VII Congresso SIFaCT Bologna, 24-26 Ottobre 2019

Poster n°80
Sezione 12: La Farmacia per il paziente oncologico

Effectiveness of systematic chemotherapy combined with target therapy in second-line treatment of metastatic colorectal carcinoma

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Background

In patients with unresectable metastatic colorectal cancer (mCRC) receiving second-line treatment, the clinical management primarily consists of the combination of chemotherapy regimen with or without targeted agents. In the second-line treatment of mCRC the role of target therapies in association with systemic chemotherapy is controversial. The objective of this meta-analysis was to identify, describe and summarise the effect of combination therapy with targeted agent (cetuximab, panitumumab, bevacizumab, icrumumab, ramucirumab, aflibercept, cediranib, regorafenib, vatalanib, conatumumab, ganitumumab, simtuzumab or trebananib) and standard chemotherapy regimen (FOLFOX, FOLFIRI or CAPOX) on overall survival (OS) and progression-free survival (PFS).

Patients and methods

The study was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Statement. An electronic literature search was carried out in MEDLINE, EMBASE, Web of Science, Cochrane library, and ClinicalTrials.gov, for all studies published until July 2019. The trials investigated the addition of target therapy to chemotherapy regimen compared with either chemotherapy regimen alone. The targeted agents were categorized according to the mechanism of action. The studies included in the meta-analysis met the following criteria: randomized controlled trial; eligible patients histologically or cytologically diagnosed as mCRC and second-line therapy. Data analysis was performed using OMA.

Results

Our literature search identified 17 trials resulting in 22 comparisons for a total of 8,785 patients. Globally, the HR for PFS was 0.820 (95% CI, 0.770 – 0.869; P<.001), in detail for the anti-VEGF subgroup HR was 0.760 (95% CI, 0.699– 0.822 P<.001), for EGFR-I HR was 0.855 (95% CI, 0.763– 0.948 P<.001), while the group of molecules with other mechanism of action showed a worse outcome in terms of PFS, with a HR of 1.212 (95% CI, 1.027– 1.397 P<.001). Globally, the HR for OS was 0.890 (95% CI, 0.841– 0.939; P<.001); in detail for the anti-VEGF subgroup HR was 0.855 (95% CI, 0.797-0.914 P<.001), for EGFR-I HR was 0.924 (95% CI, 0.825-1.023; P<.001) and for the subgroup mixed and novel mechanism of action HR was 1.190 (95% CI, 0.977-1.404 pz.001).

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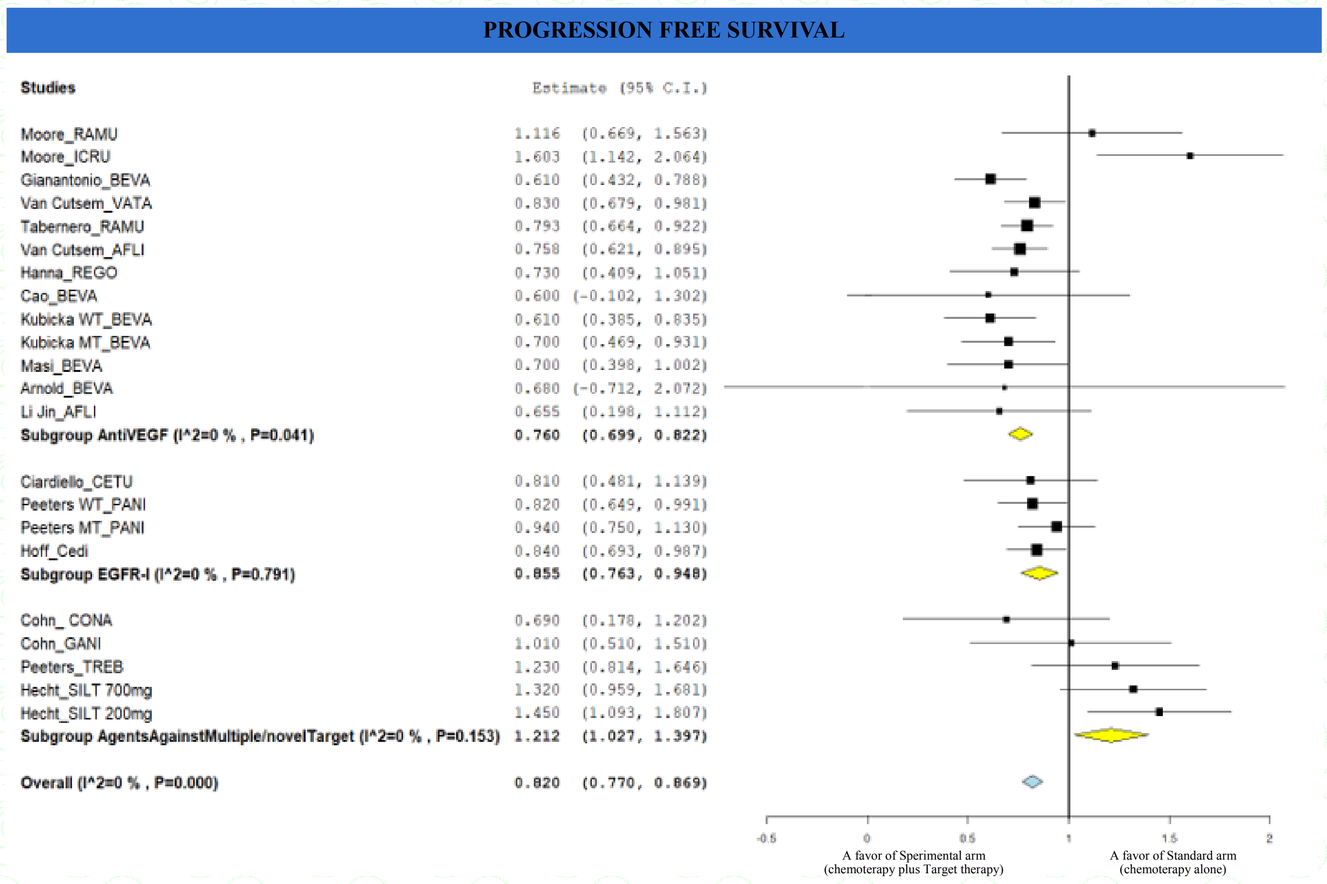

Conclusions

In patients with advanced CRC disease that receiving a second-line of treatment, the combination of target therapy with cytotoxic systemic chemotherapy, respect to chemotherapeutic regimen treatment alone, is the most effective therapeutic option. The subgroups of EGFR-I and anti-VEGF agents both demonstrated to improve PFS while only the subgroup of anti-VEGF improved OS. The group of newer targeted agents ever showed HR values related to a very low efficacy; none of these molecules completed their clinical development for colorectal cancer.

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