1.0 Abstract

Title

Venetoclax (ABT-199) in Patients with Chronic Lymphocytic Leukemia: Experience through the Pre-Approval Access Program in European Countries: A Medical Chart Review

Keywords

Venetoclax, chronic lymphocytic leukemia, pre-approval access cohort, retrospective chart review, ramp-up, effectiveness, safety

Rationale and Background

Venetoclax has been given conditional marketing authorization by the European Medicines Agency (EMA) for the treatment of chronic lymphocytic leukemia (CLL) in the presence of 17p deletion or TP53 mutation in adult patients who are unsuitable for or have failed a B-cell receptor pathway inhibitor; and for the treatment of CLL in the absence of 17p deletion or TP53 mutation in adult patients who have failed both chemo immunotherapy and a B-cell receptor pathway inhibitor. Due to a high unmet need, pre-approval access (PAA) programs for this indication were offered in several European countries, including France, Germany, the Netherlands, Sweden and the United Kingdom (UK).

The rationale for this retrospective chart review of patients who had participated in the PAA programs was to obtain effectiveness, safety and tolerability data to complement the early safety data received during the PAA programs. These additional data will provide further understanding regarding the clinical use, treatment management during the venetoclax dose ramp-up period, treatment duration, effectiveness and tolerability of venetoclax in a context outside of clinical trials.

Research Question and Objectives

The overarching goal of this study was to collect real-world evidence on the effectiveness, safety and tolerability of venetoclax treatment for CLL among patients who received venetoclax as part of PAA cohort programs in Europe.

The primary objective was to describe:

- The effectiveness of venetoclax, measured as overall response rate (ORR) according to physician assessment at week 36.

Secondary objectives were to describe:

- ORR and complete response rate (CRR) according to physician assessment at week 52;
- CRR according to physician assessment at week 36;
- Overall survival (OS) at week 52;
- Time to progression (TTP) at week 52;
- Progression-free survival (PFS) at week 52;
- Proportion of patients starting treatment in the PAA cohorts and remaining on treatment at week 36; and
- Adverse events (AEs) experienced during ramp-up and throughout treatment.

Study Design

Multi-center retrospective chart review in France, Germany and the UK. Netherlands and Sweden were included; however the sites in those two countries did not participate.

Results

Data were collected from the charts of 47 patients. The median patient age was 68 years (range 48-90), 72.3% of patients were male, and 83.0% had at least one documented comorbidity.

The ORR at week 36 was 51.1%, with 12.8% of patients achieving a complete response and an additional 4.3% achieving a complete response with incomplete marrow recovery; the ORR at 52 weeks was 57.4%, with 19.1% of patients achieving a complete response and an additional 6.4% a complete response with incomplete marrow recovery.

Median survival was 72 weeks from venetoclax initiation. As only 11 patients (23.4%) had documented progression during the study period, TTP and PFS were not calculated due to the small sample size.

At week 36, 24 patients (51.1%) remained on treatment, and at week 52, 18 patients (38.3%) remained on treatment.

Clinically relevant AEs possibly related to venetoclax were experienced by a total of 22 patients (46.8%), with 39 distinct AE instances documented. Five of these were serious AEs (SAEs), including one death. The majority of AEs occurred during the first few weeks of treatment (i.e. during ramp-up).

The most common class of AEs was ‘blood and lymphatic system disorders’ (13 AEs), with neutropenia being especially prevalent (7 neutropenia, 2 febrile neutropenia); ‘gastrointestinal disorders’ was another relatively common class (9 AEs). Only four patients (8.5%) experienced tumor lysis syndrome (TLS), one of which was determined to be clinical TLS, two were determined to be laboratory TLS and one was unknown classification.

Discussion

Despite a lower than target sample size, some of the results from this chart review study are in line with findings from clinical trials and other recently published real-world evidence for the treatment of CLL with venetoclax. The ORR and OS were lower than expected but these results could be due to a high number of Unknown responses (21%) and the heavily pre-treated population reviewed here.