Long-Term Fiscal Implications of MEPACT in the Treatment of High-Grade Nonmetastatic Osteosarcoma: A Budget-Impact Model and a Lifetime Tax Perspective

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BACKGROUND

- Nonmetastatic osteosarcoma is a type of bone cancer that primarily affects children, adolescents, and young adults.
- It is an ultra-orphan disease, a term used to describe very rare diseases.
- MEPACT (mifamurtide) is indicated for use in children and adults aged between 2 and 30 years of age for the treatment of high-grade resectable nonmetastatic osteosarcoma after macroscopically complete surgical resection to remove the tumour.
- MEPACT is used in combination with postoperative multiagent chemotherapy.
- The largest ever completed phase 3 randomized trial in osteosarcoma (INT-0133 study, N = 662) comparing add-on MEPACT to three- or four-agent adjuvant therapy alone[1] demonstrated a survival benefit with the addition of MEPACT to chemotherapy: a statistically significant increase in 6-year overall survival from 70% to 78% (P = 0.03).

OBJECTIVES

- To assess the budget impact to the United Kingdom (UK) National Health Service (NHS) of adding MEPACT to the standard three- or four-agent adjuvant therapy.
- To evaluate the long-term financial impact on the UK government of introducing MEPACT.

METHODS

Budget-Impact Model Overview

- A Microsoft Excel–based budget-impact model was developed to evaluate the trajectory of spending over 1- to 5-year time horizons in a hypothetical population of 54 patients (in year 1) with nonmetastatic osteosarcoma from an NHS perspective.
- The estimate of 54 patients with nonmetastatic osteosarcoma was derived based on prevalence data from the Automated Childhood Information System and population data from the Office of National Statistics, UK (Table 1).
- It was assumed that 80% of all osteosarcomas are newly diagnosed, nonmetastatic, and resectable.
- Patients received the average number of mifamurtide doses administered in the INT-0133 study (i.e., 38.4 doses).
- The model assumes 89% of the total UK population is located in England and Wales.

Table 1. Eligible Number of Patients

Population Data		2009	2010	2011	2012	2013
Total UK population (millions)		62.6	63.1	63.5	63.9	64.4
England and Wales population	0.89	55.7	56.2	56.5	56.9	57.3
Incidence in children (0-14 years)	3.0	29	29	29	29	30
Incidence in adolescents (15-19 years)	7.3	26	26	25	24	24
Incidence in young adults (20-24 years)	3.3	13	13	13	13	13
% of patients with nonmetastatic osteosarcoma	80	67	67	67	66	67
Potential patient population		**54**	**54**	**53**	**53**	**53**

Budget-Impact Model Input Parameters

- The model was populated with clinical and economic data obtained from a variety of sources, including:
  - Clinical trial data for MEPACT
  - Published literature
  - Treatment guidelines
  - Other information from published and unpublished sources
- The cost per MEPACT dose for the UK is £2,375; additional costs directly related to MEPACT include outpatient costs and pharmacy costs.
- Additional outpatient visits due to MEPACT treatment were based on patients receiving in excess of 36 doses, because it was assumed that patients who receive 36 doses or less will receive their MEPACT dose when they receive a part of their maintenance chemotherapy dose. The average number of additional outpatient visits per MEPACT patient is 7.4, at a cost of £189 per visit.
- The only adverse event included was an infusion reaction, with a cost of £1.65. It was assumed that 98% of MEPACT-treated patients would have an infusion reaction, compared with 0% of patients who didn't receive MEPACT.
- The probabilities of recurrence for both the MEPACT and non-MEPACT arms were calculated using the transition probabilities derived from the phase 3 trial. The cost of recurrence is £23,298 and includes diagnostic and treatment costs.
- The probability of postrecurrence (disease progression) was derived from the calculated results in a MEPACT cost-effectiveness model.
- It was assumed that all patients who have a postrecurrence (disease progression) will die within the year that this event occurs; palliative care costs of £3,481 are applied to these patients.
- The model considers use and associated costs of drug acquisition, administration, recurrence, and palliative care under two scenarios and calculates the budgetary impact:
  - Base case: No patients received MEPACT as an add-on treatment
  - Scenario 1 and Scenario 2: Patients received MEPACT as an add-on treatment in line with the formulary share (Table 2)

Table 2. Formulary Shares

Scenario	Treatment	2009	2010	2011	2012	2013
Base case	MEPACT	0%	0%	0%	0%	0%
	No MEPACT	100%	100%	100%	100%	100%
Scenario 1	MEPACT	50%	50%	50%	60%	60%
	No MEPACT	50%	50%	50%	40%	40%
Scenario 2	MEPACT	100%	100%	100%	100%	100%
	No MEPACT	0%	0%	0%	0%	0%

Lifetime Tax Perspective

- Given the young age at which the average patient may be treated for high-grade resectable osteosarcoma, the societal impact may be significant.
- The contribution osteosarcoma survivors can provide to the economy in terms of their economic activity (i.e., how much tax the survivors contribute) was investigated. The aim of this was to show whether the initial cost of treating patients with MEPACT is recouped in tax payments later in the patient's life.
- The model assumes that a patient who survives after being treated with MEPACT will be a person with average characteristics (an individual with average education, health, and life expectancy).

- The average characteristics in the model were based on a generalized accounting framework described by Cardarelli et al. (2000)[2] and used by Connolly et al. (2009)[3] to model direct financial transactions between an in vitro fertilization (IVF)-conceived singleton and the UK government over the projected lifetime.
- By examining the lifetime financial transfers between individuals and the government, the model derives the lifetime net tax contribution of an individual.
- The model calculates the net present value (NPV), which is an estimation of the size of return on investing in MEPACT in present value.
- The net tax contribution or net tax deficit of an individual at any stage of life is calculated using the following formula:

$$N_t(t) = T(t) - E(t) - H(t) - C(t) - P(t)$$

where $T(t)$ is the gross tax revenue paid to the government at time t, $E(t)$ and $H(t)$ are the education and health care costs to the state, $C(t)$ is the child tax credits, and $P(t)$ is the pension. The net tax contribution at any point in time is represented by $N_t(t)$.

- Average age-stratified income was obtained from the 2007-2008 survey of personal income from a representative sample of those liable to pay UK taxes,[4] which showed income varying with age. These data were fitted to a statistical function and adjusted for labour productivity growth.
- The other government transfers used to derive the net tax contribution are shown in Table 3. In the model, these also grow according to labour productivity growth estimates.

Table 3. Societal Impact Unit Costs and Parameters

Cost	Unit Values	Source
Age at start of treatment	14	
Education	£4,830	Department for Children, Schools and Families, 2008[5]
Health care 0-4 years 5-15 years 16-44 years 45-64 years 65-74 years 75-84 years	£550 £115 £270 £450 £750 £1,500	UK Department of Health, 2001[6]
Child benefit	£539	Barnard et al., 2009[7]
State pension	£8,580	Pensioners Income Series 2007/2008[8]
Private pension	£11,648	Pensioners Income Series 2007/2009[8]
Tax (nonretired households)	35%	Barnard et al., 2009[7]
Tax (retired households)	30%	Barnard et al., 2009[7]
Mifamurtide costs	£91,189	
Labour productivity growth	1.90%	Organisation for Economic Cooperation and Development, 2008[9]
Health care expenditure growth	3.00%	Connolly et al., 2009[3]
Discount rate	3.50%	Her Majesty's Treasury, 2003[10]
Age child tax credits stop	18	Connolly et al., 2009[3]
Age education stops	19	Connolly et al., 2009[3]
Age retirement begins	68	Connolly et al., 2009[3]

RESULTS

Budget-Impact Model

- The average cost per MEPACT-treated patient is £91,189, assuming an average of 38.4 MEPACT doses.
- The overall budget impact of MEPACT is shown in Figure 1.
- The expected 1-year cost in 2011 of MEPACT would be £3,971,820 compared with £1,449,520 had all patients been treated without MEPACT. Administration costs accounted for 3% of total costs.
- The annual budget impact for the NHS in England and Wales is estimated to be a £3,971,820 in 2011, rising to £4,460,889 in 2015.
- All other significant costs associated with MEPACT treatment (Scenario 1) have been considered (Table 4, Figure 2).
- Assuming 100% uptake of MEPACT, the annual budget impact for the NHS in England and Wales is estimated to be £6,494,121 in 2011.

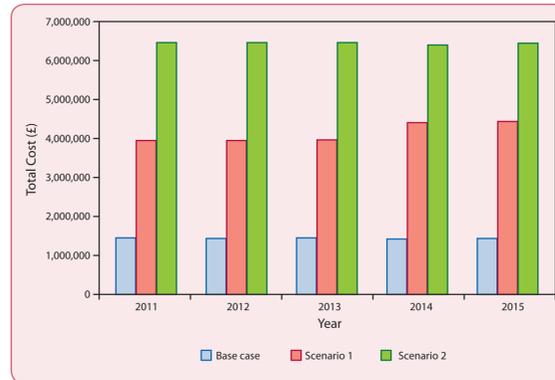**Figure 1. Total Budget Impact of MEPACT Over a 5-year Period**

Table 4. Other Significant Costs Associated With Treatment (Scenario 1)

| Parameter	2011	2012	2013	2014	2015
MEPACT-treated patients	27	27	27	32	32
Non-MEPACT-treated patients	27	27	27	21	21
MEPACT-only–related costs	£2,528,410	£2,528,410	£2,524,630	£3,010,052	£3,023,659
First-line chemotherapy costs	£1,402,255	£1,402,255	£1,400,159	£1,391,144	£1,397,434
AE—hearing loss	£0	£0	£0	£0	£0
AE—infusion reaction	£43	£43	£43	£52	£52
Recurrence-related costs					
Cost of recurrence	£40,891	£40,891	£40,830	£39,348	£39,526
Cost of palliative care	£221	£221	£220	£217	£218
Total costs	£3,971,820	£3,971,820	£3,965,883	£4,440,813	£4,460,889

AE = adverse event.

Figure 2. Significant Costs Associated With Treatment (Scenario 1)
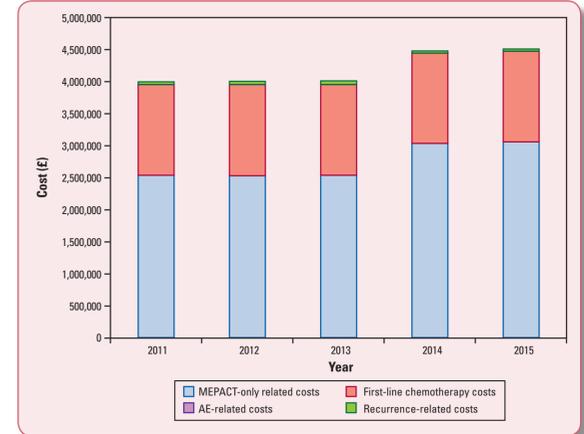
Lifetime Tax Perspective

- The projected lifetime net taxes are illustrated in Figure 3, where the varying discounted tax position between the individual and the state is seen to change over time.
- A positive value at any given point in time indicates the return on investment from IVF expenditure for the government.
- The lifetime discounted value of net taxes from a 14-year-old survivor treated with MEPACT is £78,047.
- The undiscounted net tax contribution of a 14-year-old is £325,389.
- The break-even age, defined as the point at which the net tax contribution becomes greater than zero (Figure 3), is approximately 41 years.
- On average, a patient who receives MEPACT has repaid all costs of treatment by the age of 41 years and then goes on to make significant positive contributions to society.

Figure 3. Project Present Value for a MEPACT Treated Patient
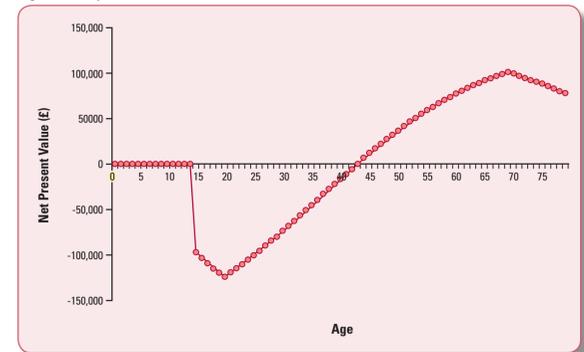
CONCLUSIONS

- Treatment with MEPACT improves survival outcomes for nonmetastatic osteosarcoma patients.
- There are no potential resource savings through the introduction of MEPACT.
- The additional budget impact due to MEPACT is mainly due to the up-front cost of the drug.
- However, given the young age at which the average patient may be treated for high-grade resectable osteosarcoma, the societal impact may be significant.
- From the tax calculations, we conclude that investment in MEPACT does not negatively impact the long-term fiscal budget of the UK government.
- Conversely, by taking a broader government perspective over an average lifetime, a surviving patient returns a positive net value to the state.
- On average, a patient who receives MEPACT has repaid all costs of treatment by the age of 41 years.

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