

Trial Scenarios: Monitoring

3. Trial of preoperative chemotherapy in oesophageal cancer¹

Background:	It has been reported that preoperative chemotherapy improves ¹ survival in oesophageal cancer, but there is little randomised evidence.
Design:	Open simple pragmatic RCT
Setting:	42 hospitals across Europe
Study population:	800 patients with oesophageal cancer due to have surgery
Eligibility criteria:	Microscopically confirmed oesophageal cancer without lymph node involvement or metastatic disease; no other malignancy; normal renal function, white-cell count and platelets
Intervention:	Group 1 – immediate chemotherapy with 2 cycles of cisplatin and fluorouracil (commonly used chemotherapies in long-standing use) followed by surgical resection Group 2 – immediate surgical resection
Randomisation:	Central telephone randomisation
Trial supplies:	From routine hospital stock
Main outcomes:	Survival time (primary) and dysphagia (secondary) recorded by treating clinician
Follow-up:	3-monthly for first year, then 6-monthly until death
Data management:	Paper CRFs
Experience:	Coordinating centre and clinical sites all experienced in conducting and participating in clinical trials

What are the particular hazards of the trial?

The main concern in this trial is whether pre-operative chemotherapy increases the peri- and post-operative surgical morbidity.

Suggested Approaches to Monitoring

Trial Oversight:

- A trial steering committee
- An independent DMC is essential
- A trial management group

¹ This scenario was based on a trial report by the MRC Oesophageal Cancer Working Party, Surgical resection with or without preoperative chemotherapy in oesophageal cancer. (*Lancet* 2002; 359:1727), but some of the details have been altered or invented.

Before the start of recruitment:*Minimum*

- Written assurance from each investigator that the setup was complete and they are ready to start; **and**
- Investigator questionnaire to check appropriate training and skills

Optimal

- Investigators' meeting(s) to review the trial and all procedures (It might be possible to organise a meeting in conjunction with a scientific conference)

During the trial

Depending on whether or not site visiting is undertaken, one of the following plans is suggested:

	Without site visiting	With site visiting
Understanding of and adherence to protocol and trial procedures	Annual investigators meetings, if feasible (alternative - several teleconferences)	Annual site visits
Verification of participant existence	<ul style="list-style-type: none"> • Collect signed consent form at coordinating centre (with patient consent) • Collect pathology reports • Central registry (eg ONS) flagging wherever possible 	Clinic records
Consent	Collect signed consent form at coordinating centre (with patient consent)	Check consent forms in patient's clinical records
Eligibility	<ul style="list-style-type: none"> • Review of eligibility prior to randomisation (by telephone or faxed form) • Pathology reports 	Check against clinic records
Outcome	Collect death certificates	Record of death and dysphagia in clinic records
Other data	Central statistical monitoring to identify sites that may require attention or visiting	Sample of records for review of accuracy of adverse event reporting

Centralised classification of outcomes blind to treatment group is recommended.

At the end of the trial

Written confirmation from each site regarding archiving.