MOPEB0287

Dolutegravir-Lamivudine as initial therapy in HIV-1 infected, ARV-naïve patients: 96 week results of the PADDLE trial

Authors: M.I. Figueroa[1], M.J. Rolón[1], P. Patterson[1], A. Gun[2], P. Cahn[1], O. Sued[1]

Affiliation: [1]*Fundacion Huésped, Clinical Research, Buenos Aires, Argentina,* [2]*Fundacion Huesped, Laboratory research, Buenos Aires, Argentina*

Background:

Based on the results of the GARDEL trial, we designed a proof of concept study to evaluate the antiviral efficacy, safety and tolerability of a dual therapy regimen with Dolutegravir (DTG) 50 mg QD plus Lamivudine (3TC) 300 mg QD as initial HAART among ARV-naïve HIV-1 infected patients. Week 48 analysis was presented at AIDS 2016: 90% (18/20) reached the primary end point of a pVL <50 copies/mL. Week 96 results are reported here.

Methods:

Pilot study including 20 HIV-1 infected ARV-naïve adults. Eligible participants had no IAS-USA defined NRTI resistance, HIV-1 RNA <100,000 copies/mL at screening and negative HBsAg. Four patients had pVL > 100,000 copies/mL at baseline. Viral load (pVL) was measured at baseline, on days 2, 4, 7, 10, 14, 21, 28 and on weeks 6, 8, 12, and thereafter every 12 weeks up to 96 weeks.

Primary endpoint was the proportion of patients with HIV-1 RNA <50 copies/mL in an ITT-exposed analysis at 48 weeks and week 96 (FDA-snapshot algorithm).

Results:

Eighteen patients completed 48 weeks and were included in the extension phase. All patients completed week 96, 100% maintained plasma HIV-1 RNA below 50 copies/mL. Two patients required viral load retest due to blips (Table 1). Mean CD4+ increase between baseline and week 96 was 271 cell/mm³, without change between 48 and 96 weeks (Figure 1). No new virologic failures, no new AIDS defining illnesses, or SAEs (related/possibly related to study drugs) were observed. No Treatment discontinuations were reported through the extension phase. Two grade 3 laboratory abnormalities were reported (high cholesterol and proteinuria), but considered unrelated to study drug.

Table 1:

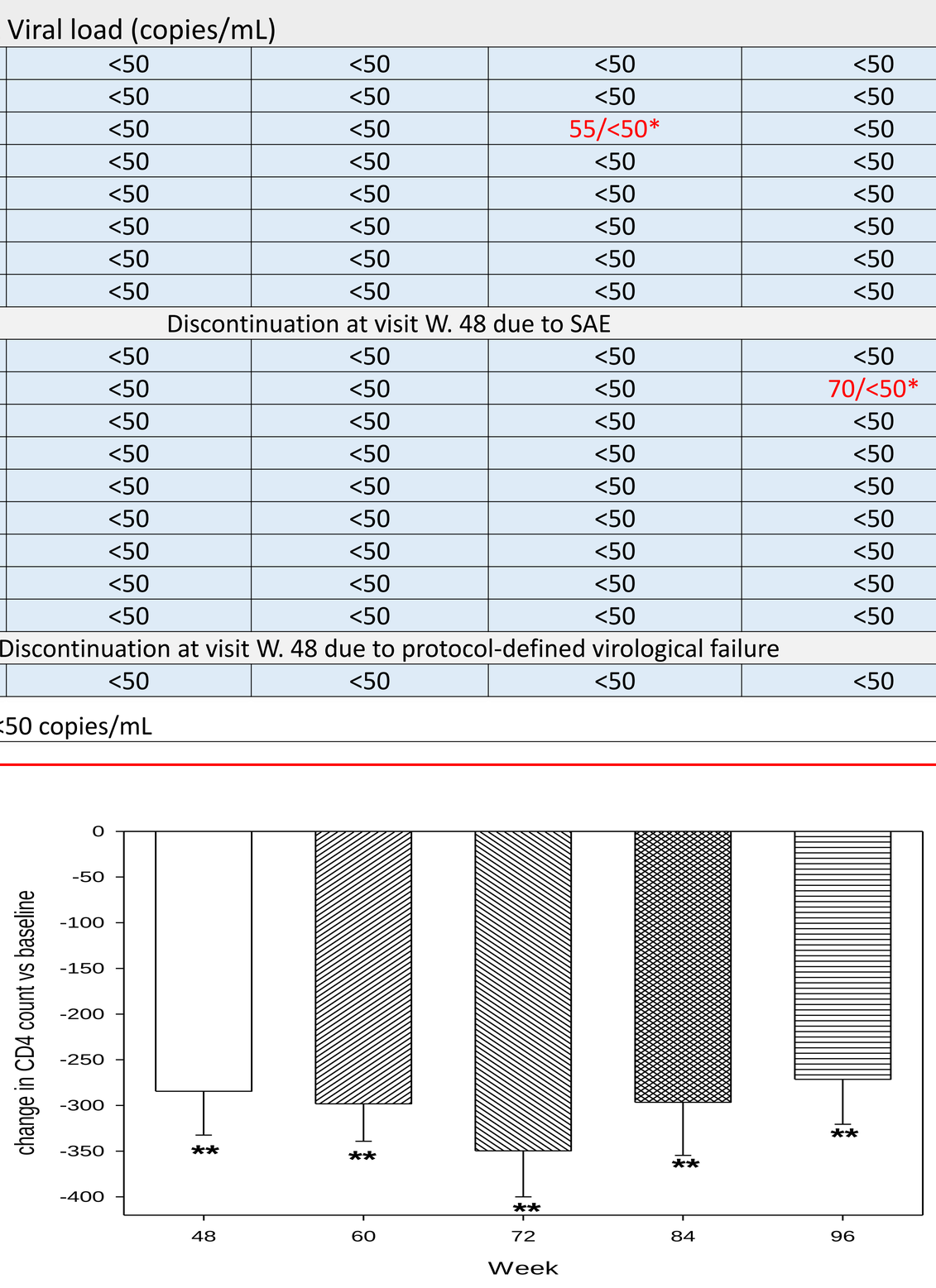
Viral load values at baseline and weeks 48, 60, 72, 84 and 96 (copies/mL).

Patient Nr.	BSL	W. 48	W. 60	W.72	W. 84	W. 96
HIV-1 Viral load (copies/mL)						
01	10,909	<50	<50	<50	<50	<50
02	10,233	<50	<50	<50	<50	<50
03	151,569	<50	<50	<50	55/<50*	<50
04	148,370	<50	<50	<50	<50	<50
05	20,544	<50	<50	<50	<50	<50
06	14,499	<50	<50	<50	<50	<50
07	18,597	<50	<50	<50	<50	<50
08	24,368	<50	<50	<50	<50	<50
09	10,832	Discontinuation at visit W. 48 due to SAE				
10	7,978	<50	<50	<50	<50	<50
11	273,676	<50	<50	<50	<50	70/<50*
12	64,103	<50	<50	<50	<50	<50
13	33,829	<50	<50	<50	<50	<50
14	15,151	<50	<50	<50	<50	<50
15	23,400	<50	<50	<50	<50	<50
16	3,910	<50	<50	<50	<50	<50
17	25,828	<50	<50	<50	<50	<50
18	73,069	<50	<50	<50	<50	<50
19	106,320	Discontinuation at visit W. 48 due to protocol-defined virological failure				
20	7,368	<50	<50	<50	<50	<50

*Two patients required retest of viral load due to blips. VL retests were <50 copies/mL

Figure 1:

Change in CD4 count vs BSL (mean ± standard error of the mean. A significant change in CD4 count was found (p<0.001). Post-hoc comparisons were performed by means of Bonferroni test. **p<0.01 vs BSL. No differences were found between weeks 48, 60, 72, 82 and 96.



Conclusion:

In this pilot study, dual therapy with DTG+3TC demonstrated efficacy, safety, tolerability and durability through 96 weeks of treatment. This strategy is being explored in a large randomized double blinded trial.