Mifamurtide

Case study

Mifamurtide for osteosarcoma

"… a clinical breakthrough"

"Reduces mortality by 25%!"

Costs £114 000

Mortality

Reduced from 30% to 22%

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Survival increased from 70% to 78%

Osteosarcoma

Rare - about 5 per million per year

Peak incidence in teenagers

5year survival 55%

NICE technology appraisal

Mifamurtide is used in combination with:

Cisplatin + doxorubicin + methotrexate +/- ifosfamide

The evidence

One randomised controlled trial

2 X 2 design

Regimen A **M,D,C**	**Regimen A+** **M,D,C + mifamurtide**
Regimen B M,D,C + ifosfamide	Regimen B+ M,D,C + ifosfamide +mifamurtide

Exclusions

- >30yr
- Low grade
- Unresectable or metastatic
- etc

Adverse effects

- Hearing loss:
- 11.5 % vs 7.1% (P = 0.047)

Modelling

- Time horizon 60 years
- Utility for disease free state = 0.85

Technical issues

- Include amputation and limb salvage cost?
- Include hearing loss?
- Mortality rate after a recurrence?
- Age adjusted utility rates?

Cost per QALY

- Manufacturer estimate: £57 000
- Expert review group estimate: £109 000

2 X 2 design

Regimen A **M,D,C**	**Regimen A+** **M,D,C + mifamurtide**
Regimen B M,D,C + ifosfamide	Regimen B+ M,D,C + ifosfamide +mifamurtide

Regimes

- Standard regime in UK is M,D,C

Effect of discounting

- Standard discount is 3.5% per annum

Discounting – sensitivity analysis (ERG estimates)

- Costs discounted at 3.5% - fixed

- Outcomes: discounted at
  - 0% >> £37 000 per QALY
  - 1.5% >> £54 000 per QALY
  - 3.5% >> £109 000 per QALY
  - 6% >> £142 000 per QALY

Committee consideration

- Technical questions:
  - Include amputation
  - *Exclude hearing loss*
  - Post recurrrence mortality
  - Age adjusted utility
- Regime
  - A+ and B+ : A and B
- Discount rate
  - ??

Discount rate

- NICE rules allow for discounting of outcome at 1.5% instead of 3.5% if
  - Long time horizon or
  - Quality of life inadequately captured

Final verdict

- Cost per QALY £36 000
- Novel mechanism of action
- 'Patient access scheme'

- 'Mifamurtide [can] be considered a cost-effective use of NHS resources'

Guidance

- "Mifamurtide in combination with multi agent chemotherapy within its licensed indication …
- for the treatment of high-grade resectable non-metastatic osteosarcoma
- after macroscopically complete surgical resection in children, adolescents and young adults
- and when mifamurtide is made available at a reduced cost…