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INTRAPERITONEAL CHEMOTHERAPY: MEDICAL PRINCIPLES

The intraperitoneal (IP) delivery of chemotherapy in the management of malignant disease principally involving this body cavity has been an active area of clinical investigation since the landmark publication of Dedrick, et al, where a solid *theoretical rationale* for this strategy was initially presented (1).

A number of factors are relevant when considering the development of a rational approach for the use of the IP route in the treatment of cancer. These include:

- (a) Major *clinical manifestations* of a disease involve the peritoneal cavity
- (b) Documented *substantial biological activity* of the drug(s) against the particular tumor type (e.g., ovarian cancer, colon cancer)
- (c) Pre-clinical or (preferably) clinical evidence for the importance of *dose* (e.g., peak level) and/or *concentration* (e.g., total AUC) in optimizing cytotoxicity (individual drugs and synergistic activity between agents)
- (d) *Favorable pharmacokinetics* for cavity exposure, compared to the systemic compartment (e.g., slow clearance from cavity; rapid clearance from circulation) following IP delivery
- (e) *No/minimal local toxicity* to peritoneal lining following IP delivery (e.g., non-irritant)
- (f) Treatment of very small tumor volumes (due to limited penetration of drugs into solid masses) or microscopic disease only
- (g) Clinical evidence of biological activity in settings where such activity would not have been anticipated (e.g., surgically-documented responses to IP cisplatin in ovarian cancer patients who had failed systemically-delivered platinum)

The safety and pharmacokinetic advantage of IP cisplatin (10-20-fold increased exposure compared to the systemic compartment) shown in phase 1 trials led to the conduct of phase 2 studies in recurrent ovarian cancer (surgically documented-objective response rates of 20-40%) (2,3), and ultimately three phase 3 randomized trials that demonstrated primary delivery of IP cisplatin improved overall survival (20-30% relative reduction in risk of death) compared to systemic administration of the agent (4-6).

IP chemotherapy may be associated with greater toxicity compared to that routinely associated with systemic treatment, due both to local effects (e.g., irritant properties) of the agent and the unique requirements for regional drug delivery (e.g., catheter placement). These issues will need to be considered, and problems resolved, before a specific strategy is likely to become accepted as “standard-of-care” in a particular clinical setting (7).

References:

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