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Poster presentation

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Incidence of infections in treatment-experienced (TE) patients in the MOTIVATE studies of maraviroc (MVC) plus optimized background therapy (OBT)

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Background

Certain infections occur more frequently in HIV-infected patients some of which are classified as AIDS-defining events. Theoretical concerns have been raised that CCR5 antagonists may have an adverse effect on the immune system. A 4-week immunotoxicology study in cynomolgous monkeys did not demonstrate any adverse effects of MVC on the immune system. MOTIVATE 1 and MOTIVATE 2 are randomized, double-blind, placebo (PBO)-controlled, Phase III studies assessing the safety and efficacy of MVC in TE patients with CCR5-tropic HIV-1. In both studies, MVC+OBT demonstrated significantly greater virologic and immunologic efficacy and a similar safety profile compared with PBO+OBT at 48 weeks.

Methods

Patients were randomized 2:2:1 to MVC QD (N = 414), MVC BID (N = 426), or PBO (N = 209) + OBT. For this analysis, data from both MVC arms were pooled (N = 840) and infections present at Day 1 were excluded. We present the incidence of infections during the first 48 weeks of treatment for patients who received MVC and PBO, in addition to exposure-adjusted incidence rates, risk ratios and 95% CI.

Summary of results

840 patients received MVC and 209 received PBO. Mean baseline CD4 (cells/μL) and viral load (VL, log10 copies/mL), respectively, were 193 and 4.9 for MVC recipients and 186 and 4.9 for PBO recipients. The unadjusted and exposure-adjusted incidence of infections, including Category C infections and exposure-adjusted risk ratio, is presented. (Table 1.)

Median baseline CD4 (cells/μL)and VL (log10 copies/mL) for patients who did and did not develop sentinel or Category C infections were 122 and 176 and 5.1 and 4.8 for MVC recipients and 99 and 188 and 5.2 and 4.8 for PBO recipients. Patients reporting infections had more previous Category C events and PBO recipients had shorter median time to the onset of infections compared with MVC recipients (0.42 years vs. 1.02 years; $p < 0.0001$).

Conclusion

To date, clinical data do not indicate that MVC is associated with clinically relevant increased rates of infections. Data from Phase III TE studies do not indicate a difference in the spectrum or severity of infections reported among patients receiving MVC and those receiving PBO, except a slightly increased rate of URTI and lower rate of pneumonia on MVC vs. PBO. Longer duration of MVC therapy (48 vs. 24 weeks) did not show any effect on the incidence of infections and no significant difference in the time of onset of these events was seen.

Table 1:

	MVC (QD+BID) [N = 840]: exposure adjusted incidence*, unadjusted incidence (%)	**Placebo [N = 209]: exposure adjusted incidence*, unadjusted incidence (%)**	**Risk Ratio (exposure adjusted): MVC/PBO (95% CI)**
Infections and infestations among sentinel infections/Category C illnesses	27.04, 159 (18.93)	31.37, 33 (15.79)	0.86 (0.59, 1.25)
Selected Category C infections			
Herpes simplex	4, 24 (2.86)	1.8, 2 (0.96)	2.22 (0.53, 9.40)
Oesophageal Candidiasis	2.5, 15 (1.79)	1.8, 2 (0.96)	1.39 (0.32, 6.07)
Oral Candidiasis	4.7, 28 (3.33)	7.4, 8 (3.83)	0.64 (0.29, 1.39)
Infections and infestations among adverse events	92.80, 447 (53.21)	132.90, 84 (40.19)	0.70 (0.55, 0.88)
Infections AEs of interest			
Nasopharyngitis	11.3, 67 (7.98)	10.4, 11 (5.26)	1.09 (0.57, 2.06)
Pneumonia	3.1, 19 (2.26)	7.4, 8 (3.83)	0.42 (0.18, 0.96)
Upper RTI	16.1, 94 (11.2)	11.6, 12 (5.74)	1.39 (0.76, 2.53)
Meningitis viral	0.4, 2 (0.2)	0, 0 (0)	ND**

*Adjusted to 100 years of subject exposure;** ND = not defined.