SYMTUZA® (darunavir, cobicistat, emtricitabine, and tenofovir alafenamide)
Safety Information of SYMTUZA – Skin Rash

SUMMARY

- In the AMBER study, the incidence of rash was 9% (32/362) for the SYMTUZA arm and 7% (25/363) for the control arm at 48 weeks.[1]
- In the DIAMOND study, rash of any grade occurred in 5% (5/109) of patients and rash of ≥Grade 2 occurred in 4% (4/109) of patients receiving SYMTUZA at 48 weeks.[2]
- In the GS-US-299-0102 study, the incidence of rash was 11.7% (12/103) for the SYMTUZA group and 8.0% (4/50) for the control group at 48 weeks.[3]
- In the EMERALD study, the incidence of rash was 4.6% (35/763) for the SYMTUZA group and 2.1% (8/378) for the control group at 48 weeks.[4]

CLINICAL STUDIES

HIV-1 Patients with No Prior Antiretroviral Treatment History

AMBER

The AMBER study was a phase 3, randomized, active-controlled, double-blind study to evaluate efficacy and safety of SYMTUZA vs darunavir [DRV]/cobicistat [COBI] fixed-dose combination co-administered with emtricitabine (FTC)/TDF in antiretroviral (ARV) treatment-naïve HIV-1-infected adults (N=725).[1]

Study Design/Methods

- Patients were stratified by screening viral load (VL;</≥100,000) and by screening CD4+ cell counts (</≥200 cells/mm^3) and then randomized to SYMTUZA with matching DRV/COBI + FTC/TDF placebo or the active-control regimen of DRV/COBI + FTC/TDF with a matching SYMTUZA placebo.

Results at 48 weeks & 96 weeks

- Through week 48, the incidence of rash was 9% (32/362) for the SYMTUZA arm and 7% (25/363) for the control arm.
  - Incidence of rash at least possibly related to study drug: SYMTUZA, 6% (22/362); control, 4% (14/363).
- Between weeks 48 to 96, there were no additional reports of rash in the SYMTUZA arm. After week 48, one patient in the control arm experienced a rash following switch to SYMTUZA.[5]
- Serious adverse events (AEs) considered study drug-related included rash in 2 control patients.
- Through week 48, AEs leading to permanent discontinuation included rash, generalized rash, and maculopapular rash in 4, 1, and 1 SYMTUZA patients, respectively, and rash/erythema in 7 control patients.[1] After week 48, there was one additional case of rash in the control arm after switching to SYMTUZA.[5]

DIAMOND

The DIAMOND study was a phase 3, single-arm, open-label, multicenter study to evaluate the safety and efficacy of SYMTUZA in newly diagnosed, HIV-1 infected, treatment-naïve patients in a rapid initiation model of care over 48 weeks (N=109).[2]

Study Design/Methods

- Eligible patients were enrolled and started on SYMTUZA orally once daily as soon as within 24 hours of the screening/baseline visit and before results of the baseline safety and resistance laboratory tests were available.

Results at week 48

- Rash of any grade occurred in 5% (5/109) of patients and rash of ≥Grade 2 occurred in 4% (4/109) of patients.

GS-US-299-0102

In the GS-US-299-0102 study, the efficacy and safety of SYMTUZA was compared to that of DRV + COBI (administered as single agents) + FTC/TDF in HIV-1 infected, treatment-naïve patients (N=153).[3]

Study Design/Methods

- Patients were stratified by baseline VL (≤100,000 and >100,000) and race (black and non-black) and randomized 2:1 to receive SYMTUZA, or a regimen consisting of DRV 400 mg x 2 + COBI 150 mg + FTC/TDF 200/300 mg tablets.

Results at week 48

- The incidence of rash was 11.7% (12/103) for the SYMTUZA group and 8.0% (4/50) for the comparator group.
- AEs leading to discontinuation included rash in 1 SYMTUZA patient.

HIV-1 Virologically-Suppressed Patients Who Switched to SYMTUZA

EMERALD Study

The EMERALD study was a phase 3, randomized, active-controlled, open-label study to evaluate the efficacy, safety, and tolerability of switching to SYMTUZA versus continuing the current regimen consisting of a boosted protease inhibitor (bPI) combined with FTC/TDF in virologically-suppressed, HIV-1-infected adults (N=1141).[6]

Study Design/Methods

- Patients were stratified according to PI (DRV/ritonavir [r] or DRV/COBI QD, atazanavir [ATV]/r or ATV/COBI QD, or lopinavir [LPV]/r BID) and then randomized 2:1 to switch to SYMTUZA or to continue their bPI regimen.
- After week 48, patients randomized to SYMTUZA continued on SYMTUZA and patients randomized to the bPI arm were switched to SYMTUZA in the extension phase until week 96.[7]

Results at 48 weeks & 96 weeks

- Through week 48, the incidence of rash was 4.6% (35/763) for the SYMTUZA arm and 2.1% (8/378) for the control arm.[4]
    - Incidence of rash at least possibly related to study drug: SYMTUZA, 1.2% (9/763); control, 0%.
    - None of the rash events were serious and none led to study discontinuation.
- Between weeks 48 to 96, there were 15 additional reports of rash in the 728 patients remaining in the SYMTUZA arm.[8]
    - None were thought to be drug-related, and none were serious or led to discontinuation.
- After week 48, 6/352 (1.7%) patients in the control arm experienced a rash following switch to SYMTUZA, 2 of which were thought to be related.[8]
    - One patient had a grade 3 rash that led to discontinuation of study drug.

LITERATURE SEARCH

A literature search of MEDLINE®, EMBASE®, BIOSIS Previews®, and DERWENT® (and/or other resources, including internal/external databases) pertaining to this topic was conducted on 08 March 2023.

REFERENCES

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