Is there any benefit of addition of Neo-adjuvant chemotherapy (FOLFOX4) to standard preoperative treatment of rectal cancer?

Thesis

Submitted for partial Fulfillment of M.D. in Clinical Oncology

BY

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2022

Abstract

Background: Neoadjuvant concomitant chemoradiotherapy followed by surgical resection and adjuvant chemotherapy is the standard of care in the treatment of locally advanced rectal cancer. This prospective study aimed to assess whether administering neoadjuvant chemotherapy (FOLFOX4) prior to standard treatment could increase pathological complete response rate and improve survival outcomes.

Methods: Patients with newly diagnosed resectable locally advanced rectal cancer were randomly assigned to either the neoadjuvant chemotherapy group or standard-of-care group. Induction FOLFOX4 regimen was given every 2 weeks over 3 months (6 cycles). In both groups, concomitant chemoradiotherapy (CRT) in a total radiotherapy dose of 50.4 Gy was administered in 28 fractions concomitantly with capecitabine 825mg/m² twice daily 5days/week or 5- Fluorouracil 400mg/m² IV bolus + leucovorin 20mg/m² IV bolus for 4 days during week1 and 5 of RTH followed by Surgery within 6-8 weeks of CRT. Six cycles of postoperative adjuvant chemotherapy (FOLFOX4) were administered in experimental group and 12 cycles in control group. The primary end point was pathological complete response(pCR) rate. The secondary endpoints were the treatment adverse events and the survival outcomes.

Results: Of the 67 patients, 35(52.2%) were female. The median age was 45 years (range 18–76 years). Stage IIIB was presented in 46.3% of patients followed by stage IIA in 22.4% of patients. Patients in experimental arm achieved a significant higher percentage of p CR as compared to control arm (28.1% vs 8.6%; P=0.001) and partial response (31.1% vs 11.4%; P=0.002). There was no significant difference between both groups in toxicity profile. After a median follow up of 24 months, there were no statistically significant differences between both treatment groups in DFS, PFS and OS. The mean PFS was 27.9 vs 24.7 months in the experimental vs the control group (P=0.14). By univariate analysis, PFS was significantly prolonged in the patients who achieved pCR (29.7 months) and pathological PR (26.6 months) versus 16.6 months in the patients who experienced tumor disease progression (P=0.001). The median overall survival of all patients was not reached, while the mean OS of the experimental group was 26.5 months versus 27.1 months in the control arm (p=0.8). By univariate analysis, the mean OS is significantly longer for patients with pCR (P=0.001), who didn't develop local recurrence(P=0.004) and patients who didn't have distant metastasis (P=0.00). Mean DFS was 17.39 months in the investigational arm versus 14.4 months in the control arm (P =0.156).

Conclusion: Our finding suggests that neoadjuvant FOLFOX4 followed by CRT for locally advanced rectal cancer improved the pathological response rate with no significant improvement in survival outcomes.

Keywords: Rectal cancer- FOLFOX4- neoadjuvant chemotherapy- pathological complete response