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Titel des Beitrags:
Phase II study to assess the efficacy, safety and tolerability of the mitotic spindle kinesin inhibitor AZD4877 in patients with recurrent advanced urothelial cancer.

Abstract:
AZD4877 is a potent inhibitor of the mitotic spindle kinesin, Eg5. Early-phase clinical studies in a broad range of cancers showed that AZD4877 is well tolerated. This Phase II study evaluated the efficacy, safety and pharmacokinetics (Cmax) of AZD4877 in patients with previously treated advanced urothelial cancer (ClinicalTrials.gov identifier NCT00661609). AZD4877 25 mg was administered once-weekly for 3 weeks of each 4-week cycle until disease progression, death, unacceptable toxicity or withdrawal. The primary objective was to determine the objective response rate (RECIST). Recruitment was to be halted if ≥ 8 weeks (including one unconfirmed PR). The most commonly reported treatment-related adverse events (TRAEs) were neutropenia (22 patients), fatigue (12), leukopenia (7) and constipation (6); the most commonly reported grade≥ 3 TRAE was neutropenia (21). Four patients had serious TRAEs. On days 1 and 8, the geometric mean Cmax of AZD4877 was 138 ng/ml (CV = 75 %) and 144 ng/ml (CV = 109 %), respectively. AZD4877 was generally tolerable in patients with advanced
urothelial cancer. Given the limited clinical efficacy, further development of AZD4877 in urothelial cancer is not planned.