

Adherence, Treatment Satisfaction and Effectiveness Of Once-Daily (QD) Vs Twice-Daily (BID) Antiretroviral Therapy (AT), in a Large Prospective Observational Cohort (CUVA Study)

Arribas JR*, Iribarren JA**, Knobel H¹, Ribera E³, Rubio R[#], Viciano P[¶] and Pérez-Molina JA[†] on behalf of CUVA Study Group

*H. La Paz, Madrid; **H. de Donostia, San Sebastián; ¹H. del Mar, Barcelona; ³H. Vall d'Hebrón, Barcelona; [¶]H. Doce de Octubre, Madrid; [†]H. Virgen del Rocío, Sevilla. [#]Bristol-Myers Squibb, Madrid, Spain (jose.perezmolina@bms.com)

Background

- Although HAART therapy has improved drastically the prognosis of patients infected by HIV, the eradication of the infection is not possible with the therapies available at the present time. For this reason, HAART contemplates the very long term, often with complex regimens.
- Adherence is one of the fundamental factors of therapeutic effectiveness. Simplicity, as well as a low number of tablets, good tolerability and little toxicity has been related to therapeutic success and reduction of mortality. All these reasons justify the present tendency towards a simplification of antiretroviral treatment with effective but convenient regimen for the patient.

Objective

- This study began when experience with QD antiretroviral therapies was still limited, so the principal aim was to describe and evaluate treatment satisfaction and adherence, as well as effectiveness, of a number of QD and BID therapies in real life conditions.

Methods

- Non-interventional, multicenter, prospective and longitudinal cohort study that compares two antiretroviral treatment schedules: administration of HAART once daily (QD) vs. twice daily (BID). Inclusion period: May-December of 2002. Patients made three visits (baseline, three and six months) in which clinical, analytical and adherence data were collected. To assess adherence a structured validated questionnaire was used (GEEMA test), and to assess treatment satisfaction a visual analogical scale was used by independent consultants who interviewed all patients at six months.
- Multivariate models were fitted on observed data to find factors predictive of adherence, treatment satisfaction and treatment effectiveness.

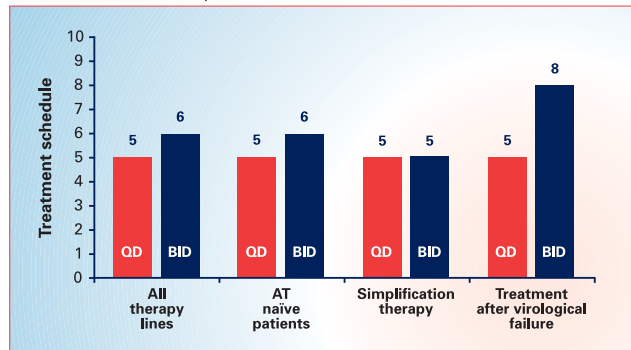
Results

- 88 investigators in 55 hospitals participated and collected information from 978 patients.

Table 1. Baseline characteristics

Basal characteristics	AT naive patients		Simplification therapy		Treatment after virological failure	
	QD	BID	QD	BID	QD	BID
Pt distribution (n=978)	123	124	372	140	116	103
Male sex (%)	73.2	71.8	73.7	75.0	68.7	69.9
Median age (year)	39	38	40	40	38	40
Risk behaviour (%)						
IVDU	39.8	30.6	42.5	45.7	59.1	56.3
Heterosexual	27.6	37.1	27.4	21.4	21.7	28.2
Homo/bisexual	22.8	20.2	23.4	22.1	13.0	11.7
IVDU+sexual	5.7	8.1	3.0	4.3	2.6	1.9
Other/Unknown	4.1	4.0	3.8	6.4	0.9	1.9
AIDS diagnosis at baseline (%)	28.5	33.9	33.9	40.0	43.0	31.3
Baseline CD4 μ L	210	176	486	516	313	261
Baseline viral load Log	5.36	5.53	3.89	3.28	4.85	5.12

Chart 1. Median number of pills in QD/BID HAART



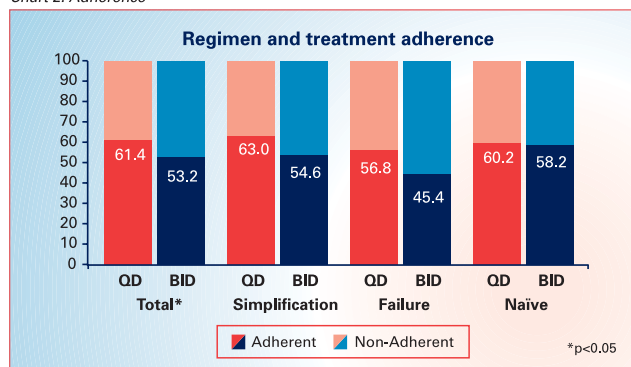
- This study was carried out when new formulations for some antiretrovirals were still unavailable (e.g.: efavirenz or lamivudine formulated in one pill, once daily), or tenofovir was not approved in first line therapy. This drove median number of pills higher than in current practice.
- Most frequent therapies in QD and BID schedules were:
 - QD: ddI+3TC+EFV (30.2%), TDF+3TC+EFV (25.7%) and ddI+TDF+EFV (11.1%).
 - BID: ddI+d4T+EFV (25.8%), d4T+3TC+EFV (15.9%), ddI+3TC+EFV (9.8%), ddI+TDF+LPV/r (7.6%), ZDV+3TC+LPV/r (6.8%) and 3TC+d4T+LPV/r (6.1%).

Table 2. Immunovirological outcome at six months (on treatment analysis)

	Therapeutic schedule		Total
	QD	BID	
AT naive patients			
% below 400 cop/ml	80.7	86.4	83.7
Average decrease in viral load	-1.2 log	-1.4 log	-1.4 log
Average increase in CD4 count	+122	+125	+125
Simplification therapy*			
% below 400 cop/ml	86.4	90.4	87.5
Average decrease in viral load	-0.7	+0.6	-0.3
Average increase in CD4 count	+20	+14	+16
Treatment after virological failure			
% below 400 cop/ml	57.1	57.8	57.4
Average decrease in viral load	-0.8 log	-0.8 log	-0.8 log
Average increase in CD4 count	+52	+79	+70

*Simplification therapy was allowed for those patients with less than 2,000 cop/mL

Chart 2. Adherence



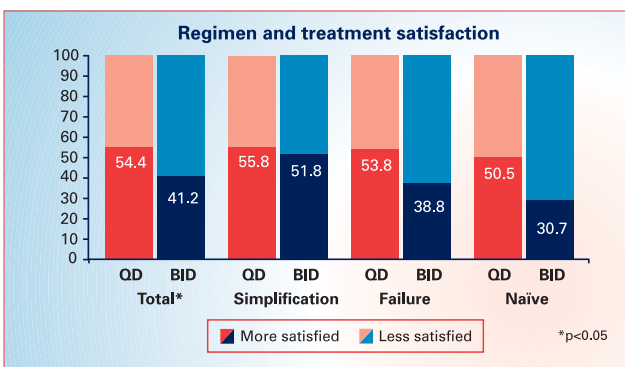
Results (cont.)

- Adherence was significantly better in QD than in BID therapies (p<0.05).
- The proportion of patients with viral load <400 copies/ml at six months was higher in those defined as adherent compared to non-adherent patients:
 - AT naive patients: 86.2% vs. 78.9% (p non significant).
 - Simplification: 91.4% vs. 83.4% (p<0.05).
 - Treatment after virological failure: 64.4% vs. 49.4% (p<0.05)

Table 3. Quality of life. Patient's treatment evaluation

Treatment evaluation (Median values - scale 1 - 10)	Total (n=978) (median)	QD (n=611) (median)	BID (n=367) (median)
In general	7.8	7.9	7.7
Efficacy against HIV	7.9	7.9	7.9
Convenient and simplicity to fulfil treatment	8.2	8.4	7.8
Tolerance	8.0	8.1	7.8
Effort needed	1.6	1.4	2.3
Able to continue correctly	9.0	9.0	9.0
Satisfaction index	8.2	8.3	7.9

Chart 3. Patient's treatment satisfaction



- The proportion of patients over the median satisfaction index was significantly better for QD than BID therapies (p<0.05).

Multivariate analysis

Factors related to treatment adherence (GEEMA Test)				
Constant = 0.1775				
	OR	95% CI		p
Treatment satisfaction	1.53	1.30	1.80	<0.0001
Family support	1.25	0.98	1.61	0.0769
Years of HIV infection (per year)	0.97	0.94	1.003	0.0763
IVDU	0.83	0.70	0.99	0.0384

Factors related to treatment satisfaction				
Constant = 0.5403				
	OR	95% CI		p
Simplification therapy	1.70	1.22	2.34	0.0016
QD therapy	1.33	1.13	1.56	0.0007
Years of HIV infection (per year)	0.95	0.92	0.98	0.0064
AIDS at baseline	0.85	0.73	1.01	0.0518

Factors related to viral load <400 copies/ml at 6 months				
Constant = -0.074				
	OR	95% CI		p
AT naive patient	5.08	3.14	8.22	<0.0001
Treatment adherent	1.57	1.13	2.17	0.0069

Conclusions

- "Early" once-daily antiretroviral therapies appear as effective as BIDs, improving significantly adherence and treatment satisfaction. This could positively affect treatment efficacy given that these features are the cornerstone for HAART success in the long term.
- The improvement in treatment adherence and quality of life, was mainly due to the QD nature of the therapy, given that these "early" once-daily AR therapies did not differ substantially with BID therapies in pill burden.
- The reduction in pill burden with the new formulations will make antiretroviral therapy easier, probably improve adherence and even efficacy.

CUVA Study Group:

Medical Researchers

- Alonso Villaverde Carlos
- Antela López Antonio
- Arranz Caso Alberto
- Arribas López José Ramón
- Barberá Gracia M[¶] Jesús
- Barreiro García Pablo
- Barros Aguado Carlos
- Berdún Chélez Miguel Ángel
- Blanch Falp Jesús
- Blanch Sancho José Javier
- Carmena Carmena Jorge
- Casado Osorio José Luis
- Casas García Esperanza
- Castro Iglesias Ángeles
- Cervero Jiménez Miguel
- Clotet Sala Bonaventura
- Condes Emilia
- Cuadra García-Tenorio Fernando
- De Otero Blasco Jordi
- Del Castillo Amaro Rafael
- Domingo Pedrol Pere
- Drona Álvarez Fernando
- Echevarría Vienna Santiago
- Elizaga Corrales Jorge
- Falco Ferrer Vincent
- Fernández Guerrero Manuel
- Ferrer Corberá Elena
- Flores Cid Juan
- Fumero Emilio
- Fuster Casas Montserrat
- García-Alcalde M[¶] Luisa
- Geijo Martínez Paloma
- González Luis
- Guellar Ginberg Ana
- Gutiérrez Rodero Félix
- Iribarren Loyarte José Antonio
- Kindelán Jaquotot José M[¶]
- Knobel Freud Hernando
- La Cruz Rodrigo José
- La Fuente García Belén
- López Calvo Soledad
- López Gómez Manuel
- López Ruz Miguel Ángel
- Losada Arias Elena
- Lozano de León Fernando
- Mariño Callejo Ana
- Martín Jiménez Teodoro
- Martínez Alfaro Elisa
- Menéndez Martínez M[¶] Antonia
- Miralles Álvarez Celia
- Moltó José
- Moreno Torrico Alfonso
- Moreno Zamora Ana
- Ocampo Herrada Antonio
- Ocaña Rivera Inmaculada
- Orti Llaverría Amat
- Pascual Liaño Francisco
- Pascual Liaño Juan
- Pedrol Clotet Enriq
- Pérez Cecilia Elisa
- Pérez Guzmán Eugenio
- Prieto Martínez Arturo
- Podzameczer Palter Daniel
- Portu Zapirain Joseba
- Pulido Ortega Federico
- Ribera Pascuet Esteve
- Ricart Olmos Carmen
- Riera Jaume Melcior
- Roca Arbones Victor
- Rosón Hernández Beatriz
- Rubio García Rafael
- Salas Aparicio Ana
- Sambat Doménech Maria
- Sánchez Ayuso Javier
- Sánchez del Río Jesús
- Sánchez Navarro Jacinto
- Santos Gil Ignacio
- Santos González Jesús
- Sanz Moreno José
- Sarriá Cepeda Cristina
- Serrano Herranz Regino
- Soler Sandra Ana
- Suárez Lozano Ignacio
- Teira Cobo Ramón
- Terrón Pernia Alberto
- Valencia Ortega Eulalia
- Vicente Ull Rogelio
- Viciano Pompeyo

Social Support Committee

- Aja Azucena
- López Muniain Peio
- Segador Auri
- Tuldrá Albert