

Conclusion

MVC+OBT resulted in durable viral suppression through week 96 in these TE patients with R5 HIV-1. Pooled analyses revealed no new or unique safety signals between 48 and 96 weeks. Serious adverse events, Category C events and malignancies occurred with similar frequency among treatment groups.

Baseline randomization assignment (includes all patients who received at least one dose of study treatment)	**PBO + OBT N=209**	**MVC QD + OBT N=414**	**MVC BID + OBT N=426**
Continuing to OBT alone or open-label MVC BID + OBT	n=111	n=239	n=259
Patients with HIV-1 RNA <400 copies/mL, n (%^)†			
Week 48	47 (22)	214 (52)	240 (56)
Week 96	14 (7)	190 (46)	212 (50)
Patients with HIV-1 RNA <50 copies/mL, n (%^)†			
Week 48	35 (17)	179 (43)	195 (46)
Week 96	12 (6)	159 (38)	171 (40)
Mean change from BL‡ in CD4+ cell count, cells/mm^3			
Week 48#	+61	+116	+124
Week 96§	+154 (n=15)	+169 (n=215)	+187 (n=227)
Study discontinuation due to adverse events, n (%^)			
From BL to Week 48	11 (5)	20 (5)	19 (4)
From Week 48 to Week 96	10 (5)	3 (1)	2 (<1)
Study discontinuation due to loss of efficacy, n (%^)			
From BL to Week 48	113 (54)	93 (22)	97 (23)
From Week 48 to Week 96	46 (22)	8 (2)	9 (2)
Median duration of study treatment exposure, years	0.7	2.4	2.5
Patients with serious adverse events (SAEs), n (%^) (from BL to Week 96)	21 (10)	53 (13)	65 (15)
Patients with Category C (AIDS-defining) event, n (%^) (from BL to Week 96)	11 (10)	16 (7)	18 (7)
Patients with malignancies, n (%^) (from BL to Week 96)	7 (3)	17 (4)	17 (4)

^ % of total number initially randomized, N
† Discontinuations/missing values classified as failures/non-responders
‡ Mean of all pre-dose assessments
# Last-observation-carried-forward approach used to impute missing values
§ Includes only those patients with a value at the Week 96 timepoint (shown in parentheses); missing values not imputed

Figure 1

References

1. Hardy WD, *et al.*: **Efficacy and safety of maraviroc plus optimized background therapy in treatment-experienced patients infected with CCR5-tropic HIV-1: 48-week combined analysis of the MOTIVATE studies.** *15th CROI* 2008. Poster 792.