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 of 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

- Patients recruited Nov 2011 → Jan 2014, in England, largest nation where STAMPEDE recruited.
- 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-cause 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 in the trial at each visit, at least up to progression.
- 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.
5. Calculate incremental cost-effectiveness ratio (ICER).
6. Validate analysis – comparison to other work.
7. Sensitivity analyses.

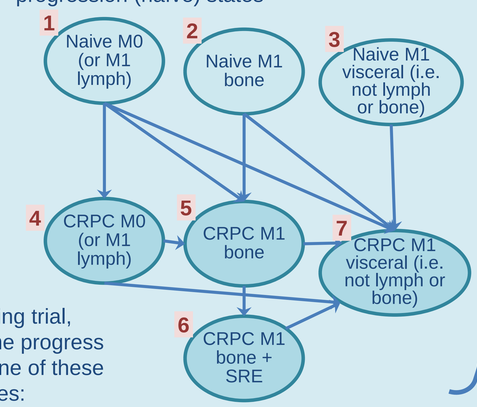
Go to [4]

Aim:

To model lifetime cost-effectiveness of abiraterone acetate plus prednisolone (AAP) vs. standard of care (SOC).

[4] Model structure; 9 health states

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



During trial, some progress to one of these states:

Naïve ≡ Pre-prog
CRPC ≡ Post-prog (castrate-resistant prostate cancer)

All naïve and CRPC states can access either type of death.

RESULTS, different costs for Abi 1000mg	ICER = Incremental Cost-Effectiveness Ratio	All AAP vs SOC	M0 AAP vs SOC	M1 AAP vs SOC
Difference in survival (y)		1.42	0.30	2.68
Difference in quality-adjusted survival (QALYs)		0.84	0.29	1.46
Abi daily cost £97.68, 100% basecase	Difference in costs (£)	£61,246	£49,486	£74,368
	ICER (£/QALY)	**£72,634**	**£170,649**	**£50,918**
Abi daily cost £73.30, 75% basecase	Difference in costs (£)	£45,703	£35,664	£56,904
	ICER (£/QALY)	**£54,201**	**£122,985**	**£38,961**
Abi daily cost £48.84, 50% basecase	Difference in costs (£)	£30,159	£21,842	£39,441
	ICER (£/QALY)	**£35,768**	**£75,320**	**£27,004**
Abi daily cost £24.42, 25% basecase	Difference in costs (£)	£14,616	£8,020	£21,977
	ICER (£/QALY)	**£17,334**	**£27,656**	**£15,047**
Abi daily cost £9.77, 10% basecase	Difference in costs (£)	£5,290	-£273	£11,499
	ICER (£/QALY)	**£6,274**	**dominates**	**£7,873**

[6] Interpretation

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

[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).

Cost saving here in M0

[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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