Prospective Trial for the Diagnosis and Treatment of Intracranial Germ Cell Tumors (SIOPCNSGCTII)

**Purpose**

**STUDY DESIGN:**
Prospective, non-randomised multicentre study with patients stratified according to risk groups

**INVESTIGATIONAL MEDICINAL PRODUCTS**
The IMPs on this trial are Carboplatin, Cisplatin, Ifosfamide and Etoposide (as approved by German competent authority).

**PRIMARY OBJECTIVES:**

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**ClinicalTrials.gov Identifier:**
NCT01424839

First received: August 11, 2011
Last updated: January 22, 2013
Last verified: January 2013

History of Changes
Germinoma

- To maintain current high event-free survival (EFS) rates using a risk adapted approach
- In localised germinoma: to omit whole brain and spinal irradiation by using combined treatment with standard chemotherapy and ventricular irradiation (+/- boosts)
- In bifocal tumours (pineal + suprasellar): to treat as non-metastatic disease and to omit whole brain and spinal irradiation by using combined treatment with standard chemotherapy and ventricular irradiation (+/- boosts)
- In metastatic disease: to maintain current excellent EFS in metastatic germinoma with craniospinal irradiation

Malignant non-germinoma

To improve EFS:
- by dose escalation of chemotherapy in patients identified as high risk at diagnosis (age < 6 years and/or AFP serum/CSF > 1000 ng/ml)
- by standardising the surgical approach for residual disease after treatment

SECONDARY OBJECTIVES:

Germinoma

- To minimise long term effects of irradiation by sparing spinal and whole brain radiotherapy in non-metastatic disease
- In standard risk to maintain EFS with chemotherapy and local irradiation
- To evaluate the influence of surgery and treatment on outcome to assist in the development of a future treatment strategy
- For all histological subtypes
- To improve accuracy of diagnosis and staging in all registered patients
- To standardise neurosurgical intervention
- For all patients requiring biopsy or resection according to protocol guidelines, to collect and to store tumour material, and CSF where possible, for use in future biological studies.

ENDPOINTS / Criteria for evaluation:

Main end point

Event-free survival, defined as minimum time from the date of diagnosis to:

- Death from any cause
- Relapse
- Progressive disease on therapy
- Or second malignancy
Secondary end points

- Overall survival, defined as time to death from any cause, measured from the date of diagnosis
- Short and long term toxicity.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Intervention</th>
<th>Phase</th>
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</thead>
<tbody>
<tr>
<td>Intracranial Germ Cell Tumors</td>
<td>Radiation: craniospinal irradiation</td>
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<tr>
<td></td>
<td>Drug: Carboplatin, Etoposide, Ifosfamide</td>
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<tr>
<td></td>
<td>Radiation: ventricular irradiation</td>
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<td></td>
<td>Drug: Cisplatin, etoposide, Ifosfamide (standard)</td>
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<tr>
<td></td>
<td>Drug: Cisplatin, Etoposide, Ifosfamide (high dose)</td>
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<td></td>
<td>Radiation: focal irradiation</td>
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</tbody>
</table>

Study Type: Interventional
Study Design: Allocation: Non-Randomized
Endpoint Classification: Efficacy Study
Intervention Model: Single Group Assignment
Masking: Open Label
Primary Purpose: Treatment

Official Title: SIOP CNS GCT II: Prospective Trial for the Diagnosis and Treatment of Children, Adolescents and Young Adults With Intracranial Germ Cell Tumors

Resource links provided by NLM:

MedlinePlus related topics: Cancer

Drug Information available for: Ifosfamide  Cisplatin  Etoposide  Carboplatin  Etoposide phosphate

U.S. FDA Resources

Further study details as provided by University Hospital Muenster:

Primary Outcome Measures:
- **survival** [Time Frame: 5 years event free survival] [Designated as safety issue: Yes]

  Survival rates in respect to applied treatment, according to Kaplan-Meier estimation, 5 years event free survival

**Secondary Outcome Measures:**

- **short and long term toxicity** [Time Frame: until 7 years after start of trial] [Designated as safety issue: Yes]
  
  Toxicity of treatment will be assessed with CTC criteria, severe toxicity will be analysed by safety desk

- **overall survival** [Time Frame: 7 years after start of trial] [Designated as safety issue: Yes]
  
  Overall survival will be measured by Kaplan-Meier Estimation, 5 years overall survival

**Estimated Enrollment:** 400

**Study Start Date:** October 2011

**Estimated Study Completion Date:** October 2018

**Estimated Primary Completion Date:** October 2018 (Final data collection date for primary outcome measure)

<table>
<thead>
<tr>
<th><strong>Arms</strong></th>
<th><strong>Assigned Interventions</strong></th>
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<tbody>
<tr>
<td>Germinoma metastatic</td>
<td>Radiation: craniospinal irradiation</td>
</tr>
<tr>
<td>• Metastatic or incompletely staged germinomas (± teratoma) Do not receive chemotherapy in this protocol</td>
<td>• Metastatic or incompletely staged pure germinoma 24 Gy (15 fractions) to craniospinal axis with a 16 Gy (10 fraction) boost to tumour bed and any intracranial metastases and spinal deposits (total tumour dose 40 Gy)</td>
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<tr>
<td>Radiotherapy</td>
<td>• Metastatic germinoma plus teratoma (incompletely resected) 24 Gy (15 fractions) to craniospinal axis; 30.4 Gy (19 fraction) boost to tumour bed and 16 Gy (10 fraction) boost to metastases (total tumour dose 54.4 Gy)</td>
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<td>• Metastatic or incompletely staged pure germinoma 24 Gy (15 fractions) to craniospinal axis with a 16 Gy (10 fraction) boost to tumour bed and any intracranial metastases and spinal deposits (total tumour dose 40 Gy)</td>
<td>• Patients with metastatic non-germinomatous disease at diagnosis After Chemotherapy: 30 Gy (20 fractions) to cranio-spinal axis with 24 Gy (15 fraction) boosts to tumour</td>
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<tr>
<td>Site and any intracranial metastases (total tumour dose 54 Gy) and 20.8 Gy (13 fraction) boosts to spinal deposits (total dose 50.8 Gy)</td>
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<tr>
<td>Drug: Carboplatin, Etoposide, Ifosfamide</td>
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<tr>
<td>Non-metastatic fully staged germinoma (± teratoma) Two courses (1 and 3) of Etoposide and Carboplatin, alternating with two courses (2 and 4) of Etoposide and Ifosfamide</td>
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<tr>
<td>Radiation: ventricular irradiation</td>
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<tr>
<td>• Non-metastatic pure germinoma in PR/SD After Chemotherapy: 24 Gy (15 fractions) to whole ventricles with a 16 Gy (10 fraction) boost to tumour bed (total tumour dose 40 Gy)</td>
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<td>• Non-metastatic germinoma in CR After Chemotherapy: 24 Gy (15 fractions) to whole ventricles</td>
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<td>• Non-metastatic germinoma plus teratoma (incompletely resected) After Chemotherapy: 24 Gy (15 fractions) to whole ventricles; 30.4 Gy (19 fraction) boost to tumour bed (total tumour dose 54.4 Gy)</td>
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<th>Non-germinoma non-metastatic standard risk</th>
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<tr>
<td>Drug: Cisplatin, etoposide, Ifosfamide (standard)</td>
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<tr>
<td>Four courses of Etoposide, Cisplatin and Ifosfamide (standard treatment)</td>
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<tr>
<td>Radiation: focal irradiation</td>
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<tr>
<td>• Patients with localised non-germinomatous disease at diagnosis After Chemotherapy: 54 Gy focal radiotherapy in 30 fractions</td>
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<th>Non-Germinoma metastatic standard risk</th>
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<td>Radiation: craniospinal irradiation</td>
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<td>• Metastatic or incompletely staged pure germinoma 24 Gy (15 fractions) to craniospinal axis with a 16 Gy (10 fraction) boost to tumour bed (total tumour dose 50.8 Gy)</td>
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<td>Craniospinal axis with 24 Gy (15 fraction) boosts to tumour site and any intracranial metastases (total tumour dose 54 Gy) and 20.8 Gy (13 fraction) boosts to spinal deposits (total dose 50.8 Gy)</td>
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<td>Patients with metastatic non-germinomatous disease at diagnosis After Chemotherapy: 30 Gy (20 fractions) to cranio-spinal axis with 24 Gy (15 fraction) boosts to tumour site and any intracranial metastases (total tumour dose 54 Gy) and 20.8 Gy (13 fraction) boosts to spinal deposits (total dose 50.8 Gy)</td>
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<td>Drug: Cisplatin, etoposide, Ifosfamide (standard) Four courses of Etoposide, Cisplatin and Ifosfamide (standard treatment)</td>
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<td>Non-germinoma non-metastatic high risk Chemotherapy Two courses of standard Etoposide, Cisplatin and Ifosfamide, followed by two dose intensified courses of Etoposide, Cisplatin and Ifosfamide with stem cell support Radiotherapy After Chemotherapy: 54 Gy focal radiotherapy in 30 fractions</td>
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- Patients with metastatic non-germinomatous disease at diagnosis: After Chemotherapy: 30 Gy (20 fractions) to cranio-spinal axis with 24 Gy (15 fraction) boosts to tumour site and any intracranial metastases (total tumour dose 54 Gy) and 20.8 Gy (13 fraction) boosts to spinal deposits (total dose 50.8 Gy)

Drug: Cisplatin, Etoposide, Ifosfamide (high dose)

Two courses of standard Etoposide, Cisplatin and Ifosfamide, followed by two dose intensified courses of Etoposide, Cisplatin and Ifosfamide with stem cell support

No Intervention: Teratoma collection of information on surgery, applied treatment and outcome

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**Eligibility**

Genders Eligible for Study: Both
Accepts Healthy Volunteers: No

**Criteria**

**Inclusion Criteria:**

- Main residence in one of the participating countries
- Primary diagnosis of an intracranial germ cell tumour
- Written consent for trial participation, treatment according to the protocol and consent for data transfer

**Exclusion Criteria:**

- Tumour entity other than primary intracranial germ cell tumour or CNS GCT as second malignancy
- Primary diagnosis pre-dating the opening of SIOP CNS GCT II in the participating country of registration
- Medical, psychiatric or social conditions incompatible with trial treatment or treatment according to protocol is not intended
Participation within a different trial for treatment of germ cell tumours and/or concurrent treatment within any other clinical trial. The only exceptions to this are trials with different endpoints, involving aspects of supportive treatment which can run parallel to SIOP CNS GCT II without influencing the outcome of this trial e.g. trials on antiemetics, antimycotics, antibiotics, strategies for psychosocial support etc.

- Pregnancy and lactation
- Any treatment not given according to protocol prior to registration

Contacts and Locations

Please refer to this study by its ClinicalTrials.gov identifier: NCT01424839

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Locations
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Principal Investigator: Gabriele Calaminus, MD

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Gesellschaft fur Padiatrische Onkologie und Hamatologie - Germany

Investigators
Principal Investigator: Gabriele Calaminus, MD University Hospital Muenster
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ClinicalTrials.gov Identifier: NCT01424839  History of Changes
Other Study ID Numbers: UKM08_0057, 2009-018072-33
Study First Received: August 11, 2011
Last Updated: January 22, 2013
Health Authority: Germany: Federal Institute for Drugs and Medical Devices

Keywords provided by University Hospital Muenster:
SIOP CNS GCT II
Patients with the primary disease of an Intracranial Germ Cell Tumors

Additional relevant MeSH terms:
Neoplasms, Germ Cell and Embryonal
Neoplasms by Histologic Type
Neoplasms
Etoposide phosphate
Isophosphamide mustard
Cisplatin
Etoposide
Ifosfamide
Carboplatin
Antineoplastic Agents
Therapeutic Uses
Pharmacologic Actions
Radiation-Sensitizing Agents
Physiological Effects of Drugs
Antineoplastic Agents, Phytotherapeutic
Antineoplastic Agents, Alkylating
Alkylating Agents
Molecular Mechanisms of Pharmacological Action