897 PUBLICATION

Combination therapy with bicalutamide 50 mg plus a luteinising hormone-releasing hormone agonist (LHRHa) is cost effective compared with an LHRHa alone in metastatic prostate cancer

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Background: Combination therapy with bicalutamide ('Casodex') 50 mg plus castration provides an estimated 20% reduction in the risk of death compared with castration alone in patients with metastatic prostate cancer (*BJU Int* 2004; 93: 1177–82). In addition to efficacy, the economic impact of clinical care is an important consideration. We compare here the cost-effectiveness of bicalutamide 50 mg/day plus LHRHa versus LHRHa alone in newly diagnosed men with metastatic (stage D2) prostate cancer.
Materials and methods: The economic model was populated using published data for the following parameters: survival probabilities, specified adverse events; cost; and utility. The key assumption for estimating the incremental cost-effectiveness ratio (ICER) was that patients receiving combination therapy remain on bicalutamide until prostate-specific antigen (ie biochemical) progression occurs and patients remain on LHRHa treatment after progression and until death.
Results: Over 5 years, combination therapy with bicalutamide plus an LHRHa was cost effective both in terms of life-years gained and quality-adjusted life-years (QALYs) gained (see table 1). The cost-effectiveness was even more noticeable at 10 years. These values are well within the acceptable range (<$100,000) for commonly reimbursed medical care interventions.

Table 1: ICER for bicalutamide plus LHRHa vs LHRHa alone

	Per life-year gained	Per QALY gained
5 years	$20,489	$33,677
10 years	$13,313	$20,053

The ICER of bicalutamide plus LHRHa versus LHRHa alone was most influenced by estimates of the survival probabilities for the two interventions. The probability of developing specific adverse events had little impact on the overall conclusions of the model. Importantly, when all the parameters used for the model were varied over a clinically reasonable range, the ICER over 5 years for bicalutamide plus LHRHa versus LHRHa alone remained cost effective (median $27,555 per QALY gained).
Conclusions: Combination therapy with bicalutamide 50 mg plus an LHRHa is a cost-effective option when compared with an LHRHa alone in treating men with metastatic prostate cancer. In light of the recently published findings of survival advantage of bicalutamide plus an LHRHa over LHRHa alone, these findings provide further support for the use of combination therapy with bicalutamide.
'Casodex' is a trademark of the AstraZeneca group of companies

898 PUBLICATION

Bicalutamide combination therapy is cost effective versus flutamide combination therapy in men with metastatic prostate cancer

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Background: Meta-analysis has shown combination hormonal therapy using castration (medical or surgical) plus a non-steroidal antiandrogen provides a significant survival advantage over castration alone in men with metastatic prostate cancer (*Lancet* 2000; 355: 1491–1498). Bicalutamide ('Casodex') and flutamide are the most frequently used non-steroidal antiandrogen components of combination therapy. We estimated the incremental cost-effectiveness ratio (ICER) of bicalutamide versus flutamide, both in combination with a luteinising hormone-releasing hormone agonist (LHRHa).
Materials and methods: An economic model was used to estimate the ICER of bicalutamide 50 mg daily plus LHRHa versus flutamide 250 mg three times daily plus LHRHa in men with metastatic (stage D2) prostate cancer. Published historical data on survival, specific adverse events, costs and utilities were used to populate the model. One- and multi-way analyses were used to assess the sensitivity of the cost-effectiveness estimates.
Results: At 5 years, the ICER for bicalutamide plus LHRHa over flutamide plus LHRHa was $20,000 per life-year gained and $22,000 per quality-adjusted life-year (QALY) gained. At 10 years, the ICER for bicalutamide plus LHRHa over flutamide plus LHRHa per QALY gained was $16,000. These values are favourable and substantially below $50,000–100,000 (the commonly accepted threshold for cost-effectiveness). According to the one-way sensitivity analysis, the cost-effectiveness of bicalutamide plus LHRHa remained favourable across a specified range of values for the predefined tolerability, cost and quality-of-life variables over 5 years (the ICER was most sensitive to differences in patient survival and drug costs). Additionally, a multi-way uncertainty analysis demonstrated that the advantageous ICER remained in the favourable cost-effectiveness range when all the variables in the decision model were varied simultaneously over a clinically reasonable range (median $13,637 per QALY gained over 5 years).
Conclusions: The study results indicate that combination therapy with bicalutamide plus LHRHa is a cost-effective treatment option compared with flutamide plus LHRHa for treating patients with metastatic prostate cancer.
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899 PUBLICATION

A phase II study of sequential chemotherapy with Docetaxel-Estramustine phosphate (DE) followed by Mitoxantrone-Prednisone (MP) in patients (pts.) with metastatic hormone refractory prostate cancer (MHRPC)

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MP and DE are active treatments in MHRPC. These drugs show different mechanisms of action and are not cross-resistent. Because of the low feasibility of concomitant polichemotherapy in MHRPC we have designed the present study with DE followed by sequential MP. Docetaxel 30 mg/sqm weekly plus bid phosphate-estramustine for a total of 12 weeks followed by two weeks rest and mitoxantrone 12 mg/sqm every 3 weeks plus bid 5 mg of prednisone for a maximum of 12 cycles, were administred to MHRPC pts. Primary endpoint was activity (>50% PSA reduction); secondary were: objective responses, toxicities, time to progression, survival and pain control. So far 39 pts have been enrolled. Pts characteristics: median age 71.5 years (55–83), median ECOG PS 1 (range 0–1), median PSA 63.4 ng/ml (7.3–595.5), metastatic sites disease: bone 22, nodes 14, pelvis 5 and liver 2. 354 cycles of Docetaxel (range 3–12) and 161 of Mitoxantrone (range 2–12) have been administred. 35 pts. are evaluable for toxicity and 34 pts for response.
Three episodes of deep venous thrombosis and two congestive heart failures occurred after DE and MP respectively. Except for NCI G3 nail changes in 12% of pts and G3 hepatotoxicity in 16% of pts, G3–4 haematological and non haematological toxicities were observed only in one pt; G1–2 nausea-vomiting occurred in 76% of pts, G1–2 diarrhoea in 76% and G1–2 stomatitis in 64% of pts. Complete PSA response were 12/34 (35%), partial response 13/34 (38%), stable disease 8/34 (23%) and progressive disease 1/25 (2%). According to RECIST criteria 8 pts are evaluable for objective response and 1 RC, 3 RP and 4 SD have been observed. Median time to progression is 7.1 months. DE and MP sequential chemotherapy is feasible and active in MHRPC pts and has a good toxicity profile; accrual is still ongoing.

900 PUBLICATION

Synergistic interaction between ionizing radiation and 8-chloro-adenosine 3', 5'-monophosphate in PC-3 human prostate carcinoma cells

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Background: A novel antineoplastic agent 8-chloroadenosine 3', 5'-monophosphate (8-Cl-cAMP) has been shown to inhibit cell growth and induce cell cycle arrest and apoptosis in a variety of cancers *in vitro* and *in vivo*. It is a new site-selective cAMP analog that down-regulates the regulatory subunit of the cAMP-dependent protein kinase I (PKA-I). The present study explored the cytotoxic and antiproliferative potential of 8-Cl-cAMP and ionizing radiation (IR) in hormone-refractory human prostate cancer cells PC-3.