BACKGROUND

- The introduction of protease inhibitors (PIs) in the mid-1990s represented a major advance in the treatment of HIV infection. It has resulted in sustained viral suppression, improved immunologic function, and marked reduction in morbidity and mortality rates.

- However, current treatment with PIs is limited by factors such as adverse effects, drug interactions, and the development of resistance.

- Darunavir (Prezista®. TMC114) is a novel PI with demonstrated superior potency against wild-type and drug-resistant strains of HIV-1 and is optimized for use in the context of both initial monotherapy and PIs-based regimens.

OBJECTIVE

- The objective of this economic evaluation was to model the impact of darunavir/r on treatment-experienced adults who have failed prior antiretroviral therapy.

- To identify darunavir’s appropriate place in therapy.

METHODS

Model Treatment Pathways

- Figure 1 illustrates the treatment pathways compared in this economic evaluation.

- After switching to darunavir/r, the model allows three sequential stages of CD4+ cell count (CD4+ cell count >200, 200–500, and >500 cells/mm3).

- Transition probabilities between the Markov model health states were based on usage rates in the clinical trials, published sources, and Canadian national statistics, respectively (Table 4).

- The model also incorporates the CD4+ cell count trajectory, duration of declining CD4+ cell counts, and duration of slowly increasing CD4+ cell counts.

Markov Model Structure and Input Parameters

- A Markov model with a 3-month cycle period was developed to follow a treatment-experienced HIV cohort through six possible health states, defined by CD4+ cell count ranges (850, 51-100, 101-200, 201-350, 351-500, and >500 cells/mm3), and eventually to the death state.

- Transition probabilities between the Markov model health states were calculated from the POWER 1 and POWER 2 clinical trial results for the darunavir/r and control regimens and from the RESIST 1 and RESIST 2 clinical trial results for the tipranavir/r and switch regimens from other published sources.

- Clinical trial data used to compute the transition probabilities included the proportion of individuals with different levels of virologic response to treatment at 24 weeks and the changes in CD4+ cell count at 24 and 48 weeks associated with the different virologic response groups for each treatment regimen.

- Antiretroviral drug costs were based on usage rates in the clinical trials, and the mean daily cost for each drug was computed using the recommended dose in U. S. DHHS guidelines. Unit costs were obtained from published sources.

RESULTS

Table 1. Virologic Response Rates at 24 Weeks

<table>
<thead>
<tr>
<th>Treatment Regimen</th>
<th>Baseline Virologic Response</th>
<th>CD4+ Cell Count (cells/mm3)</th>
<th>Mean  (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Darunavir/r</td>
<td>100%</td>
<td>&gt;200 cells/mm3</td>
<td>569 (354)</td>
</tr>
<tr>
<td>Control</td>
<td>75%</td>
<td>&gt;200 cells/mm3</td>
<td>569 (354)</td>
</tr>
<tr>
<td>Tipranavir/r</td>
<td>50%</td>
<td>&gt;200 cells/mm3</td>
<td>569 (354)</td>
</tr>
</tbody>
</table>

Table 2. Durations of CD4+ Cell-Count Changes by 24-Week Virologic Response: First and Switch Regimens

<table>
<thead>
<tr>
<th>Virologic Response</th>
<th>Duration (years)</th>
<th>First Regimen</th>
<th>Switch Regimen</th>
<th>Base case</th>
<th>Sensitivity 1</th>
<th>Sensitivity 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Log10 Drop</td>
<td>1.5 years</td>
<td>1 year</td>
<td>0.5 years</td>
<td>1 year</td>
<td>0.5 years</td>
<td>1 year</td>
</tr>
<tr>
<td>2 Log10 Drop</td>
<td>3 years</td>
<td>2 years</td>
<td>1 year</td>
<td>2 years</td>
<td>1 year</td>
<td>2 years</td>
</tr>
<tr>
<td>3 Log10 Drop</td>
<td>5 years</td>
<td>3 years</td>
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Table 4. Utility Values, HIV-Related Morbidity, and Annual Costs for Resources Other Than ARV Drugs by CD4+ Cell-Count Range

<table>
<thead>
<tr>
<th>CD4+ Cell-Count Range</th>
<th>Utility Values</th>
<th>Annual Costs (U.S. $)</th>
<th>Incremental Cost (£)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–100</td>
<td>0.78</td>
<td>3,760</td>
<td>1,865</td>
</tr>
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<td>101–200</td>
<td>0.78</td>
<td>3,760</td>
<td>1,865</td>
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<td>3,760</td>
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<tr>
<td>351–500</td>
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<td>1,865</td>
</tr>
<tr>
<td>&gt;500</td>
<td>0.78</td>
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<td>1,865</td>
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Table 5. Sensitivity Analysis

- Results were robust to changes in input parameter values and treatment scenarios (Figure 2, Table 7).

- For all ranges tested in the sensitivity analysis, the incremental cost per QALY gained remained below $50,000 (Figure 2).

CONCLUSIONS

- When compared to current PIs, darunavir/r in combination with an OBR is cost-effective in treatment-experienced adults who have failed prior antiretroviral therapy.

- The model results were most influenced by assumptions about duration of efficacy, rate of decline in CD4+ cell count after virologic failure, utility values, and other medical care costs in each CD4+ cell-count range.

- Variations in practice patterns and population and model characteristics also influenced the results of the model.

- Nevertheless, darunavir/r remained cost-effective compared to standard care over all the parameter ranges and variability factors tested.

REFERENCES

- King JT Jr et al. Abstract No. 561. 12th CROI; Feb 22-25, 2005; Boston, MA.
- Garcia et al., 2004; Deeks et al., 2002; Ledergerber et al., 2004