Addition of abiraterone to first-line long-term hormone therapy in prostate cancer (STAMPEDE): modelling to estimate long-term survival, quality-adjusted survival and cost-effectiveness

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[1] Background:
Results from randomised trials show adding abiraterone acetate plus prednisolone (AAP) to standard care (SOC) improves disease-free and overall survival in men with prostate cancer (PC) starting long-term hormone therapy for first time.

Formal assessment was required of whether funding AAP here shows appropriate resource use. This cost-effectiveness decision model tests whether giving AAP is cost-effective using English National Health Service costs, applied to the STAMPEDE treatment patterns.

This cost-effectiveness analysis focuses on one pair of arms, the abiraterone (abi) comparison
- AAP+SOC (arm G) vs. SOC (arm A).

[2] Methods:
- Health outcomes, costs and quality of life (QOL) modelled using pt data collected during STAMPEDE, with additional external information on other-cancer death.
- Included 1,917 men with high-risk, locally advanced metastatic or recurrent prostate cancer starting 1st-line hormone therapy (James et al. 2017).
- SOC was hormone therapy for ≥2 years with radiotherapy in pre-selected patients.
- If allocated to treatment arm, AAP (AA 1000mg/day, P 5mg/day) was added to SOC.
- The model makes lifetime predictions of survival, costs and quality-adjusted life-years (QALYs), with costs and QALYs discounted at 3.5% annually. Sensitivity analyses were performed.

Quality of life
- EQ-5D-3L was collected at baseline, every 6w up to 6m, then every 12w up to 2y, then every 6m up to 5y. Responses used to calculate quality of life scores for QALYs.
- Trial values were used in the models, with multiple imputation.

Costs
- Health and social care perspective, using STAMPEDE practices, British National Formulary, NHS Reference Costs and PSSRU unit costs. Estimated NHS costs applied for enzalutamide (enza), and 20% off radium and cabazitaxel.

[3] Analysis plan
1. Generate survival curves for moving between states;
   - Joint survival across some groups of transitions; remaining transitions modelled separately.
2. Regression models for costs and QALYs;
   - Mean per-patient costs and QALYs per cycle are applied later on.
3. Main simulation – creates info on how many patients spend how long in each state.
4. Apply costs and QALYs to these times in state.
6. Validate analysis – comparison to other work.
7. Sensitivity analyses.

Pts join trial in one of these pre-progression (naïve) states

During trial, some progress to one of these states:

[5] Results and limitations
- Analysis predicts trial data well; longer-term predictions validated by comparison to other work.
- Trial data less complete after ~2-3 years. Model predicted AAP would extend survival (discounted quality-adjusted survival) by 2.68y (1.46 QALYs) for metastatic (M1) patients and 0.30y (0.29 QALYs) for non-metastatic (M0).
- Cost of abi means AAP not currently cost-effective in this setting.
- If abi’s price reduces after loss of exclusivity, AAP could become cost-effective in both patient groups, with ICERs below £20,000 (US$25,330) per QALY for abi priced at 25% of basecase. AAP could dominate at lowest price in non-metastatic (M0) patients (i.e. lower costs and higher QALYs vs. SOC alone).

[6] Interpretation
If ICER less than ~£20,000 to £30,000/QALY, could be acceptable to NICE (see red line below).

RESULTS, different costs for Abi 1000mg
ICER = Incremental Cost-Effectiveness Ratio

Difference in survival (y)

<table>
<thead>
<tr>
<th></th>
<th>All AAP vs SOC</th>
<th>M0 AAP vs SOC</th>
<th>M1 AAP vs SOC</th>
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<tbody>
<tr>
<td>Difference in quality-adjusted survival (QALYs)</td>
<td>1.42</td>
<td>0.30</td>
<td>2.84</td>
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<tr>
<td>Abi daily cost £97.68, 100% basecase</td>
<td>£61,246</td>
<td>£49,486</td>
<td>£74,368</td>
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<td>Abi daily cost £73.30, 75% basecase</td>
<td>£72,634</td>
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<td>Abi daily cost £48.84, 50% basecase</td>
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<td>Abi daily cost £24.42, 25% basecase</td>
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<td>Abi daily cost £9.77, 10% basecase</td>
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<td>Abi daily cost £7.30, 100% basecase</td>
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<td>Abi daily cost £21,977</td>
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<td>Abi daily cost £21,842</td>
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<td>dominates</td>
<td>£7,873</td>
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[7] Discussion and implications
AAP could be cost-effective for M0 (off-label) and M1 pts with lower future pricing of abiraterone; may be cost-saving in the former. Results apply to STAMPEDE regimen pts.

Future policymakers could encourage license submissions and generic abi price reductions to facilitate use of AAP, given cost-saving potential in addition to improving survival.

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