

# Clinical research in cancer therapy with gemcitabine

## Protocol summaries of currently open trials

### 1. Treating Patients who are Undergoing Surgery for Stage III Non-Small Cell Lung Cancer

**Protocol Ids** # EORTC – 08013 # EUDRACT-2004-001332-23

**Title**

**Phase II Study of Neoadjuvant Induction Therapy Comprising Gemcitabine, Cisplatin, and Gefitinib in Patients With Stage IIIA Non-Small Cell Lung Cancer (NSCLC) Undergoing Surgery**

**Alternate Title**

Gemcitabine, Cisplatin, and Gefitinib in Treating Patients Who are Undergoing Surgery for Stage III Non-Small Cell Lung Cancer

**Objectives**

**Primary**

1. Determine the therapeutic activity of neoadjuvant induction therapy comprising gemcitabine, cisplatin, and gefitinib in patients with stage IIIA non-small cell lung cancer undergoing surgery.

**Secondary**

2. Determine the safety profile of this regimen in these patients.
3. Determine the stage downsizing and complete resectability rate in patients with no progressive disease who undergo surgery after treatment with this regimen.

**Projected Accrual**

A total of 55 patients will be accrued for this study

**Outline**

This is an open-label, nonrandomized, multicenter study. Patients receive induction therapy comprising gemcitabine IV over 30 minutes on days 1, 8, 22, 29, 43, and 50; cisplatin IV over 3-6 hours on days 2, 23, and 44; and oral gefitinib once daily on days 51-79. Treatment continues in the absence of disease progression or unacceptable toxicity. Within 2-7 days after completion of induction therapy, patients with no progressive disease undergo tumor resection.

After completion of study treatment, patients are followed at least every 3 months for 2 years and then every 6 months thereafter

**Study Coordinator**

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**Trial Sites and Contacts**

**Netherlands** (Amsterdam) Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital

**First published: Jan. 24, 2005**

### 2. Aggressive Non-Hodgkin's Lymphoma

**Protocol Ids** # EORTC-20021 # NCT00079261

**Title**

Phase II Randomized Study of Cyclophosphamide, Doxorubicin, Vincristine, and Prednisone With Versus Without Gemcitabine in Patients With Previously Untreated Aggressive Non-Hodgkin's Lymphoma

**Alternate Title**

Cyclophosphamide, Doxorubicin, Vincristine, and Prednisone With or Without Gemcitabine in Treating Patients With Previously Untreated Aggressive Non-Hodgkin's Lymphoma

**Objectives****Primary**

1. Compare the complete response rate (confirmed or unconfirmed) in patients with previously untreated aggressive non-Hodgkin's lymphoma treated with cyclophosphamide, doxorubicin, vincristine, and prednisone with vs without gemcitabine.

**Secondary**

2. Compare the safety profile of these regimens in these patients.
3. Compare the feasibility of these regimens, defined as the proportion of courses given as scheduled, in these patients.
4. Compare freedom from treatment failure in patients treated with these regimens.

**Projected Accrual**

A total of 76-82 patients (38-41 per treatment arm) will be accrued for this study within 2 years.

**Outline**

This is an open-label, randomized, multicenter study. Patients are stratified according to participating center, International Prognostic Index score (0-2 vs 3-5), and histology (B cell vs T cell). Patients are randomized to 1 of 2 treatment arms.

- **Arm I:** Patients receive CHOP chemotherapy comprising cyclophosphamide IV, doxorubicin IV, and vincristine IV on day 1 and oral or IV prednisone on days 1-5.
- **Arm II:** Patients receive CHOP chemotherapy as in arm I and gemcitabine IV over 30 minutes on days 1 and 8.

In both arms, treatment repeats every 3 weeks for 3 courses in the absence of unacceptable toxicity or progressive disease. Patients achieving partial response or complete or unconfirmed complete response receive an additional 5 courses of therapy (for a total of 8 courses).

Patients are followed every 3 months for 3 years, every 6 months for 2 years, and then annually thereafter.

**Study coordinator**

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### 3. Preoperative Chemotherapy in Patients With Resectable Non-Small Cell Lung Cancer

**Protocol Ids #** MRC-LU22 # ISRCTN25582437 # NCT00003159 # EU-97016

**Title**

**Phase III Randomized Study of Surgery With or Without Preoperative Chemotherapy in Patients With Resectable Non-Small Cell Lung Cancer**

**Alternate Title**

Surgery With or Without Preoperative Chemotherapy in Treating Patients With Resectable Non-small Cell Lung Cancer

**Objectives****Primary**

1. Compare the survival following surgical resection with or without preoperative chemotherapy for patients with resectable non-small cell lung cancer.

**Secondary**

2. Compare the quality of life of patients treated with these regimens.
3. Compare pre-randomization clinical and post-surgical pathological staging in patients treated with these regimens.
4. Compare resectability rates in patients treated with these regimens.
5. Compare time to and site of relapse in patients treated with these regimens.
6. Determine response in patients treated with preoperative chemotherapy.

- Determine the adverse effects of preoperative chemotherapy in these patients.

**Projected Accrual**

A total of 450-1,000 patients (225-500 per treatment arm) will be accrued for this study within 5 years.

**Outline**

This is a randomized study. Patients are randomized to 1 of 2 treatment arms.

- Arm I:** Patients undergo surgical resection no more than 4 weeks after randomization.
- Arm II:** Patients receive one of the following chemotherapy regimens immediately following randomization.

*Regimen 1:* Patients receive mitomycin IV, vinblastine IV, and cisplatin IV on day 1.

*Regimen 2:* Patients receive mitomycin IV, ifosfamide IV over 3 hours, and cisplatin IV over 1 hour on day 1.

*Regimen 3:* Patients receive cisplatin IV over 2 hours on day 1 and vinorelbine IV over 5 -10 minutes on days 1 and 8.

*Regimen 4:* Patients receive paclitaxel IV and carboplatin IV on day 1.

*Regimen 5:* Patients receive gemcitabine IV on days 1 and 8 and cisplatin IV over 2 hours on day 1.

*Regimen 6:* Patients receive docetaxel IV and carboplatin IV on day 1.

In all regimens, treatment repeats every 3 weeks for a total of 3 courses. Patients undergo surgical resection at least 4 weeks after the last course of chemotherapy.

Quality of life is assessed at 6 and 12 months, then annually thereafter.

Patients are followed 1 month after surgery, 6 months after randomization, then every 3 months for 2 years, and then every 6 months thereafter.

**Protocol chair**

Adrian Hodson,  
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## 4. Treating Patients Who Have Undergone Surgery for Pancreatic Cancer

**Protocol Ids** # EORTC-40013 # EORTC-22012 # NCT00064207 # FFCO-EORTC-40013

**Title**

**Phase II/III Randomized Study of Gemcitabine Followed By Chemoradiotherapy With Gemcitabine Versus Gemcitabine Alone After Prior Curative Resection in Patients With Pancreatic Head Adenocarcinoma**

**Alternate Title**

Gemcitabine and Radiation Therapy Compared With Gemcitabine Alone in Treating Patients Who Have Undergone Surgery for Pancreatic Cancer

**Objectives****Phase II:**

- Determine the feasibility of gemcitabine followed by chemoradiotherapy with gemcitabine vs gemcitabine alone after prior curative resection in patients with pancreatic head adenocarcinoma.
- Compare the tolerability of these regimens, in terms of acute and late toxicity, in these patients.

**Phase III:**

- Compare the disease-free and overall survival of patients treated with these regimens .
- Compare the quality of life of patients treated with these regimens.
- Compare the toxicity of these regimens in these patients.
- Determine the sites of recurrence in patients treated with these regimens.

**Projected Accrual**

A total of 538 patients (269 per treatment arm) will be accrued for this study within 3 years.

## Outline

This is a randomized, multicenter study. Patients are stratified according to ECOG/WHO performance status (0-1 vs 2), participating center, and N stage (N0 vs N1 vs NX). Patients are randomized to 1 of 2 treatment arms.

- **Arm I:** Within 8 weeks after prior surgical resection, patients receive gemcitabine IV over 30 minutes on days 1, 8, and 15. Treatment repeats every 4 weeks for 2 courses. Patients then receive additional gemcitabine IV over 30 minutes on days 57, 64, 71, 78, 85, and 92. Beginning on day 57, patients also undergo radiotherapy once daily, 5 days a week, for 6 weeks. Treatment continues in the absence of disease progression or unacceptable toxicity.
- **Arm II:** Patients receive gemcitabine IV over 30 minutes on days 1, 8, and 15. Treatment repeats every 4 weeks for 4 courses.

Quality of life (QOL) is assessed in both arms, according to the following schedules:

- **Arm I:** QOL is assessed at baseline; at 3 weeks after the beginning of chemoradiotherapy; after the completion of chemoradiotherapy; every 3 months for 2 years; and then every 6 months for 1 year.
- **Arm II:** QOL is assessed at baseline; at 12 weeks; at 16 weeks; every 3 months for 2 years; and then every 6 months for 1 year.

Patients are followed every 3 months for 2 years and then every 6 months thereafter.

## Protocol chair

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## 5. Treating Patients Who Have Undergone a Radical Cystectomy for Stage III or Stage IV Transitional Cell Carcinoma of the Bladder Urothelium

**Protocol Ids** # EORTC-30994 # UKCCCR-EORTC-30994 # NCT00028756 # ACOSOG-EORTC-30994 # CAN-NCIC-EORTC-30994 # GETUG-EORTC-30994 # JUG-EORTC-30994 # NCRI-BLADDER-EORTC-30994 # NORDIC-EORTC-30994 # SEUG-EORTC-30994 # SWOG-EORTC-30994

### Title

**Phase III Randomized Study of Immediate Versus Deferred Adjuvant Chemotherapy After Radical Cystectomy in Patients With Stage III or IV Transitional Cell Carcinoma of the Bladder Urothelium**

### Alternate Title

Comparison of Immediate and Delayed Adjuvant Chemotherapy in Treating Patients Who Have Undergone a Radical Cystectomy for Stage III or Stage IV Transitional Cell Carcinoma of the Bladder Urothelium

### Objectives

Compare the overall and progression-free survival of patients with stage III or IV transitional cell carcinoma of the bladder urothelium treated with immediate versus deferred adjuvant chemotherapy after radical cystectomy.

### Projected Accrual

A total of 1,344 patients (672 per treatment arm) will be accrued for this study within 5.37 years.

## Outline

This is a randomized, multicenter study. Patients are stratified according to participating center, tumor status (pT1 or 2 vs pT3 vs pT4), and node status (node positive vs node negative with 15 or more nodes sampled vs node negative with less than 15 nodes sampled). Patients are randomized to one of two treatment arms.

- **Arm I:** Beginning within 90 days of radical cystectomy, patients receive a total of 4 courses of

adjuvant chemotherapy.

- **Arm II:** Beginning at the time of clinical relapse, patients receive a total of 6 courses of adjuvant chemotherapy.

Patients in both arms receive one of the following chemotherapy regimens to be determined by participating center:

- **Regimen A (Classical M-VAC):** Patients receive classical M-VAC comprising methotrexate IV on days 1, 15, and 22; vinblastine IV on days 2, 15, and 22; and doxorubicin IV and cisplatin IV on day 2. Courses repeat every 28 days.
- **Regimen B (High-dose M-VAC):** Patients receive high-dose M-VAC comprising methotrexate IV on day 1 and vinblastine IV, doxorubicin IV, and cisplatin IV on day 2. Patients also receive filgrastim (G-CSF) subcutaneously once daily on days 4-10. Courses repeat every 14 days.
- **Regimen C (Gemcitabine and cisplatin):** Patients receive gemcitabine and cisplatin comprising gemcitabine IV over 30 minutes on days 1, 8, and 15 followed by cisplatin IV on day 1 or 2. Courses repeat every 28 days.

Patients are followed every 3 months for 1 year, every 6 months for 5 years, and then annually thereafter.

#### Study coordination:

##### European Organization for Research and Treatment of Cancer (EORTC)

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## 6. Treating Patients With Transitional Cell Cancer of the Urothelium

Protocol Ids # EORTC-GU-30986 # NCT00014274

#### Title

**Phase II/III Randomized Study of Gemcitabine and Carboplatin Versus Methotrexate, Carboplatin, and Vinblastine in Previously Untreated Patients With Transitional Cell Cancer of the Urothelium Who are Ineligible for Cisplatin-Based Chemotherapy**

#### Alternate Title

Combination Chemotherapy in Treating Patients With Transitional Cell Cancer of the Urothelium

#### Objectives

1. Compare the antitumor activity of gemcitabine and carboplatin vs methotrexate, carboplatin, and vinblastine in patients with transitional cell cancer of the urothelium who are ineligible for cisplatin-based chemotherapy.
2. Compare the toxicity and acute and intermediate (1-2 years) side effects of these regimens in these patients.
3. Compare the complete response rates, progression-free survival, and overall survival of patients treated with these regimens.
4. Compare the symptoms and quality of life of patients treated with these regimens.

#### Projected Accrual

A total of 156 patients (78 per treatment arm) will be accrued for the phase II portion of this study. A total of 225 patients will be accrued for the phase III portion of this study within 5 years.

#### Outline

This is a randomized, multicenter study. Patients are randomized to one of two treatment arms.

- **Arm I:** Patients receive methotrexate\* IV and vinblastine IV on days 1, 15, and 22 and

carboplatin IV over 1 hour on day 1. Courses repeat every 28 days in the absence of disease progression or unacceptable toxicity.

- **Arm II:** Patients receive gemcitabine IV over 30 minutes on days 1 and 8 and carboplatin IV over 1 hour on day 1. Courses repeat every 21 days in the absence of disease progression or unacceptable toxicity.

*[Note: \* Methotrexate is omitted for patients with pleural effusion or ascites until complete resolution and for patients with a glomerular filtration rate less than 30 mL/min or creatinine greater than 2 mg/dL]*

Patients in either arm who achieve a complete response (CR) receive 2 additional courses of chemotherapy beyond CR.

Quality of life is assessed at baseline, after every 2 courses of chemotherapy, and within 6 weeks of completion of therapy.

Patients are followed within 6 weeks, every 3 months for 1 year, and then every 6 months thereafter.

**Trial Contact Information: European Organization for Research and Treatment of Cancer (EORTC)**

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