INAHTA Briefs

Issue 2007/25

Title **Topotecan, Pegylated Liposomal Doxorubicin Hydrochloride and Paclitaxel for Second-Line or Subsequent Treatment of Advanced Ovarian Cancer: A Systematic Review and Economic Evaluation**

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Reference Health Technol Assess 2006;10(9). March 2006. www.hta.ac.uk/execsumm/summ1009.htm

Aim

To examine the clinical effectiveness and cost effectiveness of intravenous formulations of topotecan monotherapy, pegylated liposomal doxorubicin hydorocholoride (PLDH) monotherapy, and paclitaxel alone or in combination with a platinum-based compound for second-line or subsequent treatment of advanced ovarian cancer (AOC).

Conclusions and results

Nine randomized controlled trials (RCTs) were identified. Three trials included participants with both platinum-resistant and platinum-sensitive AOC. Two trials included only participants with platinum-sensitive disease. A further 4 trials were identified. Participants with platinum-resistant disease showed a low probability of response to treatment with PLDH, topotecan, or paclitaxel. Also, little difference was found between the 3 comparators as regards overall survival. Toxicity profiles of the comparators differed considerably. Paclitaxel and platinum combination therapy gave the most favorable survival times and response rates for participants with platinum-sensitive disease. Regarding single-agent compounds, the evidence suggests that PLDH is more effective than topotecan. Another trial that compared PLDH and paclitaxel found no significant difference between these two. The 3 comparators differed significantly in terms of their toxicity profiles across the trials.

Four studies met the inclusion criteria for cost-effectiveness review. Review of the economic evidence found significant limitations in studies assessing the cost effectiveness of PLDH, topotecan, and paclitaxel. Analysis 1 assessed the cost effectiveness of PLDH, topotecan, and paclitaxel as monotherapies. In the base-case results, paclitaxel monotherapy was cheapest. As regards incremental cost-effectiveness ratios (ICERs), topotecan was dominated by PLDH. Hence, the options considered in estimating ICERs were paclitaxel and PLDH. The ICER for PLDH compared with paclitaxel was GBP 7033 per quality-adjusted life-year (QALY) in the overall patient population. The ICER was more favorable in the platinum-sensitive group and less favorable in the platinum-refractory/resistant group. Incorporating the results of the additional trial data resulted in less favorable estimates for the ICER for PLDH versus paclitaxel compared with the base-case results. Analysis 2 explored the cost-effectiveness of the full range of treatment comparators for platinum-sensitive patients. The reliability of these results should be interpreted with caution. Topotecan, paclitaxel monotherapy, and PLDH were all dominated by platinum monotherapy. After excluding these alternatives, platinum monotherapy was the least costly and least effective.

Recommendations

PLDH treatment may be more beneficial than topotecan, but patient and physician choice as to the potential toxicities associated with each of the comparators and the patient's ability and willingness to tolerate these are important. Assuming the NHS is willing to pay GBP 20 000 to GBP 40 000 per additional QALY, PLDH appears to be cost effective compared with topotecan and paclitaxel monotherapy. (See Executive Summary link above.)

Methods

Seventeen databases were searched up to April 2004 for RCTs, systematic reviews of clinical effectiveness, and economic evaluations of the cost-effectiveness of PLDH, topotecan, and paclitaxel. Selected studies were quality assessed and data extracted, as were the 3 company submissions. A new model was developed to assess the costs of alternative treatments, the differential mean survival duration, and the impact of health-related quality of life. Monte-Carlo simulation was used to reflect uncertainty in the cost-effectiveness results.

Further research/reviews required

- Trial to compare paclitaxel in combination with a platinum-based therapy versus single-agent PLDH.

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ISSN 1654-501X