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## Metronomic and Targeted Anti-angiogenesis Therapy for Children With Recurrent/Progressive Medulloblastoma (MEMMAT)

**This study is currently recruiting participants.** (see [Contacts and Locations](#))

*Verified July 2016 by Medical University of Vienna*

**Sponsor:**

Medical University of Vienna

**Information provided by (Responsible Party):**

Andreas Peyrl, Medical University of Vienna

**ClinicalTrials.gov Identifier:**

NCT01356290

First received: May 17, 2011

Last updated: July 28, 2016

Last verified: July 2016

[History of Changes](#)

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[No Study Results Posted](#)

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### Purpose

Patients with relapsed medulloblastoma have a very poor prognosis whether treated with conventional chemotherapy, high-dose chemotherapy with stem cell rescue, irradiation or combinations of these modalities. Antiangiogenetic therapy has emerged as new treatment option in solid malignancies. The frequent, metronomic schedule targets both proliferating tumor cells and endothelial cells, and minimizes toxicity. In this study the investigators will evaluate the use of biweekly intravenous bevacizumab in combination with five oral drugs (thalidomide, celecoxib, fenofibrate, and alternating cycles of daily low-dose oral etoposide and cyclophosphamide), augmented with alternating courses of intrathecal etoposide and liposomal cytarabine. The aim of the study is to extend therapy options for children with recurrent or progressive medulloblastoma, for whom no known curative therapy exists, by prolonging survival while maintaining good quality of life. The primary objective of the **MEMMAT** trial is to evaluate the activity of this multidrug antiangiogenic approach in these heavily pretreated children and young adults. Additionally, progression-free survival (PFS), overall survival (OS), as well as feasibility and toxicity will be examined.

<u>Condition</u>	<u>Intervention</u>	<u>Phase</u>
Medulloblastoma	Drug: Bevacizumab Drug: Thalidomide Drug: Celecoxib Drug: Fenofibric acid Drug: Etoposide Drug: Cyclophosphamide Drug: Etoposide phosphate Drug: Liposomal cytarabine	Phase 2

Study Type: **Interventional**

Study Design: **Endpoint Classification: Efficacy Study**

**Intervention Model: Single Group Assignment**

**Masking: Open Label**

**Primary Purpose: Treatment**

Official Title: **A Phase II Study of Metronomic and Targeted Anti-angiogenesis Therapy for Children With Recurrent/Progressive Medulloblastoma**

#### Resource links provided by NLM:

Drug Information available for: [Cyclophosphamide](#) [Thalidomide](#) [Cytarabine](#) [Etoposide](#) [Fenofibric acid](#) [Etoposide phosphate](#) [Celecoxib](#) [Bevacizumab](#)

[Genetic and Rare Diseases Information Center](#) resources: [Medulloblastoma](#) [Glioma](#) [Neuroepithelioma](#)

[U.S. FDA Resources](#)

#### Further study details as provided by Medical University of Vienna:

Primary Outcome Measures:

- Efficacy [ Time Frame: 8 years ] [ Designated as safety issue: No ]

Response rate (Complete remission, partial response, stable disease = [CR+PR+SD]/n) 6 months after start of antiangiogenic treatment

#### Secondary Outcome Measures:

- Overall survival rate [ Time Frame: 8 years ] [ Designated as safety issue: No ]  
The percentage of patients in the study who are alive for a certain period of time (6, 12, 24, and 36 months) after start of treatment with an antiangiogenic multidrug-regime
- Progression free survival rate [ Time Frame: 8 years ] [ Designated as safety issue: No ]  
The percentage of patients in the study who are alive with a non-progressive disease for a certain period of time (6, 12, 24, and 36 months) after start of treatment with an antiangiogenic multidrug-regime.
- Toxicity [ Time Frame: 8 years ] [ Designated as safety issue: No ]  
To evaluate and document toxicities from chronic administration of these drugs at the doses prescribed in this protocol in patients with recurrent or progressive medulloblastoma. These will be descriptive in nature.
- Feasibility [ Time Frame: 6 years ] [ Designated as safety issue: No ]  
To evaluate the feasibility of achieving the prescribed drug doses given the reduced bone marrow tolerance after multiple relapses.
- Quality of life [ Time Frame: 8 years ] [ Designated as safety issue: No ]  
Quality of Life (QoL) will be evaluated by a generic quality of life instrument for children (the KINDL®-questionnaire).
- Prognostic factors [ Time Frame: 8 years ] [ Designated as safety issue: No ]  
To evaluate the influence of tumor biology(histologic subgroups, metastatic stage, age at first diagnosis [<3 years, >3 years]), age at start of antiangiogenic therapy, sex, duration of remission prior to antiangiogenic therapy, number of recurrences.
- Angiogenic factors [ Time Frame: 8 years ] [ Designated as safety issue: No ]  
To evaluate serum markers for in-vitro correlative studies of tumor response.

Estimated Enrollment: 40  
Study Start Date: April 2014  
Estimated Study Completion Date: April 2022  
Estimated Primary Completion Date: April 2019 (Final data collection date for primary outcome measure)

#### Intervention Details:

Drug: Bevacizumab  
10mg/kg, intravenous (iv), biweekly, 1 year  
Other Name: Avastin  
Drug: Thalidomide  
3mg/kg, oral, daily, 1 year  
Drug: Celecoxib  
50-400mg, oral bid, daily, 1 year  
Drug: Fenofibric acid  
90mg/m<sup>2</sup>, oral, daily, 1 year  
Drug: Etoposide  
35-50 mg/m<sup>2</sup>, oral, alternating 21-day cycles of daily oral etoposide and cyclophosphamide, 1 year  
Drug: Cyclophosphamide  
2.5mg/kg, oral, alternating 21-day cycles of daily oral etoposide and cyclophosphamide, 1 year  
Drug: Etoposide phosphate  
0.5mg, intrathecal, day 1-5, every four weeks, alternating with intrathecal liposomal cytarabine, 1 year  
Drug: Liposomal cytarabine  
25-35mg, intrathecal, every four weeks, alternating with intrathecal etoposide phosphate, 1 year

#### ▶ Eligibility

Ages Eligible for Study: up to 19 Years (Child, Adult)  
Genders Eligible for Study: Both  
Accepts Healthy Volunteers: No

#### Criteria

##### Inclusion Criteria:

- Relapsed or progressive medulloblastoma (at least one site of untreated recurrent disease)
- Histological confirmation of medulloblastoma at diagnosis or relapse
- Female or male, aged from 0 to <20 years (at time of original diagnosis)
- Participants must have normal organ and bone marrow function (ALT <5x institutional upper limit of normal, creatinine <1.5x institutional upper limit of normal for age, WBC >1000/mm<sup>3</sup>, platelets > 20,000/mm<sup>3</sup>. Patients with values less than WBC 2000/mm<sup>3</sup> or platelets 50,000/mm<sup>3</sup> will require initiation of treatment with etoposide and cyclophosphamide at a lower starting dose as defined within the protocol.

- Karnofsky performance status  $\geq 50$ . For infants and children less than 12 years of age, the Lansky play scale  $\geq 50\%$  will be used
- Written informed consent of patients and / or parents

Exclusion Criteria:

- Active infection
- VP-shunt dependency
- Pregnancy or breast feeding
- Conventional chemotherapy, antiangiogenic treatment or complete irradiation of all disease for current relapse (surgery may be performed before antiangiogenic treatment; patients with sites of disease not irradiated are still eligible for the protocol)
- Known hypersensitivity to any of the drugs in the protocol
- Active peptic ulcer
- Any significant cardiovascular disease not controlled by standard therapy e.g. systemic hypertension
- Anticipation of the need for major elective surgery during the course of the study treatment
- Any disease or condition that contraindicates the use of the study medication/treatment or places the patient at an unacceptable risk of experiencing treatment-related complications
- Non-healing surgical wound
- A bone fracture that has not satisfactorily healed

## ▶ Contacts and Locations

Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the Contacts provided below. For general information, see [Learn About Clinical Studies](#).

Please refer to this study by its ClinicalTrials.gov identifier: NCT01356290

### Contacts

Contact: Andreas Peyrl, MD +43 1 40400 ext 32320 [andreas.peyrl@meduniwien.ac.at](mailto:andreas.peyrl@meduniwien.ac.at)

Contact: Irene Slavic, MD +43 1 40400 ext 32320 [irene.slavic@meduniwien.ac.at](mailto:irene.slavic@meduniwien.ac.at)

### Locations

#### United States, Massachusetts

Dana-Farber Cancer Institute and Boston Children's Hospital **Recruiting**  
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#### Austria

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#### Denmark

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Recruiting

#### Sponsors and Collaborators

Medical University of Vienna

#### Investigators

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#### ▶ More Information

Responsible Party: Andreas Peyrl, MD, Medical University of Vienna  
ClinicalTrials.gov Identifier: [NCT01356290](https://clinicaltrials.gov/ct2/show/study/NCT01356290) [History of Changes](#)  
Other Study ID Numbers: MUV-MEMMAT-01  
Study First Received: May 17, 2011  
Last Updated: July 28, 2016  
Health Authority: Austria: Agency for Health and Food Safety

Keywords provided by Medical University of Vienna:

Medulloblastoma	antiangiogenic
Relapse	metronomic
Children	intrathecal

Additional relevant MeSH terms:

Medulloblastoma	Cytarabine
Glioma	Celecoxib
Neoplasms, Neuroepithelial	Fenofibric acid
Neuroectodermal Tumors	Angiogenesis Inhibitors
Neoplasms, Germ Cell and Embryonal	Angiogenesis Modulating Agents
Neoplasms by Histologic Type	Growth Substances
Neoplasms	Physiological Effects of Drugs
Neuroectodermal Tumors, Primitive	Growth Inhibitors
Neoplasms, Glandular and Epithelial	Antineoplastic Agents
Neoplasms, Nerve Tissue	Immunosuppressive Agents
Bevacizumab	Immunologic Factors
Thalidomide	Antirheumatic Agents
Etoposide phosphate	Antineoplastic Agents, Alkylating
Cyclophosphamide	Alkylating Agents
Etoposide	Molecular Mechanisms of Pharmacological Action

ClinicalTrials.gov processed this record on October 19, 2016