
The use of molecular profiling in clinical practice is increasing. Using genomic sequencing, cancers can be classified into molecular subsets. However, designing clinical trials for these molecular subsets is challenging secondary to the few numbers of available patients. Newer clinical trial designs are needed to identify novel anticancer therapy based on molecularly defined subsets.


The $3 + 3$ design is the most commonly used dose escalation scheme in phase I clinical trials. In simulation studies, adaptive designs, including the modified toxicity probability interval (mTPI), have been shown to be more efficient in identifying the maximum tolerated dose. Software is provided free of cost for utilizing the mTPI design.


Dosing based on phase 1 trials was associated with a low toxicity-related death rate in later trials. The ability to predict relevant toxicities correlates with the number of patients in the initial phase 1 trial. The final dose approved was within 20% of the recommended phase 2 dose in 73% of assessed trials.


The use of expansion cohorts has increased with time. Safety and efficacy are common objectives, but 26% of these cohorts fail to report explicit aims. Expansion cohorts may provide useful supplementary data for phase 1 trials, particularly with regard to toxicity and defining the recommended dose for phase 2 studies.


Physician education to dispel unfounded perceptions, improved access to available clinical trials, and the provision of personnel and resources to accommodate the unique requirements of an older population are possible solutions to remove the barriers of ageism.


Combining an anti-CD20 antibody with chemotherapy improved outcomes in patients with chronic lymphocytic leukemia and coexisting conditions. In this patient population, obinutuzumab was superior to rituximab when each drug was combined with chlorambucil.


Dabrafenib and trametinib were safely combined at full monotherapy doses. The rate of pyrexia was increased with combination therapy, whereas the rate of proliferative skin lesions was not significantly reduced. Progression-free survival rates were significantly improved.


The continued MAPK signaling–based resistance identified in patients with BRAF-mutant melanoma suggests that an alternative dosing of current agents, more potent RAF/MEK inhibitors, and/or inhibition of the downstream kinase ERK may be needed for durable control of BRAF-mutant melanoma.


Vemurafenib induces clinical responses in more than one-half of patients with previously treated BRAF V600-mutant metastatic melanoma. In this study with lengthy follow-up, the median overall survival rate was approximately 16 months.


The authors review recent studies on the role of programmed cell death 1 (PD-1) in immunological tolerance and discuss the possible clinical applications of manipulating PD-1.