Update results from ALTER-C-001 study: efficacy and safety of anlotinib plus XELOX regimen as first-line treatment followed by maintenance monotherapy of anlotinib for patients with mCRC-A single arm, multi-center, phase Ⅱ clinical trial

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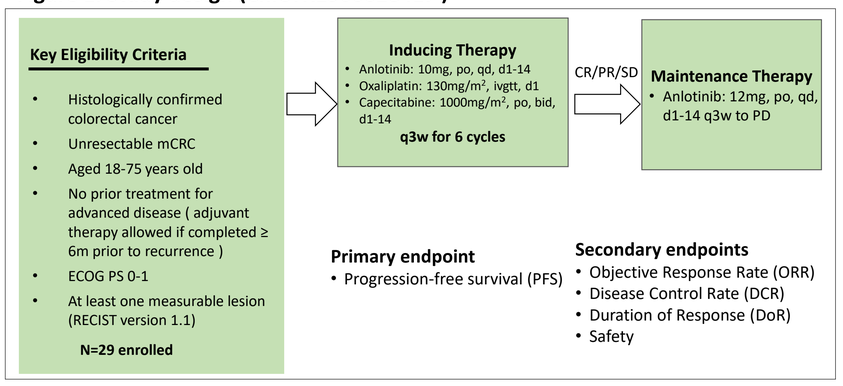
Background

- The standard therapy followed by maintenance treatment is an optional approach to balance the efficacy and toxicity for metastatic colorectal cancer (mCRC). But clinical trials have largely remained inconclusive regarding the maintenance strategy.
- Anlotinib, a novel multi-target TKI, significantly prolonged the PFS of refractory mCRC in a phase III clinical trial.
- The preliminary results of anlotinib plus XELOX regimen followed by anlotinib as first-line treatment (ALTER-C-001) exhibited antitumor efficacy and manageable toxicity for mCRC. Here we updated the results with more patients enrolled.

Methods

- This is a single-arm, open lable, multicenter phase II study (***Figure 1***)

Figure 1. Study design (ChiCTR1900028417)



Assessments

- Tumor assessment was assessed per RECIST V1.1 by investigators (every 6 weeks ± 7days).
- AEs were graded according to the National Cancer Institute Common Terminology Criteria for Adverse Event (NCI-CTCAE) V4.03.

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Results

Baseline characteristics

- At the data cut-off date of April, 2021, 21 patients were enrolled.
- Baseline characteristics were shown in ***Table 1***.

Table 1. Baseline characteristics of enrolled pts

Characteristics		Pts (n=21)
Age, median (range)		58 (48-67)
Gender, n (%)	Male	15 (71)
	Female	6 (29)
ECOG PS, n (%)	0	10 (48)
	1	11 (52)
Metastasis, n(%)	Liver	14 (67)
	Lung	11 (52)
	Bone	5 (24)
	Peritoneum	4 (19)
	Adrenal gland	2 (10)
	Ovary	2 (10)
	Enterocoelia	1 (5)
Prior chemotherapy, n (%)	No	12 (57)
	Yes	9 (43)
Primary tumor site, n(%)	Colon	7 (33)
	Rectal	14 (67)
NO. of metastases, n(%)	1	3 (14)
	≥2	18 (86)

Efficacy

- The longest duration of treatment was 12.1 months and the response was still ongoing (***Figure 2***).
- Among 17 efficacy-available patients, there were 52.9% PR (9/17), 35.3% SD (6/17) and 11.8% PD (2/17) in best overall response assessment （***Figure 3***）.
- The ORR (CR/PR) was 52.9% (9/17) and the DCR (CR/PR/SD) was 88.2% (15/17) (***Table 2***). The median PFS was not reached.

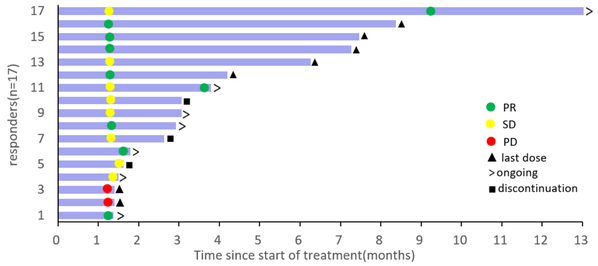

Figure 2. Duration of treatment and response with anlotinib plus XELOX regimen

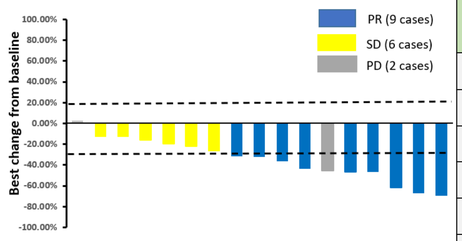

Figure 3. Best change (reductions in sum of lesion diameters) from baseline in evaluable patients with mCRC (n=17)

Table 2. Response in evaluable patients

Response Parameters	Anlotinib plus XELOX regimen (n=17)
CR, n(%)	0
PR, n (%)	9 (52.9)
SD, n (%)	6 (35.3)
PD, n (%)	2 (11.8)
ORR, n (%, 95%CI)	9 (52.9, 27.8–77.0)
DCR, n (%, 95%CI)	15 (88.2, 63.5–98.5)

Safety

- Most treatment-related adverse events (TRAEs) were grade 1-2. Grade 3 or above TRAEs were as follows (***Table 3***). One grade 5 TRAE was pancytopenia that occurred at 2.7 mths.

Table 3. Treatment-related adverse events (TRAEs) of the 21 pts with mCRC receiving anlotinib combined with XELOX

TRAEs	Any Grade , n(%)	Grade 3~4, n(%)
Leukopenia	9 (43%)	1 (5%)
Hypertension	8 (38%)	4 (19%)
Neutropenia	6 (29%)	3 (14%)
Diarrhea	5 (24%)	0 (0%)
Hypertriglyceridemia	5 (24%)	3 (14%)
Fatigue	4 (19%)	2 (10%)
Lipase elevation	3 (14%)	2 (10%)
Nausea and vomiting	3 (14%)	1 (5%)

Conclusion

- The update results suggested that anlotinib combined with XELOX as first line regimen followed by anlotinib monotherapy showed a promising clinical benefit and favorable safety profile for mCRC.
- And the results needed to be confirmed in trials continued subsequently.