

# AGMT\_NHL-15B

## Phase II single-arm “window-of-opportunity” study of a combination of obinutuzumab (GA-101) and venetoclax (ABT-199) in relapsed or refractory diffuse large B-cell lymphoma (DLBCL)

EudraCT Number: 2016-001760-10

Coordinating Investigator: U. Jäger  
AKH Wien, Medical University Vienna, Dept. of Internal Medicine I, Div. of Hematology and Haemostaseology

### Protocol Synopsis

**Indication:** Early relapsed or refractory DLBCL  
**Study design:** This is a uncontrolled, open-label, single arm phase II pilot study  
**Planned sample size:** 21 patients  
**Duration:** First patient in (FPI): Q1 2017  
**Last patient out (LPO):** Q2 2020 (expected)  
**Study medication:** Obinutuzumab, Venetoclax  
**Primary objective:**  
• To evaluate clinical activity and tolerability of obinutuzumab in combination with venetoclax in patients with relapsed/refractory DLBCL

**Secondary objectives:**  
• Safety: Incidence of dose-limiting toxicities of the combination treatment.  
• Response duration (from first documented response)  
• Progression-free survival  
• Overall survival  
• Ability to proceed to further stem cell transplantation (assessed by number of eligible patients reaching transplant)  
• Identification of genetically/biomarker defined subgroups regarding response and survival

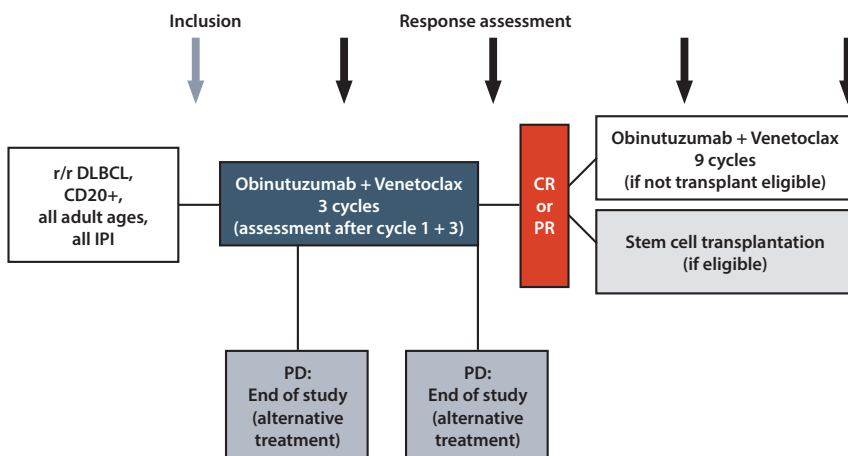
### Inclusion Criteria (selected)

- Patients ≥ 18 years of age
- Diffuse large B-cell lymphoma (DLBCL)
  - with histologically confirmed relapse within 12 months after having achieved a PR or CR with initial R-anthracycline containing therapy, or
  - with refractoriness to initial R-anthracycline containing therapy (not achieving at least a partial response)
- At least one bi-dimensionally measurable lesion on CT scan defined as > 1.5 cm in its longest dimension
- ECOG Performance Status of 0, 1, or 2
- Adequate organ function

### Exclusion Criteria (selected)

- DLBCL transformed from other malignancies or CD20 negative DLBCL
- Radiation, chemotherapy, or immunotherapy or any other anti-cancer therapy ≤ 4 weeks prior to Cycle 1 Day 1
- Ongoing corticosteroid use > 30 mg/day of prednisone or equivalent
- Acute or uncontrolled chronic infections
- Presence of positive test results for Hepatitis B, Hepatitis C and CMV
- Any sensory or motor peripheral neuropathy greater than or equal to Grade 2

### Study Design



- Obinutuzumab is given i.v. at a dose of 1000 mg on days 1, 8, 15 in cycle 1 and on day 1 of each following cycle. Venetoclax is given at 800mg daily p.o. One cycle is 21 days. This combination treatment is repeated for up to 3 cycles. Eligible patients will then proceed to stem cell transplantation (in some patients stem cells were already harvested successfully).
- A 9 cycles (27 weeks) maintenance phase with obinutuzumab and venetoclax will be given in patients ineligible for transplant.
- The study had a 6 patient run-in phase to determine safety and to adjust treatment. A futility analysis is conducted when the first 10 patients have been evaluated for response: If at least two patients had an objective response (CR or PR) the study will be continued.

#### Safety analysis:

A Data Safety Monitoring Board reviewed all safety data after the sixth patient had completed 21 days of treatment. Stopping criteria (“If one (1) treatment related death is reported or three (3) or more patients experience CTC grade 4 events other than neutropenia, anemia, or thrombocytopenia, the study will be stopped for further recruitment.”) was not met, enrollment is continuing.

#### Futility analysis:

Futility analysis was done, two patients have achieved a response so far. It was agreed that the recruitment will be extended until June 2019.

#### Recruitment (as of March 2019):

Sites	Initiation	Patients
AKH MUW / Innere Medizin I - Hämatologie	01.02.2017	5
PMU Salzburg / Innere Medizin III	20.12.2016	2
Kepler UK, Med Campus III. / UK Hämatologie	20.01.2017	0
Klinikum Wels-Grieskirchen / Innere Medizin IV	08.02.2017	2
UK Innsbruck / Innere Medizin V	16.12.2016	2
UK Graz / Innere Medizin - Hämatologie	11.04.2017	3
<b>TOTAL</b>		<b>14</b>