Elsulfavirine-based Antiretroviral Treatment in Combination with Two NRTIs: 96 weeks

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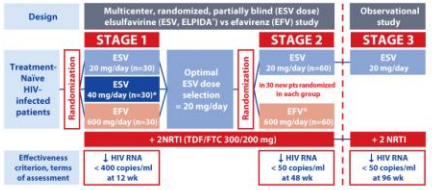
Background:

- ELPIDA® / Elsulfavirine (VM1500) is the prodrug of VM1500A, a novel potent non-nucleoside reverse transcriptase inhibitor with a favorable viral resistance profile and unique pharmacokinetic properties (T1/2 ~ 9 days). A 20 mg once daily dosing was chosen for further study based on 12-week efficacy, pharmacology and safety data; 48-week data comparing ELPIDA® 20 mg to Efavirenz-based therapy plus tenofovir/emtricitabine (TDF/FTC) has been reported effective and safe.
- The objective of this study was to assess the efficacy and safety of an ART regimen including ELPIDA® 20 mg plus two NRTI during 96 weeks.

Methods:

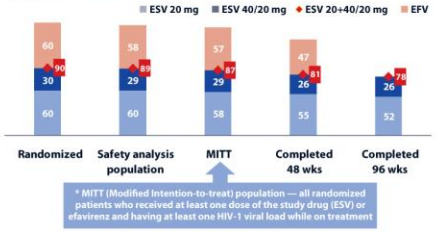
- In the parent randomized, double-blind, multicenter study, ART-naïve HIV-1-infected patients, treated initially for 48 weeks with ELPIDA® plus TDF/FTC, continued the study treatment for up to 96 weeks. During this period they received ELPIDA® 20 mg and various two NRTI regimens: TDF/FTC (35% of patients), ABC+3TC (21%), TDF+3TC (19%), ZDV+3TC (25%).

Fig.1. Study design



* 40/20 mg group: switched from 40 to 20 mg after Stage 1; at stage 3 all patients received ESV 20 mg/day; ELPIDA® received 1st global approval in Russia (June 2017).

Fig.2. Patients populations



* MITT (Modified Intention-to-treat) population — all randomized patients who received at least one dose of the study drug (ESV) or efavirenz and having at least one HIV-1 viral load while on treatment

Results:

- After initial 48 weeks of treatment, 81% of patients on ELPIDA® 20 mg and 73.7% patients on Efavirenz had VL < 50 c/mL (MITT). A total of 81 out of 87 (93%) patients, treated with ELPIDA® in the main study, continued in the follow-up study for additional 48 weeks.
- A total of 73 out of 87 (84%) patients had VL < 50 c/mL and 79/87 (91%) had < 400 c/mL at week 96. Three patients receiving ELPIDA® had VL >1000 c/mL during the study, presumably due to poor compliance; none had NNRTI resistance mutations.

Fig.3. Serum HIV RNA changes

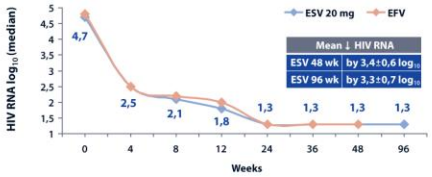
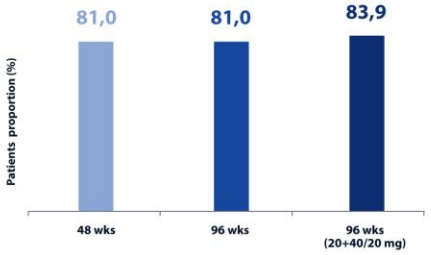


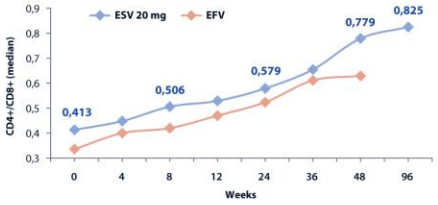
Fig.4. Patient proportion with HIV RNA < 50 copies/ml



- A CD4+ T-lymphocyte count increased by 246 ± 175.3 cells/mm³ during 96 weeks of treatment. Median CD4/CD8 ratio increased from 0.40 to 0.82.

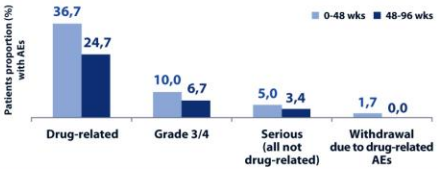
Fig.5. CD4+ and CD8+ cell count changes

Fig.6. CD4+ /CD8+ ratio changes



- No new significant AEs, related to ELPIDA®, were registered during and after 48 weeks of treatment. New AE registered in the study were mainly related to changes of two NRTI regimen, including 2/89 (2.2%) patients with Grade 3 events (i.e. decreased appetite, irritability, dyspnea and rash). No drug-related SAE were reported.
- Total exposure to ELPIDA® was 151.7 patient-years.

Fig.7. Adverse events



Tab.1. Adverse events

Adverse events (AEs)	20 mg group (n=60)	20+40/20 mg group (n=89)
Drug-related	25 (41,7%)	45 (51,0%)
Nervous system	16 (26,7%)	25 (28,1%)
Psychiatric	11 (18,3%)	19 (21,3%)
Grade 3/4	9 (15,0%)	14 (15,7%)
Serious (all not drug-related)	6 (10,0%)	7 (7,9%)

Number (proportion, %) of patients with AEs

Tab.2. Adverse events (stage 3)

Adverse events (AEs)	20 mg group (n=60)	20+40/20 mg group (n=89)
Drug-related	14 (23,3%)	22 (24,7%)
Nervous system (all not drug-related)	1 (1,7%)	2 (2,2%)
Psychiatric	3 (5,0%) incl. 1 (1,7%) drug-related	5 (5,6%) incl. 2 (2,2%) drug-related
Grade 3/4	4 (6,7%) incl. 1 (1,7%) drug-related	6 (6,7%) incl. 2 (2,2%) drug-related
Serious (all not drug-related)	3 (5,0%)	3 (3,4%)

Number (proportion, %) of patients with AEs

Tab.3. Elsulfavirine Clinical Advantages in 1st-line ART

Effectiveness	Safety and tolerability
○ Non-inferior to inferior to efavirenz ○ Sustainable to 96 weeks ○ Not dependent on baseline viral load ○ High resistance barrier	○ Favorable profile during 96 weeks – Lack of serious drug-related adverse events ○ Superior to efavirenz in safety – Low rate of nervous system/psychiatric disorders (2 times less), skin and allergic reactions

Conclusions:

- This study demonstrated that ELPIDA® was safe and well tolerated up to 96 weeks, with continued virologic efficacy, immunologic improvement and favorable resistance profile. ELPIDA®-based therapy is a safe and effective long-term strategy offering multiple potential advantages over current therapies.