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LETTER TO THE EDITOR

Long-term response to daratumumab in a patient with advanced immunoglobulin light-chain (AL) amyloidosis with organ damage

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Dear Editor,

Light-chain (AL) amyloidosis with organ damage remains an unmet medical need with significant associated morbidity and mortality, especially for those patients with relapsed or refractory (R/R) disease with cardiac involvement [1, 2]. Daratumumab, an anti-CD38 human antibody with proved efficacy in multiple myeloma recently demonstrated encouraging results also in R/R AL [3–8]. We report a durable complete response (CR) to daratumumab, in a patient with R/R AL amyloidosis after seven previous lines of therapy.

In March 2009, a 69-year-old woman referred to our institution because of dysgeusia, macroglossia, and jaw claudication. Serum lambda (λ) light chain and λ Bence Jones proteinuria were demonstrated. Free light chains (FLCs) kappa (κ) were 8.12 mg/L while λ was 4830 mg/L. Bone marrow biopsy demonstrated 35% of plasma cells restricted for λ, and umbilical fat pad aspiration showed Congo red positivity. At diagnosis, no renal nor cardiac involvement was present.

The patient received melphalan and dexamethasone treatment resulting in a temporary partial response, decrease of bone marrow plasma cells (2%), and reduction of macroglossia. From September 2010 to November 2015, she needed six subsequent lines of therapy, administered monitoring FLCs (Fig. 1) [9]. A very good hematological response was achieved twice, after bortezomib (third-line) and after pomalidomide (fourth-line) while other approaches obtained only a disease control. In March 2013, the patient developed cardiac function impairment with interventricular wall thickness increase (13.1 mm) while N-terminal prohormone of brain natriuretic peptide (NT pro-BNP) persisting in the normal range. In October 2016, the patient showed significant clinical deterioration, increase of FLCs (1140 mg/L), increase of NT pro-BNP (4159 ng/mL), and signs of renal damage (proteinuria 1.82 g/24 h). At this time, we had the opportunity to start daratumumab as compassionate use. After 4 weekly doses, FLCs concentration dropped to the normal level. Cardiac and renal function also improved after 15 doses (proteinuria 0.6 g/24 h and of NT pro-BNP 1400 ng/mL). From August 2017, the treatment was prosecuted with monthly administrations; no significant side effects were observed. In January 2018, the patient was hospitalized because of pneumonia; during this episode, the NT pro-BNP level was 1706 ng/mL. At the resolution, daratumumab was restarted. Currently, the patient is still on treatment after 18 months: although a close monitoring for infections is necessary, she is in very good general condition, with FLCs in the normal range and stable cardiac function (NT pro-BNP 1320 ng/mL).

In recent years, several retrospective reports or isolated cases demonstrated efficacy and tolerability of daratumumab in heavily treated R/R AL patients [2–5]. However, in our case the drug induced not only a rapid and deep CR but also a durable response, significantly more prolonged with respect to the previous approaches. In addition, we observed the regression of organ damage, rarely reported in this setting of patients [8]. Our case, together with the published experiences confirms a marked activity of daratumumab in R/R AL that seems to exceed that seen in relapsed myeloma. Overall, these results strongly support the current clinical trials exploring the activity of daratumumab in first-line treatment and in combination with chemotherapy.

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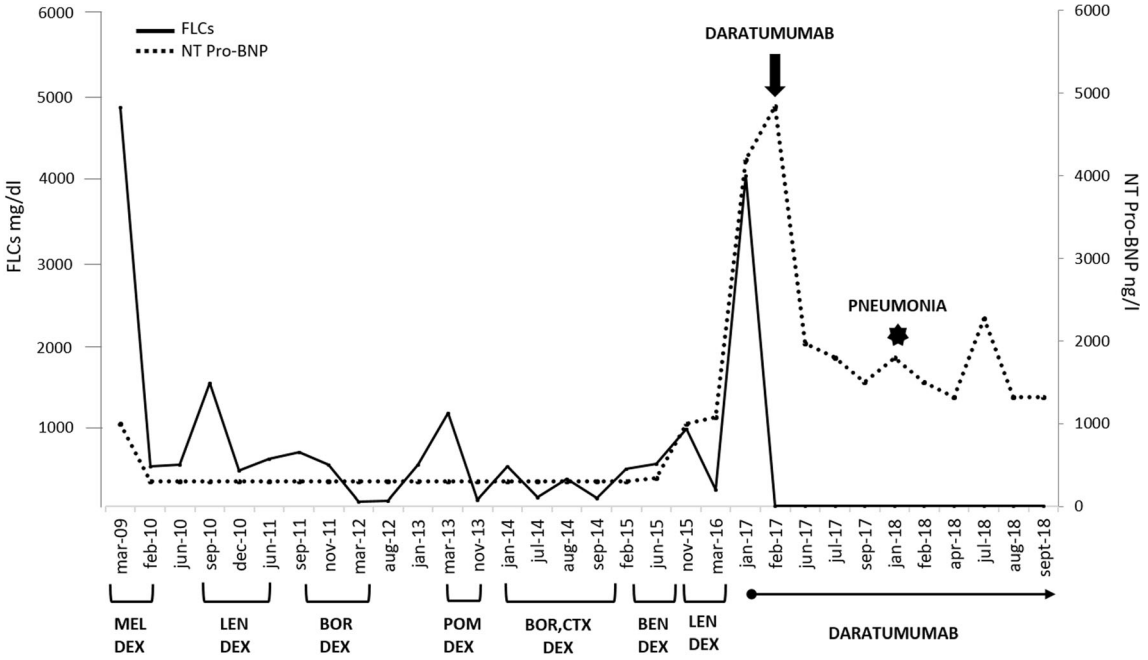

MEL: MELPHALAN
LENA: LENALIDOMIDE
BOR: BORTEZOMIB
POM: POMALIDOMIDE
CTX: CYCLOPHOSPHAMIDE
BEN: BENDAMUSTINE
DEX: DEXAMETHASONE

Fig. 1 Lamba FLCs and NT pro-BNP during treatments

Compliance with ethical standards Informed consent was obtained by the patient for the treatment. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Conflict of interest The authors declare that they have no conflict of interest.

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