Evaluation of Response and Toxicity in Patients with Locally Advanced Rectal Cancer Treated with Neoadjuvant Chemoradiation

Dr. B.K. Shewalkar¹, Dr. Arpit A. Gite², Dr. Jitendra Patel³ & Dr. Punita Pant⁴
Professor and Head¹, Junior Resident², Associate Professor³ ⁴,
Department of Radiotherapy & Oncology, Government Medical College and Cancer Hospital, Aurangabad, Maharashtra, India

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Corresponding author: Dr. Punita Pant
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Abstract:
Aims and Objective: To study response after giving neoadjuvant chemoradiation in patients with locally advanced rectal cancer with Cap capecitabine 825 mg/m² daily PO Bid with radiation in dose of 45Gy/20#/4 weeks and to study to the clinical profile of different patients with locally advanced rectal cancer and to assess the toxicity of patients treated with neoadjuvant chemoradiation

Materials and Methods: A prospective observational study was conducted in 60 patients from October 2018 to April 2020 with locally advanced Rectal carcinoma which were proven histopathologically. Neoadjuvant chemoradiation was planned with Capecitabine 825mg/m2 PO Bid with radiation to a dose of 45 Gy/20#/4 weeks. Radiological response assessed after 6 weeks of completion of treatment and then surgery was planned according to response.

Results: Thirty-seven patients received definitive surgery. Pathological complete response was observed in 1 patient, near complete response in 7, partial response in 27 and poor or no response was seen in 2 patients. Among 37 patients who have undergone surgery, 30% of patients received sphincter preserving surgery. Radiation induced acute skin and acute lower gastrointestinal were seen. Capecitabine induced diarrhea, hematological toxicities and few patients of hand foot syndrome were seen.

Conclusion: In locally advanced rectal cancer, preoperative radio chemotherapy with Capecitabine improves local control and reduces the risks of acute and late toxicity as compared to postoperative radio chemotherapy. Thus, preoperative radio chemotherapy with Capecitabine is safe and well-tolerated in locally advanced rectal cancer, especially in tumors of the lower and middle rectum.

Keywords: Rectal Cancer, Capecitabine, Neoadjuvant Chemoradiation

Introduction:
Rectal cancer is second most common cancer in large intestine and one of the major public health problems also named as colorectal or bowel cancer. Regarding its prevalence it is more common in developed regions of the world than developing countries¹. It is third
most common cancer in men and second in women in world. According to recent data (Globocan 2020) in India new cases of Colorectal cancer account for 65358 (4.9%) cases. Out of these males corresponds to 40408 (6.3%) and female to 24950 (3.7%) cases. 5-year prevalence of all ages include about 62827 cases.

Different types of treatment modalities have been proposed for patients with rectal cancer. Preoperative chemoradiation have become a part of treatment protocols nowadays in stage II and III rectal cancer. Compared to postoperative chemoradiotherapy the advantage of preoperative chemoradiation is improved compliance, reduced toxicity and down staging of tumor in substantial number of patients. It also enhances the rate of curative surgery, permit sphincter preservation in patients with low-sited tumors and has a positive impact on quality of life. Orally administered capecitabine mimics the pharmacokinetics of continuous 5-FU infusion and makes chemoradiotherapy more patient-friendly. The mechanism of capecitabine activation, preferably in tumor cells, may further enhance its efficacy and tolerability, offering the potential for an enhanced therapeutic ratio. The use of capecitabine allows chronic dosing and at the same time, avoids the discomfort and complications associated with prolonged intravenous infusion of 5-FU.

Surgery is the primary treatment modality for rectal cancer, but in patients with invasion through the rectal wall or with positive lymph nodes, the major problem is local recurrences after surgery. In case of localization in the lower third of the rectum, the surgical approach is more aggressive and destructive, with loss of sphincter function. The surgical technique can influence the local recurrence rate. In fact, after an appropriate total mesorectal excision, local recurrence rates vary from 4 to 8 % . The addition of neoadjuvant therapeutic approach, particularly in patients with low rectal cancer in whom it was possible to obtain a high rate of sphincter function preservation by using a conservative surgery having effective results. It also has lower toxicity than postoperative radiochemotherapy. The Purpose of this research study is to evaluate the response and toxicity in patients with locally advanced rectal cancer treated with neoadjuvant chemoradiation.

AIMS AND OBJECTIVES

Primary:
- To study response after giving neoadjuvant chemoradiation in patients with locally advanced rectal cancer with Cap capecitabine 825mg/m² daily PO Bid with radiation in dose of 45Gy/20#/4 weeks.

Secondary:
- To study the clinical profile of different patients with locally advanced rectal cancer.
- To assess the toxicity of patients treated with neoadjuvant chemoradiation.

MATERIALS & METHOD:
The study was conducted on patients with locally advanced rectal cancer visiting Government medical college and cancer hospital, Aurangabad from October 2018 to December 2020.

METHODS OF COLLECTIONS OF DATA:

Sample Size: Total 60 patients were recruited
Study design: Prospective, Observational study

Inclusion criteria:
1. Patient with histologically proven diagnosis of locally advanced rectal adenocarcinoma clinical stage T2N+, T3 or T4, N0 or N1-N2, M0 suitable for pre-operative for combined chemoradiotherapy
2. Ability and willingness to provide informed consent prior to participation in the study.

3. Eastern Cooperative Oncology Group (ECOG) performed status of 0-2

4. Adequate organ and bone marrow function based upon the following laboratory criteria
   a) Hb>9gm/dl
   b) Absolute neutrophil count >1500 /microliter
   c) Platelet count >1 lakh
   d) Creatinine <1.5 x ULN
   e) ALT and AST <2.5 ULN
   f) T. BILIRUBIN <1.5 ULN

Exclusion criteria:

1. Previous RT on the pelvic region or previous CT
2. Patient with metastatic rectal cancer
3. Patients with serious illness or medical illness including significant cardiac disease
4. History of significant neurological or psychiatric disorders
5. Serious uncontrolled active infection
6. Pregnant or lactating women and women with child bearing potential unless using a reliable contraceptive method.

BASELINE SCREENING PROCESS AND RECORDING:

- History of patients including presenting complaints, medical illness, drug history, personal history, past medical history and surgical history
- Clinical Examination- General and systemic examination
- Hemogram, LFT, KFT, RBS, HIV, HBsAg
- S.CEA
- CT Abdomen and pelvis
- Chest X-ray
- Sigmoidoscopy/Colonoscopy
- Biopsy

Sampling technique: Convenient sampling, the patients who are available during the duty of the investigator and were suitable in the selection criteria were included in the study as sample

PROCEDURE: All cases of locally advanced rectal cancer were registered and a detailed clinical history was taken from all patients by thorough clinical examination.

They were further investigated with routine blood investigation and special investigation- S. CEA and TNM staging were done with CT abdomen pelvis before neoadjuvant chemoradiation and after 6 weeks of completion of neoadjuvant chemoradiation. Neoadjuvant chemoradiation was planned with Capecitabine 825mg/m2 PO Bid with radiation to a dose of 45 Gy/20#/4 weeks. Radiological response was assessed by RECIST 1.1 criteria after 6 weeks of completion of treatment. Those patients who met criteria for surgery undergone surgery either Abdominoperineal resection (APR) or Anterior Resection (AR).

Pathological Response was assessed on the basis of post-operative histopathological Report by MODIFIED RYAN SCHEME FOR TUMOR REGRESSION SCORE (CAP GUIDELINE, COLLEGE OF AMERICAN PATHOLOGISTS).

RADIOThERAPY DETAILS: Radiation was delivered with 6 or 10 MV photons using a 3-field technique (posterior and both laterals). Treatment planning was performed by computerized dosimetry and a dose of 2.25Gy per fraction was prescribed to cover the planned target volume with (95% of the ICRU point dose). Patients were treated in prone position. Patients were encouraged to have a full bladder during irradiation. Radiotherapy was delivered 5 days per week, once per day,
at 2.25Gy per day. The whole pelvis received 45Gy/20# over 4 weeks.

**TARGET VOLUMES FOR GROSS AND MICROSCOPIC DISEASE IN NEOADJUVANT SETTING**

**GTV:** All gross disease on physical examination and imaging, all visible perirectal and involved iliac nodes; include any lymph node in doubt as GTV in the absence of a biopsy

**CTV:** CTV should cover the GTV with 1.5–2-cm margin expansion superiorly and inferiorly, but excluding the uninvolved bone, muscle, or air. This volume should include the entire rectum, mesorectum, and presacral space axially at these levels. A 1–2-cm margin around gross tumor invasion into adjacent organs should be added. Coverage of the entire presacral space and mesorectum should be strongly considered. Any visible mesorectal nodes on CT is to be included. Should cover the entire mesorectum and right and left internal iliac lymph nodes for T3 tumors. The right and left external iliac lymph nodes for T4 tumors with anterior organ involvement should also be included.

To cover the iliac lymphatics, a 0.7-cm margin around the iliac vessels should be drawn (excluding the muscle and bone)

To cover the external iliac nodes, an additional 1-cm margin anterolaterally around the vessels is needed. Any adjacent small nodes should be included.

Anteriorly, a margin of 1–1.5 cm should be added into bladder to account for changes in bladder and rectal filling

A 1.8-cm-wide volume between the external and internal iliac vessels is needed to cover the obturator nodes

**PTV:** Each CTV should be expanded by 0.5–1 cm, depending on the physician’s comfort level with setup accuracy.

**OBSERVATION & RESULTS:**

<table>
<thead>
<tr>
<th>CHARACTERISTICS</th>
<th>NUMBER</th>
</tr>
</thead>
<tbody>
<tr>
<td>AGE (YEARS)</td>
<td>21-85 (52)</td>
</tr>
<tr>
<td>SEX</td>
<td></td>
</tr>
<tr>
<td>MALE</td>
<td>35 (58%)</td>
</tr>
<tr>
<td>FEMALE</td>
<td>25 (42%)</td>
</tr>
<tr>
<td>ECOG PERFORMANCE STATUS</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>2 (3%)</td>
</tr>
<tr>
<td>1</td>
<td>56 (94%)</td>
</tr>
<tr>
<td>2</td>
<td>2 (3%)</td>
</tr>
<tr>
<td>PATHOLOGICAL DIFFERENTIATION</td>
<td></td>
</tr>
<tr>
<td>WELL-DIFFERENTIATED ADENOCARCINOMA</td>
<td>18 (30%)</td>
</tr>
<tr>
<td>MODERATELY-DIFFERENTIATED ADENOCARCINOMA</td>
<td>25 (42%)</td>
</tr>
<tr>
<td>POORLY-DIFFERENTIATED ADENOCARCINOMA</td>
<td>11 (18%)</td>
</tr>
<tr>
<td>OTHERS (MUCINOUS, SIGNET RING)</td>
<td>6 (10%)</td>
</tr>
<tr>
<td>TNM STAGING</td>
<td></td>
</tr>
<tr>
<td>T2N1</td>
<td>12 (20%)</td>
</tr>
<tr>
<td>T2N2</td>
<td>14 (23%)</td>
</tr>
<tr>
<td>T3N0</td>
<td>05 (08%)</td>
</tr>
<tr>
<td>T3N1</td>
<td>09 (15%)</td>
</tr>
<tr>
<td>T3N2</td>
<td>19 (32%)</td>
</tr>
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</table>
RESULTS

A) RADIATION INDUCED TOXICITIES ACCORDING TO RTOG CRITERIA:

1) ACUTE SKIN TOXICITY

<table>
<thead>
<tr>
<th>Grade</th>
<th>Week 1</th>
<th>Week 2</th>
<th>Week 3</th>
<th>Week 4</th>
<th>1 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1</td>
<td>44</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Grade 2</td>
<td>33</td>
<td>22</td>
<td>7</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Grade 3</td>
<td>35</td>
<td>26</td>
<td>0</td>
<td>3</td>
<td>1</td>
</tr>
</tbody>
</table>

Graph 1: Distribution of cases according to RTOG criteria Acute Skin Toxicity

According to RTOG criteria, Grade 2 toxicity was found 7 patients at week 3, 35 patients at week 4 and 26 patients after 1 month of completion of treatment. Grade 3 toxicity was found in 3 patients at week 4 and 1 patient after 1 month of completion of treatment. There was no Grade 4 toxicity.

Acute skin toxicity increased significantly from week 1 to after 1 month (overall for all the grades i.e., Total): Chi-square test for linear trend (Extended Mantel Haenszel method), P=0.0001.
2) ACUTE LOWER GI TOXICITY:

According to RTOG criteria, Grade 2 toxicity was found in 1 patient at week 2, 8 patients at week 3, 33 patients at week 4 and 7 patients after 1 month of completion of treatment. Grade 3 toxicity was found in 1 patient at week 3, 3 patients in week 4 and 1 patient after 1 month of completion of treatment. There was no Grade 4 toxicity.

Acute Lower GI toxicity increased significantly from week 1 to after 1 month (overall for all the grades i.e., Total): Chi-square test for linear trend (Extended Mantel Haenszel method), \( P=0.0001 \)

B) CAPECITABINE INDUCED TOXICITIES ACCORDING TO CTCAE CRITERIA:

1) DIARRHEA:

Graph 3: Distribution of cases according to CTCAE criteria Diarrhea toxicity
According to CTCAE criteria, Grade 2 toxicity was found in 1 patient at week 2, 3 patients at week 3, 28 patients at week 4. Grade 3 toxicity was found in 1 patient at week 3, 3 patients at week 4. There was no Grade 4 toxicity.

CTCAE criteria Diarrhea toxicity increased significantly from week 1 to after 1 month (overall for all the grades i.e., Total): Chi-square test for linear trend (Extended Mantel Haenszel method), P=0.0001

2) HAND FOOT SYNDROME:

Graph 4: Distribution of cases according to CTCAE criteria Hand foot Syndrome toxicity

According to CTCAE criteria, Grade 1 toxicity was found in 7 patients after 1 month of completion of treatment. Grade 2 toxicity was found in 1 patient after 1 month of completion of treatment. There were no Grade 3 and Grade 4 toxicity.

CTCAE criteria Hand Foot Syndrome toxicity increased significantly from week 1 to after 1 month (overall for all the grades i.e., Total): Chi-square test for linear trend (Extended Mantel Haenszel method), P=0.0047

RESPONSE ASSESSMENT:

1) RADIOLOGICAL RESPONSE:

Graph 5: shows distribution of cases according to Radiological Response

Non-significant trend in radiological response by RECIST category, P=0.1798
2) DISTRIBUTION OF CASES ACCORDING TO SURGERY:

Graph 6: shows distribution of cases according to Surgery

3) PATHOLOGICAL RESPONSE:

Graph 7: shows distribution of cases according to Pathological Response

A statistically significant trend in pathological response by RYAN score category, P=0.0001

RESULTS OBTAINED IN THE PRESENT STUDY INCLUDE:

- In the present study, out of 60 patients with locally advanced rectal cancer, maximum patients were found from age group > 60 years
- Maximum number of cases i.e., 35(58.3%) were males
- Maximum patients were of moderately differentiated adenocarcinoma i.e., 27 (45%)
- Out of 60 patients, maximum number of cases i.e., 27 (45%) were in stage IIIB
- 60 patients were given neoadjuvant chemoradiation with radiation dose of 45Gy/20#/4 weeks and with Capecitabine (825mg/m² PO Bid)
Acute radiation toxicity was assessed by RTOG criteria. Acute skin toxicity and Acute lower Gastrointestinal toxicity were shown in Graph No. 1 and Graph No. 2 respectively. Acute Genitourinary toxicity was seen in very few patients i.e., only in 2 (3.3%) patients in week 4 (Only grade 1) Capecitabine induced toxicity was assessed by CTCAE criteria v5.0, Diarrhea and Hand foot syndrome were shown in Graph No. 3 and Graph No. 4 respectively. Maximum anemia was seen in week 4 (Most of the were grade 1. very few grades 2) i.e., in 52 (86.6%) patients. Maximum Neutropenia was seen in week 4 (most of the Grade 1 Only) i.e., in 29 (48.3%) patients. Maximum thrombocytopenia was seen in week 3 (all were grade 1 only) i.e., in 31 (51.6%) patients

Radiological (Clinical) response was assessed by RECIST 1.1 criteria. Out of 60 patients, it was observed in 59 patients, as 1 patient died after completion of neoadjuvant chemoradiation due to disease related complication. Complete response was observed in 2 patients, partial response in 44, stable disease was seen in 4 and progressive disease was seen in 9 patients showing in Graph No. 5.

Out of 50 Patient who were eligible for surgery (excluding those with progressive disease on Neoadjuvant Chemoradiation) 37 patients have undergone surgery. Remaining 12 refused for surgery/ lost to follow as they did not want a permanent colostomy bag and hence defaulted, 1 patient who had complete clinical response following Neoadjuvant chemoradiation died due to disease related complication. Amongst 37 patients, 26 patients have undergone abdominoperineal resection (APR) and 11 undergone anterior resection (AR) surgery showing in Graph No. 6. Pathological response was seen in 37 patients those who have undergone surgery and was assessed by MODIFIED RYAN SCHEME FOR TUMOR REGRESSION SCORE (CAP GUIDELINE). Complete response was observed in 1 patient, near complete response in 7, partial response in 27 and poor or no response was seen in 2 patients showing in Graph No. 7. A statistically significant trend in pathological response by RYAN score category, P=0.0001

DISCUSSION:
The standard treatment for locally advanced rectal cancer is chemo radiation after which total mesorectal excision is performed. Preoperative chemo radiation also significantly decreased the rate of local recurrence relative to postoperative chemo radiation. Present study was conducted under radiotherapy department at Government medical college and cancer hospital, Aurangabad, Maharashtra, India, which included 60 Patients with locally advanced rectal cancer receiving external beam radiation and chemotherapy. A detailed clinical history was taken and investigated with routine blood investigation and special investigation like serum CEA. TNM staging was done with CT abdomen pelvis before neoadjuvant chemo radiation and after completion of neoadjuvant chemo radiation. Clinical profile and toxicity of patients treated with Neoadjuvant chemo radiation were assessed.

In the present study maximum patients i.e., 17 patients were from age group > 60 years (Table 1), maximum patients were male with 35 cases in maximum cases i.e., 22 patients were having weight in the range of 41 to 50 kg.

In Previous study by JUN-SANG KIM et al (2002)15 In this study, between July 1999 and March 2001, 45 patients with locally advanced rectal cancer with age from 36-80 with median age 62 (58% male and 48% female) were treated with pre-operative chemoradiation. Juergen Dunst et al (2008)16 96 patients age 34 to 81 yrs. (63% male and 37% female) with median age 65 from 7 German university center entered the study between June 2001 to
November 2003. **A De Paoli et al (2006)**\(^{17}\) A total of 53 patients were recruited to the study between September 2001 and July 2003. The median age was 63 years (range 29–80). In the present study in maximum patients i.e., 51 patients were having CEA level >5ng/ml. In maximum cases i.e., 27, moderately differentiated Adenocarcinoma was found. Stage III B was found in maximum patients i.e., 27.

In Previous study by **JUN-SANG KIM et al (2002)**\(^{15}\) 45 patients with locally advanced rectal cancer (cT3/T4 or N+) were treated with preoperative chemoradiation. Radiation dose of 45 Gy/25 fractions was delivered to the pelvis, followed by dose of 5.4 Gy/3 fractions boost to the primary tumor. Chemotherapy was given concurrent with radiotherapy and consisted of 2 cycles of 14-day oral capecitabine (1650 mg/m² /day) and leucovorin (20 mg/m² /day), each of which was followed by a 7-day rest period. Surgery was done 6 weeks after the completion of chemoradiation. **Juergen Dunst et al (2008)**\(^{16}\) Most of the patients who had a locally advanced primary tumor (cT3:57%, cT4: 40%) with lymph node involvement in 60%. All received a total radiation dose of 50.4–55.8 Gy with conventional fractions. Capecitabine was given at an oral dosage of 825 mg/m² bid on each day of the radiotherapy period with the first daily dose applied 2 h before irradiation, followed by surgery 6 weeks later. **A De Paoli et al (2006)**\(^{17}\) A total of fifty-three patients were recruited to the study between September 2001 and July 2003. The median age was 63 years (range 29–80) and the majority of patients (87%) had T3, N0–2, M0 stage of disease and were treated with capecitabine (825 mg/m², twice daily 7 days per week) and concomitant RT (50.4Gy/28fractions).

59 patients out of 60 who has done CT scan after 6 weeks of completion of Neoadjuvant Chemoradiation, **Radiological response (Clinical response)** according to RECIST 1.1 CRITERIA complete response was observed in 2 patients, partial response in 44 patients, stable disease in 4 patients and progressive disease was seen in 9 patients’ non-significant trend in radiological response was seen according to RECIST 1.1 criteria, \( P=0.1798 \), which is **approaching to significant value**.

50 Patient who were eligible for surgery amongst total 60 study subjects, 37 patients have undergone surgery. Remaining 13 refused for surgery/ lost to follow up. Amongst 37 patients, 26 patients have undergone abdominoperineal resection (APR) and 11 undergone anterior resection (AR) surgery. **Pathological response was observed according to Modified Ryan scheme for Tumor Regression score (CAP guidelines)**, complete response was observed in 1 patient, near complete response in 7 patients, partial response in 27 patients and poor or no disease was seen in 2 patients A statistically significant trend in pathological response was seen by Modified Ryan scheme for Tumor Regression score (CAP guidelines) score, \( P=0.0001 \), which is **significant**.

In Previous study by **JUN-SANG KIM et al (2002)**\(^{15}\) Thirty-eight patients received definitive surgery. Primary tumor and node downstaging observed in 63% and 90% of patients, respectively. The overall downstaging rate, including both primary tumor and nodes, was eighty four percent. A pathologic complete response was observed in 31% of patients. 21 patients had tumors situated initially 5 cm or less from the anal verge; among the 18 treated with surgery, 72% received sphincter-preserving surgery. There were no hematologic toxicities of Grade 3 or 4. Grade 2 leukopenia and anemia developed in 7% and 9% of patients, respectively. Grade 3 nonhematologic toxicities that developed included hand foot syndrome in 7%, fatigue in 4%, diarrhea in 4%, and radiation dermatitis in 2% of patients. There were no life-threatening complications associated with this chemoradiation regimen, and no postoperative death occurred.
Juergen Dunst et al (2008)\textsuperscript{16} Most of the patients suffered from an advanced primary tumor (cT3: 57\%, cT4: 40\%) with lymph node involvement in sixty percent. After preoperative treatment, with a mean of 99\% of the radiation dose actually delivered, a clinical response rate of 68\% (95\% confidence interval: 57\%–78\%) was observed. Out of 87 patients undergoing surgery, a sphincter-preserving surgery could be done in 51\% and R0 resection in 94\%. A pathologically complete response was observed in 6 patients (7\%, 95\% confidence interval: 3\%–14\%). By comparing the initial diagnosis and pathologic findings showed a downstaging in Sixty one percent. Acute toxicity with greater than five percent incidence of NCI (National Cancer Institute) grade ≥ 3 included lymphopenia (12\%), leukopenia (6\%), and diarrhea (7\%). Mild to moderate hand-foot syndrome seen in 12\% only.

A De Paoli et al (2006)\textsuperscript{17}: All patients but two completed the RT programmed and 47 (89\%) received 81\%–100\% of the capecitabine dose (100\% of dose in 72\% patients, 81\%–95\% in 17\% patients and 48\%–74\% in 11\% of patients). Grade 3 toxicity occurred in six patients (11\%) and included mainly of leukopenia (4\%) and hand–foot syndrome (4\%). Mild to moderate toxicity was seen and included leukopenia (72\%), diarrhea (40\%), proctitis (34\%) and skin toxicity (20\%). The overall clinical response rate was fifty eight percent and the downstaging rate was fifty seven percent with a pathologic complete response rate of 24\%. Among 34 patients with low-lying tumors (5 cm from anal verge), 20 (59\%) had a sphincter-saving operation.

As response to preoperative CT–RT has been reported to possibly increase the feasibility of a sphincter-preserving surgery and, potentially, to impact on disease control and survival newer strategies in preoperative treatment of rectal cancer have been directed to obtain higher complete response rates. The combination of 5-FU with new effective drugs in colorectal cancer, such as oxaliplatin and irinotecan, has demonstrated a significant increase in responses in advanced disease. Phase I–II studies evaluating the combination of RT with 5-FU and oxaliplatin or irinotecan are currently ongoing and preliminary results are becoming available.

In this study we used Capecitabine which is an active and safe oral fluoropyrimidine in combination with RT as demonstrated by our study, might simplify chemoradiation by replacing ci-5-FU and the necessity of central lines in these newer preoperative approaches.

CONCLUSION:

Preoperative Chemoradiation have become a part of treatment protocols nowadays in locally advanced Rectal Cancer. Preoperative chemoradiation can lead to tumor downstaging and improves resectability in locally advanced rectal cancer. It also permits sphincter preservation in distal rectal cancer and has a positive impact on quality of life. Present study conducted amongst histologically proven locally advanced rectal adenocarcinoma who received neoadjuvant chemoradiation with Capecitabine (825mg/m\textsuperscript{2} PO Bid) with radiation (45Gy/20#/4weeks). From the study, we conclude that preoperative chemoradiation with capecitabine is a safe, well-tolerated, and effective neoadjuvant treatment modality for locally advanced rectal cancer and it also has a considerable downstaging effect on the tumor.

REFERENCES

2. Fact Sheets by Population-CRC India ASRs.”