TRESBIEN (OGSG 2101): Encorafenib, binimetinib and cetuximab for early recurrent Stage II/III BRAF V600E-mutated CRC

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Background

- The standard of care for early recurrent BRAF V600E-mutated colorectal cancer (CRC) during or after adjuvant chemotherapy has not been established.
- Recently, a novel combination of molecular-targeted agents, encorafenib (BRAF inhibitor), binimetinib (MEK inhibitor), and cetuximab (anti-EGFR antibody) showed significantly longer overall survival and a higher response rate than standard chemotherapy in patients with previously treated metastatic BRAF V600E-mutated CRC [1].
- Furthermore, in first-line treatment for BRAF V600E-mutated CRC, triplet therapy (encorafenib, binimetinib and cetuximab) showed a promising response rate and disease control rate [2].
- These results suggest that triplet therapy may be effective even in early recurrent BRAF V600E-mutated CRC during or after adjuvant chemotherapy; however, there are no reports demonstrating its efficacy in this population.

Methods

- The TRESBIEN study is an open-label, multicenter, single-arm phase II study designed to evaluate whether encorafenib, binimetinib, and cetuximab are effective in patients with early recurrent BRAF V600E-mutated CRC, during or after adjuvant chemotherapy.
- Patients will receive oral encorafenib at 300 mg daily, oral binimetinib at 45 mg orally twice daily, and cetuximab IV weekly at 250 mg/m² after the first dose of 400 mg/m² until disease progression, unacceptable toxicity, death, patient refusal, or investigator’s decision.
- The planned enrollment period is from January 2022 to December 2024, and the observation period will include a one-year follow-up period from the time the last patient is enrolled. No interim analyses will be performed.

Eligibility (N = 25)

- Recurrent BRAF V600E-mutated CRC during or within six months of adjuvant chemotherapy
- No prior treatment with encorafenib, binimetinib or cetuximab
- Performance status 0 to 2

Primary endpoint:
- Overall Response Rate (ORR)
- Disease Control Rate (DCR)
- Duration of Response (DoR)
- Time to Treatment Failure (TTF)

Secondary endpoints:
- Overall Survival (OS)
- Progression-Free Survival (PFS)
- Disease Control Rate (DCR)
- Duration of Response (DoR)
- Time to Treatment Failure (TTF)

Key Eligibility Criteria

1. Histologically confirmed wild-type RAS and BRAF V600E-mutated stage II/III colorectal adenocarcinoma
2. After radical resection, imaging evidence of recurrence during or within six months of adjuvant chemotherapy
3. Age ≥ 18 years
4. ECOG performance status 0-2
5. Written informed consent
6. No prior treatment with encorafenib, binimetinib, or cetuximab
7. Adequate organ function within 14 days before enrollment

Statistical Consideration

The primary endpoint of this study is the ORR. There are no specific data on the effect of ORR on early recurrence of BRAF V600E-mutated CRC. Based on BEACON CRC study[1], the expected ORR in this study was 26.0%. To achieve 90% power to show a significant response benefit with a one-sided alpha level of 0.05, and assuming a threshold ORR of 6.0%, we estimated that 23 patients would be necessary. Considering dropouts, a total of 25 patients will be enrolled.

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Conflict of Interest

Shogen Boku has received honoraria from Daiichi-Sankyo Co. Ltd., Taiho Pharmaceutical Co. Ltd., Chugai Pharmaceutical Co. Ltd.

References