A population study of correlation between the treatment rate for monoclonal antibodies (Mabs) and mortality rate in patients with metastatic colorectal cancer (mCRC) in Russia

Introduction: There is a large number of published Phase 3 trials exploring the efficiency of chemotherapy combination with Mabs in mCRC patients. Some of them appear not demonstrating a significant gain in overall survival. A direct additive impact of Mabs to chemotherapy at population level has not yet been assessed previously. The aim of this study was to evaluate the correlation between penetration (treatment rate) for different chemotherapeutic drugs and Mabs and mortality in a population of mCRC patients across 82 regions of Russia.

Methods: We have compared the mortality rate for mCRC patients sourced by the National Russian State Cancer Register and the Russian Government purchasing published data on hospital tenders for oxaliplatin, irinotecan, capcitabine and Mabs (bevacizumab, cetuximab, panitumumab) at regional level across 82 regions within the period of 2012-2014. Given that the expected median overall survival for mCRC patients varies from 18 to 29 months, the correlation was explored between penetration recorded for 2013 and mortality rate recorded for 2014. The penetration was defined as a number of mCRC patients that were enrolled on a particular drug treatment divided by the total number of patients suitable for the particular treatment. The mortality rate was defined as percentage of deaths among all patients with CRC. Spearman correlation test and regression analysis were applied. Statistical analyses were performed using SPSS v22.0 (SPSS Inc., Chicago, IL).

Results: Mortality from mCRC has been significantly decreased from 2012 to 2014: 10.5% (7-16%, SD 1.6) in 2012 and 9.5% (3-19%, SD 2) in 2014 (p = 0.002). For the all patients the inverse significant correlation of mortality with the penetration was detected: for irinotecan (k = -0.324, p = 0.003), for capcitabine (k = -0.223, p = 0.04), for bevacizumab (k = -0.229, p = 0.04) and for panitumumab (k = -0.232, p = 0.04) and in total for Mabs combined group (k = -0.256, p = 0.02). We found only a numerical trend to significance in inverse correlation of mortality with oxaliplatin (k = -0.172, p = 0.1) and cetuximab (k = -0.154, p = 0.16) penetration. According to the regression analysis the relationship of penetration for anti-EGFR antibodies (β = -0.186, p = 0.08) and irinotecan (β = -0.271, p = 0.01) with the mortality decrease has been detected. With regards to the multivariate regression analysis the penetration for irinotecan had a significant impact on a mortality reduction (β = -0.271, p = 0.01) only. The increase of penetration for irinotecan drives the increase of penetration for anti-EGFR antibodies (k = 0.35, p = 0.01), but does not the one for bevacizumab (k = 0.151, p = 0.2). This fact indicates on irinotecan based combinations as the most common chemo regimens going along with anti-EGFR Mabs in routine clinical practice in Russia. Also we found a relationship with the penetration for capcitabine and for bevacizumab’s one (k = 0.443, p < 0.01).

Conclusion: Emerging penetration for irinotecan and for anti-EGFR Mabs (panitumumab and cetuximab) in mCRC patients population appear to have a significantly correlation with the mortality reduction. The impact of irinotecan penetration on mortality decrease can be explained by the high administration rate of FOLFIRI/XELOIRI regimens in a second line local routine clinical practice. Consequently the few lines (more than 1) exposure is associated with the significant survival increase.