Induction Chemotherapy Plus Chemoradiotherapy With or Without Aspirin in High Risk Rectal Cancer (ICAR)

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BACKGROUND

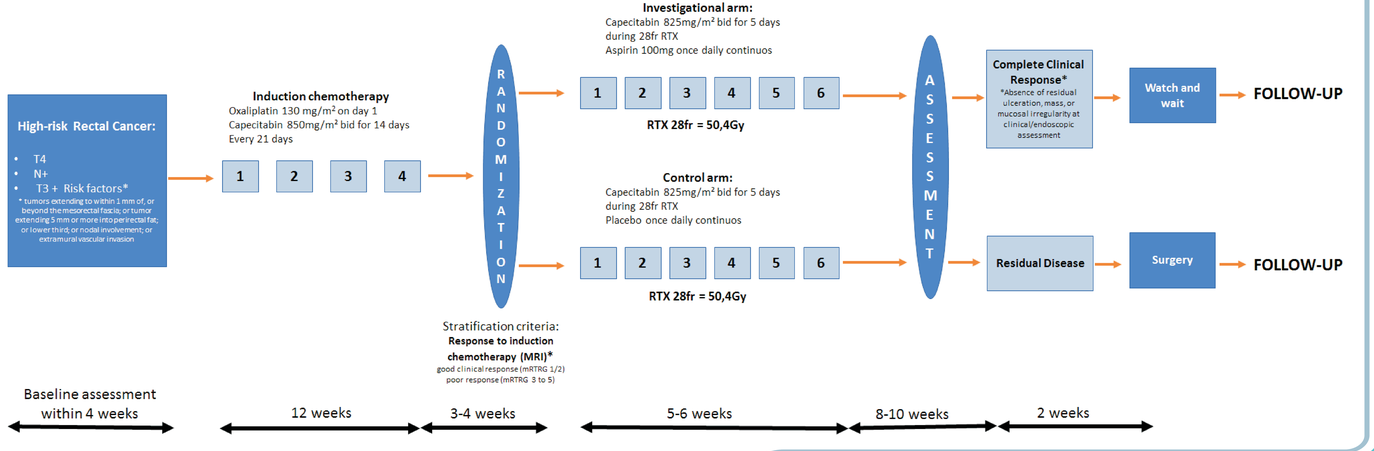
Induction chemotherapy followed by chemoradiation is an attractive approach, with favorable compliance and toxicity profiles. Furthermore, the benefit of aspirin in cancer of the colon and rectum is already known. Recently, it was described its potential activity during chemoradiotherapy, with higher rate of tumor downstaging. The aim of this study is to evaluate the efficacy of total neoadjuvant treatment and the aspirin use during chemoradiotherapy for high-risk rectal cancer.

METHODS

This is a randomized double-blind trial to evaluate induction treatment with XELOX and Capecitabine-based chemoradiotherapy with aspirin or placebo in a high risk population selected by MRI. High-risk will be defined by presence of at least one of the following criteria on high-resolution thin-slice MRI (3 mm): tumors extending to within 1 mm of, or beyond the mesorectal fascia; tumor extending 5 mm or more into perirectal fat; resectable cT4 tumors; lower third; nodal involvement; extramural vascular invasion.

The primary objective of this study is to evaluate the tumor downstaging after total neoadjuvant treatment with or without aspirin. All the patients enrolled in the study will receive XELOX every 21 days for four cycles, unless unacceptable toxicity or progression is detected. After this treatment, patients will be randomized to receive Capecitabine-based chemoradiotherapy with aspirin or placebo (Capecitabine 850 mg/m² 5 days per week combined with radiotherapy with total dose of 50.4 Gy in 28 days). Random assignment of treatment will be stratified by MRI tumour regression grade. After 8-10 weeks, they will be evaluate by MRI. Patients with incomplete clinical response will be referred to immediate surgery and patients with complete clinical response will be managed with “watch and wait” approach. Patients with progression disease during the treatment phase will be withdrawn from the study and will receive their treatment according to the investigator's judgment.

The sample size was calculated according to Simon's optimal two-stage design. Accordingly, 11 patients must be included in each group during the first stage. If 6 patients or fewer show downstaging, the trial will be stopped (interim efficacy analysis). Inclusion of patients will continue until 31 patients are included, in order to detect a difference of 26% or greater in downstaging. A treatment regimen will be considered effective if more than 18 patients of the total 31 show downstaging (final analysis), reaching 90% power with an alpha of 0.05 level of significance. Considering the loss of 20% of the included patients, the sample size should be 80 patients.



Projeto Gráfico: Serviço de Edição e Informação Técnico-Científica / INCA

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