

# DRV CONCENTRATIONS AND VIRAL LOAD IN CSF OF PATIENTS ON DRV/r 600/100 OR 800/100 mg ONCE DAILY, PLUS TWO NRTI

Di Yacovo S<sup>1</sup>, Moltó J<sup>2</sup>, Ferrer E<sup>1</sup>, Curran A<sup>3</sup>, Else L<sup>4</sup>, Clotet B<sup>2</sup>,  
Tiraboschi J<sup>1</sup>, Niubó J<sup>1</sup>, Barrera G<sup>1</sup>, Podzamczer D<sup>1</sup>.

<sup>1</sup>Hospital Universitari de Bellvitge, <sup>2</sup>Germans Triás, <sup>3</sup>Vall d'Hebron, Barcelona, Spain, and <sup>4</sup>University of Liverpool, UK.



# BACKGROUND

- Darunavir/r (DRV/r) is currently used at a dose of 800/100 mg once daily (OD) in a high proportion of patients
- Pharmacokinetic data suggest that 600/100 OD may be effective, reducing toxicity and cost
- However, drug concentrations in reservoirs such as cerebrospinal fluid (CSF) might not be adequate to inhibit viral replication

# OBJECTIVE

- **The objective of this substudy is to assess if a reduced dose of DRV/r may still achieve good CSF concentrations and contribute to inhibit viral replication in CNS.**

# PATIENTS AND METHODS (I)

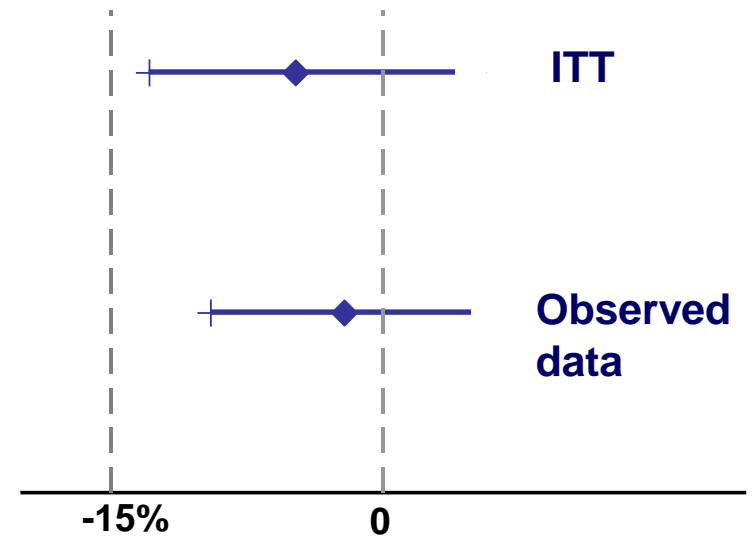
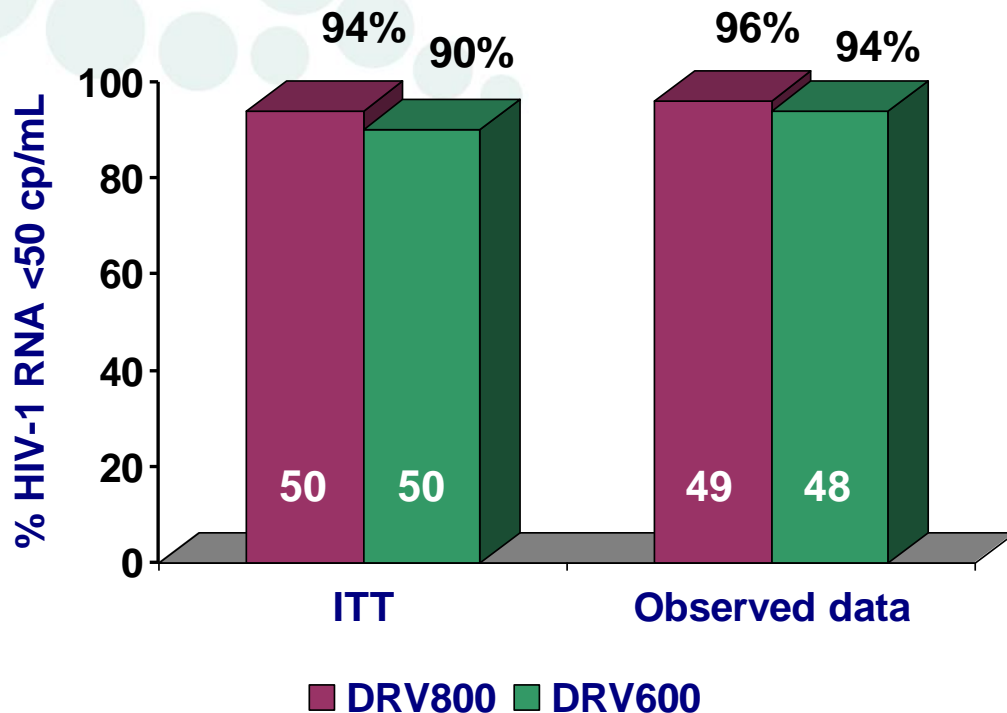
- **Design** : Substudy of the DRV600 study (eudraCT 2011-006272-39). DRV600 is an ongoing randomized open clinical trial comparing DRV/r 800/100 mg (DRV800) vs. 600/100 mg (DRV600) OD plus TDF/FTC or ABC/3TC in 100 virologically suppressed patients

*(Moltó J, et al. 15th IWCPHHT, Washington, May 2014)*

- **Setting**: Hospital Universitari de Bellvitge, Hospital Germans Trías, Hospital Vall d'Hebron, Spain, University of Liverpool, UK.

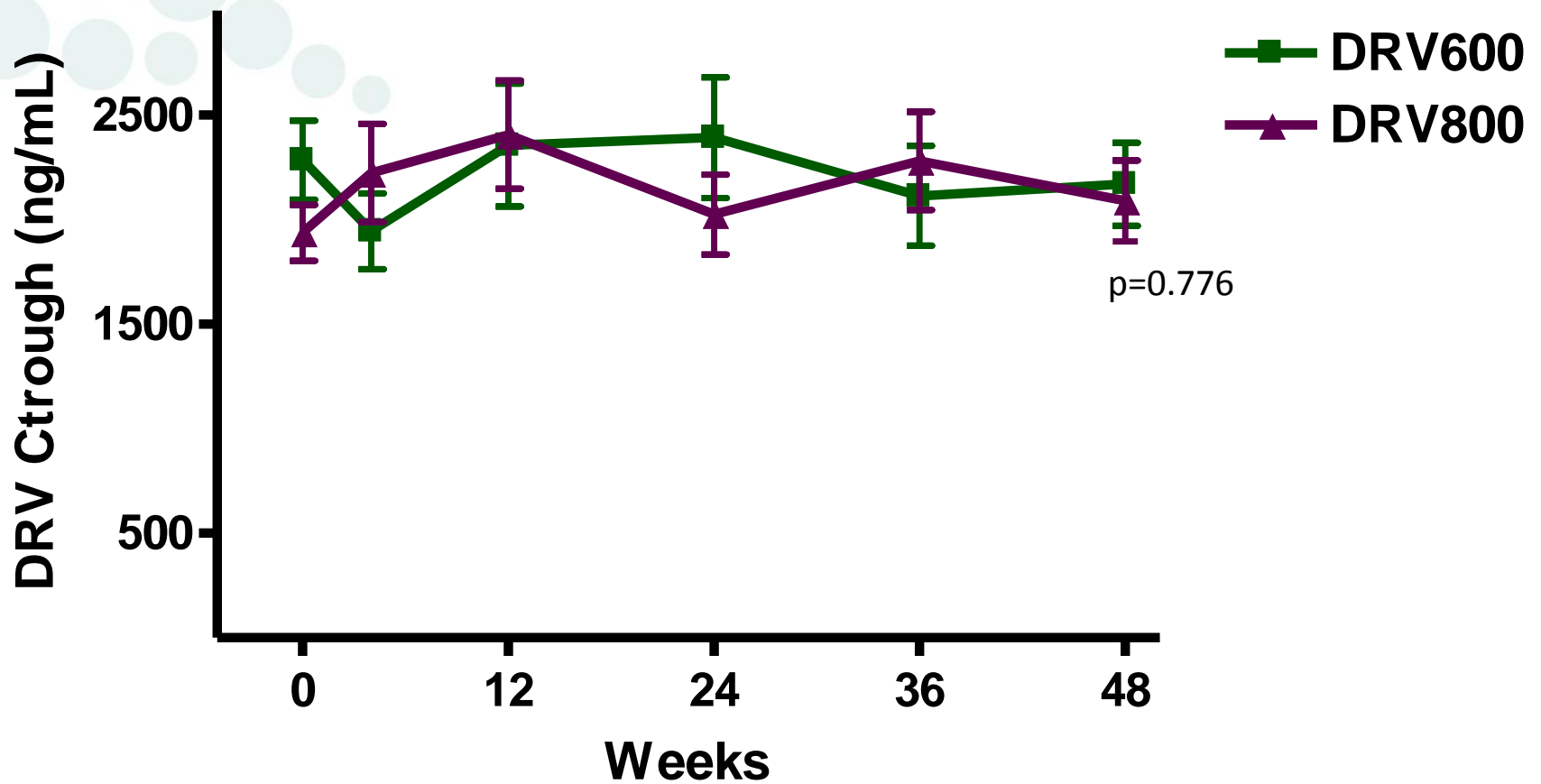
# Results w48

## Non inferiority of DRV/r 600/100 mg QD



	95% CI for the difference
ITT	-4.0 (-12.9; 4.9)
Observed data	-2.2 (-9.6; 5.2)

# Pharmacokinetics. DRV C<sub>trough</sub>



# PATIENTS AND METHODS (I)

- **Design** : Substudy of the DRV600 study (eudraCT 2011-006272-39). DRV600 is an ongoing randomized open clinical trial comparing DRV/r 800/100 mg (DRV800) vs. 600/100 mg (DRV600) OD plus TDF/FTC or ABC/3TC in 100 virologically suppressed patients

*(Moltó J, et al. 15th IWCPHHT, Washington, May 2014)*

- **Setting**: Hospital Universitari de Bellvitge, Hospital Germans Trías, Hospital Vall d'Hebron, Spain, University of Liverpool, UK.

# PATIENTS AND METHODS (II)

- **Patients:** 16 asymptomatic and virologically suppressed HIV-infected patients were included (8 in each arm). All DRV600 patients and 4 out of 8 DRV800 patients received TDF/FTC, and the other 4 patients, ABC/3TC.
- **Procedures:** Paired blood and CSF samples were obtained between 24 and 28 hours after the previous DRV dose by peripheral venous puncture and by LP, respectively. Samples were centrifuged and frozen at  $-70^{\circ}$  C until analysis.



# PATIENTS AND METHODS (III)

- Total DRV concentrations were determined in plasma by high-performance liquid chromatography (HPLC; LLQ = 50 ng/ml) and in CSF by liquid chromatography-tandem mass spectrometry (LC-MS/MS; LLQ = 2 ng/ml)
- The HIV-1 VL in plasma and CSF (LOD 40 copies/mL) was quantified using a real-time PCR technique (Abbot Molecular, Des Plaines, IL, USA), performed according to the manufacturer's recommendations

# BASELINE CHARACTERISTICS

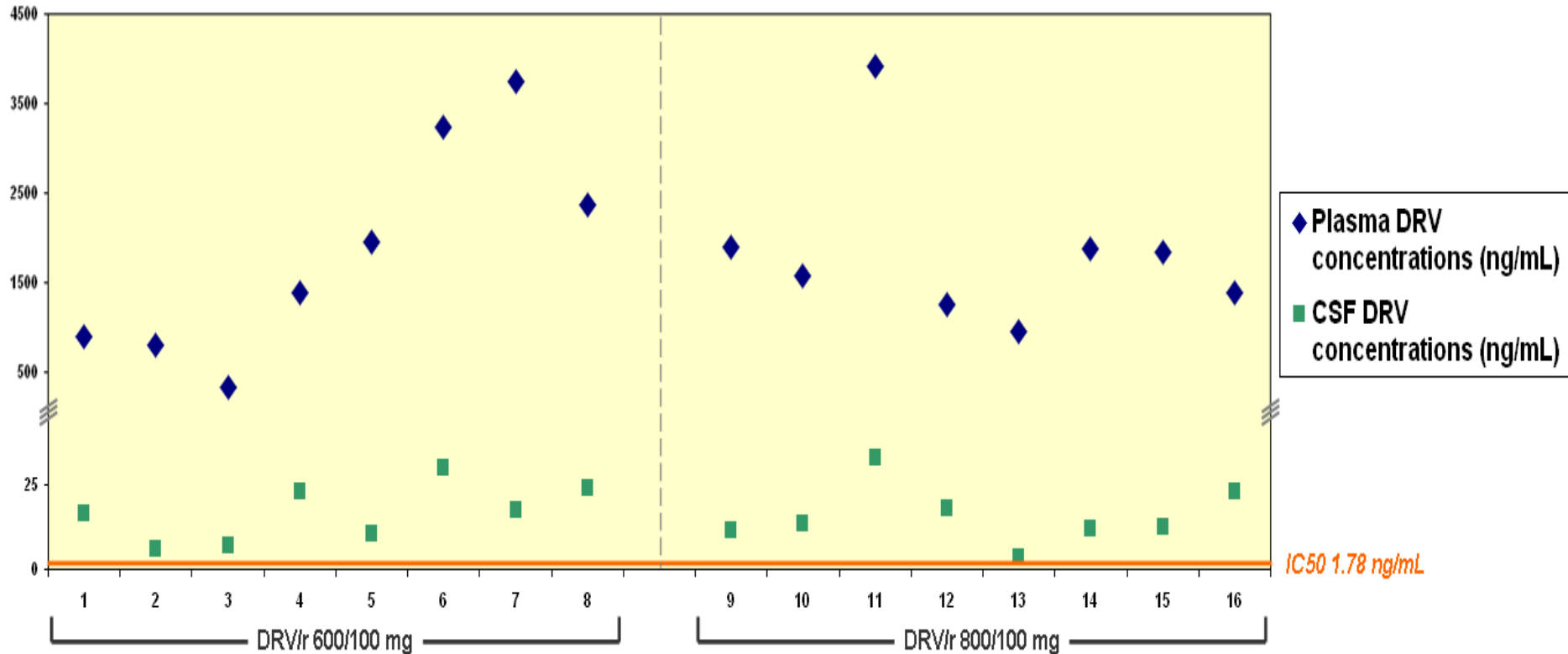
Number	Age	Gender	Risk group	CD4 Count (cel/uL)	Months under DRV	Plasma VL (cop/ml)	cART
1	71	Male	Heterosexual	207	12	<40	600/100+ TDF/FTC
2	36	Male	Homosexual	247	12	<40	600/100+ TDF/FTC
3	48	Male	Homosexual	330	11	<40	600/100+ TDF/FTC
4	50	Male	Drug user	617	8	<40	600/100+ TDF/FTC
5	27	Female	Heterosexual	527	10	<40	600/100+ TDF/FTC
6	43	Male	Heterosexual	190	10	<40	600/100+ TDF/FTC
7	58	Male	Heterosexual	360	7	<40	600/100+ TDF/FTC
8	64	Female	Heterosexual	1394	7	<40	600/100+ TDF/FTC
<b>Median (range)</b>	<b>49 (27-71)</b>			<b>345 (190-1394)</b>	<b>10 (7-12)</b>	<b>&lt; 40</b>	
9	34	Female	Heterosexual	549	12	<40	800/100+ TDF/FTC
10	61	Male	Unknown	451	9	<40	800/100+ TDF/FTC
11	41	Male	Homosexual	674	9	<40	800/100+ ABC/3TC
12	69	Male	Homosexual	1380	6	<40	800/100+ TDF/FTC
13	38	Male	Heterosexual	300	11	<40	800/100+ TDF/FTC
14	48	Female	Heterosexual	1000	7	<40	800/100+ ABC/3TC
15	17	Male	Heterosexual	536	7	<40	800/100+ ABC/3TC
16	52	Male	Heterosexual	612	7	<40	800/100+ ABC/3TC
<b>Median (range)</b>	<b>44 (17-69)</b>			<b>581 (300-1380)</b>	<b>8 (6-12)</b>	<b>&lt; 40</b>	

VL (Viral load); cART (combined Antiretroviral therapy) ; TDF/FTC (Tenofovir/Emtricitabin); ABC/3TC (Abacavir/lamivudin)

# CD4 AND VIRAL LOAD RESPONSES

cART	Number	Post doses time (Hours)	Plasma VL copies/mL	Plasma DRV (ng/ml)	CSF VL copies/mL	CSF DRV (ng/ml)	CSF:Plasma Ratio
600/100+ TDF/FTC	1	26	<40	896	<40	16.62	0.019
	2	27	<40	802	280	5.79	0.007
	3	28	<40	326	<40	7.14	0.022
	4	25	<40	1390	<40	23.04	0.017
	5	24	<40	1957	<40	10.56	0.005
	6	26	<40	3235	<40	30.19	0.009
	7	26	<40	3742	<40	17.54	0.005
	8	26	<40	2363	<40	23.99	0.010
cART	<b>Median (range)</b>	<b>26 (24-28)</b>	<b>&lt;40</b>	<b>1674 (326-3742)</b>	<b>&lt;40 (40-280)</b>	<b>17.08 (5.79-30.19)</b>	<b>0.010 (0.004-0.022)</b>
800/100+ ABC/3TC	9	26	<40	1890	<40	11.42	0.006
	10	26	<40	1569	<40	13.81	0.009
	11	24	<40	3910	<40	32.98	0.008
	12	26	<40	1258	<40	17.96	0.014
	13	24	<40	958	159	3.47	0.004
	14	26	<40	1876	<40	12.02	0.006
	15	28	<40	1845	<40	12.65	0.007
	16	25	<40	1389	<40	23.12	0.017
	<b>Median (range)</b>	<b>26 (24-28)</b>	<b>&lt;40</b>	<b>1707 (958-3910)</b>	<b>&lt;40 (40-159)</b>	<b>13.23 (3.47-32.98)</b>	<b>0.008 (0.004-0.017)</b>

# PLASMA AND CSF DRV CONCENTRATIONS



# CONCLUSIONS

- DRV concentrations and CSF VL were similar between patients receiving DRV/r 800/100 mg or 600/100 mg OD
- Low CSF DRV concentrations may be associated with viral escape in CNS
- This may be taken into account in patients receiving OD DRV/r
- Larger studies should confirm these findings