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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INTRO & AIM

In the pivotal phase III RECOURSE trial, trifluridine/tipiracil (FTD/TPI) significantly improved progression-free and overall survival (PFS, OS) in patients with pre-treated metastatic colorectal cancer (mCRC) compared to placebo [1, 2].
While such 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.

METHOD

In this prospective, multi-centre, open-label, non-interventional study, patients with pre-treated mCRC or who were not suitable for other available therapies 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 [3]:

Subgroup	Time from diagnosis of metastatic disease to inclusion [months]	Number of metastatic sites at inclusion
Best prognostic characteristics (BPC):	≥ 18	1 - 2 (no liver metastasis)
Good prognostic characteristics (GPC):	≥ 18	1 - 2
Poor prognostic characteristics (PPC):	< 18	≥ 3

Treatment-emergent adverse events (TEAEs) were classified into defined categories of severity according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE) version 4.03.

Here, we present the final results of this study.

RESULTS

From June 2018 to August 2021, 307 patients were treated with FTD/TPI (mean treatment duration 3.4 months) at 52 German sites. Baseline characteristics of 300 treated patients who were evaluable for effectiveness are listed in Table 1. Median age was 67.7 years and 17.0% of patients had an ECOG PS 2/3.

Results of OS according to subgroups BPC, GPC and PPC are listed in Table 2 and illustrated in Figure 1.

Median PFS of all evaluable patients 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 are listed in Table 3 among which anaemia (20.5%), leukopenia (18.6%) and neutropenia (16.9%) were most common.

Figure 1: overall survival - stratified according to subgroups (any ECOG)

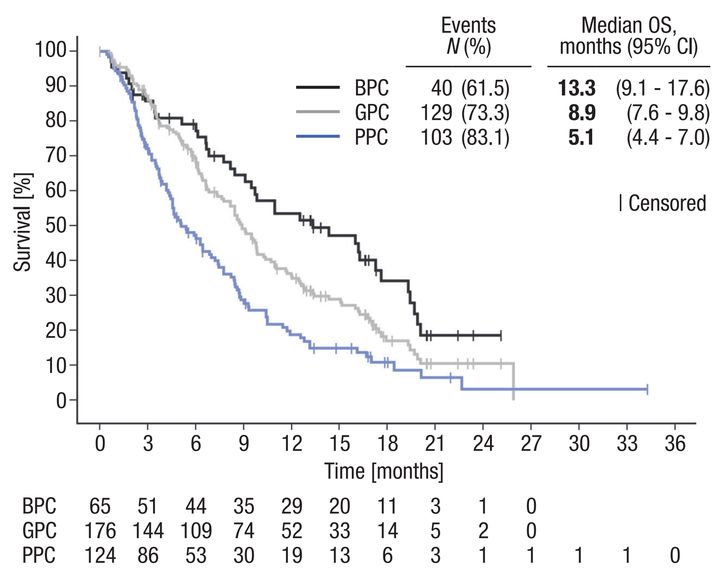

Table 1: baseline characteristics (*N* = 300)

Age, years	Median (range)	67.7 (33.3 - 90.5)
Gender, *n* (%)	Male	174 (58.0)
ECOG performance status, *n* (%)	0	72 (24.0)
	1	171 (57.0)
	2	47 (15.7)
	3	4 (1.3)
	Missing	6 (2.0)
RAS status, *n* (%)	Mutation	119 (39.7)
	Wild-type	132 (44.0)
	Unknown	49 (16.3)
Metastatic sites at inclusion, *n* (%)	Bone	20 (6.7)
	Brain	4 (1.3)
	Distant lymph nodes	51 (17.0)
	Liver	207 (69.0)
	Lung	157 (52.3)
	Peritoneum	57 (19.0)
	Other	33 (11.0)
Number of prior palliative treatment lines, *n* (%)	0	2 (0.7)
	1	61 (20.3)
	2	130 (43.3)
	≥3	107 (35.7)
Substances of previous systemic anti-CRC therapies, *n* (%)	Fluoropyrimidine-based	294 (98.0)
	Irinotecan-based	268 (89.3)
	Bevacizumab	226 (75.3)
	Anti-VEGF	59 (19.7)
	Oxaliplatin-based	225 (75.0)
	Anti-EGFR	101 (33.7)
	Other	10 (3.3)
	Regorafenib	1 (0.3)

Table 2: median OS (months, 95% CI) of FTD/TPI treated pts in subgroups of the RECOURSE vs TACTIC trial

	RECOURSE [2, 3]	TACTIC	
ECOG PS	≤ 1	≤ 1	any
Median age (years)	63	67.6	67.7
All pts	**7.1** [6.5 - 7.8] *n* = 534	**8.6** [7.4 - 9.3] *n* = 243	**7.4** [6.4 - 8.6] *n* = 300
BPC	**16.4** *n* = 97	**16.2** [9.7 - 19.4] *n* = 54	**13.3** [9.1 - 17.6] *n* = 65
GPC	**9.3** *n* = 261	**9.8** [8.6 - 11.7] *n* = 147	**8.9** [7.6 - 9.8] *n* = 176
PPC	**5.3** *n* = 273	**6.3** [4.5 - 7.8] *n* = 96	**5.1** [4.4 - 7.0] *n* = 124

Table 3: most frequent treatment-emergent adverse events (*N* = 307)

	Any grade		Grade ≥ 3	
	Cases	*n* (%)	Cases	*n* (%)
Any	1,000	238 (77.5)	291	146 (47.6)
Anaemia	81	63 (20.5)	27	25 (8.1)
Leukopenia	110	57 (18.6)	32	23 (7.5)
Neutropenia	101	52 (16.9)	60	40 (13.0)
Nausea	50	40 (13.0)	3	3 (1.0)
Diarrhoea	42	36 (11.7)	1	1 (0.3)
Fatigue	39	36 (11.7)	3	3 (1.0)
Vomiting	29	23 (7.5)	1	1 (0.3)
Decreased appetite	19	18 (5.9)	0	0
Thrombocytopenia	21	17 (5.5)	3	3 (1.0)

CONCLUSIONS

Administration of FTD/TPI to patients with pre-treated mCRC or who were not suitable for other available therapies 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.

Whereas BPC pts profited the most, pts from all prognostic subgroups evidently benefitted from treatment with FTD/TPI.

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