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Combined daratumumab-pomalidomide and ultra-fractionated whole breast irradiation is safe!

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Abstract

Background: The management of multiple myeloma (MM) has evolved in the modern era, partially owing to the increasing number of innovative therapies. The safety of their combination with concurrent radiation therapy (RT) remains unknown, in particular CD38 monoclonal antibody or derivative of thalidomide.

Case presentation: We describe a 76-year-old woman complicated with a stage 3b cardiac light chain kappa amyloidosis (AL) with smoldering multiple myeloma (MM) treated with Daratumumab, Pomalidomide and Dexamethasone undergoing whole right breast irradiation. She had whole breast irradiation (WBI) following the Fast-forward protocol delivering 26Gy in 5 fractions in one week and no toxicity was observed.

Conclusion: This case suggests that the concurrent use of Daratumumab and Pomalidomide together with adjuvant ultra-hypofractionated breast over a week is safe.

1. Introduction

The management of multiple myeloma (MM) has evolved in the modern era, partially owing to the increasing number of targeted therapies. Unlike standard chemotherapy (CT), these new therapies can impact cancer cell proliferation and death by interfering with specific proteins, enzymes, or other molecules that are essential for disease progression By targeting these specific molecular pathways, targeted therapies aim to inhibit the growth of tumors and potentially lead to better outcomes with lower risk of side effects. While these innovative therapies, in particular CD38 monoclonal antibody or derivative of thalidomide; administered alone have been studied extensively, the safety of their combination with concurrent radiation therapy (RT) remains unknown.

~~2.~~ Case description

In this report, we describe a 76-year-old woman complicated with a stage 3b cardiac light chain kappa amyloidosis (AL) with smoldering multiple myeloma (MM) treated with Daratumumab, Pomalidomide and Dexamethasone undergoing whole right breast irradiation. Her light chain kappa amyloidosis (AL) with smoldering MM was diagnosed a year ago.

The main other comorbidities were history of left breast cancer (BC), hypothyroidism, cardiac arrhythmia, high blood pressure, smoking and right total hip prosthesis. The patient was treated ten years ago for left breast cancer with breast conservative surgery and sentinel node biopsy, adjuvant RT (40 Gray in 15 fractions) and endocrine therapy (ET).

The current right BC history started with one year after diagnosis of MM. She had conservative surgery and sentinel lymph node biopsy for T1c (13mm) invasive ductal carcinoma, grade 2 without lymphovascular invasion, hormone receptor positive, and human epidermal growth factor 2 negative. The sentinel node removed was uninvolved.

After oncogeriatric evaluation, the patient was considered as eligible for adjuvant RT and ET. She had whole breast irradiation (WBI) following the Fast-forward protocol delivering 26Gy in 5 fractions in one week, using 3D conformal plan with 6 MV tangential fields (Figure 1). Mean ipsilateral lung dose and V8 Gy were respectively 3.6 Gy and 12.5% respectively. For the heart constraints, V1.5 Gy and V7 Gy were respectively 0.04% and 0% (Figure 2).

For MM therapy, the patient received during RT her second line of treatment consisting of Daratumumab, Pomalidomide and Dexamethasone for several months in the Hematology Department. This combination therapy was continued during the course of WBI with the infusion of Daratumumab on day 2 of WBI.

No toxicity was observed during WBI. A clinical reassessment was performed at 3 and 6 months. No toxicity, mainly cutaneous or hematological, was found. There were no decrease in blood value

3. Discussion and conclusion

Fast Forward trial [1] is a phase 3 randomized clinical trial which demonstrated non-inferiority of the 1-week course (26Gy in 5 fractions) of curative WBI over a standard 3 week schedule (40Gy in 15 fractions). In that trial, the worst acute rate of skin toxicity of grade 0, 1, 2, 3 and 4 who were treated in the 26Gy in 5 fractions arm was 6%, 62%, 27%, 6% and 0% respectively [2].

Daratumumab is a CD38 monoclonal antibody approved for the management of newly diagnosed, relapsed, refractory MM [3] or light chain amyloidosis [4]. Little is known about the combination of Daratumumab and RT. In the literature, one of the first reports concerned a woman with a MM with central nervous system involvement who received a large volume of craniospinal RT (36 Gy to the brain and 27 Gy to the spine) with concurrent systemic therapy combining pomalidomide and daratumumab. No significant adverse effect was reported in that case [5]. One retrospective study analyzed outcomes of 18 patients treated for MM treated with Daratumumab and concomitant palliative RT. Nine (50%) presented acute toxicities and 4 (22%) subacute toxicities, mostly hematological [6]. This study did not report any severe toxicity rates from the combined Daratumumab-RT.

The concurrent administration of immunotherapy and anti-angiogenic drugs are also a subject of debate in case of RT indication. Pomalidomide, a derivative of thalidomide that is antiangiogenic and immunomodulatory, is associated with improved the overall survival of MM patients [7]. One case report showed no adverse effect with concurrent Pomalidomide and RT in a 59years-old-woman with MM treated for a plasmocytomic bulky abdominal mass with conventional fractionated palliative RT (30 Gy in 15 fractions) [8].

To our knowledge, our case is the first report using ultra-fractionated regimen with high dose per fractions during one week for breast cancer. As for all other conventional schedules, we did not report any particular side effect with these new drugs and concurrent WBI. A longer follow-up is required to ensure the long-term safety of the combination.

We suggest that the concurrent use of Daratumumab and Pomalidomide for the treatment of MM together with curative intent adjuvant ultra-hypofractionated breast over a week is safe and can be routinely used without risk of acute and late cutaneous side effects.

4. Ethics statement

Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

5. Conflict of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

6. Author Contributions

KD, GL, NG and YB did the literature search and drafted the manuscript. LR, CB and AS reviewed the pathology. KB and LR treated the patient with Daratumumab and Thalidomide. All authors read and approved the final manuscript.

Figure 1.

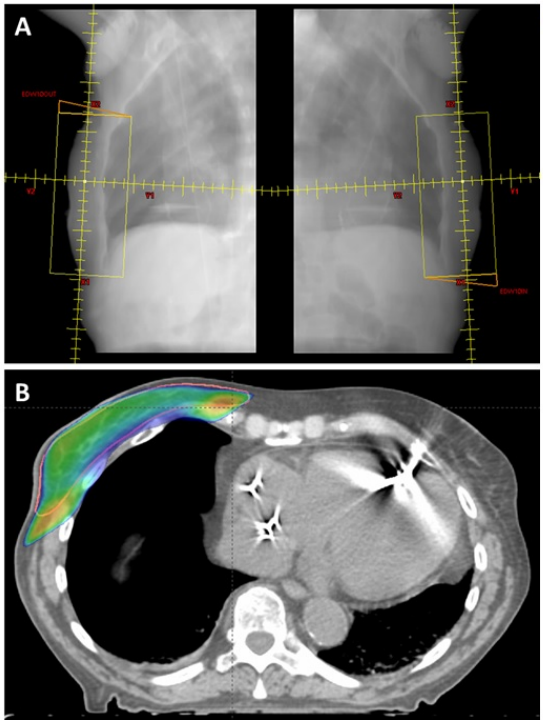
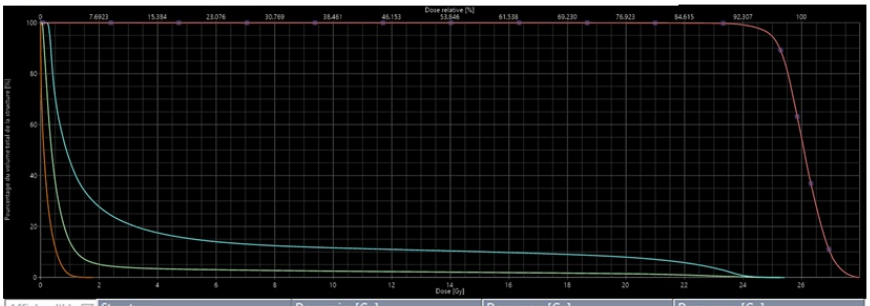


Figure 1 Dosimetry illustration. (A) Tangential fields. (B) Right breast dose distribution

Figure 2

Figure 2 Dose volume histogram



Afficher l'H...	Structure	Dose min. [Gy]	Dose max. [Gy]	Dose moy. [Gy]
☑	Poumon D	0.141	25.436	3.559
☑	Foie	0.021	25.288	1.035
☑	Cœur	0.000	1.810	0.201
☑	CTV sein	13.561	27.981	26.075
☐	Poumon G	0.000	0.290	0.027
☐	PTV sein	2.337	27.981	24.958
☐	Moelle	0.000	0.151	0.019
☐	Mamelon	16.349	26.706	24.566
☐	BODY	0.000	27.981	1.486

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