

Abstract

58

Background: Regorafenib and trifluridine/tipiracil (TAS-102) are the only therapeutic options for patients with chemorefractory metastatic colorectal cancer (mCRC) with demonstrated benefit in overall survival (OS). However, they are not accessible worldwide. In Brazil, they have been recently approved, but they have not yet been provided by public health system or private health insurances. We aimed to describe the treatment patterns and clinical outcomes of that population in a setting with limited access to those drugs. **Methods:** Retrospective study evaluating 510 patients with mCRC who were treated at five Oncoclinicas centers in Brazil from January 2011 to December 2019. Demographic and clinical data were retrieved from electronic medical records. The median OS was calculated by Kaplan-Meier method and prognostic factors were evaluated via multivariable Cox Regression, calculating the Hazard Ratio (HR) and the confidence interval (CI95%). **Results:** A total of 163 patients (33% of the overall population) received third-line and 73 (15%) fourth-line systemic therapy. Median age was 62 years, 59% were male. Tumors were right-sided in 19%, *RAS* mutated 44%, *BRAF* mutated 3%, and high-frequency microsatellite instability 3%. Metastasectomy prior to third-line was performed in 62% of the patients. From the start of third-line therapy, median follow-up was 9.0 months, with 67% of deaths, and median OS was 13.7 months (CI95% 11.8m–20.0m). Most adopted regimens in third-and fourth-line were (1) rechallenge with oxaliplatin-based therapy (39% and 26%, respectively); (2) rechallenge with irinotecan-based therapy (32% and 34%); (3) rechallenge with anti-EGFR monoclonal antibodies (20% and 29%); (4) regorafenib (13% and 25%); and (5) TAS-102 (2% and 4%). In multivariable model including clinical and molecular variables, prior metastasectomy was the only significant prognostic factor for OS (HR 0.51, CI95% 0.31–0.83, $p=0.007$). **Conclusions:** In real-world, a meaningful proportion of patients with mCRC are eligible for third and later lines of therapy. Rechallenge with chemotherapy and anti-EGFR agents is overused in a setting of limited access to therapies with demonstrated OS benefit, such as regorafenib and TAS-102. Barriers to drug access impair the adoption of the best evidence-based continuum of care and strategies to overcome them are urgently needed. Refractory patients in later lines of therapy derive survival benefit from prior metastasectomy.