LBA23 FOLFOX4/XELOX in stage II–III colon cancer: Efficacy and safety results of the Italian Three Or Six Colon Adjuvant (TOSCA) trial

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Background: Among the 6 randomized comparisons between 6 months and 3 months of adjuvant FOLFOX/XELOX for early stages colon cancer of the IDEA collaboration (International Duration Evaluation of Adjuvant), TOSCA was the first to start and the first to close the accrual, has already published the compliance and toxicity data (Annals of Oncology, 2016) and has now the most mature follow-up.

Methods: TOSCA is an open-label, phase III, multicenter, non-inferiority trial randomizing patients with high-risk stage II or III radically resected colon cancer to receive 3 months versus 6 months of FOLFOX4/XELOX (regimen at physician's choice). Primary end-point is relapse-free survival (RFS).

Results: From June 2007 to March 2013, 3759 patients were accrued from 130 Italian sites, 64% receiving FOLFOX4 and 36% XELOX in either arm. Two thirds were stage III. At the cut-off time for analysis the median time of follow-up was 62 months and 772 relapses or deaths have been observed. At 8 years the RFS rate is 75% and OS rate 80%. This analysis was done when 82% of the planned number of events was reached, with a power of 72% instead of 80%: the decision to anticipate the analysis was based on the participation to the IDEA joint collaborative analysis of studies sharing this clinical question. The Hazard Ratio of the 3 months vs 6 months for relapse/death was 1.14 (95%CI 0.99-1.31, p for non inferiority = 0.506) and the confidence interval crossed the non inferiority limit of 1.20. Counterintuitively, while RFS curves were very similar for stage III and for XELOX treated patients, they were not for stage II and for FOLFOX treated patients (HR: 1.41 and 1.23, respectively, in favour of 6 m). The HR for OS was 1.07 (95% CI 0.89-1.29, p for non-inferiority=0.249).

Conclusions: TOSCA was not able to demonstrate that 3 months of oxaliplatin-based adjuvant treatment is as efficacious as 6 months. Nevertheless, because the absolute difference in RFS between the two treatment durations is small (less than 2% at 5 years) and clinically not meaningful, the decision to complete the whole 6-month program should be individualized based on toxicity and patient attitude.

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