LymphomaHub

HL

Brentuximab vedotin (BV) with dacarbazine better tolerated in the treatment of elderly treatment naïve Hodgkin lymphoma patients compared with BV+bendamustine combination treatment

Karl Kemp-O'Brien | Oct 27, 2017

In the early online section of Blood (16-Oct-17), Jonathan Friedberg, from the University of Rochester Wilmott Cancer Institute, Rochester, New York, and colleagues, reported results from a phase II trial studying brentuximab vedotin (BV) monotherapy and two different brentixuimab combination therapies.

The results of the BV monotherapy arm of this open-label, non-randomized, multi-center phase II trial were previously reported. This study assessed the safety and efficacy of BV+dacarbazine (DITC) and BV+bendamustine in patients with treatment naïve classical Hodgkin lymphoma who were 60 or over at the time of enrollment and declined or were not eligible for chemotherapy. The primary endpoint was overall response rate (ORR), with secondary endpoints including complete response rate (CR), safety and PFS. Overall survival (OS) was treated as a separate endpoint.

Key Highlights:

- Patients required to have ECOG performance status of ≤3 and bidimensional measurable disease of ≥1.5 cm
- BV+DITC regimen:
  - 8 mg/kg BV and 375 mg/m^2 DTIC on day one of each three-week cycle, for 12 cycles, and then BV alone for four more cycles
- BV+bendamustine regimen:
  - 8 mg/kg BV on day one and 90 mg/m^2 bendamustine on days one and two or each three-week cycle, for up to six cycles, and then BV alone for up to 10 more cycles
  - Protocol was amended to reduced dose to 70 mg/m^2 after initial five patients reported severe adverse events (SAEs)

Efficacy

- BV+DITC
  - Included 22 patients, median age 69 years, of which 21 patients were evaluable for efficacy
  - ORR = 100%, CR = 62%
  - Median PFS = 17.9 months

- Median OS = Not reached

- BV+bendamustine
  - Enrolled 20 patients in total of an intended 30, median age 75 years, of which 17 patients were evaluable for efficacy
  - ORR = 100%, CR = 88%
  - Median PFS and median OS not reached

Safety

- BV+bendamustine arm terminated early by sponsor following reported AEs
- ≥ Grade 3 adverse events:
  - BV+DITC = 45%
  - BV+bendamustine = 90%
- SAEs:
  - BV+DITC = 18%
  - BV+bendamustine = 65%
- Treatment-emergent peripheral sensory neuropathy was higher in BV+DITC group (77%) than BV+bendamustine group (40%)
- Discontinuations due to AEs:
  - BV+DITC = 55%
  - BV+bendamustine = 60%
- One patient died in the BV+DITC group vs. five in the BV+bendamustine group during follow-up

In summary, the authors concluded that high activity was shown in both BV combinations in elderly patients with treatment naïve Hodgkin lymphoma, but BV+bendamustine was poorly tolerated, whereas BV+DITC was well tolerated. Given the similarity in efficacy, but a difference in tolerability, it was concluded that the results suggest BV+DITC may be suitable for elderly patients with newly diagnosed Hodgkin lymphoma who decline or are not eligible for chemotherapy, but that larger trial data is needed to confirm this.

Abstract: Patients aged ≥60 years with treatment-naïve Hodgkin lymphoma (HL) have few treatment options and inferior survival due to treatment-related toxicities and comorbidities. This phase 2, non-randomized, open-label study evaluated tolerability, activity, and response duration with brentuximab vedotin (BV) monotherapy (results previously reported), BV+dacarbazine (DTIC), and BV+bendamustine. Patients had classical HL and were ineligible for or declined frontline chemotherapy. Twenty-two patients received 1.8 mg/kg BV+375 mg/m2 DTIC for up to 12 cycles, then 20 more received 1.8 mg/kg BV+90/70 mg/m2 bendamustine for up to 6 cycles (dose reduced due to toxicity). Subsequent BV monotherapy was allowed. Approximately 30 patients were to receive BV+bendamustine; however, serious adverse event incidence (65%) and 2 deaths on study led to discontinuation of bendamustine treatment and cessation of enrollment in this arm. Most patients had Stage III/IV disease and approximately half had ≥3 comorbidities or were impaired in ≥1 aspect that significantly interfered with quality of life. For BV+DTIC, objective response rate (ORR) was 100% and complete remission (CR) rate was 62%. To date, median progression-free survival (PFS) was 17.9 months (range, 4.2+, 29+) and median overall

survival (OS) was not reached (range, 14.8+, 29+ months). For BV+bendamustine, ORR was 100% and CR rate was 88%. Neither the median PFS nor OS were reached (ranges, 2.9, 18+ months, and 2.9, 18.2+ months, respectively). For elderly patients with HL, BV+DTIC may be a frontline option based on tolerability and response duration. Despite activity, BV+bendamustine is not a tolerable regimen in these patients. The study is registered to www.clinicaltrials.gov as NCT01716806.

References

1. Friedberg J.W. *et al*. Frontline brentuximab vedotin in combination with dacarbazine or bendamustine in patients aged ≥60 years with HL. Blood. 2017 Oct 16. DOI: https://doi.org/10.1182/blood-2017-06-787200. [Epub ahead of print].