BIOLOGIC THERAPY IN THE MANAGEMENT OF LOCALLY ADVANCED RECTAL CANCER, EXPERIENCE OF 20 DE NOVIEMBRE ISSSTE MEDICAL CENTER, MEXICO CITY

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Introduction

In Mexico, colorectal cancer is within the top 5 causes of death, with an annual incidence of 6,356 cases for both sexes, being more common in men.
The treatment of rectal cancer involves the administration of chemoradiotherapy (CT / RT) and surgery in locally advanced stages. The median time to radiotherapy start is two months therefore a neoadjuvant CT program was established for these patients.
The use of bevacizumab or cetuximab based on KRAS during a neoadjuvant phase or CT/RT, has not been associated with a better relapse-free survival and pathological complete response rate.

Objetives

Assess weather the use of bevacizumab or cetuximab in locally advanced rectal cancer based on KRAS status, during neoadjuvant CT and CT/RT, has an impact on progression-free survival compared to a control group.
The primary end point was progression-free survival
The secondary end point was overall survival and pathologic response

Methods

It is a cases- controls retrospective study, at the department of medical oncology, Medical Center 20 de Noviembre ISSSTE.

The experimental (Bev/Cet) group was selected from March 4, 2009 to March 10, 2011,according_to an internal clinical trial designed to evaluate the use of targeted therapy in the treatment of rectal cancer. The control group was selected from March 6, 2012 to June 12, 2014. The mean follow up for the (Bev/Cet) group was 27 months and 20 months for the control group .

For patients at the Bev/Cet group, bevacizumab was delivered at a dose of 7.5 mg/Kg every 3 weeks with XELOX 2 cycles for all cases. Based on the result of KRAS status (results were often delayed 1-2 months), the biological therapy was chosen: KRAS mut or unknown received only CT/RT with capecitabine (1650 mg/m2/day) and KRAS wt received CT/RT with capecitabine and cetuximab (400 mg/m2/load and 250 mg/m2/week). For the control group, the same treatment was used without bevacizumab or cetuximab.

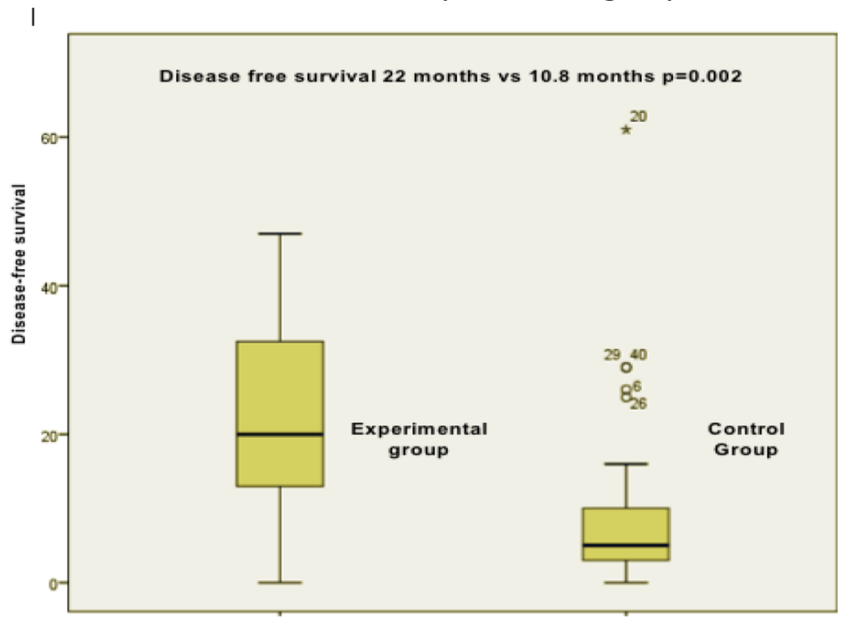
Patients underwent surgery (abdominoperineal resection or low anterior resection), All patients had colonoscopy, abdominal CT scan, and some patients underwent IRM. Delivered radiotherapy dose was 50.4 Gy / 25 fractions. Two patients did not accept surgery after CT/RT, and were kept in close surveillance. Only 5 patients in each group received adjuvant therapy with XELOX.

Poblation and results

Characteristics of the population	Bev/Cet group n=20	Control Group n=25
Age	59 years	58 years
Stage II **Stage III** **Stage IVa**	8 10 2	11 13 1
KRAS • **Wild type** • **Mutaded** • **Uknown**	13 7	6 19
Bevacizumab/Neodjuvant	20	0
Concomitant CTRT/Cetuximab **Concomitant CTRT/Bevacizumab*** **Only CT/RT**	8 2 10	0 0 25
Surgery **Unresectable** **No Surgery****	16 3 1	18 6 1
Results		
Complete Pathologic response **Complete responses by studies**** **Persistent disease after CT/RT (locoregional)** **Partial response**	7 1 3 9	4 1 6 14
Relapse after CT/RT **Yes** **No**	 8 12	 9 16
Dead by surgical complications **Follow-up without progression**	2 10	1 15
CHEMOTHERAPY **Adjuvant therapy** **1st line of relapse** **2nd line after progression**	 5 (pts XELOX) XELOX/Bevacizumab (8 pts) FOLFIRI/Cetuximab (6pts)	 5(pts XELOX) XELOX/Bevacizumab (9 pts) FOLFIRI/Cetuximab(2pts)

* Bev during CTRT was delivered in 2 patients following a local clinical trial .
** Patient refuse don't want to go to surgery after CT/RT and continue surviellance

The rate of pathologic complete was (8pts) 40% in the Bev/Cet group vs 20%(5pts)
The overall survival was 27.4 months in the experimental group vs 16.4 months of control group, p=0.67



Discussion and conclusions

The EXPERT[1] trial compared the use of neoadjuvant cetuximab and CT/RT with XELOX and the complete responses were observed in 20%.The N-SOG 03[2] experience using neoadjuvant bevacizumab, complete responses reported were 30%, with 45% perioperative complications.
In our study the observed pCR rate was 40% with two not-CT related deaths at the experimental group.
The use of targeted therapy increases pCR but we can not confirm a clear relation between KRAS status and pCR, because the KRAS was not performed for all the patients at the control group.
Prospective studies are needed to define a benefit of the targeted therapy at the neoadjuvant and concomitant CT/RT setting for a RAS WT population.

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