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

Protocol Number: AGMT_ALCL1
EudraCT Number: 2013-003505-26

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Protocol Synopsis:

Indication:	Relapsed or refractory ALCL, ALK-positive
Study design:	This is a multi-center, uncontrolled, open-labelled phase I/II pilot study to be performed in relapsed or refractory ALK+ ALCL patients.
Planned sample size:	10 patients
Status:	2 patients (AKH Wien[1])
Recruitment:	18 months (prolongation of recruitment planned in 2017)
Duration:	First patient in (FPI): Q4 2015 Last patient in (LPI): Q4 2016 (expected) Last patient out (LPO): Q2 2021 (expected)
Study medication:	Brentuximab vedotin, Imatinib

Primary objective:

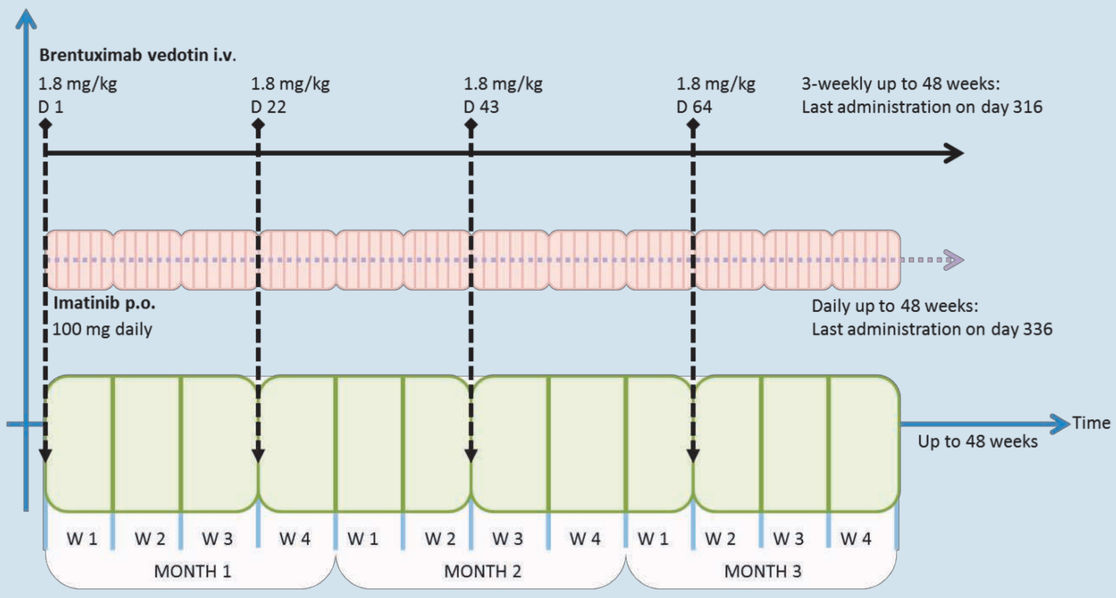
- To determine the safety and tolerability of simultaneous administration of brentuximab vedotin and imatinib mesylate in substitution of conventional chemotherapeutic treatment.

Secondary objectives:

- 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

Apart from clinical response rates with BV and imatinib, it seems important to evaluate, how many patients can go on to stem cell transplantation. sCD30 and PDGF can be determined in blood samples and should be evaluated as biomarkers.

Study Design:



This is an open label pilot study of combining BV in a licensed indication with imatinib in patients with ALCL. It is intended as a “window of opportunity” trial in which the study drugs will be given as an initial substitute for conventional chemotherapy with the intention to achieve a remission enabling the patients to proceed to autologous or allogeneic stem cell transplantation, if eligible.

Patients will be included in this trial if they have relapsed or refractory ALK+ ALCL after at least one line of conventional chemotherapy or if they are ineligible for conventional chemotherapy.

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) i.e. haematological toxicity ≥ grade 2, non- haematological toxicity ≥ grade 3, 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.
In case of progression at any time during the study the patient will go off trial and receive salvage treatment.

Inclusion Criteria (selected):

- 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

Exclusion Criteria (selected):

- 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
- 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

An academic clinical trial
Sponsor: Arbeitsgemeinschaft medikamentöse Tumortherapie gemeinnützige GmbH, Clinical-Scientific Director: R. Greil