PHASE I PHARMACOKINETIC STUDY OF S-1 GRANULE AND NEDAPLATIN FOR PATIENTS WITH RECURRENT/METASTATIC HEAD AND NECK CANCER

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Background: S-1 granule is developed to meet the needs for patients, especially with dysphagia. The current study is the first phase I trial of S-1 granule to evaluate the safety, efficacy and pharmacokinetics of the combination with nedaplatin in patients with squamous cell carcinoma of the head and neck (SCCHN).

Methods: Patients with advanced or refractory SCCHN were treated with i.v. nedaplatin at doses starting at 80 mg/m² (level 1) and escalating to 90 mg/m² (level 2), and S-1 granule at a fixed daily oral dose of 80 mg/m² on days 1 to 14 every 3 weeks. The primary end-point was to determine the recommended dose for nedaplatin given in combination with a fixed dose of S-1 granule.

Results: Twenty patients (median age, 63 yr) were enrolled in this study. One of the first six patients at dose level 1 and all three patients at dose level 2 experienced a dose limiting toxicity (the delay of >2 weeks in administering the second treatment cycle in one and two patients at dose level 1 and 2, respectively, grade 4 thrombocytopenia in one patients at dose level 2. The recommended dose was thus determined as level 1, and an additional 11 patients were assigned this level. The most frequent toxicities were leucopenia, neutropenia, thrombocytopenia, fatigue, and anorexia. All observed adverse events were well managed and no treatment-related death occurred. The response rate was 42.1% (8 of 19 patients), and the median progression-free and overall survival time was 5.5 and 12.0 months, respectively. Pharmacokinetic parameters of S-1 granule did not appear to differ substantially from those obtained previously for S-1 capsule and no pharmacokinetic interaction between S-1 granule and nedaplatin was detected.

Conclusions: The combination of S-1 granule and nedaplatin is well tolerated and appears to potentially possess activity in HNSCC.