Principles of combined treatment

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Non-surgical treatments are often used in combination. For example, radiotherapy and chemotherapy are often given together as an alternative to surgery , e.g. in the treatment of rectal, cervical, head and neck or brain cancers (Table 12.5 The rationale behind combination, as opposed to single- modality therapy , is straightforward and is somewhat analogous to that used for combined antibiotic therapy: it is a strategy designed to combat resistance. By the time of diagnosis many tumours will contain cancer cells that, through spontaneous mutation, have acquired resistance to individual modalities of treatment. Unlike antibiotic resistance, there is no need for previous exposure to the treatment. Spontaneous mutation rates are high enough to allow chance to permit the occur rence, and subsequent expansion, of clones of cells resistant to a treatment to which they have never been exposed. If only single-modality treatments were used, then the further expansion of these de novo resistant subclones would limit cure. The problem can be mitigated by , from the outset of treatment, combining treatment modalities. drugs for combination therapy is based: (i) use drugs active against the diseases in question; (ii) use drugs with distinct modes of action; (iii) use drugs with non-overlapping toxicities . By using drugs with di ff erent biological e ff ects, for example by combining an antimetabolite with an agent that actively dam - ages DNA, it may be possible to obtain a truly synergistic e ff ect, i.e. where the e ff ects of the two modalities together are supe - rior to the additive e ff ects of both separately . It is inadvisable to combine drugs with similar adverse e ff ects: combining two highly myelosuppressive drugs may produce an unacce ptably - high risk of neutropenic sepsis. Where possible, combinations - should be based upon a consideration of the toxicity profiles of the drugs concerned. In considering the combination of radiotherapy and che - motherapy , radiation could be considered as just another drug. There is, in addition to synergy and toxicity , another factor to consider in the combination of drugs and radiation – the concept of spatial cooperation. Chemotherapy is a systemic treatment, radiotherap y is not. Radiotherapy is, however, able - to reach sites, such as the central nervous system and testis, that - drugs may not reach e ff ectively . This is why , for example in patients treated primarily with chemotherapy for leukaemias, lymphomas and small cell lung cancer, prophylactic cranial irradiation may be part of the treatment protocol. Summary box 12.4 Principles of combined treatment /uni25CF /uni25CF - /uni25CF /uni25CF -

Use effective agents Use agents with different modes of action (synergy) Use agents with non-overlapping toxicities Consider spatial cooperation

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