Study objectives:

Primary objective:

To determine the safety and tolerability of simultaneous administration of brentuximab vedotin and imatinib mesylate in substitution of conventional chemotherapeutic treatment.

Secondary objective:

Clinical response rate (ORR, CR, PR)
Ability to receive further treatment (stem cell transplantation)
Progression-free survival and overall survival
Identification and assessment of biomarkers

End of study:

End of Study will be 6 years after inclusion of first patient (including a Follow up phase).

Study phase:

This is a multi-center, uncontrolled, open-labelled phase I/II pilot study.

Study population:

A total of 10 patients with relapsed or refractory ALK-positive ALCL will be included. Patients must have received at least one prior line of conventional chemotherapy for ALCL. Patients who are not eligible for conventional chemotherapy can also be included.

Inclusion criteria (selected):

Details see protocol pages 28

- Patients ≥ 18 years of age
- ALK+ ALCL
- Histologically confirmed relapse after having achieved a PR or CR with conventional therapy
- Refractoriness to conventional chemotherapy (SD or PD after conventional chemotherapy)
- Not able to receive conventional chemotherapy (e.g. due to comorbidities)
- Adequate organ function
- Written, voluntarily signed informed consent

Exclusion criteria (selected):

Details see protocol pages 29

- Patient has received any other investigational treatment within 28 days before study entry
- Known hypersensitivity to recombinant proteins, murine proteins, or to any excipient contained in the drug formulation of brentuximab vedotin or imatinib
- ECOG performance status ≥ 3
- Acute or chronic infections
- Female patients who are pregnant or breast-feeding
- Known diagnosis of HIV
- Known hepatitis B surface antigen-positive, or known or suspected active hepatitis C infection
- Known cerebral or meningeal disease (HL or any other etiology), including signs or symptoms of PML

AGMT | ARBEITSGEMEINSCHAFT MEDIKAMENTÖSE TUMORTHERAPIE

AGMT_ALCL 1

A “window of opportunity” trial with Brentuximab Vedotin and Imatinib in patients with relapsed or refractory ALK+ anaplastic large cell lymphoma or patients ineligible for chemotherapy

EudraCT-Nr.: 2013-003505-26

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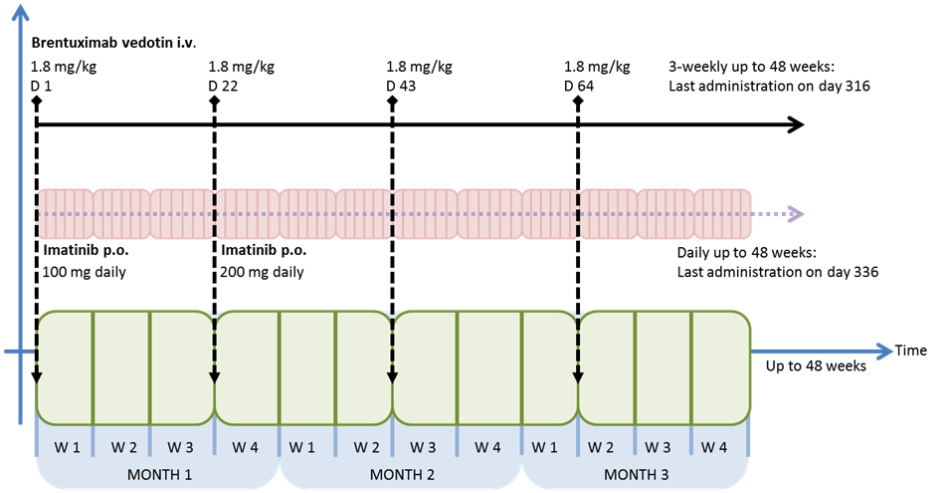
An academic clinical trial by AGMT
Arbeitsgemeinschaft medikamentöse Tumortherapie GmbH
Univ. Prof. Dr. Richard Greil

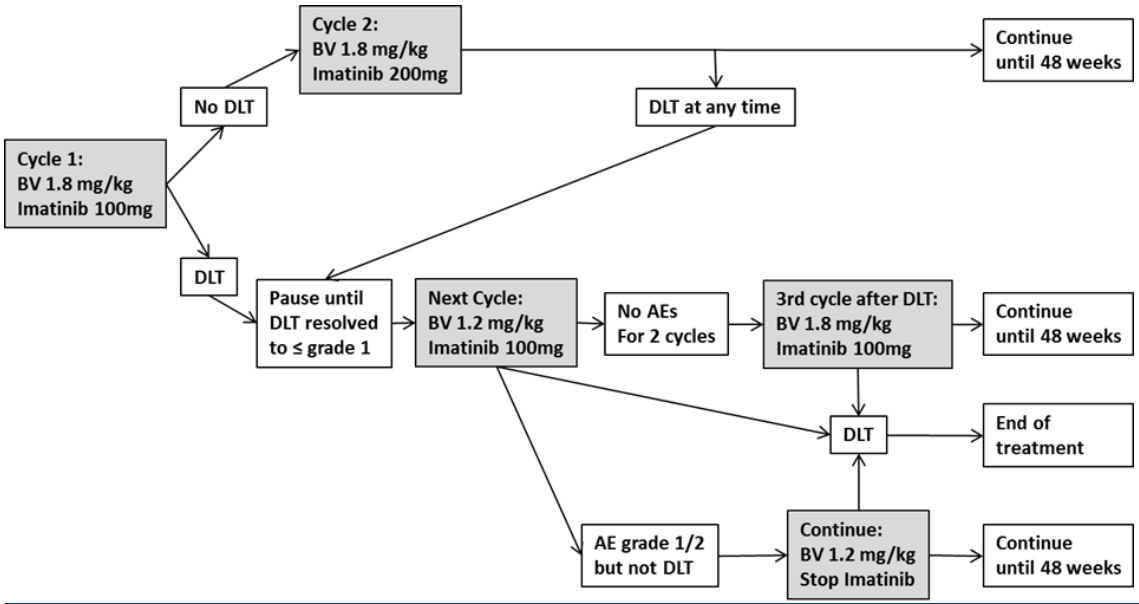
Study design:



Imatinib will be given continuously starting from day 1 of the first cycle at an oral dose of 100mg daily. The dose will be increased to 200mg daily starting from day 1 of the second cycle if no DLT occurs during the first cycle. BV will be given 3 weekly starting on day 1 at a dose of 1.8 mg/kg body weight. In the absence of a dose limiting toyicity (DLT) after 3 weeks of therapy, and in the presence of a clinical response (CR or PR) after cycle 1, the BV dose will continue every 3 weeks for 48 weeks.

Dose modification:

(Details see protocol pages 31)



A dose limiting toxicity (DLT) is defined as grade 2 or more haematological or grade 3 or 4 non haematological adverse event.

If the patient experiences a DLT both study drugs must be withheld until the toxicity has resolved to ≤ grade 1.

BV can be reintroduced at a dose of 1.2mg/kg i.v. Imatinib may be reintroduced at a dose of 100mg p.o. daily.

Treatment:

Patients with relapse or refractory ALK+ ALCL are treated with combination therapy with BV and imatinib for 48 weeks.

Basic Design:

Brentuximab vedotin and Imatinib are administered simultaneously.

Adaptive Design:

In case of a complete or partial resonse to BV/ imatinib at the end of cycle 4, therapy will be continued.

In case of stable disease or progression at any time during the conduct of the trial the patient will go off trial and rescue therapy (conventional chemotherapy, radiation therapy or other) will be initiated.

Dose adjustments will be made according to protocol. Patients may go on to receive autologous or allogeneic transplant, if remission is achieved.

Brentuximab vedotin will be provided as study drug. Imatinib may be prescribed on a compassionate use basis.

Biomarker Evaluation (sCD30) :

Biomarkers for both targets (sCD30, PDGF) are available and will be assessed in patient blood samples throughout the study and after a follow-up period of 12 weeks. Samples will be taken every 3 weeks before each cycle of BV, at the end of treatment and at final visit. The goal of the biomarker study is to develop reliable surrogate markers which indicate the efficacy of treatment of allow to predict for response.