Adverse Event Profile of Maraviroc in Treatment-experienced Patients Infected with R5 HIV-1

A. Rybus1, J. Goodenough2, J. van der Riet2, J. Kaslow2 and H. Mayer2

1Pfizer Global Research and Development, Sandwich, UK; 2Pfizer Global Research and Development, New London, CT, USA

For further information, please contact Ayman Ayoub at Ayman.Ayoub@pfizer.com

Introduction

Maraviroc (MVC, marketed as Celsentri®) is a potent CCR5 antagonist approved for treatment-naive (TN) and treatment-experienced (TE) patients infected with CCR5-tropic (R5) HIV-1. The efficacy and safety of MVC have been assessed in single- and multiple-dose studies in both healthy volunteers and HIV-infected patients, including the large Phase 2b/3 studies MERIT (MVC vs. olapoxozol) and MAVEN (MVC vs. placebo) in TN and MATIVE 1 and MATIVE 2 in TE patients.1-3

In the MATIVE studies, adults with R5 HIV-1 infection, prior experience of or resistance to at least one ARV (drug or resistance), and evidence of ongoing HIV replication, were enrolled in two 24-week randomized clinical trials of MVC QD (400 mg) or MVC BID (200 mg twice daily) with optimized background therapy (OBT) (3-6 antiretroviral therapies).1

Methods

MVC and placebo (PBO)-controlled, exposure-adjusted incidence of adverse events (AEs) in TE patients enrolled in 1,049 patients receiving MVC (QD or BID) or PBO over 46 weeks in the combined MATIVE 1 and 2 study dataset.

Results

A safety summary of AE frequencies at Week 48 is shown in Table 1. Despite the lower total exposure to MVC plus OBT, caused by the higher rate of discontinuations in patients receiving PBO, both all-causes and treatment-related rates of MVC QD vs. BID were similar to the PBO arm. AEs were reported in 390 (91.6%) of the MVC QD arm and 385 (90.9%) of the BID arm. Events were similar between study arms, as was the proportion of AE-related discontinuations and deaths (Table 1).

Exposure-adjusted incidence rates for AEs that occurred in at least 5% of treatment-arm patients are shown in Figures 1a (all-causes) and 1b (treatment-related). The majority of AEs noted were not considered to be related to study drug.

Exposure-adjusted rates of Category C events (Table 2) and non-Category C malignancies (Table 3) were low and similar between arms, other than a cluster of esophageal candidiasis events in the MVC QD arm that was not seen on MVC BID (Table 2). A slightly higher exposure-adjusted incidence of all malignant neoplasms (Category C and non-Category C combined) was noted in the PBO arm (Table 1). Exposure-adjusted rates of all infections and infestations were similar between arms and drug exposure was not noted (Table 4).

Conclusions

The safety profile of MVC in two large studies in treatment-experienced patients with few treatment options is similar to PBO.

MVC was not associated with increased rates or severities of infections, malignancies, Category C adverse events (AEs) and serious AEs (SAEs) in treatment-experienced patients with non-R5 HIV-1 infection in Study A300503.5

References


Table 1. MATIVE 1 and 2 post-treatment safety summary

Table 2. MATIVE 1 and 2 exposure-adjusted incidence of Category C events (unadjusted for exposure)

Table 3. MATIVE 1 and 2 exposure-adjusted incidence of non-Category C malignancies (unadjusted for exposure)

Table 4. MATIVE 1 and 2 grade 3/4 liver function test results by hepatitis status or inclusion of Vireo in the OBT (preliminary results)