O – 013 Safety and efficacy of trifluridine/tipiracil in previously treated metastatic colorectal cancer (mCRC): Preliminary results from the phase IIIb, international, open-label, early-access PRECONNECT study

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Introduction: Trifluridine/tipiracil (FTD/TPI) was approved following the results of the RECOURSE study (Mayer et al. N Engl J Med 2015;372:1909-19), which demonstrated that FTD/TPI significantly improved overall survival (OS) and progression-free survival (PFS) versus placebo. FTD/TPI is approved for treatment of previously treated mCRC patients, in the same setting as regorafenib. In October 2016, a phase IIIb PRECONNECT study was set up in mCRC patients to assess safety and efficacy of FTD/TPI in daily practice (NCT03306394).

Methods: PRECONNECT is enrolling patients who have histologically confirmed mCRC previously treated with, or who are not considered candidates for, available therapies, with an ECOG PS of 0 or 1. Patients receive FTD/TPI (35 mg/m2 twice daily) orally on days 1–5 and 8–12 of each 28-day cycle. Patients were followed-up up to end of study treatment. Withdrawal criteria include disease progression, unacceptable toxicity and commercial availability of FTD/TPI. Primary endpoint is safety and PFS as key secondary endpoint.

Results: A study cohort of 462 patients from 10 countries had received at least one dose of treatment at cutoff (1 November 2017). Median age was 64 years (range 28–87); 63.6% were male; 46.5% were ≥65 years old. Of the 450 patients evaluable for PS, 46% and 54% had ECOG PS 0 and 1, respectively at baseline. 52.2% had known RAS mutation. Primary site of disease was left-sided for 62.8%, right-sided for 24.5%, and not specified for 12.8%. Prior to study start, more than 94% received fluoropyrimidine and/or oxaliplatin and/or irinotecan, while 83%, 41% received anti-VEGF, anti-EGFR respectively and only 35% patients received regorafenib. Emergent adverse events (AEs) were reported in 92.4%. Drug-related AEs were reported in 74.5%; most common were neutropenia, nausea and diarrhea, which occurred in 49.5%, 27.7%, and 20.6% of patients, respectively. Drug-related grade ≥3 AEs were reported in 48.6%; most common hematological were neutropenia (38%), anemia (7.1%), febrile neutropenia (1.7%), and thrombocytopenia (1.3%) while most common non-hematological were diarrhoea (3.5%) and fatigue (2.2%). At cutoff time, 29 patients remained on treatment (6.2%). Of the 435 patients withdrawn from the study, 77.4% withdrew for

progressive disease, 6.7% for AE and 6.4% for commercial availability of FTD/TPI that remained on treatment at withdrawal. Median FTD/TPI treatment duration and number of cycles were 12.9 weeks (range 2–48) and 3 (range 1–12), respectively. Median relative dose intensity was 89%. Dose of FTD/TPI was reduced due to AE in 8% of patients mainly due to neutropenia (2.8%). FTD/TPI was associated with a median PFS of 3.2 months (95% CI 2.8–3.4) and disease control rate of 41.1% (95% CI 36.3–46.0) in the 414 patients who received FTD/TPI and had one post-baseline tumor evaluation. Median time to ECOG PS $\geq$ 2 was 8.7 months. At cutoff time, 91.3% were still alive; therefore median OS was not yet reached.

Conclusion: These are first data on the widespread clinical use of FTD/TPI outside US and Japan. Preliminary encouraging safety and efficacy data obtained make FTD/TPI a favorable treatment option for mCRC patients.