# Safety and effectiveness in CLL patients treated with Venetoclax Monotherapy in Austria, Germany, and Switzerland

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## CONCLUSIONS

Under real-world conditions, Ven monotherapy is used in heavily pre-treated elderly patients.

Rate of del(17p) and TP53 mutation was high in treated patients. Unmutated IGHV was present in the majority of patients tested, however 50.0% had not been tested for IGHV at all.

Most patients finished ramp-up and continued venetoclax at the standard dose.

Rates of PFS, OS, and best overall response rate reflect data from Phase-II studies of venetoclax monotherapy.

AEs commonly occurred but were mainly (>70%) mild in nature (CTCAE grade 1 or 2) and no new or unexpected AE effects were seen.

9 patients had TLS, 6 patients according to laboratory values, 3 of these patients had also reported clinical TLS.

8 out of 9 patients with TLS, including those with documented clinical TLS, continued venetoclax treatment and completed the ramp-up phase.

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## REFERENCES

1. Venetoclax SmPC, October 2022
2. Hallek M, Cheson BD, Catovsky D et al. Guidelines for the diagnosis and treatment of chronic lymphocytic leukemia: A report from the international workshop on chronic lymphocytic leukemia updating the national cancer institute-working group 1996 guidelines. Blood 2008;111:5446-5456.
3. Hallek M, Cheson BD, Cativsky D, et al. iwCLL guidelines for diagnosis, indications for treatment, response assessment, and supportive management of CLL. Blood. 2018 Jun 21;131(25):2745-2760.

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## Background

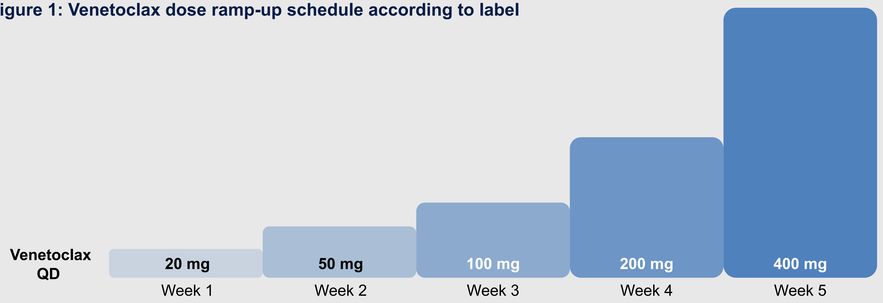
In clinical trials, treatment of chronic lymphocytic leukemia (CLL) with venetoclax (Ven) has shown promising efficacy and good tolerability. However, patients treated in clinical trials often represent a selected group and prospective real-world data are limited.

We conduct a prospective non-interventional observational study assessing effectiveness, safety, and quality of life in patients treated with Ven in Austria, Germany, and Switzerland. The population enrolled is representative for patients treated with Ven according to local label[1]. This report focuses on patients treated with Ven monotherapy.

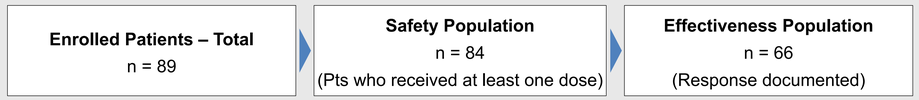
## Methods

Adult patients with CLL requiring therapy treated with Ven according to local label are eligible for the study. Patient visits are scheduled at the physicians discretion and according to clinical practice. Study documentation is possible at baseline, weekly during ramp-up, monthly until the end of 6 months and 3-monthly afterwards up to a maximum of 2 years. Response assessment according to iwCLL criteria can be documented at the end of ramp-up, after 3, 12, and 24 months.

### Figure 1: Venetoclax dose ramp-up schedule according to label




### Figure 2: Patient Flow during the study




Enrolment period was 11.2017–11.2022

### Demographics

Table 1: Patient characteristics[1]

| Characteristics | Patients |
|---|---|
| **Age at first diagnosis, median (range), year** | 64 (33-90) |
| **Sex (n=89), n (%)** | |
| Female | 36 (40.4) |
| Male | 53 (59.6) |
| **Binet Stadium at treatment start (n=89), n (%)** | |
| A | 22 (24.7) |
| B | 33 (37.1) |
| C | 34 (38.2) |
| **Prior therapies (n=89), n (%)** | |
| Yes | 80 (89.9) |
| No | 9 (10.1) |
| **Number of prior therapies, median (range)** | 2 (1-10) |
| **Patients with prior therapies, n (%)[2]** | 60 (67.4) |
| Chemoimmunotherapy | 60 (67.4) |
| Fludarabin | 21 (23.6) |
| Bendamustin | 50 (56.2) |
| B-cell receptor inhibitors | 59 (66.3) |
| Ibrutinib | 54 (60.7) |
| Idelalisib | 14 (15.7) |
| **Patients with comorbidity, n (%)[3]** | 68 (76.4) |
| Cardiovascular | 50 (56.2) |
| Metabolic / endocrine | 28 (31.5) |
| Psychological | 16 (18.0) |
| Gastrointestinal | 14 (15.7) |
| Skeletal system / joints | 13 (14.6) |
| **CIRS based on comorbidity/comedication, median (range)** | 5 (0-10) |
| **Pts with comedication, n (%)** | 60 (67.4) |

[1] Includes only patients who received prior therapy.
[2] Multiple therapies possible for one patient.
[3] Comorbidity categories with ≥15% are listed.
(CIRS = Cumulative Illness Rating Scale)

Table 2: Molecular genetics

| Molecular genetic | Patients, n (% of tested) |
|---|---|
| **Del(17p), (n=78)*** | |
| Deleted | 39 (49.4) |
| Not deleted | 39 (49.4) |
| Not tested | 10 (11.9% of total) |
| ***TP53*, (n=72)*** | |
| Mutated | 36 (48.6) |
| Not mutated | 36 (48.6) |
| Not tested | 15 (17.9% of total) |
| **IGHV, (n = 44)*** | |
| Mutated | 14 (29.8) |
| Not mutated | 30 (63.8) |
| Not tested | 42 (50.0% of total) |

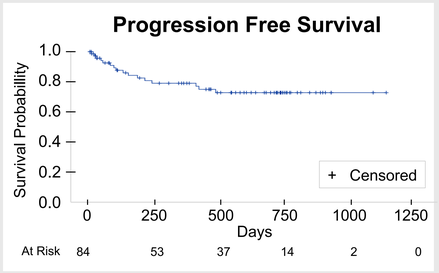
* Patients were not documented.

- In patients tested, del(17p), TP53 mutation, and presence of unmutated IGHV was diagnosed in 49.4 %, 48.6 %, and 63.8 %, respectively.

## Results

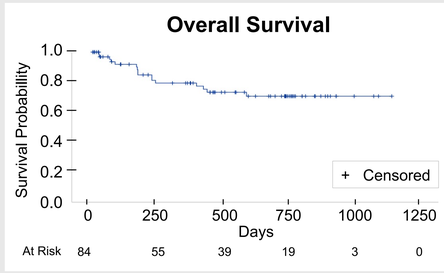
The median follow-up was 461 days.

### Figure 3: Progression Free Survival (PFS)



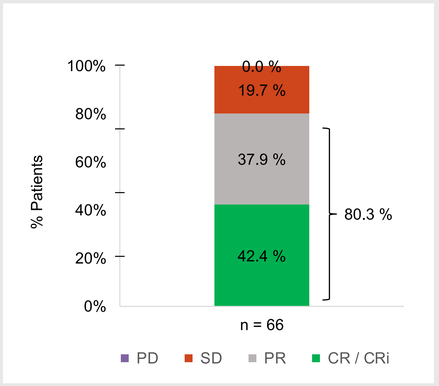

- The estimated PFS-rate after 24 months was 75.0 % (SD: 4.6 %).

### Figure 4: Overall Survival (OS)




- The estimated OS-rate after 24 months was 75.7% (SD: 5.4 %).
- 16 patients (median age 76.5 years; median number of previous therapies 2.5; median CIRS 4.5; 14/16 with comorbidities; 12/16 with comedication) died after a median of 27 days after initiating Ven.

### Figure 5: Best response after 24 months




- Response increased continuously during treatment with 57.4 %, 69.0 %, and 76.6 % responding at the end of ramp-up, after 3 months, and after 12 months, respectively.
- Best overall response rate after 24 months was 80.3 % (CR+CRi 42.4 %; PR: 37.9 %).
- 1 disease progression was documented.
- 67 patients completed ramp-up, 6 are currently in the ramp-up phase, and 11 treatment discontinuations occurred during ramp up, due to physicians decision (n=2), patient wish (n=4), or AE/SAE (n=5)
- The median duration of ramp-up was 35 d (range 1-178) and
- 90 % of patients reached standard daily dose of 400 mg.
- In total, 31 (36.9 %) patients had treatment deviation.
- The most common reason for treatment deviations were hematological AEs/ SAEs (Table 3).

### Table 3: Reasons for treatment deviation

| Reasons for treatment deviation | Patients, n (%) |
|---|---|
| Hematological AE / SAE | 27 (32.1) |
| Non-hematological AE / SAE | 16 (19.0) |
| Physicians decision | 9 (10.7) |
| Patient wish | 5 (6.0) |

Multiple answers possible for multiple deviations within one dose step (AE = Adverse event; SAE = Serious adverse event)

### Table 4: Patients with AEs

| AE* | Patients, n (%) |
|---|---|
| **Patients with AE** | **77 (91.7)** |
| Diarrhoea | 15 (17.9) |
| Thrombocytopenia | 14 (16.7) |
| Neutropenia | 12 (14.3) |
| Fatigue | 10 (11.9) |
| Leukopenia | 10 (11.9) |
| Anemia | 9 (10.7) |
| Nausea | 9 (10.7) |
| Infections | 8 (9.5) |
| **Patients with AE CTCAE grade 3–5** | **52 (61.9)** |
| Neutropenia | 9 (10.7) |
| Thrombocytopenia | 8 (9.5) |
| **Any SAE** | **36 (42.9)** |
| Fever | 3 (3.6) |
| Infection | 3 (3.6) |
| Syncope | 3 (3.6) |

*AEs and AEs with CTCAE grade 3 – 5 ≥10% and SAEs with ≥3% are listed.
(CTCAE = Common Terminology Criteria for Adverse Events)

- 91.7 % and 42.9 % of patients had ≥1 AE and SAE, respectively (Table 5).
- There were 5 CTCAE grade 5 AEs: Infection, urosepsis with shock, 2 worsening of general condition, progressive disease.
- Prevention of hyperuricemia with allopurinol and/or rasburicase, and/or febuxostat/adenuric was given to 72.6 % of patients.

### Table 5: Patients with documented TLS

| TLS | Patients, n (%) |
|---|---|
| Any TLS | 9 (10.7) |
| Only laboratory | 6 (7.1) |
| Only clinical | 1 (1.2) |
| Laboratory and clinical | 2 (2.4) |

(TLS = Tumor Lysis Syndrome)

- 8 patients with suspected or documented TLS completed ramp-up, one during ramp-up, 1 discontinued therapy due to physician's decision.
- 3 patients experienced clinical TLS (Table5):
  - Two patients were diagnosed with Binet C, had a high lymphocyte count (94000/µl and 69900/µl), and received venetoclax in the 9th and 5th line. Treatment with venetoclax was continued and the ramp-up phase was completed. TLS was confirmed by treating physician.
  - One patient was diagnosed with Binet B and exhibited a leukocyte and lymphocyte count of 840/µl. Venetoclax was the 8th line of treatment. No laboratory abnormalities were documented for this patient. Patient died during ramp-up after resolution of TLS due to worsening of general condition (not related to treatment).