Irish Journal of Medical Science (1971 -) (2019) 188:1079–1080
https://doi.org/10.1007/s11845-018-1951-6

LETTER TO THE EDITOR

Dialysis independence following single-agent daratumumab in refractory myeloma with renal failure

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Received: 19 November 2018 / Accepted: 10 December 2018 / Published online: 19 December 2018

Keywords Daratumumab · Dialysis-dependant renal failure · Dialysis independence · Multiple myeloma

Dear Editor,

Although outcomes for multiple myeloma (MM) patients have improved dramatically, MM patients with dialysis-dependent renal failure (DDRF) are a subgroup with an adverse prognosis [1]. In particular, patients with MM not achieving independence from dialysis (DI) despite intensive therapy fare very poorly [2]. Thus, providing treatments that induce rapid disease responses and result in DI is essential if outcomes are to be improved [3, 4]. Here, we report a MM patient with refractory MM with DDRF who achieved DI with single-agent daratumumab, an anti-CD38 monoclonal antibody that has shown significant single-agent activity in relapsed/refractory myeloma [5].

A 67-year-old male was diagnosed with IgA-kappa MM at another institution in 2016. There was widespread lytic-bone disease, serum IgA-kappa paraprotein 15 g/L, and 80% kappa-restricted plasma cells in the bone marrow (BM). Baseline parameters are as follows: beta-2-microglobulin 2.3 mg/L, albumin 31 g/L, creatinine 66 μmol/L serum free-light chain ratio (SFLCr): kappa 58 mg/L:lambda 6.6 mg/L (ratio 8.8). Unfortunately, fluorescence in situ hybridization (FISH) was not performed. He received 6 cycles of bortezomib, lenalidomide, and dexamethasone (RVD) after which no paraprotein was detectable and SFLCr was 3.8. Fourteen months later, he presented to our center with acute kidney injury (AKI) with creatinine 468 μmol/L, calcium 2.33 mmol/L, paraprotein 30 g/L, kappa > 1800 mg/dl, lambda 0.9 mg/L (SFLCr > 2000). BM again showed 80% plasma cells (renal biopsy not undertaken). He commenced hemodialysis three times a week with high-dose dexamethasone (D 40 mg OD days 1–4) and bortezomib (Bz) 1.3 mg/m^2 on days 1, 4, 8, and 11 every 21 days. Weekly oral cyclophosphamide was added to BzD after 2 cycles; however, after 3 cycles of Bz-based therapy, renal function was unchanged and he remained DD with paraprotein 21 g/L, kappa > 8000 mg/L, lambda 0.9 mg/L and imaging showing progressive bony disease. Given the refractory disease and dialysis-requirement, daratumumab (alone) was commenced at 16 mg/kg/week post-dialysis. Infusion commenced at 50 mls/h, titrated per protocol with standard dilution volumes with no infusion-related reactions. Four weeks later, renal function had dramatically improved and he discontinued dialysis completely just 27 days post-commencing daratumumab with repeat assessment showing creatinine 114 μmol/L, paraprotein < 2 g/L, kappa 56.9 g/L, and lambda 12.9 mg/L. He has now completed 19 weeks of treatment and remains DI.

Rocchi et al. recently reported a case of daratumumab use in MM with DDRF, and our case adds to this experience but importantly shows single-agent daratumumab can lead to DI [6]. DI rates of approximately 50% can be achieved in de novo disease complicated by DDRF with intensive therapy; however, the expected rate of DI with regimens used in RRMM is unclear [7]. In a recent

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study of pomalidomide and dexamethasone in RRMM with RF, none of 14 patients with DDRF became DI with a median OS of just 5.2 months [8]. Studies of Bz-based therapy in MM with DDRF have included both patients with de novo MM and RRMM making it difficult to interpret DI rates in RRMM alone. For example, one of the first studies included 24 MM patients with advanced RF (23 with DDRF; 15 > 2 lines of therapy) and led to DI in just three patients [9]. In conclusion, our report of DI following single-agent daratumumab highlights the role for this agent in MM cases with DDRF.

Compliance with ethical standards

Informed consent The patient gave informed consent for this letter to be written.

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