Pathologic Complete Response (pCR) To Neoadjuvant Chemoradiation (CRT) Of uT2N0 Rectal Cancer (RC) Treated By Local Excision (LE): Results Of The ACOSOG Z6041 Trial

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BACKGROUND

Early rectal cancer treated with total mesorectal excision (TME) benefits from high cure rates and low recurrence rates. However, TME is associated with significant morbidity (1-8) and mortality. Local excision (LE) is an alternative to TME with lower morbidity and mortality. LE alone results in a high rate of local recurrence. Chemoradiation (CRT) after or before LE may lower the recurrence rate. To investigate this, the American College of Surgeons Oncology Group (ACOSOG) designed a single-arm, non-randomized, multi-center Phase II clinical trial using neoadjuvant CRT followed by LE in patients with ulcerated-stage T2N0 rectal cancer (Z6041). Here, we report preliminary findings from this trial, describing the pathologic complete response (pCR) rate.

STUDY DESIGN

Prior to enrollment patients underwent complete colonoscopy, rigid proctoscopy, endorectal ultrasound (ERUS) or endorectal coil MRI, abdominal and pelvic CT, and chest x-ray. Central review of all staging ERUS or endorectal coil MRI images was performed by a single reader. Patients had an ECOG PS of ≤ 2 and had histologically confirmed invasive adenocarcinoma with a lesion located within 5 cm of the anal verge. TN staging was T2N0 in all cases, established by ERUS or endorectal coil MRI. Greatest tumor diameter was ≤ 5 cm. Patients with tumors fixed to adjacent structures on digital rectal examination were not eligible.

Patients were treated with capecitabine (825 mg/m²), oxaliplatin (50 mg/m²), and 45% reduction of radiation (54 Gy) (Original dose, OD group). Due to toxicity, the dose of RT was reduced to 50.4 Gy and capecitabine to 725 mg/m² in 35 patients (22% of trial dose, RD group). Patients without LE were treated with capecitabine (825 mg/m²) and oxaliplatin (50 mg/m²) for 6 weeks, 1, 2, 4 and 5 during radiation (RT) (total dose 54 Gy) (Original dose, OD group). Due to toxicity, the dose of RT was reduced to 50.4 Gy and capecitabine to 725 mg/m² in 35 patients (22% of trial dose, RD group). Patients performed approximately 4–8 weeks after completing neoadjuvant CRT, using either a conventional transanal approach or a transanal endoscopic microsurgery technique. After LE tumors were staged according to AJCC criteria.

Secondary study endpoints included pathologic complete response (pCR) rate of primary tumor to neoadjuvant CRT, surgeon satisfaction and quality of CRT prediction prior to surgery, and feasibility rate with respect to negative margins, adverse events (AEs) relating to CRT and postoperative complications (PCs). Note that AEs and PCs are not presented here.

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PATIENTS AND METHODS

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TREATMENT REGIMEN

The trial was supported by the ACOSOG grant no. N01 (U10 CA76001), Beadle-Weiner.

CONCLUSIONS

The pCR rate is higher than that reported for Stage II and III tumors and this regimen results in one of the highest pCR rates observed in a co-operative group trial for early stage rectal cancer.

Nearly all eligible patients that received neoadjuvant CRT underwent LE with negative margins.

A negative surgical margin is an important predictor of a pCR.

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