

A Note of Caution re VRD in AL"

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Bortezomib, lenalidomide and dexamethasone (VRD) treatment in systemic AL Amyloidosis - a note of caution

With PBS reimbursement from 1 June 2020 of the bortezomib, lenalidomide and dexamethasone (VRD) triplet as frontline treatment for newly diagnosed myeloma, the Australian Amyloidosis Network would like to highlight the reported international experience of VRD in systemic AL amyloidosis, and provide a note of caution.

Bortezomib-based induction with an alkylator (either cyclophosphamide or melphalan; VCD or VMD) has been extensively evaluated and demonstrated as beneficial in several large RCTs.^{1,2}

VRD has not been assessed in any prospective clinical trials in systemic AL amyloidosis. The only report of VRD in AL amyloidosis is a retrospective case series in 34 patients reported in October 2019 by Kastritis *et al* in *Blood Advances*.³ While response rates were promising (CR 32%), patients could only tolerate a dose of lenalidomide of 5 mg, and the authors concluded that VRD is associated with significant toxicity.

Supporting these concerns, bortezomib, pomalidomide, and dexamethasone (VPD) was assessed in a prospective trial in AL amyloidosis, but this was closed early due to toxicity.⁴ The IMiDs as a class are less well tolerated in AL amyloidosis than in myeloma.

Thus, it is the recommendation of the Australian Amyloidosis Network that until further prospective clinical studies are undertaken, VCD should still be considered the standard of care as frontline treatment in systemic AL amyloidosis. Future optimisation of this backbone is likely to be with the addition of an anti-CD38 mAb rather than with an IMiD.³

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References

1. Kastritis E, Leleu X, Arnulf B *et al*, Bortezomib, melphalan and dexamethasone for light chain amyloidosis. *J Clin Oncol*. 2020 July. Online pre-print.

2. Kastritis E, Palladini G, Minnema MC *et al*, Subcutaneous daratumumab and cyclophosphamide, bortezomib and dexamethasone in patients with newly diagnosed light chain (AL) amyloidosis: primary results from the Phase 3 Andromeda Study. *EHA 2020*. LB2604.
3. Kastritis E, Gavriatopoulou, Roussou M, *et al*. Primary treatment of light-chain amyloidosis with bortezomib, lenalidomide, and dexamethasone. *Blood Adv*. 2019 Oct 22; 3(20): 3002–3009
4. Zonder, JA, Santhorawal V, Kukreti V, *et al*. Phase I Trial of Pomalidomide, Bortezomib, and Dexamethasone as Frontline Treatment of AL Amyloidosis. *Blood* 2017; 130 (Supplement 1): 3158.