Annals of Oncology 27 (Supplement 6): vi526–vi544, 2016
doi:10.1093/annonc/mdw392.34

translational research

1553P The role of immune system on the efficacy of bevacizumab in patients with metastatic colorectal cancer (mCRC)

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Background: We aimed to investigate the role of anti-bevacizumab antibodies, regulatory T, CD4+ and CD8+ cells on the efficacy of bevacizumab plus chemotherapy combination in patients with mCRC.

Methods: Thirty consecutive patients treated with bevacizumab plus either irinotecan or oxaliplatin based chemotherapy regimens were included. The levels of Tregs (CD4 + CD25(hi)FoxP3+), CD4+ and CD8+ cells from peripheral blood were assayed by flow cytometry before the onset and after 4 cycles of bevacizumab. The anti-bevacizumab antibody levels were assayed by ELISA 3 months after the onset of bevacizumab.

Results: The median age was 59 years. The majority of the patients had metastatic disease at the time of diagnosis. The chemotherapy backbone was FOLFIRI in 75% of the patients. The median number of treatment cycles was 7. The objective response (OR) and disease stabilization rates were 30% and 73.3%, respectively. The median progression-free survival (PFS) and overall survival times were 8.0 and 16.0 months. Four patients had measurable anti-bevacizumab levels. There was no OR in patients with measurable anti-bevacizumab antibody levels. The levels of Treg cells were between 0.15 and 4.82% (median 0.40%) and the ratio of CD4 + /CD8+ cells between 0.91 and 4.30 (median 1,9) on peripheral blood before the treatment. There were no significant changes in the levels of Tregs and the ratio of CD4 + cell/CD8+ cells on bevacizumab treatment. The patients with higher CD4 + /CD8+ cells before the bevacizumab had favorable PFS times (14 vs 6 mos, P = 0.065). The patients having low Treg levels after 4 cycles of bevacizumab had favorable PFS time (14 vs 7 mos, p = 0.061). The chemotherapy backbone had no significant effect on trial parameters.

Conclusions: The Tregs and the ratio of CD4+ /CD8 + cells could be predictors of PFS for bevacizumab treatment in patients with mCRC. The pre-treatment ratio of CD4+ /CD8+ cells, the levels of Tregs and anti-bevacizumab antibodies might influence the efficacy of long term use of bevacizumab in patients with mCRC. The improved PFS in patients having lower Tregs after bevacizumab treatment may provide a rationale for the combination of bevacizumab and immune checkpoint inhibitors.

Legal entity responsible for the study: N/A

Funding: TUBITAK (The Scientific and Technological Research Council of Turkey) (Grant# 114S496)

Disclosure: All authors have declared no conflicts of interest.