



The use of single-agent versus multiple-agent neoadjuvant chemoradiotherapy in the treatment of locally advanced rectal cancer.

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1. BACKGROUND

The use of neoadjuvant chemoradiotherapy is frequently recommended in the treatment of locally advanced rectal cancer however the ideal chemotherapy regimen remains unknown and there is variability in the chemotherapeutic agents used among different institutions.

2. OBJECTIVE

Our goal was to examine differences in overall survival between patients receiving single versus multiple-agent neoadjuvant chemoradiotherapy.

3. METHODS

- National Cancer Database (NCDB) was queried from 01/2006 to 12/2016.
- All patients with locally advanced rectal cancer who received neoadjuvant chemoradiotherapy were included.

- Comparison between patients that received single-agent chemotherapy with those who received multiple-agent neoadjuvant chemoradiotherapy.
- Primary outcome: Overall survival.

4. RESULTS

- Single-agent chemotherapy: 18,544 patients
- Multiple-agent chemotherapy: 12,481 patients

Patients that received multiple-agent chemotherapy were older with more comorbidities (higher Charlson-Deyo Scores). Those receiving multiple-agent chemotherapy were more likely to have clinical Stage III disease (52.9% vs 43.3%, $p < 0.001$) and less likely to have well-differentiated cancer (6.9% vs 7.7%, $p < 0.001$).

The rates of negative resection margin were identical ($p = 0.225$) between the two groups. On multivariable analysis after adjusting for comorbidities, radiation dose, and resection margins, single-agent chemotherapy was associated with worse overall survival (HR 1.09, 95% CI 1.057-1.124, $p < 0.001$).

Other factors associated with overall survival were age, white and black race, income in the lowest quartile, and systemic therapy administered both pre- and post-op (Cox regression analysis).

Variable	Hazard Ratio	95% Confidence Interval	p-value
Age at diagnosis	0.997	0.996 - 0.999	0.003
Race			
White	0.896	0.843 - 0.952	<0.001
Black	0.921	0.852 - 0.995	0.037
Income Less than 38,000 \$	1.327	1.07 - 1.645	0.01
At least two courses of chemotherapy both pre and postop (vs only preop)	0.827	0.802 - 0.854	<0.001
Single agent chemotherapy (vs multiple)	1.09	1.057 - 1.124	<0.001

5. CONCLUSIONS

Multiple-agent chemoradiotherapy is associated with improved overall survival in locally advanced rectal cancer, however chemotherapy regimen does not affect resection margins. The modest overall survival benefit with multiple agent chemotherapy must be balanced with the potential associated toxicity.