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## Characterizing Glucose Homeostasis and Metabolic Response to Exercise in Patients with Metastatic Colorectal Cancer: Two Embedded Sub-Studies within the REACH Trial

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**Background:** A systematic review and meta-analysis found that patients with cancer are insulin resistant, which has been associated with poorer treatment tolerance and survival. Exercise may counteract these abnormalities, but mechanistic evidence in metastatic colorectal cancer (mCRC) during first-line chemotherapy is limited.

**Objectives:** To characterize glucose homeostasis at baseline and to examine (1) whether patients with newly diagnosed, unresectable mCRC exhibit impaired glucose homeostasis compared with matched non-cancer controls, and (2) metabolic adaptations to an 18-week structured exercise intervention during systemic therapy.

**Methods:** Two exploratory sub-studies are embedded within the ongoing REACH trial (Randomized controlled trial of the Effects of combined resistance and Aerobic exercise on Health-related quality of life in patients undergoing first-line chemotherapy for metastatic colorectal cancer), a randomized controlled trial with health-related quality of life as the primary outcome.

- In Sub-study I, baseline glucose homeostasis is assessed using 2-hour oral glucose tolerance test (OGTT), and continuous glucose monitoring (CGM; Dexcom G6) for 10 days in patients with mCRC (n=24) and age-, sex-, ethnicity- and BMI-matched non-cancer controls (n=24).

- In Sub-study II, n=60 participants (~30 per randomized arm) undergo the same assessments pre- and post-intervention to evaluate changes in insulin sensitivity, glucose tolerance, and incretin responses (GLP-1, GIP). Blood samples collected during OGTT are analyzed for glucose, insulin, C-peptide, and related metabolic markers. The primary endpoint is a composite combining 2-hour glucose from OGTT and time-in-range (TIR) from CGM for both sub-studies.

**Results:** Recruitment and assessments are ongoing. We anticipate presenting initial baseline characteristics and feasibility indicators (including participation and adherence to CGM/OGTT procedures), alongside preliminary baseline glucose profiles in mCRC.

**Perspectives:** These embedded sub-studies will provide clinically relevant insight into real-life glycemic patterns and glucose tolerance in advanced colorectal cancer and may inform future precision exercise strategies targeting metabolic health during oncology treatment.

### Keywords

Exercise oncology glucose homeostasis

### Conflict of Interest & Ethical Approval

yes

### Abstract submitters declaration

yes

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