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Patients' and doctors' preferences for adjuvant chemotherapy in resected non-small-cell lung cancer: What makes it worthwhile?

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Abstract ***Background:*** Adjuvant chemotherapy (ACT) in non-small-cell lung cancer (NSCLC) improves overall survival, but the benefits must be weighed against its harms. We sought to determine the survival benefits that patients and their doctors judged sufficient to make ACT in NSCLC worthwhile.
Methods: 122 patients completed a self-administered questionnaire at baseline and 6 months (before & after ACT, if they had it); 82 doctors completed the questionnaire once only. The time trade-off method was used to determine the minimum survival benefits judged sufficient in four hypothetical scenarios. Baseline survival times were 3 years & 5 years and baseline survival rates (at 5 years) were 50% & 65%.
Results: At baseline, the median benefits judged sufficient by patients were an extra 9 months (Interquartile range (IQR) 1–12 months) beyond 3 years & 5 years and an extra 5% (IQR 0.1–

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10%) beyond 50% & 65%. At 6 months ($n = 91$), patients' preferences had the same median benefit (9 months & 5%) but varied more (IQRs 0–18 months & 0–15%) than at baseline. Factors associated with judging smaller benefits sufficient were deciding to have ACT ($P = 0.01$, 0.02) and better well-being ($P = 0.01$, 0.006) during ACT. Doctors' preferences, compared with patients' preferences, had similar median benefits (9 months & 5%) but varied less (IQR 6–12 months versus 1–12 months, $P < 0.001$; 5%–10% versus 0.1–10%, $P < 0.001$).
Conclusion: Most patients and doctors judged moderate survival benefits sufficient to make ACT in NSCLC worthwhile, but the preferences of doctors varied less than those of patients. Doctors should endeavour to elicit patients' preferences during discussions about ACT in NSCLC.

1. Introduction

Adjuvant chemotherapy (ACT) is standard treatment for patients with resected non-small-cell lung cancer (NSCLC) following the demonstration of a survival advantage in modern randomised trials. A meta-analysis of the five largest of these trials [1–5] confirmed the benefits of platinum-based ACT in stages II and IIIA NSCLC as an 11% relative reduction in the hazard of death (95% CI 4% to 18%, $P = 0.005$) with an absolute benefit in overall survival of 5% at 5 years (from 44% to 49%) [6]. ACT was, however, toxic as shown by one quarter of the patients allocated ACT ($n = 2281$) having less than their planned treatment due to toxicity (34%) and patient refusal (35%).

Patients making decisions about ACT for NSCLC must trade-off its possible benefits versus its harms and inconveniences. This trade-off is a value judgement and reflected in their preferences for ACT [7]. Studies can quantify these preferences by determining the survival benefits needed to make the harms and inconveniences of a treatment worthwhile. Patients have judged small survival benefits sufficient to make worthwhile the harms and inconveniences of ACT in breast cancer and colon cancer (median benefits judged sufficient of an extra 1% in survival rate or an extra 1 month in survival time) [8–10], but patients' preferences for ACT in NSCLC have not been reported.

Thoracic surgeons and medical oncologists are key contributors to the process of decision making about ACT in NSCLC, as the main referrers for, and prescribers of, the treatment. The final treatment decision about ACT should, however, reflect the preferences of each patient rather than their doctors. Better understanding of how doctors may influence decisions about ACT in NSCLC requires knowledge of doctors' preferences. We previously showed that lung cancer clinicians ($n = 156$) attending a national lung cancer conference judged moderate survival worthwhile, but there were few thoracic surgeons ($n = 6$) included in the study sample [11].

The purpose of this prospective observational study was to determine the survival benefits judged sufficient, by both patients and their doctors (medical oncologists and thoracic surgeons), to make ACT worthwhile for resected NSCLC, the factors associated with their judgments, and comparisons of patients' and doctors' preferences.

2. Methods

2.1. Patients and doctors

Patients were included if they had stage I to stage III NSCLC resected within 12 weeks of referral to a medical oncologist at a participating centre who were able and willing to complete the study questionnaire. Patients were excluded if they had evidence of metastatic disease or if they had received previous chemotherapy for NSCLC. All patients provided written, signed and informed consent. Medical oncologists at each participating centre and referring thoracic surgeons were also invited to participate. Ethical approval was obtained from each of the 17 participating centres.

2.2. Preferences

Patients' and doctors' preferences were elicited with a written, validated, self-reported questionnaire [10]. The questionnaire used the time trade-off method to determine the minimum survival benefits judged sufficient to make ACT in NSCLC worthwhile. There were two survival time questions and two survival rate questions for a total of four hypothetical scenarios. The scenarios had baseline survival times without ACT of 3 or 5 years, and baseline survival rates at 5 years without ACT of 50% or 65%.

The survival time questions asked patients and doctors to consider the benefit of ACT as adding extra time to the baseline of 3 or 5 years without ACT. The extra time benefits were discrete and incremental from a minimum of an extra 1 day to a maximum of an extra15 years. For example, patients and doctors were asked to choose between living 3 years *without* the harms and inconveniences of ACT or 3 years plus 1 day (or 1 month, 3 months and so on) *with* the harms