Impact by age on dose-limiting toxicities in phase 1 oncology trials of cytoxic agents and molecular targeted agents

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Background: Elderly cancer patients aged 65 or more are generally frail compared with younger patients. They are considered to be the age group of less fitting for clinical trials, especially investigating feasibility. For the past decade, the types of the agents have been changing and the number of drug classes has been increasing. The aim of our study was to investigate the impact by age on dose-limiting toxicities (DLT) in each type of agents.

Methods: Retrospective analysis was implemented on patients who participated in phase 1 oncology trials between 1995 and 2016 in our institution. DLT was defined in each trial protocol. The rate of DLT was compared between younger patients (< 65 year) and elderly patients (≥ 65 year) for cytotoxic agents and molecular targeted agents.

Results: In this period, 973 patients underwent 214 enrolments in trials of cytotoxic agents and 996 enrolments for molecular targeted agents. For cytotoxic agents, 165 enrolments with 23 DLT events (13.9%) occurred in the younger group and 49 enrolments with 13 DLTs (26.5%) in the elderly group (p = 0.05). With molecular targeted agents, 728 enrolments with 57 DLTs (7.8%) occurred in the younger group and 268 enrolments with 31 DLTs (11.6%) in elderly group (p = 0.08).

Conclusions: In phase 1 trials, enrolment of elderly patients should be carefully discussed especially in trials of cytotoxic agents. With molecular targeted agents, age groups exert less impact on DLT.

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