Dermatology Practical & Conceptual

Real-Life Safety and Effectiveness of Dupilumab in Patients with Concomitant Malignancies: a Case Series

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Introduction

Dupilumab is a human monoclonal antibody which targets the alpha subunit of the interleukin (IL)-4-Receptor, blocking the signaling of both IL-13 and IL-4 and it is the first biologic drug approved for moderate-to-severe atopic dermatitis [1]. According to a systematic review from Braddock et al [2], data on the role of IL-13 and IL-4 in carcinogenesis are conflicting and there is paucity of evidences regarding the use of dupilumab in patients with concomitant malignancies [3].

We report our experience with 10 patients with previous history of cancer and 4 patients who developed a malignancy during treatment with dupilumab, from January 2019 to June 2022.

Case Presentation

Ten patients started dupilumab after receiving a diagnosis of cancer (Table 1):

- Three patients had previously undergone partial thyroidectomy for papillary thyroid carcinoma (4, 6 and 29 years before receiving dupilumab, respectively).
- Two women had a history of ductal breast cancer: one received chemotherapy 12 years before the start of dupilumab, while the second patient underwent surgery 6 years before.
- Two patients had a diagnosis of prostatic cancer: one started dupilumab 4.5 years after the prostatectomy, while

Table 1. Demographic data and characteristics of the malignancies of patients with history of cancer before the start of dupilumab and patients who developed cancer after the start of dupilumab

N°	Sex	Age	Type of Cancer	Cancer Treatment	Date of Cancer Diagnosis	Date of Dupilumab Treatment Start	Time Between Cancer Diagnosis and Dupilumab (Months)	EASI at Baseline	P-NRS at Baseline	Date of Last Observation	EASI at Last Observation	P-NRS at Last Observation
1	M	26	Papillary Thyroid Carcinoma	Surgery	Jan-16	Jul-20	55	28	9	Feb-22	3,5	5
2	F	32	Papillary Thyroid Carcinoma	Surgery	Jan-16	Jan-22	73	24	9	May-22	0	0
3	F	88	Papillary Thyroid Carcinoma	Surgery	Jan-93	Jun-22	358	28,2	10	n/a	n/a	n/a
4	F	46	Ductal Breast Cancer	Chemotherapy	Jan-08	Feb-20	147	26	10	Jun-22	2	3
5	F	66	Ductal Breast Cancer	Surgery	Jan-16	Mar-22	75	24	10	Jul-22	3	9
6	M	74	Prostatic Adenocarcinoma	Surgery	Dec-16	May-21	54	24	10	Jul-22	0	3
7	M	59	Prostatic Adenocarcinoma	Radiotherapy + Hormonal therapy	May-21	May-22	12	24	8	n/a	n/a	n/a
8	M	70	Lung Adenocarcinoma	Surgery	Jan-16	Jan-20	49	24	9	Apr-22	2	4
9	M	92	Squamous cell carcinoma	Surgery	Jun-13	Jun-20	85	26	9	May-22	3	3
10	F	74	Ovarian Cancer	Chemotherapy	Jan-09	Jun-20	139	26	9	May-22	2	7
N°	**Sex**	**Age**	**Type of Cancer**	**Cancer Treatment**	**Date of Dupilumab Treatment Start**	**Date of Dupilumab Treatment Start**	**Time Between Cancer Diagnosis and Dupilumab (Months)**	**EASI at Baseline**	**P-NRS at Baseline**	**Date of Last Observation**	**EASI at Last Observation**	**P-NRS at Last Observation**
1	M	74	Melanoma	Surgery	May-21	Dec-21	7	24	10	Jul-22	0	3
2	M	75	Melanoma	Surgery	Jun-19	Jan-20	7	27	9	Apr-22	0	0
3	M	61	Prostatic Adenocarcinoma	Surgery + Hormonal Therapy	May-21	May-21	2	25	9	Jul-22	1	1
4	M	71	Squamous Cell Carcinoma	Surgery	Jun-19	Jan-20	7	26	10	May-22	0	0

EASI = Eczema Area and Severity Index; P-NRS = Pruritus-Numerical Rating Scale.

the other received dupilumab one year after radiotherapy and hormonal therapy.

- One woman had history of ovarian cancer, treated with chemotherapy 11 years before starting dupilumab.
- One patient underwent pulmonary lobectomy for a lung adenocarcinoma 4 years before dupilumab.
- One patient was diagnosed with multiple squamous cell carcinomas (SCCs).

All patients are currently undergoing a specific oncologic follow-up, according to guidelines from the Italian Association of Medical Oncology. Overall, 4 patients started dupilumab less than 5 years after the cancer diagnosis. One patient received dupilumab one year after completing radiotherapy. Six patients have already completed one year of treatment with dupilumab, without any cancer progressions or recurrences.

Among our patients treated with dupilumab, 4 developed malignancies during therapy (Table 1). After 7 months of therapy, two patients were diagnosed with a melanoma in situ and a pT1a melanoma respectively, both completely excised. Another patient was diagnosed with a SCC. Another patient was diagnosed with prostatic carcinoma two months after starting dupilumab; he is currently receiving hormonal therapy after prostatectomy. All of these patients never interrupted dupilumab and they are still on treatment, completing one year of follow-up.

Conclusions

The role of IL-4 and IL-13 in carcinogenesis is still unclear. A systematic review did not show a higher risk of malignancy when specifically targeting the IL-13 and IL-4 pathway [2]. In literature, several case series on patients with concomitant malignancies have been described, showing no elevated risk of cancer recurrences or relapses [4-5]. In our experience, three of the four cancers diagnosed during treatment with dupilumab were cutaneous malignancies. The fourth patient was diagnosed with a prostatic adenocarcinoma two months after the start of dupilumab: considering his age (61 years old) and the short timespan between the diagnosis and the start of the treatment, no causal effect could be observed. Finally, none of our patients experienced cancer progressions or relapses during treatment.

We have described a case series of patients with concomitant malignancies treated with dupilumab. Larger prospective studies with longer follow-up are needed to further assess this topic. Larger prospective studies with longer follow-up are needed to further assess this topic.

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