Session E. Gastrointestinal (colorectal) cancer

Prognostic significance of KRAS mutation rate in metastatic colorectal cancer patients


1Department of Medical Oncology, Campus Bio-Medico University of Rome, Roma
2Azienda Ospedaliero-Universitaria Pisana, Istituto Toscano Tumori, Pisa
3Niguarda Cancer Center, Ospedale Niguarda Ca’ Granda, Milano
4Unit of Medical Oncology - Department of Oncology - AOUPI, Palermo
5Università Cattolica del Sacro Cuore, Roma
6Department of Anatomical Pathology, Campus Bio-Medico University of Rome, Roma
7Department of Medical Oncology, Azienda Ospedaliero-Universitaria, Udine
8Dipartimento di Patologia Chirurgica, Medica, Molecolare e dell’Area Critica, Università di Pisa, Pisa

Background: Activating mutations of K-Ras gene have a well-established role as predictors of resistance to anti-EGFR monoclonal antibodies in metastatic colorectal cancer (mCRC) patients. Their prognostic value is controversial, and no data regarding the prognostic value of mutation rate, defined as the percentage of mutated alleles/tumor sample, are available. We aimed to evaluate the prognostic value of K-Ras mutation rate in a homogenous cohort of mCRC patients receiving first-line doublet plus bevacizumab.

Patients and methods: This retrospective study enrolled 397 K-Ras mutant mCRC patients from 6 Italian centers, and 263 patients were fully evaluable for our analysis. K-Ras mutation rate was assessed by means of pyrosequencing analysis. Patients with less than 60% of cancer cells in tumor tissue were excluded. No patients received anti-EGFR containing anticancer therapy, at any time. Median mutation rate was 40% and was adopted as cut-off value. The primary endpoint was PFS, OS was a secondary endpoint.

Results: At univariate analysis, a K-Ras mutation rate higher than 40% was significantly associated with lower PFS (7.3 vs 9.1 months; P < 0.0001) and OS (21 vs 31 months; P = 0.004). A multivariate model adjusted for age at diagnosis, site of origin of tumor tissue (primary cancer vs metastases), referral center, number of metastatic sites, and first-line chemotherapy backbone, showed that K-Ras mutation rate remained a significant predictor of PFS and OS in the whole population.

Conclusions: Our data demonstrate an association between K-Ras mutation rate and prognosis in patients treated with bevacizumab-containing first-line therapy for mCRC. These data deserve to be verified in an independent validation set.