Adding tumor debulking to palliative chemotherapy in multi-organ mCRC

Safety and Feasibility of the ORCHESTRA trial

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BACKGROUND

For selected patients with oligometastatic colorectal cancer (mCRC), local treatment of metastases is standard of care based on retrospective reports showing long term survival rates. In patients with multi-organ mCRC local treatment is technically feasible and therefore increasingly performed. However, it is unknown if adding tumor debulking to first line palliative chemotherapy improves overall survival in patients with multi-organ mCRC.

PURPOSE

The ORCHESTRA trial is designed to prospectively evaluate overall survival benefit from tumor debulking in patients with multi-organ mCRC.

METHODS

Primary endpoint: Overall Survival (OS)

Aim: OS benefit from added tumor debulking of > 6 months

Planned accrual: 478 patients

ARM A: Systemic therapy

ARM B: Systemic therapy and maximal tumor debulking

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BASELINE

Baseline tumor load (% of n [N])

- Liver metastasis
- 3 x CAPOX(B) or 4 x FOLFOX(B)

Randomization

Tumor Debulking

Tumor Debulking

Main inclusion criteria

Patients with mCRC metastases in ≥ 2 organs with an indication for first line palliative systemic therapy.

>80% Tumor debulking deemed feasible by expert panel by (combination of)

- Surgery
- Radiotherapy (SABR)
- Thermal ablative therapy (RFA/MWA)

RESULTS

All patient received 3 cycles 5-FU/oxaliplatin-based combination chemotherapy and bevazcuzumab as at physician discretion. In case of stable disease or response, patients were randomized to continuation of chemotherapy or to tumor debulking followed by continuation of chemotherapy. Serious Adverse Events (SAE) related to debulking were reported, 83.7% of patients accomplished.

Conclusion

Tumor debulking is feasible and safe and does not prohibit administration of palliative chemotherapy in the majority of patients with multi-organ mCRC.

FUTURE PERSPECTIVES

To date, 160 patients have been included in 30 participating hospitals in the Netherlands. The ORCHESTRA trial will continue accrual to determine whether the aim of > 6 months OS benefit from tumor debulking will be achieved.

SAFETY AND FEASIBILITY

Feasibility

From the first 100 patients included, 88 were randomized. No patients withdrew their consent after randomization. In the intervention arm, tumor debulking was performed in 37 of 45 patients (82.2%). In 32 of these patients (83.8%) >80% tumor debulking was accomplished.

Serious adverse events (SAEs) related to tumor debulking

In 15 of 37 patients (40.5%) who underwent tumor debulking, 21 SAEs related to debulking were reported, 83.7% of patients recovered within 30 days or had no SAEs. Postoperative 90-day mortality was 2.7%.

Chemotherapy was resumed in 86.5% of patients, in a median time of 12.7 weeks (range 4.7 – 35) and 78% completed a total of 8 cycles of CAPOX(B) or 12 cycles FOLFOX(B) chemotherapy versus 70% in arm A.

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