Letter to the Editor

Durable complete response after stereotactic body radiation therapy in immunotherapy-resistant non-small cell lung cancer

Sir,

We report the case of a patient with advanced PD-L1 negative non-small cell lung cancer (NSCLC), who was started on second-line treatment with nivolumab in August 2015, achieving a complete response. One year later, monotopic oligoprogression occurred in a right adrenal metastasis, that was treated with stereotactic body radiation therapy (SBRT) and subsequent maintenance nivolumab, achieving a sustained complete response.[1] In February 2019, after 43 months of continued treatment with nivolumab, with ^{18}F-fludeoxyglucose-positron emission tomography scan showing no evidence of active disease [Figure 1], treatment was discontinued after a discussion with the patient. Ever since, periodic imaging (every 3 months) has shown no evidence of disease, confirming a durable complete response that lasts for >4 years so far.

While the optimal duration of immunotherapy (IO) in NSCLC is not established, a protracted treatment course could be associated with a greater benefit without an increase in toxicity,[2] although with a higher economic burden. In an exploratory analysis on 163 patients randomized to the CheckMate 153 study, treatment with nivolumab for >1 year prolonged progression-free survival and showed a positive trend for overall survival, compared to 1 year of treatment.[3] On the other hand, there are data suggesting that the reintroduction of IO in patients who discontinued it in the absence of PD, could continue to be effective.[4] Indeed, while most pembrolizumab studies on NSCLC established a maximum treatment duration of 2 years, in Keynote-010, 14 out of 79 patients received a second course of pembrolizumab due to PD after withdrawing it due to a sustained response after a 2-year initial treatment course, achieving six partial responses (43%) and five stabilizations (36%).[5] Therefore, after a durable complete response, the pros and cons of discontinuing IO should be discussed with patients.

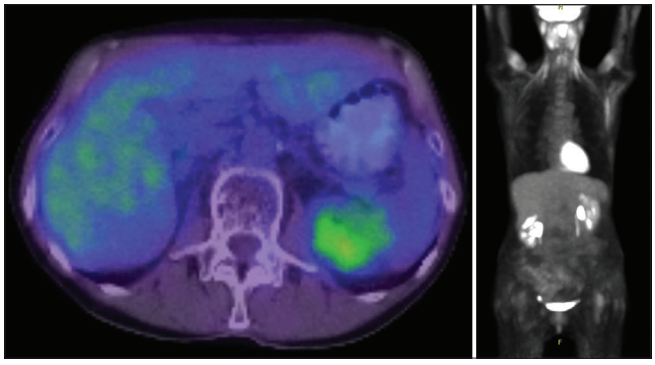

Figure 1: ^{18}F-Fludeoxyglucose-positron emission tomography scan in February 2019, showing no evidence of macroscopic disease

This case suggests that the synergistic effects of sequential treatment with radiotherapy (RT) and IO may have had a prominent role in the patient's outcome. RT has the ability to enhance the antitumor activity of immune checkpoint inhibitors and in some cases even reverse primary or secondary resistance.[6]

When our patient received SBRT, the only site of macroscopic disease was the right adrenal metastasis. However, as a principle in oncology, metastatic macroscopic disease theoretically also means the presence of microscopic disease. In this regard, the sequence nivolumab → SBRT → nivolumab not only eliminated the irradiated adrenal metastasis but also have elicited a still ongoing immune response against micrometastases because no new lesions have appeared to date, >4 years after SBRT. Indeed, there is evidence that supports the hypothesis that the combination of IO and RT can favor a powerful immune response that, in addition to acting on macroscopic disease, will also permanently act on microscopic disease,[7] functioning as a vaccine.

As our case illustrates, and considering the few therapeutic options in patients with advanced NSCLC progressing to IO, in those patients who oligoprogress after an initial response to IO, SBRT followed by maintenance IO may be an effective and well-tolerated approach.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

Miguel J. Sotelo[1,2,3], Santiago Cabezas-Camarero[4], Alejandro Riquelme[5], Coralia Bueno[5]

[1]Department of Medical Oncology, Hospital María Auxiliadora, [2]Aliada Oncological Center, [3]Oncological Research Unit, Clínica San Gabriel, Lima Peru, [4]Department of Medical Oncology, Hospital Universitario Clínico San Carlos, [5]Department of Medical Oncology, Hospital Universitario Infanta Cristina, Madrid, Spain

For correspondence:
Dr. Miguel Jhonatan Sotelo,
Department of Medical Oncology, Hospital María Auxiliadora, Aliada Oncological Center, Oncological Research Unit, Clínica San Gabriel, Avda. Miguel Iglesias 968, San Juan de Miraflores, 15801 Lima, Peru.
E-mail: miguel.sotelo.lezama@gmail.com

Submitted: 11-Jul-2020
Revised: 29-Aug-2020
Accepted: 07-Oct-2020
Published: 22-Jun-2022

REFERENCES

1. Sotelo MJ, Cabezas-Camarero S, Riquelme A, Bueno C. Long-term survival of a patient with programmed death ligand 1-negative lung adenocarcinoma and oligoprogressive disease treated with nivolumab and stereotactic body radiation therapy. J Cancer Res Ther 2020;16:941-5.
2. Antonia SJ, Borghaei H, Ramalingam SS, Horn L, De Castro Carpeño J, Pluzanski A, *et al*. Four-year survival with nivolumab in patients with previously treated advanced non-small-cell lung cancer: A pooled analysis. Lancet Oncol 2019;20:1395-408.
3. Friedlaender A, Kim C, Addeo A. Rethinking the optimal duration of immune checkpoint inhibitors in non-small cell lung cancer throughout the COVID-19 pandemic. Front Oncol 2020;10:862.
4. Reck M, Rodríguez-Abreu D, Robinson AG, Hui R, Csőszi T, Fülöp A, *et al*. OA14.01 KEYNOTE-024 3-year survival update: Pembrolizumab vs platinum-based chemotherapy for advanced non-small-cell lung cancer. J Thorac Oncol 2019;14:S243.
5. Herbst RS, Garon EB, Kim DW, Cho BC, Pérez-Gracia JL, Han J-Y, *et al*. Long-term outcomes and retreatment among patients with previously treated, programmed death-ligand 1-positive, advanced non-small-cell lung cancer in the KEYNOTE-010 study. J Clin Oncol 2020;38:1580-90.
6. Wang X, Schoenhals JE, Li A, Valdecanas DR, Ye H, Zang F, *et al*. Suppression of Type I IFN signaling in tumors mediates resistance to Anti-PD-1 treatment that can be overcome by radiotherapy. Cancer Res 2017;77:839-50.
7. Cushman TR, Gomez D, Kumar R, Likacheva A, Chang JY, Cadena AP, *et al*. Combining radiation plus immunotherapy to improve systemic immune response. J Thorac Dis 2018;10:S468-S479.

Access this article online

Website: www.cancerjournal.net

DOI: 10.4103/jcrt.JCRT_954_20

Quick Response Code:

Cite this article as: Sotelo MJ, Cabezas-Camarero S, Riquelme A, Bueno C. Durable complete response after stereotactic body radiation therapy in immunotherapy-resistant non-small cell lung cancer. J Can Res Ther 2022;18:868-9.