International Scholars Journals

African Journal of Internal Medicine ISSN 2326-7283 Vol. 7 (11), pp. 001-003, November, 2019. Available online at www.internationalscholarsjournals.org © International Scholars Journals

Review

Colorectal cancer: What news after the 2014 ESMO GI congress?

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Accepted 05 December 2019

In the European Society for Medical Oncology (ESMO) 16th World Congress on Gastrointestinal cancer which took place in Barcelona between 25 and 28 June 2014, colorectal cancer was the subject of various oral presentations and posters. A selection of the more innovative researches, likely to change the patients' management was performed.

Key words: ESMO GI congress, colon cancer, rectum.

INTRODUCTION

The Gastrointestinal cancer congress of the European Society of Medical Oncology (ESMO) is the largest Congress specifically designed for practicing clinicians, gastroenterologists, hepatologists, surgeons, medical oncologists, radiation oncologists, and clinical researchers who wish to review and update their knowledge and management of cancers of the gastrointestinal tract.

This16th World Congress on Gastrointestinal cancer which took place in Barcelona between 25 and 28 June, 2014, colorectal cancer was the subject of various oral presentations and posters that are likely to change our daily practice like a news methods of screening for colorectal cancer, assessement of the role of addition of cetuximab to standard chemotherapy in patients with resectable colorectal liver metastasis and the benefit of maintenance treatment in patients with mCRC.

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SCREENING FOR CRC IN 2014

A meta-analysis was conducted to evaluate the role of fecal immunochemical tests (FITs) to screen for colorectal cancer (CRC) (Jeffrey et al., 2014) .Nineteen eligible studies were included and meta-analyzed. The pooled sensitivity, specificity were 0.79 (95% CI, 0.69 to 0.86), 0.94 (CI, 0.92 to 0.95) respectively, with an overall diagnostic accuracy of 95% (CI, 93 to 97%). It was substantial heterogeneity between studies in both the pooled sensitivity and specificity estimates but stratifying by cutoff value for a positive test result resulted in homogeneous results. In this setting, we can conclude that the Fecal immunochemical tests are moderately sensitive, are highly specific, and have high overall diagnostic accuracy for detecting CRC. Diagnostic performance of FITs depends on the cutoff value for a positive test result. In the same context Multi-target Stool DNA Test was compared with a fecal immunochemical test (FIT) in persons at average risk for colorectal cancer (Thomas et al., 2014). Of the 9989 participants who could be evaluated, 65 (0.7%)

had colorectal cancer and 757 (7.6%) had advanced precancerous lesions, The sensitivity for detecting colorectal cancer was 92.3% with DNA testing and 73.8% with FIT (P = 0.002).The numbers of persons who would need to be screened to detect one cancer were 154 with colonoscopy, 166 with DNA testing, and 208 with FIT.

The investigators concluded that the multi-target stool DNA testing detected significantly more cancers than did FIT but had more false positive results.

Furthermore, another study evaluated the accuracy of circulating methylated SEPT9 DNA (mSEPT9) for detecting CRC in a screening population. (Timothy et al. 2014) and showed that CRC signal in blood can be detected in asymptomatic average risk individuals undergoing screening. However, the utility of the test for population screening for CRC will require improved sensitivity for detection of early cancers.

SYSTEMIC CHEMOTHERAPY WITH OR WITHOUT CETUXIMAB IN PATIENTS WITH RESECTABLE COLORECTAL LIVER METASTASIS

The New EPOC trail is an open-labeled, randomized, phase 3 trial designed to assess the benefit of addition of cetuximab to standard chemotherapy in patients with resectable colorectal liver metastasis (Primrose et al., 2014).

257 Patients with KRAS exon 2 wild-type resectable or suboptimally resectable colorectal liver metastases were randomized to receive chemotherapy with or without cetuximab before and after liver resection.

Chemotherapy consisted of oxaliplatin 85 mg/m² intravenously over 2 h and fluorouracil bolus 400 mg/m² intravenously over 5 min, followed by a 46 h infusion of fluorouracil 2400 mg/m² repeated every 2 weeks (regimen one) or oxaliplatin 130 mg/m² intravenously over 2 h and oral capecitabine 1000 mg/m² twice daily on days 1-14 repeated every 3 weeks (regimen two). Patients who had received adjuvant oxaliplatin could receive irinotecan 180 mg/m² intravenously over 30 min with fluorouracil instead of oxaliplatin (regimen three). Cetuximab was given as an intravenous dose of 500 mg/m² every 2 weeks with regimen one and three or a loading dose of 400 mg/m² followed by a weekly infusion of 250 mg/m² with regimen two. The primary endpoint was progression-free survival.

117 patients in the chemotherapy alone group and 119 in the chemotherapy plus cetuximab group were included in the primary analysis.

Progression-free survival was significantly shorter in the chemotherapy plus cetuximab group than in the chemotherapy alone group (14·1 months [95% CI 11·8-15·9] vs 20·5 months [95% CI 16·8-26·7].

The investigators concluded that the Addition of cetuximab to chemotherapy and surgery for operable colorectal liver metastases in KRAS exon 2 wild-type patients results in shorter progression-free survival. Translational investigations to explore the molecular basis for this unexpected interaction are needed but at present the use of cetuximab in this setting cannot be recommended.

WHAT THE OPTIMAL ANTIBODY COMBINATION IN FIRST-LINE TREATMENTS FOR METASTATIC ADENOCARCINOMA OF THE COLON OR RECTUM (MCRC)?

CALGB/SWOG 80405 trail is an open-labeled, randomized, phase 3 designed to compare chemotherapy: (Irinotecan/5-FU/leucovorin (FOLFIRI) or oxaliplatin/5-FU/leucovorin (mFOLFOX6)), combined with bevacizumab or cetuximab in first-line treatments for metastatic adenocarcinoma of the colon or rectum (MCRC). The primary endpoint was OS (Alan et al., 2014).

The OS was 29.04 months in patients treated with bevacizumab versus 29.93 months in patients treated with cetuximab (HR = 0.92 (0.78, 1.09) (p value = 0.34).

The PFS was 10.84 for the bevacizumab arm compared to 10,45 for the cetuximab arm. Therefore, based on these results cetuximab and bevacizumab equivalent in OS in patients KRAS wild type; either is appropriate in first line treatments for metastatic adenocarcinoma of the colon or rectum (MCRC).

IS THERE ANY ROLE FOR MAINTENANCE TREATMENT IN MCRC?

The final results of the COIN-B study were communicated at the 2014 ESMO GI congress. COIN-B is a phase II trial evaluating the maintenance efficiency by cetuximab (Wasan et al., 2014). The median overall survival was 22.2 months in the maintenance arm compared to 16.8 months in the pause arm. The results of this phase II study suggest that maintenance treatment with cetuximab may have an interest after "induction chemotherapy" in patients KRAS wild. However the Instead of cetuximab maintenance should be evaluated in phase III in this subgroup of patients.

An update on the results of the CAIRO 3 trial study was presented (Miriam et al., 2014); the benefit of maintenance treatment with capecitabine plus bevacizumab (Avastin) after induction treatment with capecitabine, oxaliplatin, and bevacizumab (CAPOX-B) was evident across all subgroups of patients. The maintenance is significantly delayed disease progression, compared to observation.

The investigators also found a non-significant benefit in

the secondary endpoint of overall survival. Preplanned subgroup analysis showed that this overall survival benefit was restricted to patients with synchronous disease who had their primary tumor resected and patients with complete or partial response as best response on induction treatment.

Furthermore, another study evaluated the maintenance efficiency. The AIO trial is an open-labeled, randomized, phase 3 non-inferiority trial designed to compare maintenance strategy with fluoropyrimidines (FP) plus Bevacizumab (Bev), Bev alone, or no treatment, after a 24-week standard induction of FP, oxaliplatin (Ox), and Bev as first-line treatment for patients with metastatic colorectal cancer (mCRC) (Dirk et al., 2014).The primary endpoint was 'time to failure of strategy' (TFS) and Secondary endpoints included time to first progression (PFS1) and overall survival (OS).

TFS favored maintenance arm over no treatment arm (HR 1.31, 95% CI 1.01-1.69, p=0.038) but without difference between FP plus Bev and Bev alone (HR 1.04, 95% CI 0.81-1.36, p=0.74).

In this setting, we can conclude that the active maintenance with, FP plus Bev or Bev alone, show prolonged TFS over no treatment. With currently limited follow up, the different maintenance strategies had no impact on OS.

CONCLUSION

In the 2014 ESMO GI, Colorectal cancer was the subject of various presentations that will play a pivotal role in establishing future treatment standards for colorectal cancer in the world.

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