

Site ID:

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Date:

Completed by:

Before Treatment and every dose escalation:

- Consider if the patient should be **hospitalized** for the Venetoclax ramp-up
- For patients with an increased TLS-risk or an increased level of uric acid in the blood: Is the administration of **uric acid reducing medication** necessary? Allopurinol e.g. should be administered 2-3 days before the first dose of Venetoclax.
- For patients with electrolyte values outside the normal ranges; these must be corrected before Venetoclax is administered.
- The concomitant medication should be checked for **potential cross reactions** with Venetoclax (please pay attention with CYP3A- inhibitors und -inductors (e.g. Clarithromycin, Fluconazol, Ketoconazol) as well as P-gp-, BCRP- or OATP1B1/B3 inhibitors).

Instructions for the patient:

- Necessity of **oral hydration** (minimum 2000 ml within 24 hours) **during the complete Venetoclax ramp-up phase.**
- Consumption of **Sevilla-oranges, Grapefruit und starfruit** during the treatment with Venetoclax is forbidden
- Venetoclax should be taken **during breakfast.**
 - o Important! The intake of Ibrutinib for patients in the GIVe arm should occur before breakfast
 - o The administration of the antibody should take place after the intake of Venetoclax (and Ibrutinib if applicable)

Before the dose escalation:

- No side effects grade CTC°III/IV (unless directly attributable to the underlying CLL)
- Lab assessments**

The following values are documented on the CRF (DE-page):

Hemoglobin, Leucocytes, Thrombocytes, Lymphocytes, Neutrophils, Creatinine, GOT/GPT, Bilirubin, Uric Acid, LDH, Sodium, Potassium, Calcium, Phosphate

Further lab testing should be done according to local standards, e.g. blood count.

Option 1:

- Lab assessments within ≤24 h before dose escalation** was evaluated by the investigator and assessed as inconspicuous .
- Additional lab assessment ≤4 h before dose escalation** is considered as baseline value for the assessment of TLS (the results don't need to be evaluated by the physician before intake of venetoclax).

Option 2:

- No** lab assessment was done **≤24 h before dose escalation**.
- The results of the lab assessment **≤4 h before dose escalation** **must** be evaluated by the physician before intake of venetoclax.

Venetoclax dose:

- Intake of Venetoclax** with approx. 250ml of water during breakfast or with a small snack.
- 20mg (take 2 tablets of 10mg out of the blister card)
 - 50mg (take 1 tablet of 50mg out of the blister card)
 - 100mg (take 1 tablet of 100mg out of the blister card)
 - 200mg (take 2 tablets of 100mg out of the blister card)
 - 400mg (take 4 tablets of 100mg out of the bottle)

Document the time of Venetoclax intake: _____:_____

Lab assessments AFTER Venetoclax dose escalation:

- Lab assessments **6-8 h after Venetoclax dose escalation**
- The results of the lab assessment must be evaluated and compared to the baseline assessments by the physician on the **same day**.
 - Deregulated electrolytes must be corrected immediately.
 - The study protocol must be adhered to (Chapter „Laboratory changes and further actions“ and „Definition of tumor lysis syndrome (TLS)“).

The following values are documented on the CRF (LBC-page):

Potassium, Phosphate, Uric Acid, Creatinine, LDH, Calcium
(Documentation only if there is a change of more than 25% from baseline)

Further lab testing should be done according to local standards, e.g. blood count.

The day after dose escalation:

- Lab assessments **≥24 h after Venetoclax dose escalation**
- The results of the lab assessment must be evaluated by the physician **before intake on the next venetoclax tablet**.
- Deregulated electrolytes must be corrected immediately.
 - The study protocol must be adhered to (Chapter „Laboratory changes and further actions“ and „Definition of tumor lysis syndrome (TLS)“).

The following values are documented on the CRF (LBC-page):

Potassium, Phosphate, Uric Acid, Creatinine, LDH, Calcium
(Documentation only if there is a change of more than 25% from baseline)

Further lab testing should be done according to local standards, e.g. blood count.

- Intake of Venetoclax** (see above) with approx. 250ml of water.