SO-18 Safety and efficacy of trifluridine/tipiracil in previously treated metastatic colorectal cancer: Final results according to duration of treatment from the phase IIIb, international, open-label, early-access PRECONNECT study

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Background: Trifluridine/tipiracil (FTD/TPI) is registered in over 93 countries for the management of patients with metastatic colorectal cancer (mCRC) who have progressed on standard therapies. In the RECOURSE study, FTD/TPI significantly improved overall survival and progression-free survival (PFS) compared with placebo. 1,2 PRECONNECT was an international, multicentre, open-label, phase IIIb trial (NCT03306394) designed to provide eligible adults with mCRC access to FTD/TPI and to further characterise the safety and efficacy of FTD/TPI in daily clinical practice. Here we present the final results from PRECONNECT according to duration of treatment (DoT).

Methods: Patients aged ≥18 years with histologically confirmed mCRC who were refractory to, or not candidates for, standard chemotherapies and had an Eastern Cooperative Oncology Group performance status (ECOG PS) of 0 or 1, received oral FTD/TPI 35 mg/m 2 twice-daily on days 1-5 and 8-12 of each 28-day cycle. Treatment continued until disease progression, unacceptable toxicity, physician decision, withdrawal of consent, pregnancy, major protocol deviation, or when FTD/TPI became commercially available. The primary endpoint was safety (including incidence of treatment-emergent adverse events [TEAEs] and time to deterioration of ECOG PS to ≥2). Secondary endpoints included PFS and quality of life (QoL) as measured by QLQ-C30. Data are presented as descriptive statistics, and by DoT group — [0-3] FTD/TPI treatment cycles completed, [4-7] cycles completed and ≥8 cycles completed.

Results: Of the 914 patients (male 59%; median age 62 years; ECOG PS 0 in 49%; RAS mutant 52%; median time from first metastasis 32 months; median number of previous lines of treatment 3) analysed, 632 (69%) completed [0-3] cycles, 219 (24%) completed [4-7] cycles, and 63 (7%) completed ≥8 cycles. Patients completing [4-7] and ≥8 cycles of FTD/TPI were more likely to have a baseline ECOG PS of 0, less likely to have a RAS mutation, had a longer time from first metastasis to first FTD/TPI intake, and were less likely to have previously received regorafenib versus those completing [0—3] cycles. TEAEs were experienced by 96.6% of the overall patient population; the most frequent were neutropenia (53.5%), asthenia (36.7%), anaemia (31.1%), nausea (29.5%), and diarrhoea (24.8%). Drug-related grade ≥3 TEAEs included neutropenia (38.1%), anaemia (7.2%), and asthenia (3.4%). Severe febrile neutropenia (1.2%) and severe cardiac disorders (0.7%) were infrequent. Median [95% CI] PFS was 2.8 [2.7-3.0] months, and median PFS increased with DoT ([0-3] cycles: 2.2 [2.0-2.3] months; [4-7] cycles: 5.3 [4.6-5.6] months; ≥8 cycles: 9.4 [8.7-10.5] months). Median [95% CI] time to ECOG PS deterioration was 9.2 [8.5-NC] months and increased with DoT ([0-3] cycles: 3.8 [3.5-3.9] months; [4-7] cycles: 8.9 [8.5-NC] months; ≥8 cycles: 16.4 [14.3-NC] months). There was no clinically relevant change from baseline in QLQ-C30-GHS score overall or by DoT group.

Conclusions: The PRECONNECT study showed consistent results with the previously demonstrated safety and efficacy profile of FTD/TPI, with no new safety concerns identified. PFS and time to ECOG PS deterioration increased with DoT, and QoL was maintained during treatment. These data provide additional support for the use of FTD/TPI in the treatment of mCRC in daily clinical practice.

Clinical trial identification: NCT03306394.

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