A phase II study of TAS-102 for advanced/recurrent esophageal cancer refractory/intolerable to standard therapies


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Background: There is no effective chemotherapy for patients with esophageal squamous cell carcinoma (ESCC) refractory or intolerant to 5-FU, platinum, and taxanes. TAS-102 is an oral combination drug of trifluridine and tipiracil hydrochloride. Our preclinical study showed that TAS-102 has antitumor activity against 5-FU resistant esophageal cancer cells. We conducted this study to evaluate the safety and efficacy of TAS-102 in ESCC patients who were refractory or intolerant to standard treatment (UMIN000019268).

Methods: Patients with histologically proven advanced or recurrent ESCC, which had been refractory or intolerant to 5-FU, platinum, and taxanes, were eligible. Patients also had to satisfy following criteria: >20 years of age; ECOG performance status 0 or 1; adequate organ functions. TAS-102, 35 mg/m2 bid, was administered on days 1-5 and 8-12 for the first 2 weeks followed by 2-week rest. The regimen was repeated every 4 weeks until disease progression, serious adverse event, or refusal. Primary endpoint was progression-free survival rate at 3 months (PFS3). With expected PFS3 of 25% to 30% and the null hypothesis of 10% under 80% power and a one-sided significance level of 5%, 35 patients was needed.

Results: A total of 42 patients were enrolled. 90% of the patients were male, 95% had distant metastasis, and 98% had target lesion (s). As of data cutoff, 34 events were observed, PFS3 was 15.4% (90% CI: 7.4%, 26.0%), which did not reject the null hypothesis. Median PFS and OS were 1.3 months and 4.5 months, respectively. Response rate was 0%, although 24% (10/42) of patients achieved stable disease. There were 3 patients not evaluable for response. Major treatment related adverse events of grade ≥3 were: neutrophil count decreased (48%), febrile neutropenia (7%), and appetite decreased (5%). No treatment related death was observed.

Conclusions: TAS-102 was feasible and showed modest efficacy in patients with refractory ESCC.

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