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Associations of incidence of common adverse events (AEs) and survival outcomes in metastatic colorectal cancer (mCRC) patients (pts) treated with first line chemotherapy: Findings from 9,812 pts in the ARCAD database.

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Abstract Disclosures

Background:

There is limited, often conflicting evidence about AE timing, severity or associations with outcomes with the use of cytotoxic agents in cancer treatment. We investigated the impact on overall survival (OS) and progression-free survival (PFS) of selected common AEs (neutropenia, diarrhea, nausea, vomiting, neuropathy) occurring in patients receiving first line oxaliplatin (Oxa)- and/or irinotecan(Iri)-based regimens for mCRC.

Methods:

The CTCAE grading scores of at least one AE of interest were available on 9812 pts treated with chemotherapy alone (median age 63; 62.4% male, 50.1% ECOG PS 0) from 17 1st-line randomized trials. Patients who also received biologics were excluded in the primary analyses. AEs occurring during the first 6 weeks of treatment and entire treatment were analyzed by stratified multivariable Cox models in relationship to OS/PFS. 55.7% pts received Oxa- regimens, 35.7% Iri-regimens, and 8.6% combined Oxa- and Iri-regimens.

Results:

Within the first 6 weeks of treatment, G3+ neutropenia (HR_{adj}= 1.3, 95% CI, 1.06-1.59, p_{adj} 0.01), diarrhea (HR_{adj}= 1.48, 95% CI, 1.23-1.79, p_{adj}< .0001), nausea (HR_{adj}= 1.53, 95% CI, 1.17-1.99, p_{adj} 0.002) and vomiting (HR_{adj}= 1.56, 95% CI, 1.18-2.07, p_{adj} 0.002) were associated with significantly worse OS for Iri-regimens, but only G3+ nausea predicted for worse OS for Oxa- regimens (HR_{adj}= 1.61, 95% CI, 1.18-2.21, p_{adj} 0.003). For AEs experienced at any time, G3+ neutropenia and neuropathy were significantly associated with longer PFS and OS for Oxa-regimens, while G3+ vomiting and nau ere associated with worse OS for both Oxa- and Iri-based regimens. Sensitivity analysis showed la gely concordant results by including pts who also received biologics.

Conclusions:

The association between more severe selected AEs and outcome varies between AEs and is influenced by timing of the occurrence. More severe selected AEs occurring early in treatment are associated with worse outcomes. In contrast, for AEs occurring at any time, G3+ neutropenia and neuropathy predicted for longer PFS and/or OS in Oxa-treated pts.