P-54 Phase 2a study of NT-I7, a long-acting interleukin-7, plus pembrolizumab: Cohort of subjects with checkpoint inhibitor-naïve advanced MSS-colorectal cancer

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Background: Checkpoint inhibitor (CPI) monotherapy is ineffective for microsatellite stable colorectal cancer (MSS-CRC). NT-I7 (efineptakin alfa) is a long-acting IL-7 that can increase T-cell infiltration in the tumor microenvironment (TME). We hypothesize that NT-I7 may create a favorable immune-reactive TME to enhance the efficacy of CPI when combined with pembrolizumab (pembro).

Methods: This is an open-label, phase 2a study in subjects with relapsed/refractory (R/R) tumors, including CPI-naïve R/R MSS-CRC. Subjects were enrolled following Simon's 2-stage minimax design; 17 were enrolled in the first stage, and 8 additional subjects were enrolled for the second stage. Subjects received the recommended-phase-2-dose of NT-I7 intramuscularly at 1200 µg/kg every 6 weeks (Q6W) plus pembro 200 mg intravenously Q3W. Preliminary anti-tumor activity based on Overall Response Rate (ORR) was assessed by Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 and iRECIST. Biomarker analyses in peripheral blood and tumor biopsy were performed.

Results: As of 14-Jan-2022, 28 subjects were enrolled in the CPI-naïve R/R MSS-CRC cohort. Median age was 56.0 years [37-81], with ECOG PS 0 (28.6%) and 1 (71.4%). Twenty-three (82%) subjects received $\geq$ 2 prior therapies. All subjects had metastatic or locally advanced disease at enrollment. The median duration of follow-up was 5.3 months. Among these 25 evaluable subjects ORR and disease control rate (DCR) was 4% (1/25 subjects) and 40% (10/25) per RECIST v1.1; 12% (3/25 subjects) and 44% (11/25) per iRECIST. In addition to 3 subjects with iPR, 11 subjects are still ongoing to follow up responders. Interestingly, in patients with rectal malignancy both ORR and DCR by iRECIST were 50% (2/4). The ORR and DCR by iRECIST were 25% (1/4) and 50% (2/4) in 2L; 17% (1/6) and 33% (2/6) in 3L; and 13% (1/8) and 50% (4/8) in 4L. Among subjects without/with $\geq$ 2 liver mets, the ORR was 33.3% (2/6) vs 5.3% (1/19); DCR was 83.3% (5/6) vs 31.6% (6/19) and PFS was 11.6 weeks vs 6.1 weeks. All subjects with responses continue on treatment. Treatment-related adverse events (trAEs) occurred in 27 (96.4%) subjects, 12 (42.8%) G1-2 events and 14 (50%) G3 events; 1 (3.6%) G4 and no G5 trAEs were reported. No subjects discontinued from the study due to trAE. One iPR subject with available biopsy data showed an enhanced T-cell infiltration in the TME at week 5.

Conclusions: The chemotherapy-free combination of NT-I7 + pembro was well tolerated in heavily pretreated subjects with CPI-naïve R/R MSS-CRC. The encouraging antitumor activity showed that subjects without liver metastasis sites especially benefited from the combination of NT-I7 and pembro therapy. Biomarker analyses demonstrated improved peripheral and intratumoral T cell responses. Plan is to enroll 25 more patients to further evaluate efficacy of NT-I7 + pembro in CPI-naïve subjects with R/R MSS-CRC.

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P-55 Efficacy and safety data from patients with pre-treated metastatic colorectal cancer receiving trifluridine/tipiracil: Real-world data from the non-interventional TACTIC study

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Background: In the pivotal phase III RECOURSE trial, trifluridine/tipiracil (FTD/TPI) significantly improved overall and progression-free survival (OS, PFS) in patients with pre-treated metastatic colorectal cancer (mCRC) compared to placebo [1]. While randomised controlled trials represent the most reliable method of hypothesis testing, in- & exclusion criteria inevitably impede translation of their results to a real-world patient collective. Omitting restrictive in- & exclusion criteria we challenged the observations from the RECOURSE trial on a patient population which more accurately reflects daily clinical practice in Germany.

Methods: In this prospective, multi-centre, open-label, non-interventional study, patients with pre-treated mCRC were treated with oral FTD/TPI (35 mg/m2 bid on days 1 — 5 and 8 — 12 of each 28-day cycle). Primary endpoint was OS. Secondary endpoints included PFS and safety. Additionally, 3 subgroups were defined according to a post-hoc analysis of the RECOURSE trial [2]: best, good and poor prognostic characteristics (BPC, GPC, PPC). Patients with $<$ 3 metastatic sites at inclusion and $\geq$18 months from diagnosis to inclusion were considered to have GPC. GPC patients without liver metastasis at inclusion were considered to have BPC. All remaining patients were considered to have PPC.

Results: From June 2018 to August 2021, 307 patients were treated with FTD/TPI (mean treatment duration 3.4 cycles) at 52 German sites. Median age was 67.7 years and 17.0% of patients had an ECOG PS2/3. When focusing on patients with ECOG PS$\leq$1, median OS of patients in the full analysis set (n=243: 8.6 months; 95% CI 7.4 — 9.3) as well as of the defined subgroups (BPC n=54 vs GPC n=147 vs PPC n=96: 16.2 vs 9.8 vs 6.3 months; 95% CI 9.7 — 19.4 vs 8.6 — 11.7 vs 4.5 — 7.8) were in line with results of RECOURSE study (all patients n=534: 7.1 months/ BPC n=97 vs GPC n=261 vs PPC n=273: 16.4 vs 9.3 vs 5.3 months) [1] with a longer survival of patients with BPC and GPC compared to PPC. Similar results observed when analysing data from patients with ECOG PS$\leq$3 (all patients n=300: 7.4 months; 95% CI 6.4 — 8.6/ BPC n=65 vs GPC n=176 vs PPC n=124: 13.3 vs 8.9 vs 5.1 months; 95% CI 9.1 — 17.6 vs 7.6 — 9.8 vs 4.4 — 7.0). Median PFS of all patients in the full analysis set was 2.9 months (95% CI 2.8 — 3.3). BPC (n=65) and GPC (n=176) patients were characterised by a longer median PFS compared to PPC (n=124) patients (4.0 vs 3.4 vs 2.6 months; 95% CI 3.3 — 5.3 vs 3.0 — 3.7 vs 2.4 — 2.8). The most frequent TEAEs were anaemia (20.5%), leukopenia (18.6%) and neutropenia (16.9%).

Conclusions: Administration of FTD/TPI to patients with pre-treated mCRC was associated with prolonged survival, delayed progression and a manageable toxicity profile confirming efficacy and safety of FTD/TPI in a real-world population. Independent of other baseline characteristics such as ECOG PS and age, low metastatic burden and indolent disease were factors of good prognosis with regards of OS and PFS. [1]Mayer et al,NEnglJMed2015 [2]Tabernero et al,ESMOOpen2020.