Cisplatin plus Capecitabine (CisCape) and radiotherapy (RT) for the neoadjuvant treatment of rectal cancer: final update of previously reported data

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Background

Complete pathological response (pCR) after neoadjuvant therapy is recognized as a powerful favourable prognostic factor for many cancer types, and strategies to potentiate chemotherapy regimens in the hope to increase pCR rate have been attempted[1].
We evaluated the potential for increasing pCR rate by adding a widely used radiosensitizer , cisplatin, to standard capecitabine – based chemoradiotherapy (CRT) in the neoadjuvant setting of rectal cancer (RC)[2].We previously reported results on 17 rectal cancer patients (pts) treated with neoadjuvant CisCape-RT (ESMO World GI 2011)[3]. Here we present the final report of 52 patients treated with the CisCape-RT regimen

Methods

51 pts (male:female, 35:16, median age 63 years, range 41-77), clinically staged with endoscopic ultrasound and chest/abdomen/pelvis CT scan as Stage II (18 pts) or III (33 pts) with histologically confirmed moderately (43pts) or poorly (8 pts) differentiated RC (median distance from the anal verge 5 cm, range 2-13) were treated with standard pelvic radiotherapy (45 Gy/25 fractions) and concurrent capecitabine (825 mg/m2 twice daily days 1 through 14 and 22 through 35) plus cisplatin (40 mg/m2 once every three weeks)(Table 1). Surgery was planned at 8-10 weeks after the end of CRT. 8 cycles of standard adjuvant FOLFOX4 was offered to all patients independently of pathological stage.

Table 1: Patients Characteristics

Characteristics	Number of Points
Sex (F, M)	16:35
Age (y)	63(41-77)
Clinical Stage	
cT3cN0	18
cT2cN1	5
cT3cN1-2	25
cT4cN1	4
Distance from anus (cm)	5 (1-12)
Longest dim (cm)	5 (2-16)
Grading G2:G3	39:13
Mucinous yes:no	9:42
Median CRT duration (days)	41(21-75)
CRT dose reduction yes:no	7:44
CRT delay yes:no	9:42
Hb (g/dL)	13.7 (9.3-16.8)

Results

Radical abdominoperineal and anterior resection was performed in 36 and 12 pts, respectively, 3 pts underwent palliative surgery. pCR (regression AJCC grade 0) was documented in 7 pts (14%), nearly complete response (AJCC grade 1) in 10 pts (20%).

Tumour Regression and Survival

In the whole cohort, median disease-free (DFS) was not yet reached after a median follow-up of 30 months.
There was a strong association between DFS and AJCC grade, with no relapse observed for AJCC grade 0-1 and a 4-year DFS rate of 78% and 22% for AJCC grade 2 and 3, respectively, HR 3.47 (95% CI 0.64-18.9), p 0.03 (Figure 1).

Hemoglobin and tumour regression

Logistic regression was used to assess for potential predictors of pCR (AJCC grade 0). Baseline Haemoglobin levels were significantly associated with the chance of having a complete histological response with an OR= 0.57, p= 0.049, meaning a 43% increased chance of having a pCR for 1-unit increase in baseline Hb[4].As expected, a significant reduction in Hb levels were recorded after on month of CRT according to Wilcoxon test, p< 0.001, making post-CRT Hb not suitable as a predictor of response.

Toxicity and adjuvant chemotherapy

A high frequency of Grade 3-4 toxicities, mainly diarrhoea, was observed (52% of pts). Adjuvant FOLFOX4 was completed in 52% of pts.

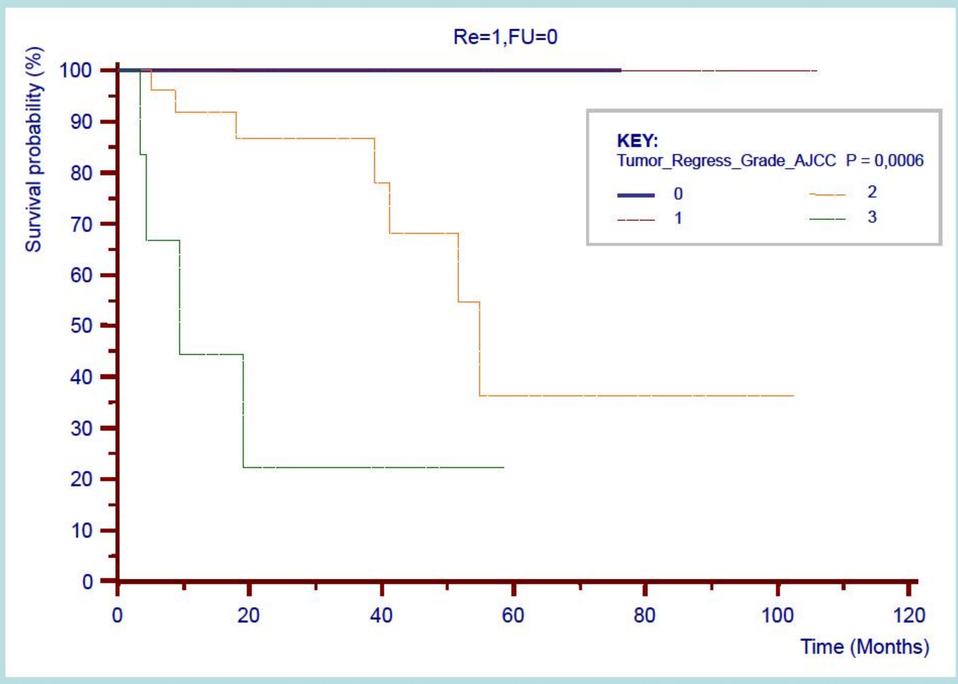

Figure 1: Disease free survival according to AJCC regression grade

Conclusions

Despite a good tumour AJCC regression rate, the high occurrence of grade 3-4 toxicities with CisCape CRT makes this regimen not suitable for larger phase III trials in all RC patients. However, baseline Hb may be a possible patient selection criteria for this intensive treatment strategy.

References

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