

■ CONFERENCE REPORTS

Non-curative chemotherapy for cancer – is it worth it?

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For most patients with cancer, treatment achieves only modest prolongation of survival and limited improvements in the quality of life. So is it worth giving non-curative treatment for cancer?

Delay in diagnosis, poor communication and support, inequalities in treatment and inadequate funding have contributed to poor survival figures for cancer in the UK. However, there has now been an unprecedented increase in financial support, with an increase of 30% over four years in cancer health care expenditure, to be spent on augmenting the workforce and cancer treatments. Among other laudable aims, the cancer plan aims to reduce the economic and professional inequalities between regions in the UK, and to establish a system of treatment appraisal by an independent body (NICE). By summer 2002, it is hoped to end the lottery in the availability of cancer treatments. Health authorities will need to ensure funding for all approved drugs.

New cancer treatments – will they make a difference?

In the past five to ten years the introduction of taxoids, topo-isomerase 1 inhibitors and novel antimetabolites such as gemcitabine and capecitabine for the treatment of breast, lung, colorectal and ovarian cancer has led to substantial symptomatic improvement and longer survival. However, there is also a great urgency to make better use of existing drugs and to develop more selective treatments for cancer cells.

Drug resistance and the non-selectivity of current conventional therapies limit their use. Several trials employ antibody, gene or virus-directed enzyme pro-drug therapies to overcome the problem of pharmacological drug resistance, whilst cell resistance might be defeated by incorporating drugs that could modify defective transport or apoptotic mechanisms, eg herceptin (monoclonal antibody treatment for breast cancer).

Novel approaches to cancer treatment might employ agents that affect cancer growth, eg angiogenesis inhibitors or signal transduction inhibitors, in combination with conventional treatment to prevent metastases or to increase cell sensitivity. The most recent example of how this approach may affect future practice comes with the development of STI 1761, which inhibits the fusion protein bcr-abl, expressed by patients with chronic myeloid leukaemias (CML). Preliminary trials into this signal transduction inhibitor have produced complete response (CR) rates of around 100%.

Thus the future for cancer treatments is entering a new domain. Whilst cytotoxic agents will remain the cornerstone of therapy, the development of agents that influence, modify or modulate accessory pathways may substantially improve the effectiveness of such treatments and minimise the side effects.

Lung cancer

Non-small cell lung cancer (NSCLC) is a cruel and symptomatic disease. Unfortunately, cisplatin-based chemotherapy can be toxic, particularly in patients who are elderly and frail and who have multiple pathologies. In 1998 a survey showed that of 81

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Dr Martin Gore, The Royal Marsden Hospital

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Should old age influence cancer treatment?

Professor Ian Tannock, Princess Margaret Hospital, Toronto, Canada

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Ms Margaret King, cancer patient

Dr Ian Gibson MP

patients with cancer, 68% would accept chemo-therapy if it was likely that they would gain symptomatic control. A review in 1995 of outcome of responders versus non-responders showed that even in the latter group 54% of patients improved symptomatically. In the majority of patients relief of symptoms occurred after one cycle of therapy. Cisplatin reduced the risk of death by 27%, with a median increase in survival of six weeks. Other drugs, eg irinotecan, also reduce symptoms and prolong life in patients with lung cancer. Thus the concept of non-curative chemotherapy for lung cancer should be embraced with enthusiasm.

Breast cancer

In 1998, Tannock published the results of a study into palliative chemotherapy and metastatic breast cancer (MBC), comparing a higher versus a lower dose regimen. The response rate, duration of survival and toxicity were significantly greater in the higher dose group, with better pain control, mobility and less anxiety. In the same year, Ramirez demonstrated that MBC patients who responded to first line palliative chemotherapy were more likely to conclude that the treatment had been worthwhile, regardless of toxicity. There is a significant relationship between response to palliative chemotherapy and symptom improvement in women with metastatic breast cancer.

With the new agents such as taxotere, docetaxel, capecitabine and herceptin becoming available for metastatic breast cancer, there is great enthusiasm for the role of non-curative chemotherapy. Whether it is appropriate can only be answered by the patient herself.

Ovarian cancer

The majority of patients with ovarian cancer present with advanced disease. Over the past twenty years with the advent of platinum and now taxane containing treatments, the overall survival and disease free interval for such patients has increased significantly, due at least in part to the exquisite sensitivity of ovarian cancer to chemotherapy, both at presentation and relapse. Chemotherapy can be extremely useful in circumstances where surgery is unhelpful, eg for bowel obstruction secondary to disease.

Greater difficulty comes in deciding the correct time to retreat a patient, whether to re-challenge the patient with platinum, either as a single agent or in combination, and at which point to stop treatment in patients with either refractory or stable disease. The issue of maintenance forms part of this debate and the role of weekly taxanes is currently being assessed as part of a phase II study.

Colon cancer

For the patient with advanced colon cancer, four trials have demonstrated benefit in terms of overall survival and quality of life. These trials also, however, reveal a significant attrition rate in recruitment and wide variations in both patient selection and in the delivery of best supportive care.

The greatest advances in colorectal cancer therapy have occurred in the past five years, with the advent of two new agents to add to the limited armamentarium of active drugs: oxaliplatin and irinotecan. In patients who had previously received 5FU, second line irinotecan increased overall survival compared to best supportive care, whilst oxaliplatin improves progression-free survival, without impairment of quality of life, compared to 5FU. Further studies are needed to assess their place in treatment regimens.

Prostate cancer

The incidence of prostate cancer has trebled in the past 30 years, and is the second highest cause of death from cancer in men. However, fewer than 50% of patients see an oncologist, which may explain why the five year survival from the disease is a paltry 43% in the UK, compared to 69% in France and 68% in Germany. The role of maximum androgen blockade (MAB) in advanced prostate cancer was reviewed in *The Lancet* this year. Compared with monotherapy, MAB led to a significant improvement in five year survival. The addition of mitozantrone to MAB has also shown survival benefit in patients with locally advanced disease.

Quality of life is important, but quality of death is more important. Survival benefits are conferred by maximising androgen blockade and by the addition of chemotherapy. We need to be more aggressive and actively pursue chemotherapy options, if we are to improve the care of patients with advanced prostate cancer.

Should age influence cancer treatment?

The goals of palliative chemotherapy, ie survival, quality of life or both, are aspired to irrespective of age. Cancer is predominantly a disease of the elderly, and increasingly becomes a concern as to who should receive palliative chemotherapy. There is no zero cost option in terms of treatment: all have potential side effects. However, whilst co-morbidity undoubtedly increases with age and may affect the ability of any patient to tolerate chemotherapy, age alone is not a contraindication for treatment. A 1983 review of 19 studies in eight cancers revealed that patients over the age of 70 years experienced the same levels of toxicity as their younger counterparts. The elderly are often underrepresented in these trials, however, and patient selection tends towards the recruitment of fitter patients with less co-morbidity.

One method that allows an oncologist to select the most appropriate treatment for patients comes in the form of the comprehensive geriatric assessment (CGA). This categorises patients into three groups:

1. Those who are functionally independent and without co-morbidity: candidates suitable for most standard cancer treatments.
2. Those who are frail, dependent, and with three or more co-morbid conditions: candidates for supportive care.

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3. Those in between, who may benefit from a modified regimen of therapy.

Thus age should not influence cancer treatment, but functional status and likely benefit should.

How much is life worth?

Only the patient can answer the question, and only when in possession of the full facts. The main issues are quality of life, improvement of symptoms, and survival. Quality of life must be balanced against side effects. Survival too is important, and whilst a few weeks' extra benefit may not appear much to the doctor, to the patient it may be highly significant.

It is vital that health care professionals are considerate with their words when talking to patients. In particular, it is the treatment that has failed the patient, not vice versa; the word 'cure' is used liberally and inaccurately, and while – for the best of motives – doctors are hesitant with the truth, many patients would prefer a more candid approach.

There is an urgent need for a British strategy for cancer care,

encompassing research, palliative care and the patient's voice. The aim is to develop a cancer plan that is promoted irrespective of the presiding political party, one which seeks to promote and develop cancer standards, engender teamwork and ensure delivery of a first class service. Huge investments are needed to achieve this, but every life must be valued, and consumers and politicians alike must fight to improve the quality of life for every cancer patient.

Conclusion

This was a fascinating and stimulating conference. The invited speakers presented convincing data: non-curative chemotherapy has an enormous potential to improve the quality of life and possibly survival for the majority of cancer patients. Encouragement must be given at all levels to increase the referral rates to medical oncologists. With the advent of increased funding, better drugs and more awareness of the potential benefits of treatment, there should now be real optimism in cancer care.