

Principles underlying the non-surgical treatment of cancer

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Medical and clinical (radiation) oncology are rapidly changing fields. Both understanding of cancer and the technology available are expanding at a rapid pace. Nevertheless, there are basic principles that remain constant. These are to ascertain as precisely as possible the diagnosis, stage of disease and molecular characteristics of the tumour and, from this information, assess via the multidisciplinary team the management options for the patient. In general terms, where a local treatment, i.e. surgery or ablation, is as effective as a systemic treatment, the local treatment will be preferred. The range of options will be specific to each tumour type and is constantly evolving. This is most true of the systemic therapy options available to patients. The purposes of oncology treatment can be conveniently divided into:

- curative primary : the effect of non-surgical treatment alone is highly effective, e.g. head and neck cancers (Table 12.5);
- neoadjuvant : where non-surgical treatment prior to surgery can substantially reduce the morbidity of treatment and increase its chances of success, e.g. radiotherapy to downstage rectal carcinoma prior to surgery;
- adjuvant : where non-surgical treatment after surgery can increase the chance of cure, e.g. radiotherapy and chemotherapy after breast cancer;
- life-prolonging/palliative : these terms are better separated, especially in the case of life-prolonging treatments in a non-curative setting that may add years to life, e.g. use of olaparib in BRCA - mutated ovarian cancer.

Systemic therapies In recent decades, drug development has evolved from screening large libraries of chemicals for their ability to interfere with cellular processes. Increased understanding of the molecular pathophysiology of cancers has identified key molecules essential to tumour function. Many of these molecules can be inhibited and are termed 'druggable targets'. Three-dimensional characterisation of these targets and synthesis of molecules to inhibit them has produced a large number of highly effective targeted therapies. The pace of change is sufficiently rapid that it is now only possible for an individual clinician to keep abreast of developments in a limited number of cancers. The following principles are key in decision making over systemic therapy administration to individual patients:

- Assess the fitness and willingness of the patient to tolerate each of these options. Most cancers occur in middle-aged or older patients. The older a patient is, the more likely they are to have comorbidities or be frail. It is important to note that middle-aged patients may be unfit or have serious comorbidities and that older patients may actually be very fit. Organ dysfunction and frailty may substantially increase the risks of treatment and reduce its chance of success. This must be assessed on an individual basis.
- Support the patient to understand the options and choose the most

appropriate management approach. Discussions about prognosis and treatment options are complex, difficult and any decisions made are often irrevocable. They also take place when the patient and their family are at their most anxious and vulnerable. It is often necessary to provide information in digestible amounts and to do so repeatedly. There are few oncological situations where an immediate decision needs to be taken by the patient. The difficulties of drawing a balance between risk and benefit are illustrated by considering adjuvant therapy for a solid malignancy. In the absence of a good test to ascertain individual risk of relapse, it is necessary to treat Max Wilms, 1867–1918, Professor of Surgery, Heidelberg, Germany. often around 10% (Figure 12.5). Although 10% is a small proportion, it represents a small chance of a major benefit, namely cure. If there were a test that could accurately determine patients with no residual disease after resection, then a lower proportion of patients would need to have adjuvant therapy, each of whom would have a higher chance of benefit (Figures 12.5 and 12.6). Frequently reassess the balance of risk and benefit during treatment. For patients receiving repeated cycles of treatment, there are three key questions to consider before proceeding with the next cycle of treatment: 1 Is the treatment working? Where there is measurable disease, this is usually assessed by radiological restaging at intervals of 6–12 weeks. The test for whether the treatment is working will depend on the goals of treatment: if the goal is stabilisation of disease then it may be sufficient that the tumour is not growing; if the goal is elimination of disease then progressive shrinkage of the radiological abnormalities will be necessary. 2 Is the patient tolerating treatment? This can only be discovered by asking the patient what side effects they are experiencing. Clinicians should be used to detecting and managing the side effects of the drugs they are prescribing. In addition to open questions, the clinician should enquire specifically about common or dangerous side effects. If the patient is not tolerating treatment, then it may be necessary to delay the next cycle or to reduce the dose, even though this may be at the expense of reducing the effectiveness of treatment. 3 Is it safe to give the next cycle of treatment? To answer this question, the clinician will have to assess what side effects the patient is experiencing and also ensure that laboratory measures are within acceptable limits. The necessary laboratory tests will commonly include full blood count, urea and electrolytes and liver function tests as well as other tests determined by which treatments are being used.

without the need for surgical excision. Malignancy Potentially curative treatment Leukaemia Chemotherapy (+/- radiotherapy) Lymphoma Chemotherapy (+/- radiotherapy) Small cell lung cancer Chemotherapy (+/- radiotherapy) Chemotherapy (+/- Tumours of childhood radiotherapy) (rhabdomyosarcoma, Wilms' tumour) Early laryngeal cancer Radiotherapy Advanced head and neck Chemoradiation (synchronous cancer chemotherapy and radiotherapy) Oesophageal cancer Chemoradiation (synchronous chemotherapy and radiotherapy) Squamous cell cancer of the Chemoradiation (synchronous anus chemotherapy and radiotherapy) Advanced cancer of the cervix Radiotherapy (+/- chemotherapy) Medulloblastoma Radiotherapy (+/- chemotherapy) Skin tumours (BCC, SCC) Radiotherapy BCC, basal cell carcinoma; SCC, squamous cell carcinoma.

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