POSTER SESSION III
Poster # PIN48

Comparative Cost-Efficacy Analysis of Darunavir/r and Other Ritonavir-Boosted Protease Inhibitors for First-Line Treatment of HIV-1 Infection in Germany

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Background

- Once-daily darunavir (PREZISTA), in combination with low-dose ritonavir (/r) and nucleoside reverse transcriptase inhibitors (NRTIs), has demonstrated robust efficacy among treatment-naïve adults with HIV-1 infection.[1]
- A comparison of the cost and efficacy of all available boosted protease inhibitors (PIs) used in first-line treatment is important to help health care decision makers identify the value of once-daily darunavir/r and other ritonavir-boosted PIs in first-line treatment.

Objective

The objective of the economic model was to perform an integrated comparison of the cost and virologic efficacy of darunavir/r 800/100 mg once daily (QD) and the other ritonavir-boosted PIs currently licensed for use as first-line highly active antiretroviral therapy (HAART) in treatment-naïve adults with HIV-1 infection in Germany. The model also assessed the impact of the introduction of darunavir/r 800/100 mg QD on the efficiency frontier of first-line PI-based HAART. The model took a payer perspective.

Methods

Comparators

- Darunavir/r 800/100 mg QD
- Lopinavir/r 800/200 mg total daily dose (400/100 mg twice daily [BID] or 800/200 mg QD)
- Fosamprenavir/r 1400/100 mg QD or 1400/200 mg QD
- Atazanavir/r 300/100 mg QD
- Saquinavir/r 1000/100 mg BID

All boosted PIs were used in combination with a dual NRTI backbone:

- In the base-case analysis, tenofovir disoproxil fumarate plus emtricitabine (TDF/FTC) 300/200 mg QD or TDF 300 mg plus lamivudine (TDF/3TC) 300 mg QD;
- In the scenario analysis, TDF/FTC, TDF/3TC, or abacavir plus lamivudine (ABC/3TC) 600/300 mg QD.

Virologic Efficacy

- The percentage of individuals with a virologic response (i.e., plasma HIV-1 RNA < 50 copies/mL) was calculated using the intention-to-treat time to loss of virologic response (also known as ITT-TLOVR) analytic algorithm at 48 weeks of therapy.
- Data were obtained from a systematic review and meta-analysis of recently published trials of boosted PI regimens used in first-line therapy.[2, 3]
- Virologic efficacy was analyzed by the combination of boosted PI and NRTI backbone. Adjustments were made to account for differences in the baseline characteristics of the study populations across trials.
- Virologic efficacies of darunavir/r 800/100 mg QD and saquinavir/r used in combination with an ABC/3TC (ABC-based) backbone were estimated from the regression model developed for the meta-analysis.[3]

Antiretroviral Drug Costs

- Antiretroviral (ARV) therapy costs for each boosted PI regimen were calculated in 2009 Euros and were based on dosages of boosted PIs and NRTI backbones used in each of the clinical trials (Table 1).
- Unit costs of all drugs were based on the Pharmacy Purchase Price (PPP) and were derived from the September 15, 2009 Lauer Taxe.[4]
- The cost of the TDF/FTC or TDF/3TC (TDF-based) NRTI backbone was the average cost of TDF/FTC and TDF/3TC weighted by the total number of individuals using each regimen in clinical trials.

Table 1. Antiretroviral Drug Costs (in 2009 Euros)

Drug Name	Total Daily Dose (mg)	Daily Cost
PIs		
Darunavir (PREZISTA)	800	€23.58
Atazanavir (Reyataz)	300	€22.90
Fosamprenavir (Telzir)	1400	€17.74
Lopinavir/ritonavir 200/50 mg meltrex tablets (Kaletra)	800/200	€22.87
Saquinavir (Invirase)	2000	€17.60
Ritonavir (Norvir) boosting	100 or 200	€1.48 per 100 mg
NRTIs		
ABC/3TC (Kivexa)	600/300	€20.35
TDF/FTC (Truvada)	300/200	€21.90
3TC (Epivir)	300	€8.03
TDF (Viread)	300	€14.06

Model Outcomes

- **Incremental cost efficacy ratio (ICER):** incremental annual cost per additional individual with virologic response at 48 weeks.
- **Efficiency frontier:** graphical representation of the most efficient mix of current treatment regimens, created by plotting the modeled regimens on the cost-efficacy plane and connecting only the regimens that are not *dominated**:
  - Along the efficiency frontier, treatment regimens are incrementally more efficacious and more expensive.
  - The area below the efficiency frontier represents regimens that are dominated by (i.e., inferior to) the existing regimens. The area above the efficiency frontier represents potential new regimens that would be superior to the existing ones, should they become available.[5]
- **Other outcomes:** absolute annual cost per individual with virologic response at 48 weeks; number of individuals successfully treated (i.e., with virologic response at 48 weeks), given a fixed budget.

*A *dominated* regimen is a regimen that is less efficacious but more expensive than another regimen or a combination of regimens.

Base-Case Results

Cost-Efficacy Estimates

- When comparing all boosted PIs with TDF-based backbones, fosamprenavir/r and darunavir/r 800/100 mg QD combination therapies were the only HAART regimens on the efficiency frontier; all other regimens were dominated (Table 2 and Figure 1).
- Darunavir/r 800/100 mg QD combination therapy had an incremental cost of €26,316 per additional individual with a virologic response at 48 weeks, compared with fosamprenavir/r combination therapy (Table 2 and Figure 1).

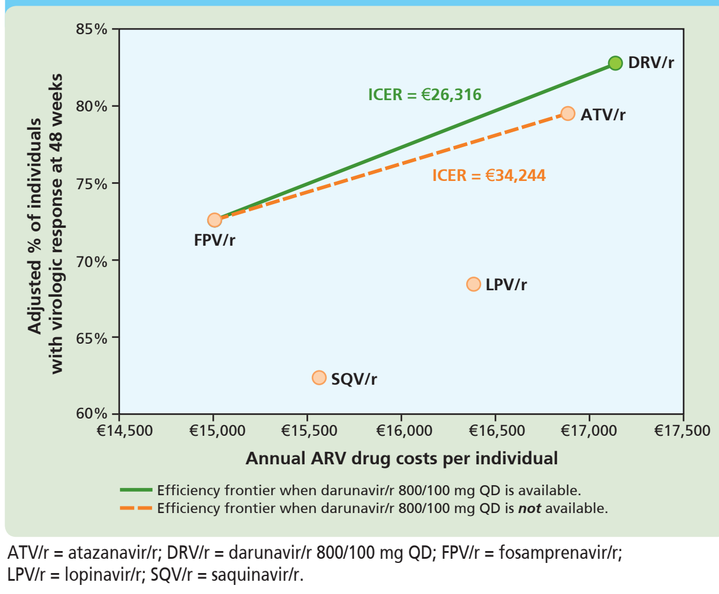
Table 2. One-Year Cost-Efficacy Analysis of First-Line Boosted PIs With TDF-Based NRTI Backbones (TDF/FTC or TDF/3TC)

Boosted PI	Annual ARV Drug Costs per Individual	Incremental Cost	Adjusted Virologic Response at 48 Weeks (%)	Incremental Efficacy	Incremental Cost per Individual With HIV-1 RNA < 50 Copies/mL
Fosamprenavir/r	€15,009	—	75.1%	—	—
Saquinavir/r	€15,567		66.9%		Dominated[a]
Lopinavir/r	€16,384		71.7%		Dominated[a]
Atazanavir/r	€16,892		80.6%		Dominated[a]
Darunavir/r 800/100 mg QD	€17,140	€2,132	83.2%	8.1%	€26,316

[a]The incremental cost-efficacy ratio was calculated for non-dominated regimens only. Therefore, the incremental cost and incremental efficacy of any dominated regimen were omitted from this table.

- If darunavir/r 800/100 mg QD were not available as a treatment option, the efficiency frontier would include only fosamprenavir/r- and atazanavir/r-based combination therapies (Figure 1).
- Darunavir/r 800/100 mg QD resulted in a lower incremental cost per additional individual with a virologic response at 48 weeks (€26,316) than atazanavir/r (€34,244), the most efficacious boosted PI prior to the introduction of darunavir/r 800/100 mg QD. Following the introduction of darunavir/r 800/100 mg QD, atazanavir/r was no longer on the efficiency frontier (Figure 1).

Figure 1. Efficiency Frontier of First-Line Boosted PIs With TDF-Based NRTI Backbones (TDF/FTC or TDF/3TC)



ATV/r = atazanavir/r; DRV/r = darunavir/r 800/100 mg QD; FPV/r = fosamprenavir/r; LPV/r = lopinavir/r; SQV/r = saquinavir/r.

Other Outcome Measures

- The absolute annual ARV drug cost per individual with a virologic response at 48 weeks for darunavir/r 800/100 mg QD combination therapy was €20,601, which was lower than that for other combination therapies such as those containing lopinavir/r (€22,850) and atazanavir/r (€20,958), the two most commonly prescribed boosted PIs in first-line therapy in Germany (calculated from Table 2).
- Given a fixed budget of €10 million per year, the number of individuals that could be treated successfully over 1 year ranged from 430 to 500; this number was highest for regimens containing fosamprenavir/r (500) and darunavir/r 800/100 QD (485) (calculated from Table 2).

Scenario Analysis Results

- When comparing all combinations of boosted PIs with TDF-based backbones and with ABC-based backbones, the regimens on the efficiency frontier included the following:
  - Fosamprenavir/r with ABC-based backbone
  - Fosamprenavir/r with TDF-based backbone
  - Darunavir/r 800/100 mg QD with TDF-based backbone.

  All other regimens were dominated (Table 3 and Figure 2).
- As in the base-case analysis, the ICER of darunavir/r 800/100 mg QD with TDF-based backbone was €26,316 per additional individual with a virologic response at 48 weeks, compared with fosamprenavir/r with TDF-based backbone (Table 3 and Figure 2).
- If darunavir/r 800/100 mg QD were not available as a treatment option, the regimens on the efficiency frontier would include the following:
  - Fosamprenavir/r with ABC-based backbone
  - Fosamprenavir/r with TDF-based backbone
  - Atazanavir/r with TDF-based backbone (Figure 2).
- As in the base-case analysis, darunavir/r 800/100 mg QD with TDF-based backbone resulted in a lower incremental cost per additional individual with a virologic response at 48 weeks (€26,316) than atazanavir/r with TDF-based backbone (€34,244), the regimen at the highest point on the efficiency frontier prior to the introduction of darunavir/r 800/100 mg QD (Figure 2).

Table 3. One-Year Cost-Efficacy Analysis of First-Line Boosted PIs With TDF-Based and ABC-Based NRTI Backbones

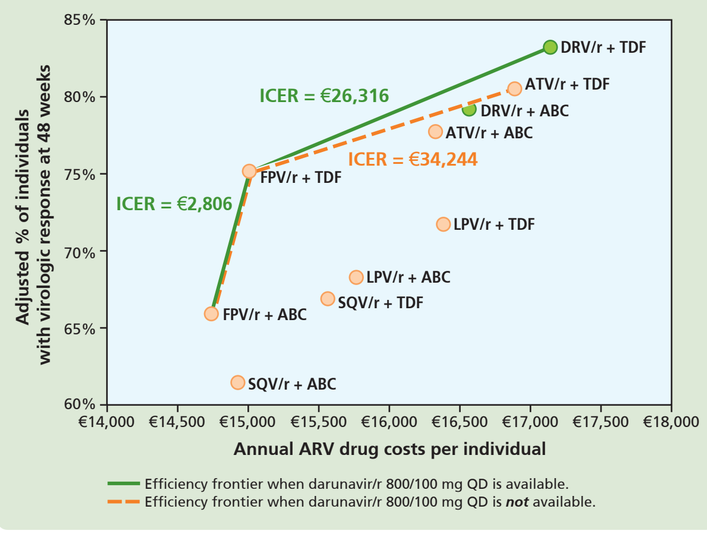
Boosted PI + NRTI Backbone	Annual ARV Drug Costs per Individual	Incremental Cost	Adjusted Virologic Response at 48 Weeks	Incremental Efficacy	Incremental Cost per Individual With HIV-1 RNA < 50 Copies/mL
Fosamprenavir/r + ABC[a]	€14,748	—	65.8%	—	—
Saquinavir/r + ABC[a]	€14,932		61.5%		Dominated[c]
Fosamprenavir/r + TDF[b]	€15,009	€261	75.1%	9.3%	€2,806
Saquinavir/r + TDF[b]	€15,567		66.9%		Dominated[c]
Lopinavir/r + ABC[a]	€15,775		68.2%		Dominated[c]
Atazanavir/r + ABC[a]	€16,326		77.8%		Dominated[c]
Lopinavir/r + TDF[b]	€16,384		71.7%		Dominated[c]
Darunavir/r 800/100 mg QD + ABC[a]	€16,575		79.6%		Dominated[c]
Atazanavir/r + TDF[b]	€16,892		80.6%		Dominated[c]
Darunavir/r 800/100 mg QD + TDF[b]	€17,140	€2,132	83.2%	8.1%	€26,316

[a] + ABC = ABC-based backbone = ABC/3TC.

[b] + TDF = TDF-based backbone = TDF/FTC or TDF/3TC.

[c] The ICER was calculated for non-dominated regimens only. Therefore, the incremental cost and incremental efficacy of any dominated regimen were omitted from this table.

Figure 2. Efficiency Frontier of First-Line Boosted PIs With TDF-Based and ABC-Based NRTI Backbones



Conclusions

- In the base-case analysis (considering a TDF-based NRTI backbone), among the ritonavir-boosted PIs analyzed, darunavir/r 800/100 mg QD and fosamprenavir/r were the only regimens on the efficiency frontier of first-line PI-based HAART for HIV-infected adults. Darunavir/r 800/100 mg QD combination therapy had an incremental cost of €26,316 per additional individual with a virologic response at 48 weeks, compared with fosamprenavir/r combination therapy. All other boosted PIs were dominated.
- Darunavir/r 800/100 mg QD combination therapy had a lower cost per individual with a virologic response at 48 weeks than combination therapies containing lopinavir/r and atazanavir/r, the two most commonly prescribed boosted PIs in treatment-naïve, HIV-infected adults.
- The results of the cost-efficacy analysis were robust when ABC-based NRTI backbones were included in the analysis, in addition to TDF-based NRTI backbones.
- These conclusions do not account for the economic consequences associated with the more favorable gastrointestinal and lipid-related tolerability profile of darunavir/r 800/100mg QD when compared with other ritonavir-boosted PIs such as fosamprenavir/r and lopinavir/r.
- The cost per patient with a virologic response is a measure of value for money that is relevant to decision makers when comparing HIV treatments. This measure eventually may become a key element in the assessment of the economic value of ARV therapy and other HIV-related interventions, as part of a set of complementary economic analyses.

References

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