

544LB A Randomized, Placebo-Controlled, Double-Blind Study of VM-1500 in HIV-Naïve Patients

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Background: VM-1500 is the pro-drug of the active compound VM-1500A, a potent, highly selective NNRTI. Its antiviral profile is superior to that of efavirenz and other currently marketed NNRTIs. The PK profile suggests once daily dosing. Together with minimal side effects, VM-1500 may be a good NNRTI to be started in HIV treatment.

Methodology: A randomized, placebo-controlled, multiple dose, double-blind study for 7 days in patients with HIV infection who are antiretroviral therapy-naïve with HIV-1 RNA > 5,000 copies/ml and CD4 > 250 cells/mm³. Eight patients were randomized to VM-1500 (20 mg) or placebo (7:1). After positive DSMB review the dose was escalated from 20 mg to 40 mg. A second cohort of 8 patients was randomized to VM-1500 (40 mg) or placebo (7:1).

Results: Seven patients who received 20 mg of VM-1500 for 7 days the average HIV-1 RNA decreased from 82,944 copies/ml to 2,133 copies/ml while one patient who received placebo, HIV-1 RNA was 303,000 copies/ml at day 1 and 248,000 copies/ml at days 8. The average CD4 increased from 551 cells/mm³ to 592 cells/mm³ in VM-1500 group and the CD4 of one patient in placebo arm was 492 cells/mm³ at day 1 and 517 cells/mm³ at day 8. For the second cohort with VM-1500 40 mg, 7 patients who received 40 mg of VM-1500 for 7 days the average HIV-1 RNA decreased from 93,671 copies/ml to 1,316 copies/ml while one patient who received placebo, HIV-1 RNA was 126,000 copies/ml at day 1 and 116,206 copies/ml at days 8. The average CD4 increased from 471 cells/mm³ to 525 cells/mm³ in VM-1500 group and the CD4 of one patient in placebo arm was 424 cells/mm³ at day 1 and 388 cells/mm³ at day 8. For the side effects, 3 patients in the first cohort (20mg) had mild dry mouth and polyuria, 1 patient had mild headache. However, patients in the second cohort (40mg) had no side effects for the whole seven days of VM-1500 treatment.

Conclusions: VM-1500 showed excellent activity with a 1.8 log reduction in HIV-1 RNA after 7 days of treatment with only minimal side effects. VM-1500 is a good once daily candidate NNRTI to treat HIV-infected patients.

Patients' characteristics, CD4, and HIV-1 RNA									
Group and Patient's number	HIV-1 RNA Day-1 copies/ml	HIV-1 RNA Day-8 copies/ml	CD4 Day 1 cell/mm ³	CD4 Day 8 cell/mm ³	Group and Patient's number	HIV-1 RNA Day-1 copies/ml	HIV-1 RNA Day-8 copies/ml	CD4 Day 1 cell/mm ³	CD4 Day 8 cell/mm ³
Group I VM-1500 20 mg	83,800	681	448	416	Group I VM-1500 40 mg	8,664	226	678	694
Group II VM-1500 20 mg	46,200	1,940	632	642	Group II VM-1500 40 mg	21,557	611	606	522
Group III VM-1500 20 mg	198,000	7,590	576	577	Group III VM-1500 40 mg	47,336	757	324	386
Group IV VM-1500 20 mg	17,200	281	908	1,103	Group IV VM-1500 40 mg	314,191	4,686	226	297
Group V VM-1500 20 mg	40,600	755	377	456	Group V VM-1500 40 mg	7,640	129	440	513
Group VI VM-1500 20 mg	188,000	3,390	491	528	Group VI VM-1500 40 mg	154,276	2,169	543	594
Group VII VM-1500 20 mg	6,810	294	424	424	Group VII VM-1500 40 mg	102,000	634	480	671
Group VIII VM-1500 20 mg	303,000	248,000	492	517	Group VIII VM-1500 40 mg	126,000	116,206	424	388