Circulating endothelial cell (CEC) monitoring in metastatic colorectal cancer (mCRC) patients treated with first-line bevacizumab-based combination regimens: results of the randomized phase II FNCLCC-ACCORD 13/0503 trial

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**Background**
Bevacizumab is a targeted monoclonal antibody that inhibits vascular endothelial growth factor, a key mediator in angiogenesis.1–3 In metastatic colorectal cancer (mCRC), bevacizumab improved objective response rate (ORR), progression-free survival (PFS), and overall survival (OS) when combined with chemotherapy.4-6 No biomarker able to predict the efficacy of anti-angiogenic therapy in patients with cancer has been identified.7-9 Although these preliminary reports were promising, the high levels of CEC detected in these studies as well as the very important discrepancies in CEC values reported in healthy individuals, led to considerable cautioning of the reliability of the only preliminary clinical trial for CEC measurement.10

Recently, the cells identified as CEC in these studies have been shown to be, in fact, large platelets.11 Because of the technical difficulties and challenge associated with CEC measurement, reliable data on CEC in cancer patients are still lacking today.

**Patients & Methods**

**Patients Population**
- ACCORD 13/0503 Design: Patients with metastatic colorectal cancer (mCRC) and normal platelet count were randomly assigned to receive bevacizumab (BV) at varying doses (2.5-7.5 mg/kg) in combination with FOLFOX or CAPEOX and chemotherapy.
- CECA: Patients with mCRC treated with BV at 13 mg/kg and FOLFIRI.
- BL and EOC1 CEC Levels: Combined Analysis & Progression at 6 months

**CEC Quantification:** Study Population
- Baseline CEC Levels & Patient Characteristics

**Results**

**Discussion & Conclusion**

**→ Discussion**
- High BL or EOC1 CEC levels: predictive of disease progression (PD) status at 6 months (primary endpoint):
  - BV 13 mg/kg + FOLFIRI: PD = 15%
  - High BL CEC level (≥16) at EOC1: PD = 17%
  - High CEC levels at BL & EOC1: PD > 25%

**→ Conclusion**
- CEC quantification by 4-color flow cytometry:
  - Reliable and reproducible
  - Moderate baseline (BL) CEC level (≤16) similar to that observed in our previous retrospective study in 159 patients with metastatic colorectal cancer (mCRC) treated with BV at 13 mg/kg and FOLFIRI.

**References**
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