gastrointestinal tumours, colorectal

PREOPERATIVE CHEMORADIOTHERAPY AND POSTOPERATIVE CHEMOTHERAPY WITH CAPECITABINE +/- OXALIPLATIN IN LOCALLY ADVANCED RECTAL CANCER: INTERIM ANALYSIS FOR DISEASE-FREE SURVIVAL OF PETACC 6


Aim: The PETACC-6 trial investigates the role of oxaliplatin in addition to preoperative chemoradiation (CRT) and adjuvant chemotherapy (CT) with capcitabine to improve disease-free survival (DFS) in locally advanced rectal cancer.

Method: Patients with rectal adenocarcinoma within 12 cm from the anal verge, T3/4 and/or node-positive, without evidence of metastatic disease, considered either resectable at the time of entry or expected to become resectable, were randomized to 5 weeks of preoperative CRT with capcitabine, followed by surgery and 6 cycles of adjuvant CT with capcitabine (standard control arm 1) or capcitabine + oxaliplatin before and after surgery (arm 2). 440 DFS events were required to have 80% power to detect an improvement in 3-year DFS from 65% to 72% (HR = 0.763), with two-sided alpha of 5% and allowing for an interim analysis for early efficacy at 200 events.

Results: 1094 patients were randomized (547 in each arm). From 1081 eligible patients, 543 in arm 1 and 528 in arm 2 started preoperative treatment (3/528 patients without oxaliplatin in arm 2), and of these 77.3% and 72.6% patients started postoperative chemotherapy within protocol. In arm 2, 11.8% patients did not receive the planned postoperative oxaliplatin. Major reasons for protocol discontinuation were progressive disease (3.9% in arm 1 vs. 3.8% in arm 2), toxicity (7.7% vs. 16.5%), surgery complication (8.7% vs. 9.1%), patient's refusal (5.9% vs. 10.8%). At planned interim analysis, the independent data monitoring committee recommended the early release of the results. At a median follow-up of 31 months, 124 and 121 DFS events were observed in arm 1 and 2 (adjusted HR = 1.036, 95% CI: 0.81 - 1.33, P = 0.78). 3-year DFS was 74.5% (95% CI: 70.1% - 78.3%) in arm 1 (which is higher than anticipated) vs. 73.9% (95% CI: 69.5% - 77.8%) in arm 2; conditional power under HR = 0.763 is only 7%. Less locoregional and distant failures were recorded in the experimental arm with oxaliplatin (95 in arm 2 vs. 109 in arm 1) but a higher rate of deaths without progression (26 in arm 2 vs. 15 in arm 1).

Conclusions: Interim results at a median follow up of 2.6 y currently indicate no DFS-benefit for the addition of oxaliplatin to capcitabine-based CRT and adjuvant CT. However, with actually only 245 out of the required 440 events, final evaluation cannot be done before at least 2 further years follow-up.

Disclosure: H.J. Schmoll: has a consultant or advisory relationship to disclose with Roche, Sanofi and Bayer; has honoraria to disclose from Roche; has research funding to disclose from Merck and Roche; K. Haustermans: has research funding to disclose from Roche; T.J. Price: has a consultant or advisory relationship to disclose with Roche; R. Hofheinz: has a consultant or advisory relationship to disclose with Roche; has honoraria and research funding to disclose from Roche; B. Brenner: has a consultant or advisory relationship to disclose with Sanofi-Aventis; has research funding to disclose from Sanofi-Aventis; J. Zalcberg: has a consultant or advisory relationship to disclose with Sanofi-Aventis and Roche; has honoraria, research funding and other remuneration to disclose from Sanofi-Aventis and Roche. M.P. Lutz: has a consultant or advisory relationship to disclose with Roche; E. Van Cutsem: has research funding to disclose from Roche and Sanofi. All other authors have declared no conflicts of interest.