Results: Safety and efficacy of trifluridine/tipiracil in previously treated metastatic colorectal cancer (mCRC): Preliminary results from the phase 3b, international, open-label, early-access PRECONNECT study

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Results: participants and exposure

Background

- Trifluridine/tipiracil (FTD/TPI, or TAS-102) is registered in over 48 countries (including Europe, USA and Japan) for the management of patients with metastatic colorectal cancer (mCRC) who had progressed on standard therapies.
- FTD/TPI has a different mechanism of action to 5-fluorouracil (S-FLU), and has demonstrated efficacy in mCRC patients refractory to S-FLU.1
- In the pivotal phase 3, RECOURSE study (NCT01607857; N=680), FTD/TPI significantly improved overall survival (OS) and progression-free survival (PFS) versus placebo in patients with mCRC who had progressed on standard therapies.2 In the final survival analysis, median OS with FTD/TPI was 7.2 months versus 5.2 months with placebo (hazard ratio [HR] 0.69; P<0.0001)3.
- The international, phase 3b PRECONNECT early-access study was initiated to provide a large cohort of eligible adult patients with mCRC access to FTD/TPI and to further assess the safety and efficacy of FTD/TPI in daily practice (NCT03006394). Presented herein are the safety and efficacy data of the first 462 patients included and treated in the program up to a cut-off date of 1 November 2017.

Methods

• PRECONNECT is an on-going, open-label, prospective, single-arm study.
• The primary objective of PRECONNECT is to determine the safety of FTD/TPI. - Safety was assessed by the incidence of adverse events (AEs), as well as changes in laboratory tests, physical examination, Eastern Cooperative Oncology Group performance status (ECOG PS) and vital signs.
- EOG P5 deterioration was also assessed and was defined as the time from start of treatment to the first patient EOGC deterioration (changing from an EOGC P5 of 0-1 baseline to ≥2 post baseline). - AEs were graded using NCI CTCAE version 4.03.
• The secondary objectives of PRECONNECT include assess the efficacy of FTD/TPI in terms of investigator-assessed PFS, objective response rate (ORR), and disease control rate (DCR).
• Descriptive statistics are provided, depending on the nature of the variable.

Figure 1. Inclusion criteria, treatment schedule and withdrawal criteria for patients participating in PRECONNECT

- Patients aged ≥18 years with histologically confirmed mCRC
- Receipt of ≥1 prior regimens of standard chemotherapy (fluoropyrimidines, oxaliplatin, irinotecan, anti-VEGF mAb, anti-EGFR mAb for KRAS wt).
- Refractory, intolerant or not a candidate for those chemotherapies
- ECOG PS of 0 or 1
- Patients with adequate organ function

Table 1. Patient demographics, characteristics and previous therapies at baseline.

- Between October 2016 and May 2017, 462 patients were enrolled and received at least one dose of FTD/TPI.

Conclusions

- Analysis of the safety and efficacy of FTD/TPI in this large interim analysis of the prospective, phase 3b PRECONNECT study in patients with mCRC who have been previously treated with standard therapy demonstrated that:
- The safety profile of FTD/TPI was acceptable and consistent with that reported in the randomized phase 3 RECOURSE trial and other previous randomized trials.4
- Median PFS based on investigator assessment was 2.3 months (95% CI: 2.7-3.3) compared with 2.0 months (95% CI: 1.9-2.1) in FTD/TPI treatment arm based on a radiological assessment (N=533).2
- DCR was 36.8% compared with 44% in RECOURSE treatment arm (N=533).2
- Median time to deterioration of EOGC P5 was 8.7 months compared with 5.7 months in RECOURSE treatment arm (N=533).2
- The PRECONNECT data provide further support of FTD/TPI as a safe and efficacious treatment option for pre-treated mCRC patients.
- PRECONNECT will also assess the quality of life of patients; preliminary data are anticipated in 2019.

References


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