

SO-15 **Quality of life and physical functioning in older patients with metastatic colorectal cancer receiving palliative chemotherapy: The randomized NORDIC9-study**

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Background: Quality of life (QoL) data from randomized trials is lacking in older patients with metastatic colorectal cancer (mCRC). In the randomized NORDIC9-study, reduced-dose combination chemotherapy S1+oxaliplatin (SOx) showed superior efficacy compared to full-dose monotherapy S1 (Teysuno). Here, we hypothesized, that treatment with reduced-dose SOx does not result in inferior QoL and physical functioning compared to treatment with full-dose S1.

Methods: In the NORDIC9-study, we included patients with mCRC aged ≥ 70 years, who were not candidates for full-dose combination chemotherapy. Patients received either full-dose S1 (30 mg/m² orally twice daily on days 1-14, q3w), or reduced-dose SOx (S1 20 mg/m² orally twice daily on days 1-14 + oxaliplatin 100 mg/m² on day 1, q3w). Reduced-dose SOx significantly prolonged the primary end-point PFS from 5.3 to 6.2 months (HR 0.72, $p=0.047$). Secondary pre-planned endpoints were patient-reported outcome (PRO) measures evaluated through the domains global QoL and physical functioning from the EORTC QLQ-C30 questionnaire. PROs were completed at baseline, after 9, and 18 weeks of treatment with the 9-week follow-up being the primary data assessment time point. For statistical analysis, a non-inferiority design was chosen applying linear mixed effects model for repeated measures. Mean difference of coefficient (95%CI) values between the two treatment arms were estimated from baseline to 9-, and 18-week. The results were interpreted according to the EORTC anchor-based, clinically relevant minimally important differences (MID) for between-group difference in change, developed in patients with mCRC receiving chemotherapy.

Results: From March 2015 to Oct 2017, 160 patients with a median age of 78 years (IQR 76-81) were included in the NORDIC9-study. The EORTC QLQ-C30 questionnaire was completed by 150, 94, and 60 patients at baseline, at 9-, and at 18-week. Patient and disease characteristics were well balanced between the treatment arms. The difference of global QoL was 6.85 (95%CI -1.94; 15.65) at 9-week in favor of SOx (SOx: 2.63 [-4.84; 10.11], S1: -4.22 [-9.16; 0.72], $p=0.127$). In the physical functioning domain, the difference was 7.37 (0.70; 14.05) likewise in favor of SOx (SOx: -0.14 [-4.73; 4.44], S1: -7.52 [-12.23; -2.80], $p=0.03$). The difference in global QoL and physical functioning in favor of the SOx group exceeded the threshold values for MID between groups and is thus considered clinically relevant. At 18-week, no clinically relevant between-group difference was observed regarding global QoL, while the clinically relevant difference in physical functioning was preserved in favor of the SOx group.

Conclusions: The NORDIC9-study showed that reduced-dose SOx was more effective in maintaining global QoL and physical function compared to full-dose S1, resulting in a clinically relevant difference according to the EORTC MID values at 9 weeks of treatment. No clinically relevant difference in global QoL was observed after 18 weeks, while the clinically relevant difference was maintained in physical functioning in favor of the SOx group. Considering our findings, and the significantly improved PFS seen in the SOx group, reduced-dose combination chemotherapy may be the treatment of choice in vulnerable older patients with mCRC, rather than full-dose monotherapy.

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