MultipleMyelomaHub

General MM, Relapsed/refractory patients

Phase III study finds no significant benefit with bortezomib retreatment versus standard retreatment therapy

Sara Valente | Aug 29, 2017

Longer survival rates in Multiple Myeloma (MM) can mean that patients are more likely to experience relapse, and therefore require retreatment regimens. In order to prevent exhausting all available treatment options it may be necessary to retreat at an early stage of relapse. Evangelos Terpos, from the Department of Clinical Therapeutics, University of Athens School of Medicine, and colleagues, assessed the effects of experimental retreatment with subcutaneous bortezomib and dexamethasone (VD), followed by prolonged bortezomib therapy versus standard VD treatment in relapsed and refractory MM (RRMM). The study was published in the European Journal of Haematology in August 2017.

Study design:

- The study took place between April 2013 and February 2016 across 61 sites in Europe
- The study was terminated early due to insufficient patient enrolment
- Patients (pts) included in the study must have previously been treated with, and responded to, bortezomib
- Pts (n=80) were randomized (2:1) to receive either standard or subcutaneous VD retreatment
- Median age = 68 years (44-81 years)
- The primary endpoint of the study was Progression Free Survival (PFS)
- Secondary endpoints included: Overall Response Rate (ORR), Duration of Response (DoR), Time to Progression (TTP), Overall Survival (OS), Time To Next (myeloma) Therapy (TTNT) and safety

Key Findings:

- Median follow-up = 21.2 months experimental *vs* 20.0 months standard arms
- Median PFS: experimental arm = 7.2 months (95% CI, 5.7-9.0) *vs* standard arm = 7.8 months (95% CI, 4.9-11.7)
- ORR: experimental arm = 66% *vs* standard arm = 52%
- DOR: experimental arm = 6.8 months (95% CI, 5.6-10.4) *vs* standard arm = 5.6 months (95% CI, 2.3-8.8)
- Median TTP: experimental arm = 7.4 months (95% CI, 6.2-9.0) *vs* standard arm = 7.8 months (95% CI, 4.9-11.7)
- Median OS: not evaluable
- OS at 18 months: experimental arm = 84% *vs* standard arm = 77%
- Median TTNT: experimental arm = 8.6 months (95% CI, 7.1-12.2) *vs* standard arm = 9.0 months (95% CI, 4.4-11.4)

Safety:

- Common grade ≥3 Adverse Events (AEs):
  - Thrombocytopenia: experimental = 9% *vs* standard = 22%
  - Anemia: experimental = 8% *vs* standard = 7%
  - Pneumonia: experimental = 8% *vs* standard = 4%
  - Atrial fibrillation: experimental = 6% *vs* standard = 7%
- No new safety signals were detected

Conclusion

The results of the study were only considered descriptive as the expected sample size was not reached and there was not enough data to compare the two retreatment therapies. The authors reported that re-exposing patients to bortezomib was not favourable, which subsequently affected the recruitment numbers. From the data collected, it was concluded that no improvement in median PFS was observed with experimental VD retreatment therapy, compared with standard VD therapy. It was also noted that better tolerability was seen with weekly bortezomib treatment compared with twice-weekly, which revealed higher rates of grade ≥3 AEs and serious AEs. The authors suggested that since weekly treatment was more tolerable than twice-weekly, patients may be able to stay on treatment longer by having better disease control, though further research would be needed. The study was registered at ClinicalTrials.gov (NCT01910987).

Abstract

OBJECTIVES: This randomized, international, multicenter, open-label phase III study investigated the effects of experimental retreatment with subcutaneous bortezomib plus dexamethasone (VD) followed by prolonged bortezomib therapy vs. standard VD retreatment in patients with relapsed/refractory multiple myeloma. **METHODS:** Patients were randomized (2:1) to receive either experimental (n = 53) or standard (n = 27) retreatment, stratified by the number of prior therapy lines. **RESULTS:** The study was terminated prematurely with insufficient enrollment to adequately compare the retreatment therapies; results should be considered descriptive. After a median follow-up of 21.2 and 20.0 months in the experimental and standard arms, respectively, the median progression-free survival (primary endpoint) was 7.2 months (95% confidence interval 5.7-9.0) vs. 7.8 months (4.9-11.7). The overall response rate was 66% and 52% for experimental and standard retreatment regimens, respectively. Thrombocytopenia was the most common and most differentially observed grade ≥3 adverse event (experimental: 9% vs. standard: 22%). Any-grade peripheral neuropathies (including peripheral sensory neuropathies) were reported in 23% vs. 37% of patients. **CONCLUSIONS:** This study showed no significant benefit with experimental vs. standard VD retreatment therapy. Further investigations are required to determine whether the experimental retreatment regimen is a suitable alternative to the current standard retreatment regimen.

References

1. E Terpos. *et al.* Retreatment and prolonged therapy with subcutaneous bortezomib in patients with relapsed multiple myeloma: A randomized, controlled, phase III study. European Journal of Haematology. 2017 Aug 12. DOI: 10.1111/ejh.12937. [Epub ahead of print]