Background

Elpida® or Elsulfavirine (VM1500) is the prodrug of VM1500A, a new potent non-nucleoside reverse transcriptase inhibitor with unique pharmacokinetic properties (T1/2 is ~8 days). A 20 mg once daily dosing was chosen for further study based on 12-week efficacy, pharmacology and safety data. The objective of this study was to compare the efficacy and safety of an ART regimen including Elpida or Efavirenz (EFV) plus tenofovir/emtricitabine (TDF/FTC).

Methods

Phase IIb randomized, placebo-controlled, double-blind, multicenter study in ART-naïve HIV-1-infected patients treated for 48 weeks. Patients were randomized 1:1 to receive; 1) Elpida 20 mg QD, or 2) EFV 600 mg QD. All patients were treated with TDF/FTC.

Results

120 patients enrolled, 60 Elpida/60 EFV. Baseline plasma HIV RNA median was 4.7-4.8 log10 copies/ml; median CD4+ T lymphocyte count was 349 and 379 cells/mm3 for Elpida and EFV, respectively. A total of 55/60 (91.7%) Elpida and 47/60 (78.3%) EFV patients had HIV-1 RNA values < 400 copies/ml (MITT). Patients with baseline HIV-I RNA > 100 000 copies/ml, 14/18 (77.7%) and 15/22 (68.2%) had HIV RNA <400 copies/ml, respectively. CD4+ T lymphocyte counts increased at Week 48 by 179 and 182 cells/mm3 respectively. Median CD4/CD8 ratio increased in both groups from 0.41 to 0.78 and from 0.34 to 0.63 respectively. Study drug-associated adverse events were observed in 22/60 (36.7%) of Elpida patients and 45/58 (77.6%) of EFV patients (p<0.0001). The most frequent were headache (15% and 24.1%), dizziness (6.7% and 27.6%), sleep disorders (5% and 20.7%). Only EFV patients had abnormal dreams (17.2%), skin rash (17.2%), and pruritus (5.2%). Only 5 patient discontinued Elpida (2 AE [1 pregnancy], 1 lack of adherence, 1 LTFU, 1 withdrew consent), and 13 patients discontinued EFV (7 AE, 5 LTFU, 1 withdrew consent).

Conclusions

This 48-week study demonstrated equivalent virologic and immunologic efficacy of ART regimens including Elpida or EFV in ART-naive HIV-1 infected patients. Elpida was significantly safer than EFV-based therapy offering a better tolerated alternative to EFV-based ART. Based on these findings and the pharmacokinetic properties of Elpida, future studies will examine parenteral and oral administration at less frequent dosing intervals.