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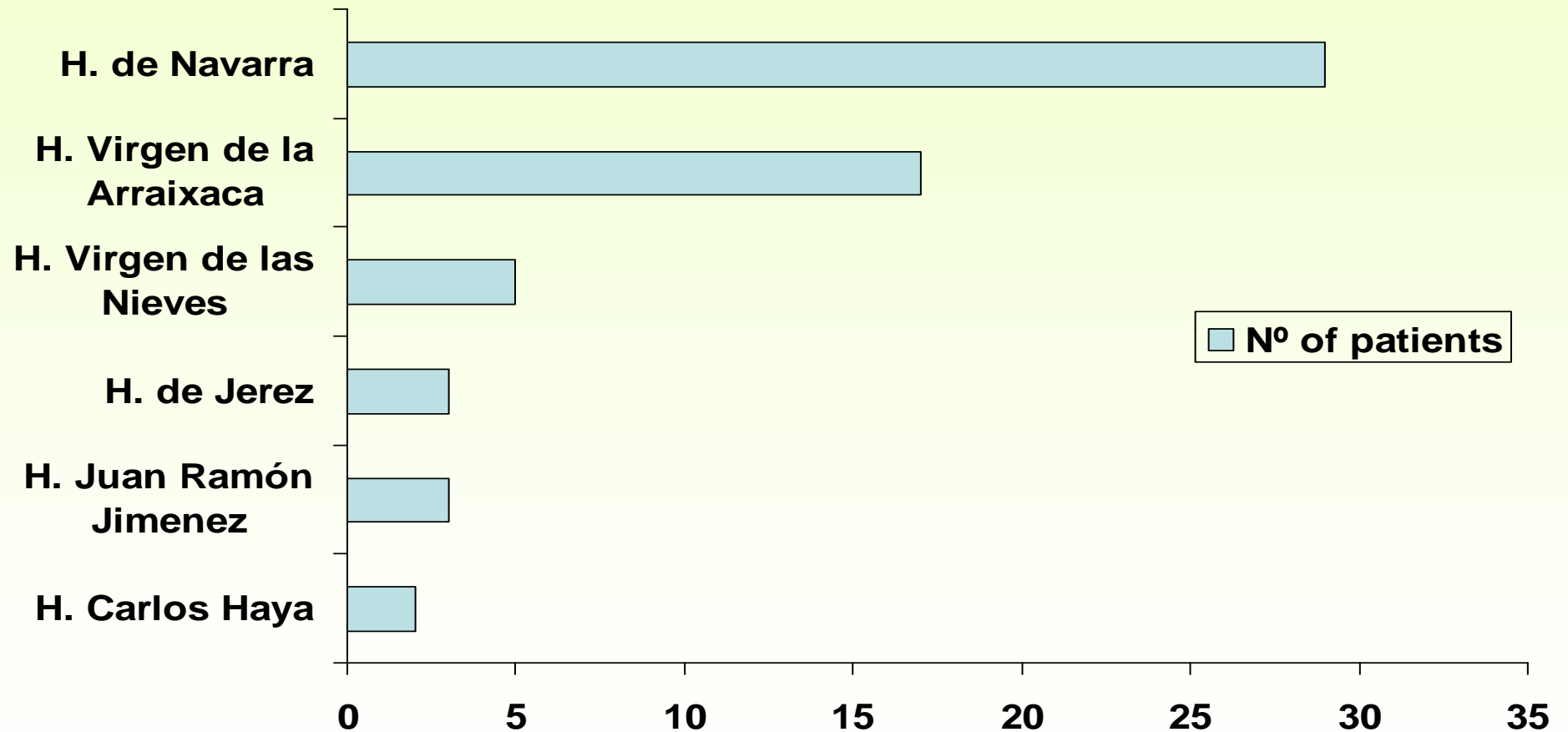
**PHASE II TRIAL OF PREOPERATIVE  
CAPECITABINE WITH CONCURRENT  
RADIOTHERAPY IN PATIENTS WITH  
LOCALLY ADVANCED RECTAL CANCER.**

# BACKGROUND

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- **Preoperative chemoradiation (CRT) has become standard treatment for locally advanced rectal cancer.**
- **Preoperative radiotherapy with continuous infusional 5-FU improves sphincter preservation and produces complete pathological responses.**
- **Capecitabine (Xeloda), an oral fluoropyrimidine, is preferentially converted to 5-FU by high intra-tumor thymidine phosphorylase that can be activated by radiotherapy.**
- **The recommended dose for phase II evaluation is 825mg/m<sup>2</sup> bid, administered during a conventional radiotherapy period of about 6 weeks.**
- **The aim of this prospective study was to assess pathologic response, sphincter preservation and acute toxicity of preoperative CRT with capecitabine.**

# PARTICIPATING CENTERS



Patients have been included between March 2004 and June 2005

# OBJECTIVES

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## **Primary endpoint**

- Complete pathologic response rate

## **Secondary endpoints**

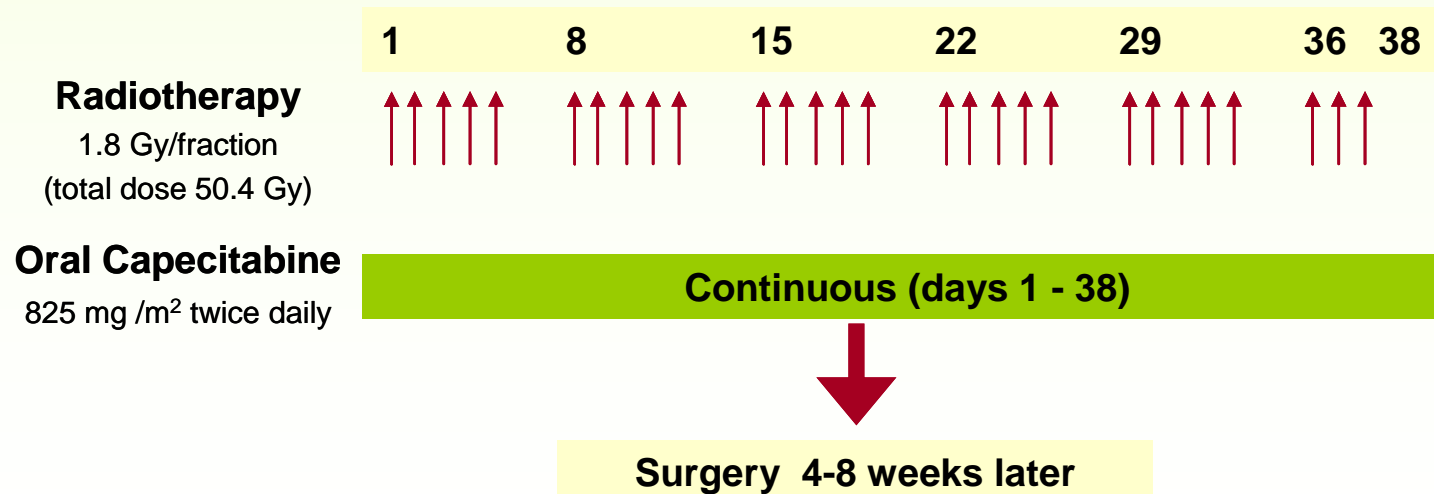
- Overall response rate
- Safety profile
- Overall survival
- Progression free survival
- Sphincter-preservation

# INCLUSION CRITERIA AND TREATMENT PLAN

## Inclusion criteria

Histological or cytological diagnosis of rectal cancer  
Clinical T3-T4 or N+  
Age 18 - 80 years old  
ECOG 0-2  
Adequate bone marrow, renal and hepatic functions.  
Inform consent

## Treatment plan



# PATIENT CHARACTERISTICS (N=59)

	n (%)
<b>Median age, years (range)</b>	<b>64 (30-78)</b>
<b>ECOG</b>	
<b>ECOG 0</b>	<b>16 (28)</b>
<b>ECOG 1</b>	<b>41 (72)</b>
<b>Sex</b>	
<b>Male</b>	<b>36 (61)</b>
<b>Female</b>	<b>23 (39)</b>
<b>Histologic type</b>	
<b>Adenocarcinoma</b>	<b>59 (100)</b>
<b>AJC Stage</b>	
<b>Stage II</b>	<b>26 (44)</b>
<b>Stage III</b>	<b>33 (56)</b>
<b>Lower rectum (&lt; 7cm from anal verge)</b>	<b>35 (59)</b>

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# RESULTS

# EFFECTIVENESS

<b>% Patients</b>	<b>(N=59)</b>
<b>Complete pathologic response (pCR)</b>	<b>10.3</b>
<b>Partial response (PR)</b>	<b>60.3</b>
<b>Stable disease (SD)</b>	<b>24.1</b>
<b>Progressive disease (PD)</b>	<b>3.4</b>
<b>Non-evaluable (NE)</b>	<b>1.8</b>

95% CI; pCR (10.3%): 2.8-18.2

95% CI; pCR + PR (70.6%): 58.5-82.3

**Overall response occurred in 70.6% of patients.**

**Median follow-up was 7.0 months.**

# SAFETY

- There were no grade 4 toxicities\*

<b>% Patients</b>	<b>Grade 1/2</b>	<b>Grade 3</b>
<b>Anemia</b>	<b>36.2</b>	<b>-</b>
<b>Leucopenia</b>	<b>43.1</b>	<b>1.7</b>
<b>Neutropenia</b>	<b>24.1</b>	<b>-</b>
<b>Cardiac</b>		<b>1.7</b>
<b>Gastrointestinal</b>	<b>56.8</b>	<b>8.6</b>
<b>Asthenia</b>	<b>6.9</b>	<b>1.7</b>
<b>Skin</b>	<b>6.9</b>	<b>3.4</b>

Only 18% of patients had Grade 3 toxicity

\* *CTC v. 2.0*

# TREATMENT COMPLIANCE

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## Administered treatment

Forty-five (76%) patients completed preoperative CRT as planned.

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<b>% Patients</b>	<b>(N=59)</b>
<b>Treatment modifications, (%)</b>	
<b>Capecitabine</b>	<b>20</b>
<b>Radiotherapy</b>	<b>12</b>
<b>Treatment delays, (%)</b>	<b>9</b>

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# TREATMENT AND SURGERY

Surgery was performed in 57 patients (97%).

	(N=57)
<b>Histologic type , (%)</b>	
<b>Adenocarcinoma</b>	<b>100</b>
<b>Lymph nodes, (%)</b>	
<b>Negative</b>	<b>76</b>
<b>Positive</b>	<b>24</b>

**72% of patients had sphincter-preservation**

## PREOPERATIVE CHEMORADIOTHERAPY IN RECTAL CANCER A COMPARISON AMONG TWO SCHEMES: INFUSIONAL 5FU & CAPECITABINE

	<b>GRCSG (Sauer)</b>	<b>Our series</b>
Number of patients	405	59
CT scheme	5FU, 1 gr/m <sup>2</sup> /day, 120h, 1 and 5w	CAP, 825 mg/m <sup>2</sup> /12h
T3-4, N+	100%	100%
N+	54%	56%
Full dose radiotherapy	92	88%
Full dose chemotherapy	89%	80%
Complete response	8%	10%
pN+	25%	24%
Sphincter preservation	69%	72%

# PREOPERATIVE CHEMORADIOTHERAPY IN RECTAL CANCER A COMPARISON AMONG TWO SCHEMES: INFUSIONAL 5FU & CAPECITABINE

## Acute toxicity (Grades 3-4)

	<b>GRCSG (Sauer)</b>	<b>Our series</b>
Diarrhea	12%	7%
Hematologic effects	6%	2%
Dermatologic effects	11%	3%
Any Grade 3-4	27%	18%
RT modifications	8%	12%
CT modification	11%	20%

# CONCLUSIONS

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**These results strongly suggest that preoperative CRT using capecitabine is a well-tolerated and effective neoadjuvant treatment for locally advanced rectal cancer**

**The next step is to compare in a randomized trial capecitabine and infusional 5-FU concurrently with preoperative RT. There is an active Phase III Trial (NSABP R-04) designed to do this.**

# NSABP- R 04 Randomized Trial

**Radiation Therapy and Either Capecitabine or Fluorouracil With or Without Oxaliplatin Before Surgery in Treating Patients With Resectable Rectal Cancer**

A total of 1,606 patients will be accrued within 4 years, from July 2004

<b>Sponsors and Collaborators:</b>	<b>National Surgical Adjuvant Breast and Bowel Project (NSABP)</b> <a href="#">National Cancer Institute (NCI)</a> Cancer and Leukemia Group B
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