Phase Ib trial of the Toll-like receptor 9 agonist IMO-2055 in combination with 5-fluorouracil, cisplatin, and cetuximab as first-line palliative treatment in patients with recurrent/metastatic squamous cell carcinoma of the head and neck.

This Phase Ib trial assessed the maximum tolerated dose (MTD) and safety of the Toll-like receptor 9 agonist IMO-2055 combined with 5-fluorouracil, cisplatin, and cetuximab (PFE) as first-line palliative treatment in patients with relapsed and/or metastatic squamous cell carcinoma of the head and neck (R/M SCCHN). A standard 3+3 study design was used. Patients were sequentially enrolled to be treated with IMO-2055 (0.16, 0.32, or 0.48 mg/kg/day; days 1, 8, 15), 5-fluorouracil (1,000 mg/m$^2$/day; days 1-4), cisplatin (100 mg/m$^2$/day; day 1) and cetuximab (400 mg/m$^2$/day first dose; then 250 mg/m$^2$/day; days 1, 8, 15) every 3 weeks. Thirteen patients received IMO-2055. Dose-limiting toxicities (DLTs; ie, any Grade [G]3/4 treatment-related adverse events [TEAEs] in cycle 1) occurred in 2/4 patients treated with IMO-2055 0.32 mg/kg (G4 hypokalemia and hypomagnesemia [n=1]; G4 septicemia, hyperthermia, febrile neutropenia, and G3 hypotension [n=1]). In the IMO-2055 0.16-mg/kg expansion cohort, 1 patient experienced DLTs of G3 sepsis, bacteremia, and hyperthermia. The most common G$\geq$ 3 TEAEs were neutropenia (n=9; not including febrile...
neutropenia (n=1), hypokalemia (n=5), and hypomagnesemia (n=4). Serious adverse events (SAEs) occurred in 8 patients, including 4 with SAEs considered IMO-2055 related; 1 of these patients died. Best response achieved overall was partial response in 3 patients and stable disease in 9 patients. The overall safety profile led to early trial termination; the safety monitoring committee did not confirm the MTD (formally IMO-2055 0.16 mg/kg). Regimens combining IMO-2055 and PFE cannot be recommended for further development in R/M SCCHN patients.