COMBINING CYTOTOXIC CHEMOTHERAPY WITH ANTIANGIOGENIC AGENTS AND COMPLETE RESPONSES IN CANCER PATIENTS: A META ANALYSIS OF PUBLISHED TRIALS

Y. Li1, X. Liang2, G. Chen1
1Urology, Jinshan Hospital, Fudan University, Shanghai, CHINA
2Drug Monitoring Center, Qilu Hospital, Shandong University, Jinan, CHINA

Aim: The approach of combining chemotherapy with antiangiogenic agents (AAs) has been explored in many trials. In most cases, the addition of AAs to chemotherapy have shown greater activity compared to chemotherapy alone. However, a clinically relevant increase in complete responses (CRs), which is a rare but important event in patients receiving chemotherapy, was not reported. We meta-analyzed the incidence and risk of CRs in patients treated with AAs and chemotherapy in randomized controlled trials (RCTs) for first-line therapy of cancer.

Methods: PubMed was reviewed up to March 2014. We included RCTs in which the FDA approved VEGFR tyrosine-kinase inhibitors (sorafenib, sunitinib, axitinib, vandetanib, pazopanib, regorafenib, cabozantinib), VEGF-ligand-binding fusion protein (aflibercept) or VEGF antibody (bevacizumab) in combination with chemotherapy was compared with chemotherapy alone in patients with cancer. CRs was considered as the main outcomes and determined according to the Response Evaluation Criteria in Solid Tumors. Statistical analyses were conducted to calculate the incidence, relative risks (RRs) and 95% confidence intervals (CIs).

Results: A total of 12547 patients from 27 RCTs were included. A total of 6021 patients received AAs plus chemotherapy (3596 for bevacizumab, 1613 for sorafenib, 426 for axitinib, and 386 for sunitinib) and a total of 5298 patients in control arms received chemotherapy alone. The incidence of CRs in patients treated with AAs plus chemotherapy was 1.4% (95% CI, 1.0–1.9) compared to 1.0% (95% CI, 0.6–1.4) in the chemotherapy arm. Comparing the different type of AAs, the incidence of CRs was 2.4% (95% CI, 1.5–3.3) in the bevacizumab group and 0.3% (95% CI, 0.0–0.7) in the TKIs group. Compared with the chemotherapy alone, the addition of bevacizumab was associated with an increased risk of CRs, with a RRs of 1.84 (95% CI: 1.35–2.50, p = 0.00). The RRs to have a CRs was 0.87 (95% CI, 0.51–1.49; p = 0.61) in patients treated with TKIs plus chemotherapy compared to chemotherapy alone.

Conclusions: Our meta-analysis shows that bevacizumab, but not TKIs, increase the curative rate of patients receiving chemotherapy. Further efforts are needed to identify the characteristics of CRs patients and investigate biomarkers that can predict the efficacy of addition of AAs to cancer patients receiving chemotherapy.

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