(S806) IBRUTINIB LEAD-IN FOLLOWED BY VENETOCLAX IN PATIENTS WITH CHRONIC LYMPHOCYTIC LEUKEMIA: PHASE 2 CAPTIVATE EARLY SAFETY AND EFFICACY RESULTS

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Abstract: S806

Type: Oral Presentation

Presentation during EHA23: On Saturday, June 16, 2018 from 12:00 - 12:15

Location: Victoria Hall

Background

Ibrutinib (ibr), a first-in-class, once-daily BTK inhibitor, is approved in the US for CLL/SLL and in the EU for CLL treatment, including patients with del(17p). Single-agent ibr results in improved survival; however, rates of complete remission (CR) are low, and continuous therapy is required. Ibr and venetoclax (ven), a BCL-2 inhibitor approved by FDA, have complementary therapeutic activity, and synergistic anti-tumor activity has been shown in preclinical and clinical studies with these agents. Ven improves CR rates and can lead to minimal residual disease-negative (MRD(-)) responses in CLL, but increases tumor lysis syndrome (TLS) risk. Tumor debulking by single-agent ibr lead-in followed by combination ibr + ven (I+V) may improve clinical outcomes and lower TLS risk.

Aims

PCYC-1142 (CAPTIVATE) is a phase 2, multicenter study of I+V in first-line CLL (NCT02910583). The study is conducted in 2 phases. The first phase evaluates the MRD(-) clinical response rate of I+V, followed by MRD status-guided randomized treatment discontinuation. The overall objective is to evaluate whether achievement of MRD(-) remission after I+V allows for treatment holidays.

Methods

PCYC-1142 (CAPTIVATE) is a phase 2, multicenter study of I+V in first-line CLL (NCT02910583). The study is conducted in 2 phases. The first phase evaluates the MRD(-) clinical response rate of I+V, followed by MRD status-guided randomized treatment discontinuation. The overall objective is to evaluate whether achievement of MRD(-) remission after I+V allows for treatment holidays.

Results

At time of analysis, a total of 163 patients (median age, 58 years) were enrolled. The first 14 patients had completed the safety run-in of ibr lead-in and ≥6 cycles of I+V; 97 patients (including the safety run-in patients) had completed ibr lead-in and had initiated ven treatment (I+V Exposed). No dose-limiting toxicities occurred during safety run-in. At baseline, 14% of patients had del(17p), 15% had del(11q), and 33% had bulky disease with longest lymph node diameter (LDi) ≥5 cm. Of the 14 safety run-in patients, ORR was 100% (14/14; CR confirmed in 1/5 patients with early BM results at time of analysis and 13/14 confirmed PR); 9/11 assessed patients had MRD(-) status in PB. Common AEs (occurring in ≥20% of I+V Exposed patients) were diarrhea (39%), fatigue (23%), nausea (23%), and arthralgia (21%); grade ≥3 AEs in ≥3% were neutropenia (10%), hypertension (3%), and thrombocytopenia (3%). No patients met the clinical criteria for TLS; laboratory TLS was seen in 1/163. Of 30 I+V Exposed patients with baseline LDi ≥5 cm, 19 (63%) were reduced to LDi <5 cm after ibr lead-in. TLS risk was reduced to medium/low in 17/22 of high risk patients (77%). Overall, the proportion of patients with high-risk TLS decreased from a baseline of 23% to 3% after ibr lead-in.

Conclusion

These early study results support the safety, activity, and TLS risk reduction potential of ibr lead-in. The early data show promising activity of an I+V oral regimen with MRD(-) responses in 82% in first-line CLL. Safety profiles were consistent with AE profiles of single-agent ibr or ven. The protocol-specified efficacy analysis in the first 30 patients (including ORR) will be presented.

Session topic: 6. Chronic lymphocytic leukemia and related disorders - Clinical

Keyword(s): Chronic Lymphocytic Leukemia, Clinical Trial, Minimal residual disease (MRD), Tumor lysis