A cost-effectiveness analysis of erythropoiesis-stimulating agents for treating cancer-treatment induced anaemia

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INTRODUCTION AND OBJECTIVE

- Erythropoiesis-stimulating agents (ESAs) are licenced for use in conjunction with red blood cell transfusions (RBCTs) to improve cancer-treatment induced anaemia (CIA) and reduce the need for transfusions. Since there is currently mixed evidence on the cost-effectiveness of ESAs in CIA , we aimed to assess the cost-effectiveness of ESAs from the perspective of the UK NHS, as part of an update from a previous NICE assessment.[1]

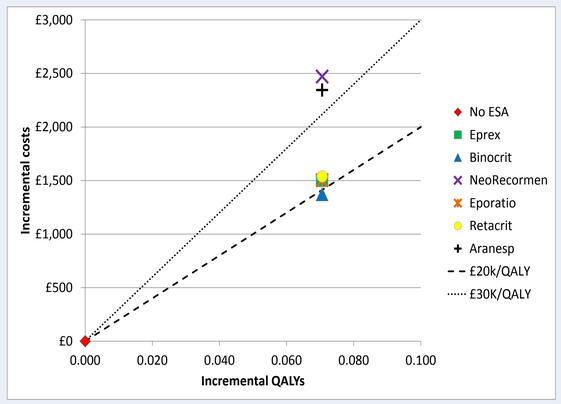
METHODS

- We built a simplified, empirical model, which compares patients receiving ESA therapy to patients not receiving ESA therapy and is split into two temporal sections. One evaluates short-term costs and QALYs (while patients are anaemic) and one long-term QALYs. A diagrammatic representation of the model is given in Figure 1. The perspective adopted was NHS and Personal Social Services.
- Short-term costs accrued are: ESA drug acquisition and administration, red blood cell transfusion costs and costs of adverse events. Cancer costs are assumed equal for all patients. Long term costs are not modelled due to the uncertainty and to avoid an arbitrary value disadvantaging a strategy with a survival benefit. Costs were inflated to 2014/15 prices.
- Short-term QALYs are accrued as the utility associated with observation of Hb over time. This includes time receiving ESA therapy and the time post-ESA therapy called normalisation where patients return to their 'normal' Hb level (in the base case this is set to 12g/dL).
- Long-term QALYs are accrued due to potential differences in overall survival (OS) between the two arms. An exponential distribution is assumed for OS in the base case , consistent with results from a number of trials. A hazard ratio is applied to OS for lifetime for patients receiving ESA therapy.
- Most parameters were estimated from the systematic review of clinical effectiveness (for details see poster 1498P), which assumed equal effectiveness for ESAs. However, some parameters specific to each ESA, such as drug doses and costs, are varied between ESAs.

RESULTS

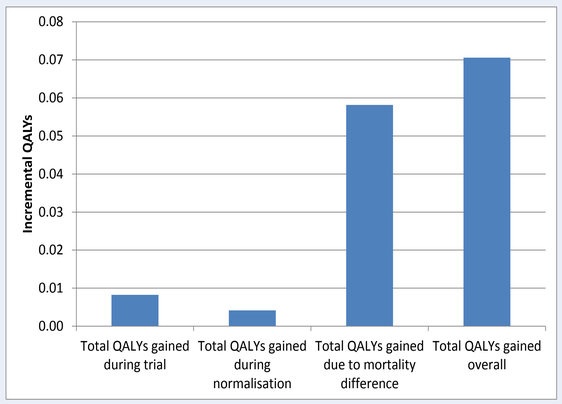
- We find that the deterministic base case, which uses drug prices from British National Formulary (BNF), has incremental cost-effectiveness ratios (ICERs) for ESA treatment versus no ESA treatment range from £19,429–£35,018 per QALY gained. These are plotted on the cost-effectiveness plane in Figure 2. Figure 2 shows clearly that in our model ESAs are assumed to have the same effectiveness (incremental QALY gain versus no ESA is the same for all ESAs) in line with our systematic review of clinical effectiveness. As such, when the ESAs are directly compared, ESAs with a higher cost are dominated by the ESA with the lowest cost.

Figure 2. Cost-effectiveness of ESAs vs. no ESA use



Abbreviations: ESA, erythropoiesis-stimulating agents; QALY(s), quality-adjusted life year(s)

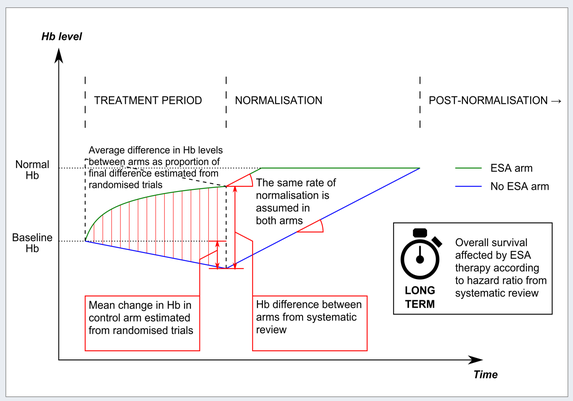
Figure 3. QALYs gained from ESA use vs. no ESAs



Abbreviations: ESA, erythropoiesis-stimulating agents; QALY(s), quality-adjusted life year(s)

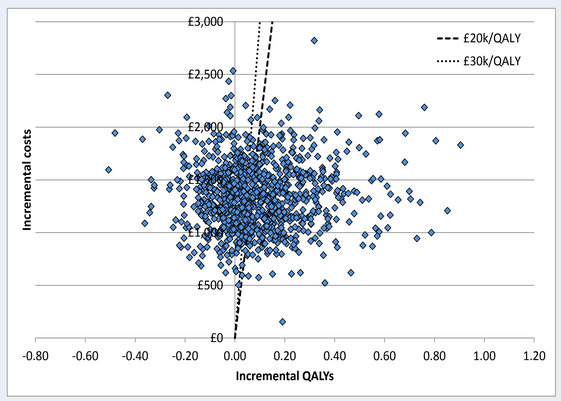
- The largest cost for all ESA arms is the cost of the ESA itself, which is calculated on an intention-to-treat basis to be £1,510–£2,485 per patient. The largest cost for a patient not receiving ESA is the cost of red blood cell transfusions (£799). Due to assumptions of equal effectiveness and dosing schedule, all other ESA costs are assumed the same in the base case.
- The total discounted QALYs gained when ESAs are used versus no ESA is 0.071 QALYs per patient. The majority of these are accrued in the long term (0.058), due to the difference in life years from ESA use as a result of the overall survival hazard ratio of 0.97 favouring ESA use. In the short term, most QALYs were gained in the cancer treatment period (0.008 QALYs) and 0.004 were accrued during the period of normalisation. The different QALY gains are shown in Figure 3.

Figure 1. Model diagram



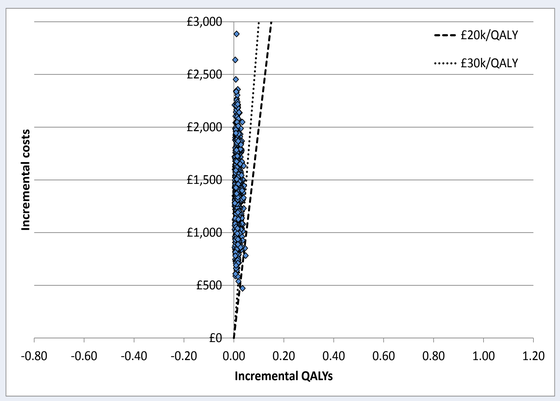
Abbreviations: ESA, erythropoiesis-stimulating agents; Hb, haemoglobin

Figure 4. PSA results, base case



Abbreviations: ESA, erythropoiesis-stimulating agents; QALY(s), quality-adjusted life year(s)

Figure 5. PSA results, overall survival assumed equal



Abbreviations: ESA, erythropoiesis-stimulating agents; QALY(s), quality-adjusted life year(s)

SENSITIVITY ANALYSES

- Probabilistic sensitivity analysis (PSA) results for the most cost-effective ESA are shown in Figure 4. This shows that there is great uncertainty in the base case results, particularly with regards the QALY gains of using ESAs. The confidence interval for QALY gain was -0.264 – 0.447 QALYs. In 31.4% of simulations there was an estimated QALY loss from ESA therapy.
- Scenario analyses found that the main source of uncertainty was the overall survival estimates.
- The PSA results of the scenario analysis where OS is assumed equal for patients receiving ESAs or not, are shown in Figure 5. We find that the QALY gain has greatly reduced, but so has as the confidence interval: 0.014 (95% CI 0.001–0.027) QALYs gained compared to not using ESAs. The reduction in QALYs also increases the ICERs, with the most cost-effective ESA achieving an ICER of £96,754 per QALY gained (95% CrI: £36,500 to >£300,000 per QALY gained) in the PSA. None of the credible intervals for the ICERs fall below £30,000 per QALY gained, suggesting in this scenario that ESAs are unlikely to be cost-effective.
- As the model deals with relatively small increments of costs and QALYs, it is sensitive to changes in many of its parameters, but OS is one of the most significant drivers of cost-effectiveness. Another is the cost of ESAs.

CONCLUSIONS

- **Evidence for survival benefits from ESAs is highly uncertain and therefore the cost-effectiveness of these ESAs is also uncertain.**
- **If ESAs are assumed not to affect survival and lower wholesale acquisition costs can be agreed, the likelihood of ESAs being cost-effective increases.**

IMPLICATIONS FOR FURTHER RESEARCH

- **Further investigation into overall survival seems necessary. Long-term follow-up RCT evidence would be the ideal, but we are also conducting further research into the available evidence (see poster 1502P)**
- **A limitation of the model is the lack of evidence on utilities associated with Hb level and normalisation, so this is an important area of further research.**

ASSOCIATED POSTERS

1498P: What is the clinical effectiveness of erythropoiesis stimulating agents for the treatment of cancer treatment-induced anaemia? *Crathorne L, Huxley N, Haasova M, Snowsill T, Jones-Hughes T, Hoyle M, Briscoe S, Coelho H, Long L, Medina-Lara A, Mujica-Mota R, Napier M, Hyde C.*

1502P: What is the clinical and cost effectiveness of erythropoietin-stimulating agents for the treatment of patients with cancer-treatment induced anaemia? Insights from cumulative meta-analyses (CMA) and lessons for cost-effectiveness analyses. *Haasova M, Huxley N, Crathorne L, Hyde C.*

REFERENCES

1. Wilson J, Yao GL, Raftery J *et al*. (2007). A systematic review and economic evaluation of epoetin alpha, epoetin beta and darbepoetin alpha in anaemia associated with cancer, especially that attributable to cancer treatment. Health Technol Assess. **11,** 1-202, iii-iv.

DISCLOSURES

- This project was commissioned by the NIHR HTA Programme.

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