LymphomaHub

CLL/SLL

Results of extended treatment with 420mg ibrutinib daily in ND and R/R CLL

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In January 2017, Steven E. Coutré from the Stanford Cancer Center, Stanford University School of Medicine, Stanford, California, and colleagues reported the results of up to 44 months continued follow-up from the phase Ib/II study PCYC-1102, and its extension study PCYC-1103. The trials were evaluating the efficacy and safety of daily ibrutinib monotherapy at 420mg in the treatment of Treatment Naïve (TN) or Relapsed/Refractory (R/R) CLL, administered until disease progression or discontinuation.

Key Highlights:

- 94 CLL pts, TN = 27pts, R/R = 67 (two or more prior therapies, median 4)
  - TN group = ≥65 years old, average = 71 yrs
  - R/R group: average age = 66 yrs, del17p = 34% (23pts), del11q = 33% (18pts)
- TN group ORR = 85%, CR = 26%, PR = 52%
- R/R CLL group ORR = 94%, CR = 9%, PR = 82%
- Estimated 30-month PFS: TN = 96% (95% CI, 74–99), R/R = 76% (95% CI, 63–85)
- Median PFS was not reached in both groups
- Estimated 30-month OS: TN = 96% (95% CI, 76–99), R/R = 87% (95% CI, 76–93)
- Within R/R group:
  - 30-month OS: del17p = 81% (95% CI, 58–93), del11q = 88% (95% CI, 61–97), no del = 90% (95% CI, 66–98)
  - 30-month PFS: del17p = 60% (95% CI, 34–78), del11q = 82% (95% CI, 55–94), no del = 85% (95% CI, 60–95)
- Adverse events (AEs):
  - 13% discontinued due to progressive disease (4% of TN pts, 16% of R/R pts)
  - 13% discontinued due to AEs (11% of TN pts, 13% of R/R pts)
  - Most common ≥ Grade 3 AEs in TN: hypertension = 26%, pneumonia = 4%, neutropenia = 4%, and thrombocytopenia = 4%
  - Most common ≥ Grade 3 AEs in R/R: hypertension = 22%, pneumonia = 19%, neutropenia = 16%, thrombocytopenia = 7%, and anemia = 1%
  - Infectious events ≥ Grade 3 higher in R/R than TN group
  - Treatment-related AEs ≥ Grade 3: TN = 22%, R/R = 37%

In conclusion, the authors state that 66% pts remained on ibrutinib in the extension study at the 420mg dose, and that this resulted in durable responses that were tolerated well in both TN and R/R CLL settings. Future trials are investigating possible advantages of combination therapy in the treatment of CLL.

References:

- Coutré S.E. *et al.* Extended Treatment with Single-Agent Ibrutinib at the 420 mg Dose Leads to Durable Responses in Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma. Clinical Cancer Research. 2017 Jan 10. DOI: 1158/1078-0432.CCR-16-1431.

Abstract:

Purpose: Ibrutinib, a first-in-class, once-daily, oral inhibitor of Bruton tyrosine kinase, promotes apoptosis, and inhibits B-cell proliferation, adhesion, and migration. Ibrutinib has demonstrated single-agent efficacy and acceptable tolerability at doses of 420 and 840 mg in patients with chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) who were treatment-naïve (TN) or had relapsed/refractory (R/R) CLL after ≥1 prior therapy in a phase Ib/II study (PCYC-1102). Subsequently, the ibrutinib 420 mg dose was approved in CLL. Experimental Design: We report data with 44 months of follow-up on 94 patients with TN and R/R CLL/SLL receiving ibrutinib 420 mg once-daily in PCYC-1102 and the long-term extension study PCYC-1103. Results: Ninety-four CLL/SLL patients (27 TN, 67 R/R) were treated with ibrutinib (420 mg/day). Patients with R/R disease had received a median of four prior therapies (range, 1–12). Responses were rapid and durable and median duration of response was not reached. Best overall response was 91% [85% TN (complete response, CR 26%) and 94% R/R (9% CR)]. Median progression-free survival (PFS) was not reached in either group. The 30-month PFS rate was 96% and 76% for TN and R/R patients, respectively. Ibrutinib was well tolerated with extended follow-up; rates of grade ≥3 cytopenias and fatigue, as well as discontinuations due to toxicities decreased over time. Conclusions: Single-agent ibrutinib at 420 mg once-daily resulted in durable responses and was well tolerated with up to 44 months follow-up in patients with TN and R/R CLL/SLL. Currently, 66% of patients continue on ibrutinib.
