



Eosinophilic Fasciitis Triggered by Nivolumab: A Remarkable Efficacy of the mTOR Inhibitor Sirolimus

Erwan Le Tallec, Alain Lescoat, Alice Ballerie, Berengere Cador, Hervé Lena,
Charles Ricordel, Damien Sene, Celeste Lebbe, Patrick Jégo, Nicolas
Belhomme

► To cite this version:

Erwan Le Tallec, Alain Lescoat, Alice Ballerie, Berengere Cador, Hervé Lena, et al.. Eosinophilic Fasciitis Triggered by Nivolumab: A Remarkable Efficacy of the mTOR Inhibitor Sirolimus. *Journal of Thoracic Oncology*, 2020, 15 (2), pp.E29-E30. 10.1016/j.jtho.2019.09.011 . hal-02470585

HAL Id: hal-02470585

<https://univ-rennes.hal.science/hal-02470585>

Submitted on 24 Mar 2020

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Eosinophilic fasciitis triggered by nivolumab: a remarkable efficacy of the mTOR inhibitor Sirolimus

*E. Le Tallec MD, A. Lescoat MD, A. Ballerie MD, B. Cador-Rousseau MD, H. Lena MD,
C. Ricordel MD, D. Sene MD-PhD, C. Lebbe MD-PhD, P. Jego MD-PhD, N. Belhomme MD**

Corresponding Author: Nicolas Belhomme, MD, Service de Médecine Interne, CHU de Rennes, 2 rue Henri-Le-Guilloux, 35033 Rennes, France. Email : nicolas.belhomme@chu-rennes.fr

Erwan Le Tallec, MD

Internal Medicine Department
Hôpital Sud, Rennes, France
Rennes 1 University, Rennes, France

Tel : +33 2 99 28 79 36

Mail : erwan.le.tallec@chu-rennes.fr

Alain Lescoat, MD

Internal Medicine Department,
Hôpital Sud, Rennes, France
UMR Inserm U1085, Institut de recherche en santé, environnement et travail (IRSET)
Rennes 1 University, Rennes, France

Mail : alain.lescoat@chu-rennes.fr

Alice Ballerie, MD

Internal Medicine Department,
Hôpital Sud, Rennes, France
Rennes 1 University, Rennes, France

Mail : alice.ballerie@chu-rennes.fr

Bérengère Cador, MD

Internal Medicine Department,
Hôpital Sud, Rennes, France
Rennes 1 University, Rennes, France

Mail : berangere.cador@chu-rennes.fr

Hervé Lena, MD

Department of Respiratory Medicine
Pontchaillou Hospital, Rennes, France
Chemistry, Oncogenesis, and Stress Signaling INSERM U1242

Rennes 1 University
Centre Eugène Marquis, Rennes, France

Mail : herve.lena@chu-rennes.fr

Charles Ricordel, MD
Department of Respiratory Medicine
Pontchaillou Hospital, Rennes, France
Chemistry, Oncogenesis, and Stress Signaling INSERM U1242
Rennes 1 University
Centre Eugène Marquis, Rennes, France

Mail : charles.ricordel@chu-rennes.fr

Sène Damien, MD, PhD
Internal Medicine Department
Lariboisière Hospital, Paris, France.
INSERM UMR
Paris Diderot University, Paris, France

Mail : damien.sene@aphp.fr

Céleste Lebbe, MD, PhD
Dermatology Department, AP-HP, Saint Louis Hospital, Paris, France
Paris University, INSERM U976

Mail : celeste.lebbe@aphp.fr

Patrick Jego, MD, PhD
Department of Internal Medicine
Hôpital Sud, Rennes, France
UMR Inserm U1085, Institut de recherche en santé, environnement et travail (IRSET),
Rennes 1 University, Rennes, France

Mail : patrick.jego@chu-rennes.fr

* **Nicolas Belhomme, MD (corresponding author)**
Department of Internal Medicine
Hôpital Sud, Rennes, France
Rennes 1 University, Rennes, France

Mail : nicolas.belhomme@chu-rennes.fr

Disclosure statement: The authors declare no conflict of interest

Fundings: none.

This manuscript has not been published elsewhere, and is not currently under review in any other peer-reviewed media.

Erwan Le Tallec takes full responsibility for the content of this manuscript, including validity of data and statistical analysis.

Eosinophilic fasciitis triggered by nivolumab: a remarkable efficacy of the mTOR inhibitor Sirolimus

*E. Le Tallec MD, A. Lescoat MD, A. Ballerie MD, B. Cador-Rousseau MD, H. Lena MD,
C. Ricordel MD, D. Sene MD-PhD, C. Lebbe MD-PhD, P. Jego MD-PhD, N. Belhomme MD*

To the Editor:

We previously reported in the JTO the case of a 56-year-old woman with a metastatic pulmonary adenocarcinoma in complete remission under Nivolumab, who developed a typical eosinophilic fasciitis with a concomitant immune cholangitis, both found considered as adverse events of the immune checkpoint inhibitor (ICI)¹.

Nonetheless, no improvement was observed after ICI discontinuation, and a dramatic worsening was noticed despite a combination of corticosteroids and methotrexate therapy, as the fasciitis extended to the whole body-involving the face- and causing a diffuse and painful stiffness.

Because the immune disease was still worsening, 9 months after Nivolumab withdrawal, and considering the absence of malignancy relapse on CT scan reassessment, methotrexate was switched for Sirolimus, a m-TOR inhibitor which had also shown efficacy in a case of idiopathic eosinophilic fasciitis².

A remarkable improvement was rapidly obtained, and after 6 months of therapy, the patient regained a close to normal range of motion of her large joints, with a clear improvement in skin thickening involving the fingers and the dorsum of the hands, which were previously stuck in flexion contracture, as illustrated in Figure 1. So far, the cancer is still in remission, despite the absence of antineoplastic agents.

Data regarding the management of steroid refractory idiopathic eosinophilic fasciitis are scarce. Concerning the specific situation of ICI-immune-mediated fasciitis, no practical guidelines are available, and especially in the case of fasciitis that are refractory to ICI cessation and classical corticosteroids therapy. Although considered as a rare affection, ICI-immune mediated fasciitis should deserve special attention to explore new therapeutic approaches, as the treatments that have

proven efficient in other rheumatic toxicities, e.g. in arthritis, might not be broadened to this specific ICI adverse event even if their pathophysiology share some similarities^{3,4}.

Hence, this observation suggests a noticeable efficacy of Sirolimus in Nivolumab related fasciitis, raising the question that the mTOR pathway could be a promising target in the field of ICI-immune-mediated diseases.

Captions

Figure 1. Clinical evolution after 6 months of Sirolimus therapy:

A (upper left picture), B (lower left picture): Skin thickening with contracture of the fingers

C (upper right picture), D (lower right picture): After 6 months of Sirolimus, marked improved mobility of the joints

References:

1. Le Tallec E, Ricordel C, Triquet L, et al. An Original Case of an Association of Eosinophilic Fasciitis with Cholangitis Induced by Nivolumab. *J Thorac Oncol*. 2019;14:e13-e15.
2. Oza VS, Walsh R, North J, Berger TG, Murase JE. Treatment of Eosinophilic Fasciitis with Sirolimus. *JAMA Dermatol*. 2016;152:488-90
3. Thompson JA, Schneider BJ, Brahmer J, et al. Management of Immunotherapy-Related Toxicities, Version 1.2019. *J Natl Compr Canc Netw*. 2019;17:255-289.
4. Baroudjian B, Arangalage D, Cuzzubbo S, et al. Management of immune-related adverse events resulting from immune checkpoint blockade. *Expert Rev Anticancer Ther*. 2019;19:209-222