Combined treatment with low-dose interferon plus vinblastine is associated with less toxicity than conventional interferon monotherapy in patients with metastatic renal cell carcinoma


Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
The use of high-dose interferon (IFN) monotherapy (15 x 10^6 U, three times weekly) versus low-dose IFN (5 x 10^6 U, three times weekly) plus vinblastine (VBL, 6 mg/m2 every 14 days) for the treatment of metastatic renal cell carcinoma.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with metastatic renal cell carcinoma who did not have serious infection, hypertension, cardiac disease or other malignancies. In addition, the patients had to be 70 years old or younger, and be naive to the agents used in this study.

Setting
The setting was secondary care. The economic study was carried out in Athens, Greece.

Dates to which data relate
The effectiveness data were collected between 1988 and 1993 inclusive. The resource use data appear to apply to the same period. No price year was reported.

Source of effectiveness data
The effectiveness data were derived from a single study.

Link between effectiveness and cost data
The resource use data appear to have been collected from the same sample as the effectiveness data. It was not stated whether these data were collected prospectively or retrospectively.

Study sample
This study enrolled 100 consecutive patients (50 in each group) presenting at two hospitals between January 1988 and May 1993. The sample would appear to have been appropriate for the clinical question. A power calculation estimated that 44 patients in each group would be sufficient to detect a 20% difference in the response rates (effectiveness) with 80% power at the 5% significance level.
Study design
This was a randomised, non-blinded study carried out at two hospitals. The patients were assigned to one of the two groups using sealed envelopes. The duration of the study was 12 weeks. Thirteen patients (13%) withdrew before the end of the 12 weeks, including 5 in the control (IFN) group and 8 in the intervention (IFN+VBL) group. The control group patients all withdrew due to severe toxicity. The reasons for withdrawal were more varied among the intervention group. Two refused to continue, 2 suffered progression in their bone metastases, 1 had severe toxicity, 1 suffered a nonfatal myocardial infarction and 2 died.

Analysis of effectiveness
The data were analysed on an intention to treat basis. The authors reported "no obvious clinically important differences between the two treatment groups at baseline". The primary effectiveness outcomes were:

- the rates of complete response ("disappearance of all tumour markers and clinically measurable disease"),
- partial response ("50%-100% decrease in the sum of the products of the two longest perpendicular diameters of measurable lesions"), and
- stable disease ("<50% decrease or <25% increase in ... parameters").

The incidence of various treatment-related adverse events was also measured.

Effectiveness results
There were no statistically significant differences in the response rates or estimated survival between the two groups. Forty-two per cent of the IFN monotherapy patients versus 34% of the IFN+VBL patients had either complete response, partial response or stable disease.

More IFN+VBL patients (52%) experienced leukopenia than IFN monotherapy patients (24%), (p=0.013).

More IFN patients suffered severe fatigue (53%) than IFN+VBL patients (17%), (p=0.0008).

More IFN patients had greater than 10% weight loss (58%) than IFN+VBL patients (24%), (p=0.002).

The mean duration of fever was also greater among IFN patients.

The other toxicity results were not statistically significant.

Clinical conclusions
Combined treatment with IFN+VBL was better tolerated than IFN monotherapy, with no statistically significant decrease in the short-term effectiveness.

Measure of benefits used in the economic analysis
No summary health benefit measure was used. This was therefore a cost-consequences study.

Direct costs
The hospital costs included in the analysis were the IFN and VBL treatments and associated hospital stays, and other drugs including antibiotics. The resource use data were presumably collected alongside the trial between 1988 and 1993 inclusive. The quantities of IFN, VBL and hospital days were reported separately. No sources or dates were reported for the unit costs. Discounting was irrelevant as the costs referred to the 12-week treatment period only.
Statistical analysis of costs
A t-test was conducted to test the significance of the difference in the overall treatment costs between the two groups. The test was significant at the 5% level.

Indirect Costs
The indirect costs were not included in this analysis.

Currency
US dollars ($).

Sensitivity analysis
No sensitivity analyses were reported.

Estimated benefits used in the economic analysis
See the 'Effectiveness Results' section.

Cost results
The IFN+VBL group used less of each resource than the IFN monotherapy group.

The total cost of IFN+VBL was $75,772.

The cost of IFN monotherapy was 60% greater at $195,840, (p<0.001).

These costs appear to apply only to the 12-week treatment period. In addition, they included the costs of the drugs, the use of which was likely to be related to treatment-related adverse events.

Synthesis of costs and benefits
Not relevant.

Authors' conclusions
The combined interferon (IFN) and vinblastine (VBL) treatment appears to have been better tolerated than IFN monotherapy without compromising short-term efficacy. In addition, as it also resulted in cost-savings, the IFN+VBL treatment appears to dominate conventional treatment.

CRD COMMENTARY - Selection of comparators
IFN monotherapy was reported to be the conventional treatment in the setting of this study. You should check whether this is current practice in your own setting.

Validity of estimate of measure of effectiveness
This study was a randomised controlled trial and was, therefore, appropriate for the clinical question. The authors excluded patients on the basis of common criteria such as age, serious co-morbidities, and prior exposure to the drugs in question. However, they did not speculate on the extent to which their sample was representative of the general metastatic renal cell carcinoma population. The groups were comparable at baseline and appropriate statistical tests were conducted.

The authors appear to have estimated survival of up to 70 to 100 weeks on the basis of the observed outcomes at 12
weeks. Thus, there is likely to be much uncertainty surrounding the survival estimates, though this was not discussed in the analysis.

**Validity of estimate of measure of benefit**
No summary benefit measure was used since this was a cost-consequences study.

**Validity of estimate of costs**
The article provided few details about the cost analysis. The quantities of IFN, VBL and hospital days were reported separately and, therefore, may be generalisable to other settings. However, because no information was provided about the unit costs, the final figures are of limited generalisability. The analysis included the costs of antibiotics and "other drugs", the use of which was presumably affected by the severity of the adverse events. Thus, the analysis appears to have included all the major relevant hospital costs, although the exclusion of any lesser cost items is unlikely to have affected the conclusions of the study, as the main cost driver in the analysis was the cost of IFN and/or VBL.

**Other issues**
The authors discussed the findings of other studies though none of these appear to have included a cost analysis. The authors concluded that IFN+VBL is better than IFN for patients with metastatic renal cell carcinoma because it is better tolerated, equivalent in short-term efficacy and cheaper. Their results showed that IFN+VBL patients experienced more leukopenia, although it was of a low enough grade not to cause complications. The authors' conclusions are therefore justified given the scope of the analysis.

**Implications of the study**
The authors recommend a longer-term study to evaluate the survival effects of these treatments.

**Source of funding**
None stated.

**Bibliographic details**

**PubMedID**
10954911

**DOI**
10.1089/10799900050116381

**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Adult; Aged; Antineoplastic Agents, Phytogenic /administration & dosage /adverse effects /economics; Antineoplastic Combined Chemotherapy Protocols /administration & dosage /adverse effects /economics; Carcinoma, Renal Cell /drug therapy /secondary; Costs and Cost Analysis; Drug Tolerance; Fatigue /chemically induced; Female; Fever /chemically induced; Humans; Interferon-alpha /administration & dosage /adverse effects /economics; Kidney Neoplasms /drug therapy; Leukopenia /chemically induced; Male; Middle Aged; Recombinant Proteins; Vinblastine /administration & dosage /adverse effects /economics; Weight Loss /drug effects