LBA125

Rapid Oral Abstract Session

Low-dose aspirin to reduce recurrence rate in colorectal cancer patients with PI3K pathway alterations: 3-year results from a randomized placebo-controlled trial.

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Background: Colorectal cancer (CRC) affects 1.9 million individuals globally each year. Among patients with stage II-III CRC, 20-40% develop metastatic disease. Aspirin lowers the incidence of adenomas and CRC in high-risk patients. In addition, observational studies suggest that post-diagnosis aspirin treatment improves disease-free survival (DFS) in unselected populations. Furthermore, retrospective findings indicate that somatic PIK3CA mutations predict treatment response, but requires validation in randomized trials. **Methods:** The ALASCCA trial was a randomized, double-blind, multicenter, placebo-controlled trial with two parallel arms, across 33 hospitals in Sweden, Denmark, Finland, and Norway. Patients with stage I-III rectal cancer or stage II-III colon cancer exhibiting somatic alterations in the PI3K signaling pathway were included. Patients were randomized to receive either 160 mg of aspirin daily or placebo, initiated within three months post-surgery and continued for three years. To detect a hazard ratio (HR) of 0.36 for the primary outcome of time to recurrence (TTR) assessed at 3 years, with 80% power and a two-sided alpha of 0.05, 150 patients with PIK3CA mutations in exon 9 and/or 20 (“Group A”) were required per arm. An additional 300 patients with other somatic PI3K pathway driver alterations (PIK3CA outside exon 9/20, PIK3R1, or PTEN; "Group B") were required for secondary analyses. A stratified Cox proportional hazards model was fitted for the primary efficacy analysis. **Results:** A total of 3508 patients were screened for somatic alterations in the PI3K pathway. Of the 2980 patients with conclusive genomic analyses, 1103 patients (37%) had an alteration in the PI3K pathway: 515 patients (17.3%) in Group A and 588 patients (19.7%) in Group B. In total, 626 patients were randomized. After three years of follow-up, the HRs for TTR comparing aspirin to placebo were 0.49 (95% CI; 0.24-0.98; p=0.044) in Group A and 0.42 (95% CI; 0.21-0.83; p=0.013) in Group B. For DFS, the HRs were 0.61 (95% CI; 0.34-1.08; p=0.091) in Group A, and 0.51 (95% CI; 0.29-0.88; p=0.017) in Group B. Three patients experienced aspirin-related severe adverse events (one GI-bleeding, one hematoma, one allergic reaction). **Conclusions:** Primary endpoint was met. Adjuvant treatment with 160 mg aspirin daily for three years reduced recurrence rate in CRC patients with somatic alterations in the PI3K signaling pathway. These findings could lead to immediate changes in clinical praxis for about a third of CRC patients. Clinical trial information: NCT02647099. Research Sponsor: Swedish Research Council; Swedish Cancer Society; ALF (regional agreement on medical training and clinical research between the Stockholm County Council and Karolinska Institutet.); Private Donation; Stockholm Cancer Society.