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Effect of lean body mass on the association between oxaliplatin dose and dose-limiting neurotoxicity in colorectal cancer patients

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Background

Chemotherapy-induced peripheral neuropathy (CIPN) is a common, dose-limiting toxicity of oxaliplatin-based chemotherapy. Oxaliplatin dosing is based on body surface area and does not account for lean body mass (LBM), which may influence drug pharmacokinetics and toxicity. We assessed the independent and interactive effects of initial oxaliplatin dose and LBM on dose-limiting neurotoxicity during CAPOX chemotherapy in colorectal cancer (CRC) patients.

Methods

This study was conducted in a cohort of stage I-III CRC patients. CIPN after each chemotherapy cycle was assessed from oncologists' medical notes using the CTC-AE (v5.0), with grade ≥2 CIPN defined as dose-limiting. Initial oxaliplatin dose (mg) was obtained from medical records. LBM (kg) was estimated from diagnostic CT scans using the skeletal muscle area at the third lumbar vertebra, with sarcopenia defined by sex-specific skeletal muscle index cut-offs. A dose deviation score was calculated as the difference between the actual BSA-based dose and an LBM-based dose (3.09 mg/kg LBM) from a clinical trial. Cox regression models were used to assess associations between initial dose, deviation score, and time to grade ≥2 CIPN during the first four treatment cycles. Interaction terms were included to test whether LBM or sarcopenia modified the association between initial dose and CIPN.

Results

Data were analyzed from 136 patients treated with CAPOX between 2012 and 2019. The mean age at diagnosis was 63 years and 64% were male. The average BSA was 1.9 m^2, initial oxaliplatin dose was 249.2mg, LBM was 51.7 kg, and 33% of patients were sarcopenic. In total, 42 patients developed grade ≥2 CIPN during the first four cycles. Cox regression analysis showed no significant association between initial oxaliplatin dose or dose deviation score and time to grade ≥2 CIPN. No significant interactions were found between initial dose and LBM or sarcopenia, and no differences were observed in stratified analyses by LBM and sarcopenia.

Conclusions

Lean body mass did not modify the association between initial dose and the rate at which CIPN occurs during treatment in patients treated with CAPOX. Future research is needed to explore the effect of cumulative dose and long-term CIPN.

Legal entity responsible for the study

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Disclosure

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