Advanced gastric cancer (AGC) patients treated with S-1 in a Caucasian population. A specialized center experience in Ireland

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Introduction: S-1 is an oral combination of tegafur (a prodrug of 5-fluorouracil (5-FU)) and two modulators of 5-FU metabolism, gimeracil and oteracil. This combination was optimized to reduce the toxicity of 5-FU due to toxic metabolites. S-1 in combination with cisplatin is approved for use in AGC in Europe since 2011. We report here post-approval safety data for 11 AGC patients treated with S-1 regimens in daily practice including combination with oxaliplatin (SOX) and trastuzumab. Data were collected in the observational Study of Compliance Observed with Oral fluoropyrimidine Teysuno (SCOOP).

Methods: Laboratory, treatment, compliance, and adverse event data were recorded at baseline and after each treatment cycle for patients treated with S-1 between September 2012 and March 2014. Reasons for discontinuation were recorded at the end of the study. Patients with histologically confirmed, unresectable, advanced or metastatic gastric carcinoma, including adenocarcinoma of the gastroesophageal junction, who were being treated with S-1 (in first-line or subsequent-line treatment) and who had a performance status ≤ 2 were included. Patients with a contraindication to oral fluoropyrimidine treatment were excluded.

Results: Data for 11 patients (8 male; mean age, 60 years) were evaluated. Ten patients had stage IV disease; one had stage IIIb/c disease. Six patients had no previous treatments while 5 had received ≥1 previous treatments. Nine patients received a combination of S-1 (25mg/m2 bid for 14 days) with oxaliplatin (130mg/m2 d1) (SOX q3w) while one received S-1 plus trastuzumab (6mg/kg), and one received SOX plus trastuzumab. A total of 36% of patients (4/11) completed 6 cycles and 55% of patients (6/11) completed at least 5 cycles of therapy without S-1 dose reductions. No patients skipped or reduced S-1 during treatment. One patient discontinued for non-compliance. One patient experienced grade 3 thrombocytopenia, neutropenia, and hematoma in cycle 2 which resolved with dose reduction and discontinuation of oxaliplatin in cycle 3. Two patients experienced grade 2 nausea in cycle 1 that was considered to be related to S-1 treatment. One of these patients discontinued due to non-compliance, the other resolved without treatment and was able to continue through 5 cycles. No hand-foot syndrome or cardiotoxicity were reported.

Conclusion: S-1 regimens for AGC in Caucasian patients appear to be well tolerated in combination with oxaliplatin (SOX) in this, albeit limited, Irish cohort. Further studies have to be performed to confirm the benefit of SOX in AGC in the Caucasian population as it was recently demonstrated in the Asian population (Yamada Y, Higuchi K, Nishikawa K et al. Phase III study comparing oxaliplatin plus S-1 with cisplatin plus S-1 in chemotherapy-naïve patients with advanced gastric cancer. Ann Oncol. 2015; 26(1):141-8).