Dose-toxicity models in oncology

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INTRODUCTION: The first human exposure to a new medicine always carries a major risk. Assessment of the safety profile and determination of a therapeutic dose are formidable tasks, particularly in oncology where toxicity is seen as a surrogate for efficacy. Increasing evidence supports the adoption of innovative dose-toxicity models, as these are safer and more efficient in meeting the challenges of modern investigational oncology than traditional models used in Phase I clinical trials. AREAS COVERED: A literature review on dose-toxicity models in oncology was carried out. The objective of this study was to provide a non-mathematical, reader-friendly overview of current and innovative dose-toxicity models in oncology with an emphasis on recent clinical advances, including the benefits of a Bayesian framework. EXPERT OPINION: Innovative dose-toxicity models attempt to minimize clinical risk and maximize research performance. Of these, the Bayesian Continual Reassessment Method and the Escalation With Overdose Control are two successful contemporary designs that outperformed traditional models in clinical trials; they account for patient heterogeneity, combination therapy, and they appropriately assess molecularly targeted agents. Support by regulatory authorities is providing an additional incentive to the widespread use of innovative and efficient dose-toxicity designs: this will improve investigational oncology, and ultimately benefit patients and science alike.

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