Background: Neo-adjuvant chemo-radiotherapy in advanced rectal adeno-carcinoma aims to render unresectable tumour resectable. The efficacy of different chemo-radiotherapy schedules for sphincter preserving surgery and better disease free survival were explored in this study.

Methods: This was a multicentric prospective trial where 66 patients of low rectal adeno-carcinoma with "unresectable tumour" underwent 3 different regimens of neo-adjuvant chemo-radiotherapy from January 2010 to February 2011. Group A: External beam radiotherapy (EBRT) in conventional fractionation with 4500 cGy / 25 fractions to whole pelvis along with concomitant weekly 5-FU – 425mg/M2 IV. for 5 weeks. (N = 20)

Group B: (N = 22). 5-FU, Leucovorin (20mg/ M2 IV.), Oxaliplatin (135mg/ M2 IV.) on day-1 of EBRT and repeated on day 22. Third dose was given, 2 weeks after completion of EBRT, same as Group A.

Group C: Hyper-fractionated radiotherapy (HFRT) with 120 cGy twice daily fractionation, 6 hours apart for 14 days along with chemotherapy of 5-FU – 425mg/M2 IV on day-1, 8 and 15 of radiotherapy course. (N = 24). On completion of CRT, evaluation done after 5 - 11 weeks for feasibility of surgery.

Results: In Group A 14/20 patients (70%) were selected for surgery. 11 patients (55%) underwent APR (abdomino perineal resection) and permanent colostomy. In 3 patients (15%) sphincter sparing Surgery was possible. None had positive surgical margin. None had developed grade 3 &/ or 4 acute toxicity after chemo-radiotherapy. At 12 months loco-regional relapse occurred in 8 patients (40%) and one had (5%) had multiple sites metastasis. At 24 months 16 patients were alive (80%) with local relapse in 8 (40%) and distant metastasis in 3 patients (15%). Group B: All patients underwent surgery. 19 patients underwent APR (67.8%) and permanent colostomy; 3 patients underwent sphincter preserving surgery (10.7%). 6 patients (21.4%) on laparotomy found unresectable due to pelvic adhesions. Bladder and rectal toxicity (92.8%) delayed surgery for 9 - 13 weeks (median 11 weeks). 2 in the APR group and 1 in sphincter preserving surgery group showed pelvic recurrence at the end of 12 months and prolonged salvage chemotherapy was given. 2 patients (7.14%) developed distant metastasis. No evidence of disease till date (follow up for 27 months) was seen in 17 patients. Group C: Surgery was possible in 20 patients (83.3%). 4 patients discontinued treatment after CRT. All underwent APR. One patient (4.1%) had pelvic recurrence at 12 months and 1 at 24 months. Distal metastasis noted in 2 patients (8.2%). 5 patients had lower limb edema and swelling with no pelvic relapse. After chemo-radiotherapy acute rectal toxicity, grade 3 and 4 were (70.8%); grade 3/4 skin toxicity in 14 patients (58.3%); grade 3 diarrhoea in (37.5%).

Conclusion: Hyperfractionated chemoradiotherapy is a better option for local control of advanced rectal adenocarcinoma although distal metastasis is same as conventional chemoradiotherapy.