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Neoadjuvant mFOLFIRINOX and preoperative chemoradiation (CRT) versus preoperative CRT in patients with T3-4 rectal cancer: Surgical and quality of life results of PRODIGE 23 phase III trial

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Background

PRODIGE 23, a phase III clinical trial, investigated the role of neoadjuvant mFOLFIRINOX before preoperative chemoradiation (CRT), with TME-surgery and adjuvant chemotherapy (CT) in resectable T3-4 rectal cancer.

Methods

Eligible pts had cT3-T4 M0 rectal cancers, <76 years, and WHO PS ≤1. Primary endpoint was 3-yr DFS. Secondary endpoints were ypT0N0 rate, OS, metastasis-free survival (MFS) and QoL assessed with EORTC QLQ-C30 and QLQ-CR29. 460 pts were needed to observe 136 events to increase 3-year DFS from 75% to 85% (HR=0.56). Arm A pts received preop CRT (50 Gy, 2 Gy/fr + capecitabine), surgery, then adjuvant CT for 6 mos. Arm B pts received 6 cycles of mFOLFIRINOX, followed by the same preop CRT, surgery and 3 mos of adjuvant CT. Adjuvant CT consisted of mFOLFOX6 or capecitabine.

Results

(ITT) From 2012 to 2017, 230/231 pts were randomly assigned in Arm A/B. Median follow-up was 46.5 mos and 136 DFS events occurred. Main results are reported in the table below. Time to QoL deterioration ≥ 10 points was significantly longer in Arm A for chemotherapy symptoms (hair loss, fatigue, nausea/vomiting, appetite loss, diarrhea, dry mouth, taste) and worry about weight, and was significantly longer in Arm B for functional outcomes as dysuria (HR 0.61, p<0.01), buttock pain (HR 0.7, p=0.01), fecal incontinence (HR 0.73, p=0.05), sore skin (HR 0.67, p<0.01), bowel embarrassment (HR 0.73, p=0.05) and impotence in men (HR 0.64, p<0.01).Table: LBA21

	Control arm, %	Experimental arm, %	HR and p values
3yr DFS	68.5	75.7	0.69 (0.49-0.097), P=0.034
3 yr MFS	71.7	78.8	0.64 (0.44-0.93), P<0.02
Primary tumor resection rate	93.5	92.2	Ns
Type of resection - Low anterior or intersphincteric - Abdominoperineal	85.1 14	85.9 14.1	Ns
TME, complete mesorectum	94.9	96.3	Ns
Postoperative mortality	2.8	0	P=0.03
Overall morbidity	31.2	29.3	Ns
Median hospital stay, days	12	11	Ns
Median n^0 of postop RBCs	0	0	Ns
ypT0N0	12.1	27.8	P<0.001
R0/ R1-R2	94.4/5.6	95.3/4.7	Ns

Conclusions

Neoadjuvant mFOLFIRINOX plus CRT is safe, preserves the quality of resection and significantly increased ypCR rate, DFS, and MFS. Patients treated with neoadjuvant chemotherapy had more symptoms during chemotherapy, but benefits from longer time to QoL deterioration for rectal functional outcomes.

Clinical trial identification

NCT01804790.

Legal entity responsible for the study

R&D UNICANCER.

Funding

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Disclosure

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