

Adjuvant Aspirin Treatment in PIK3CA Mutated Colon Cancer Patients – The Phase III, Prospective-Randomized Placebo-Controlled Multicenter SAKK 41/13 Trial

Ulrich Güller, Stefanie Hayoz, Daniel Horber, Sara De Dosso, Dieter Koeberle, Sabina Schacher, Roman Inauen, Michael Stahl, Thierry Delaunoy, Thomas Ettrich, György Bodoky, Pierre Michel, Thibaud Koessler, Karin Rothgiesser, Sandra Calmonte, Markus Joerger

Background:

Many retrospective studies have provided suggestive evidence of a protective effect of aspirin as adjuvant treatment of colon cancer, particularly in patients with an activating PIK3CA mutation. The objective of the present randomized SAKK trial was to demonstrate the benefit of adjuvant aspirin in PIK3CA mutated colon cancer patients.

Methods:

This was a phase III, randomized, placebo-controlled, double-blinded, multicenter and multinational trial. Only stage II and III colon cancer patients with a centrally-assessed activating PIK3CA mutation in Exon 9 or 20 were included. Randomization was 2: 1 to aspirin 100mg daily for 3 years versus placebo for 3 years. The primary endpoint was disease-free survival (DFS), secondary endpoints included overall survival (OS) and adverse events. One-sided type I error was 5% with a power of 80% to detect a hazard ratio (HR) of <0.456. The computed sample size was 185, with a number needed to screen of 1`088. Due to financial constraints, the trial was prematurely closed.

Results:

Overall, 112 patients were enrolled and included (aspirin arm: N=74, placebo arm: N=38).

Median age was 66 years (range 29-89), 42.9% were female, baseline-characteristics were well-balanced between groups. After a median follow-up of 4 years, 19 DFS events occurred. The HR for DFS was 0.57 (90% CI 0.27-1.22) in favor of Aspirin (p=0.11). DFS rates at 3 years were 88.3% (90% CI: 80.1%-93.3%) in the aspirin and 82.4% (90% CI 68.3%- 90.7%) in the placebo arm. HR for OS was 0.70 (90% CI 0.23-2.12, p=0.3). No patient experienced aspirin-related severe adverse events.

Conclusions:

The SAKK 41/13 prospective-randomized trial provides first prospective evidence of a protective effect of adjuvant aspirin in patients with resected, PIK3CA-mutant colon cancer, with a clinically relevant 43% improvement of DFS. Even though the result is not statistically significant due to the small sample size, adjuvant aspirin warrants individual consideration in patients with resected, PIK3CA-mutant stage II and III colon cancer.

Financial support:

- Swiss National Foundation
- Swiss Cancer League
- Grant for Oncology Innovation, Merck
- Promedica Stiftung
- Fédération Francophone de la Cancérologie Digestive (FFCD)

Aspirin and placebo were provided by Bayer.

Collaboration with EORTC.

For media inquiries:

Prof. Dr. med. Ueli Güller, MHS, Head Physician Oncology

Coordination/Contact:

Marie-Anne Perrot, T : +41 58 636 20 20, marie-anne.perrot@spitalstsag.ch