

Cost-efficacy analysis of the MONET trial using German antiretroviral drug prices

Matthias Stoll, Medical University, Hannover, Germany, Andrew Hill, Pharmacology Research Laboratories, University of Liverpool, UK, Anne Anceau, Janssen-Cilag, Issy Les Moulineaux, France, Christiane Moecklinghoff, Janssen-Cilag EMEA, Neuss, Germany

Introduction

In the MONET trial recruited 256 patients with HIV RNA <50 copies/mL for over 24 weeks (NNRTI based (43%), or PI based (57%)).

Patients were switched to darunavir/ritonavir (DRV/r) 800/100 mg once daily, either as monotherapy (n=127) or with 2NRTI (n=129). Patients were followed up every three months, which is similar to routine clinical practice.

In the primary efficacy analysis, HIV RNA <50 copies/mL by Week 48 (per protocol, switch equals failure analysis) was 86.2% for DRV/r monotherapy versus 87.8% for triple therapy, proving non-inferior efficacy.

By switch included analysis, where responses at Week 48 were included if patients had switched to other treatments, efficacy was 93.5% versus 95.1%.

Nine patients in each arm had serious adverse events. No patients in either arm developed phenotypic resistance to DRV.

The aim of this analysis was to calculate the potential cost-savings from using DRV/r monotherapy versus standard triple combinations of antiretrovirals.

Methods

The German costs per patient with HIV RNA below 50 copies/mL were calculated, using a "switch included" analysis, to account for additional antiretrovirals taken after treatment switches.

Costs were based on *Pharmacy Purchase Prices Germany Lauer-Taxe* (www.lauer-fischer.de). This analysis only looked at antiretroviral drug costs.

If patients intensified with NRTIs or switched treatment during the trial, the costs of the new antiretrovirals were also included.

Results

Table 1: MONET trial: Baseline characteristics by treatment arm (ITT population)

	DRV/r mono n=127	Triple therapy n=129
Mean age, years	43	44
Gender (% male)	78%	83%
Race (% Caucasian)	92%	90%
IV drug user (%)	16%	9%
Mean weight (kg)	72	75
Mean CD4 count (cells/uL)	571	579
HCV antibody positive	17%	9%
Known duration of HIV infection (years)	9.1	7.5
Duration of ARV treatment (years)	7.4	5.9
PI naive at screening (%)	23%	28%
PI-based HAART at screening (%)	56%	57%
NNRTI-based HAART at screening (%)	44%	43%

Table 2: Percentage of patients using different antiretrovirals during the trial:

	DRV/r mono N=127		DRV/r+2NRTI N=129	
Abacavir	0	(0.0%)	3	(2.3%)
ZDV/3TC	2	(1.6%)	15	(11.6%)
Didanosine	0	(0.0%)	2	(1.6%)
Emtricitabine	7	(5.5%)	9	(7.0%)
ABC/3TC	4	(3.1%)	42	(32.6%)
Lamivudine	2	(1.6%)	18	(14.0%)
Stavudine	0	(0.0%)	5	(3.9%)
Tenofovir	9	(7.1%)	20	(15.5%)
ZDV/ABC/3TC	0	(0.0%)	0	(0.0%)
TDF/FTC	4	(3.1%)	56	(43.4%)
Zidovudine	0	(0.0%)	2	(1.6%)
Darunavir/r	127	(100.0%)	129	(100.0%)

Table 3: Annual cost per person of antiretrovirals in Germany

Antiretroviral	Daily Cost	Annual Cost
Abacavir	€ 12.06	€ 4,402
Combivir	€ 18.37	€ 6,705
Didanosine	€ 10.33	€ 3,770
Emtricitabine	€ 7.91	€ 2,887
Abacavir + lamivudine	€ 20.35	€ 7,428
Lamivudine	€ 8.03	€ 2,931
Stavudine	€ 9.52	€ 3,475
Tenofovir	€14.07	€ 5,136
ZDV + ABC + 3TC	€ 32.97	€ 12,034
Tenofovir + emtricitabine	€ 21.94	€ 8,008
Zidovudine	€10.07	€ 3,676
Darunavir/r 800/100 QD	€25.21	€ 9,202
Lopinavir/r	€ 22.87	€ 8,348
Efavirenz	€ 11.50	€ 4,198

Table 4 shows the costs of treatment before and during the trial, for patients who were taking a PI based HAART or NNRTI based HAART at the screening visit.

Patients taking a PI based HAART regimen before the MONET trial had a mean cost of 15,856 Euro per year at screening. The cost of antiretrovirals fell by 41% to 9,299 Euro in the DRV/r monotherapy arm, but rose slightly to 16,817 Euro in the triple therapy arm. For patients who were taking a PI based HAART regimen at screening, the cost of the DRV/r monotherapy arm was 45% lower than the cost of the 2NRTI + DRV/r arm.

Patients taking an NNRTI based HAART regimen before the MONET trial had a mean cost of 12,109 Euro per year at screening. The cost of antiretrovirals fell by 24% to 9,176 Euro in the DRV/r monotherapy, but rose to 16,082 Euro in the triple therapy arm. For patients who were taking an NNRTI based HAART regimen at screening, the cost of the DRV/r monotherapy arm was 43% lower than the cost of the 2 NRTI + DRV/r arm.

Table 4: mean costs of treatment (per patient year) by treatment arm

PI based HAART at screening	DRV/r N=68	DRV/r +2 NRTI N=70
Screening PI	€ 8,348	€ 8,348
Screening NNRTI	€ 0	€ 0
Screening NRTI	€ 7,537	€ 7,481
Total costs at screening	€15,884	€15,829
Treatment PI	€ 9,061	€ 9,086
Treatment NRTI	€ 237	€ 7,731
Total costs during MONET trial	€ 9,299	€16,817
NNRTI based HAART at Screening	DRV/r N=55	DRV/r +2 NRTI N=53
Screening PI	€ 0	€ 0
Screening NNRTI	€ 4,198	€ 4,198
Screening NRTI	€ 7,949	€ 7,873
Total cost at screening	€12,146	€12,071
Treatment PI	€ 8,550	€ 8,564
Treatment NRTI	€ 625	€ 7,518
Total cost during MONET trial	€ 9,176	€16,082

Cost per patient with HIV RNA <50 copies/mL

Table 5 shows the annual cost per patient with HIV RNA <50 copies/mL at Week 48. Overall, the mean annual cost of treatment per patient was 9,244 Euro in the monotherapy arm and 16,500 Euro in the triple therapy arm, a difference of 44%.

The mean cost per patient maintaining HIV RNA <50 copies/mL at Week 48 was Euro 9,887 in the monotherapy arm versus Euro 17,347 in the triple therapy arm (switch included analysis).

Assuming a fixed budget of 1 million Euros, 108 patients could be treated with DRV/r monotherapy: 101 of these patients would be expected to maintain HIV RNA levels below 50 copies/mL after 48 weeks of treatment. By contrast a fixed budget of 1 million Euros would be sufficient to treat only 60 patients with DRV/r plus 2 NRTIs: 57 of these patients would then be expected to have HIV RNA levels below 50 copies/mL at Week 48. 76% more patients could be treated successfully for a fixed budget for 1 million Euro

Figure 1: Mean annual cost of antiretrovirals by treatment arm

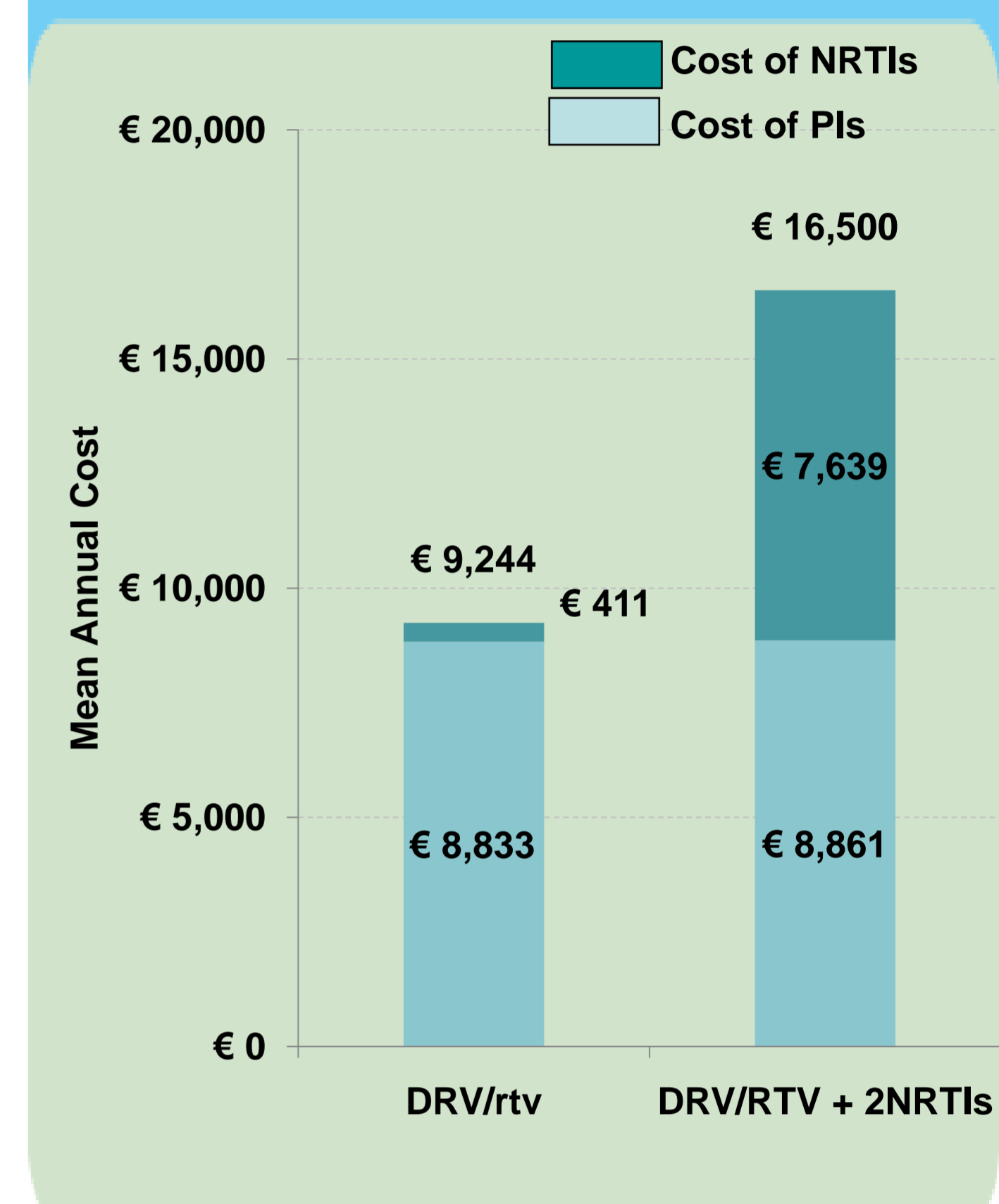


Table 5: Cost per patient with HIV RNA <50 copies/mL at Week 48 (Switch included analysis)

Total	DRV/r	DRV/r+ 2 NRTI
Mean Annual Cost	€ 9,244	€ 16,500
Number treated for € 1,000,000	108.2	60.6
% Success	93.5%	95.1%
Number of Successes	101.1	57.6
Cost per success	€ 9,887	€ 17,347

Conclusions

Based on the MONET results, the lower cost of DRV/r monotherapy versus triple therapy in Germany would allow 76% more patients to be treated for a fixed 1 million Euro budget, while maintaining HIV RNA suppression below 50 copies/mL.

DRV/r monotherapy was also cheaper than either the NNRTI based HAART or PI based HAART which patients received at screening.

The MONET trial assessed DRV/r monotherapy as a switch option for patients with HIV RNA levels below 50 copies/mL at screening and no history of virological failure. These results cannot be extrapolated to other populations, such as naïve patients, or experienced patients with detectable HIV RNA levels.