P503

The prognostic role of [18F]FDG PET/CT in patients with advanced cutaneous squamous cell carcinoma submitted to cemiplimab immunotherapy: a single-center retrospective study

Ilaria Proietti [1],Luca Filippi[2], Vincenzo Petrozza[3], Concetta Potenza[1], Oreste Bagni [4], Orazio Schillaci [5]

[1] Dermatology Unit "Daniele Innocenzi", "A. Fiorini" Hospital, Terracina, Italy.ilaria.proietti@uniroma1.it,+393334684342
[2] Nuclear Medicine Unit, Department of Oncohaematology, Fondazione PTV Policlinico Tor Vergata University Hospital, Rome, Italy
[3] Department of Medico-Surgical Sciences and Biotechnologies, Pathology Unit, ICOT Hospital, University of Rome "La Sapienza", Italy.
[4] Nuclear Medicine Unit, Santa Maria Goretti Hospital, Latina, Italy.
[5] Department of Biomedicine and Prevention, University Tor Vergata, Rome, Italy

Introduction

Advanced cutaneous squamous cell carcinoma cSCC, although rare and affecting only a minority of patients (i.e. 5%), is difficult to treat and often presents dismal prognosis.[1] Cemiplimab, a monoclonal antibody targeting programmed cell death protein-1 (PD-1) showed 40-50% objective response of cSCC patients treated with cemiplimab and immune-related adverse events (irAEs) have been reported, with grade 3 or higher adverse events occurring in about 18%. 5,6 In this scenario, there is an unmet need for molecular and imaging biomarkers suitable for patients' selection in order to promptly identity subjects who can benefit of this therapy. Indeed, no validated parameters are currently available to effectively predict patients' individual sensitivity to immunotherapy, although some interesting approaches are under investigations.[2]Positron emission tomography (PET/CT) with 2-deoxy-2[18F]fluoro-D-glucose ([18F]FDG) is a well-established imaging modality for cancer staging and response assessment, and has been also employed with promising results in the clinical field of immunotherapy.[3] Notably, PET/CT can provide quantitative parameters, such as metabolic tumor volume (MTV) and total lesion glycolysis (TLG), that reflect whole body tumor load and have been gaining an ever-increasing relevance to build predictive models in oncology.[4] In addition, recently published data have indicated that metabolic response to immunotherapy, assessed at a median 3 months after the start of treatment,present a prognostic impact on patients' survival. [4]

Study objective

Our aim was to investigate whether baseline clinical and PET-derived parameters, as well as 12-week metabolic response, have a prognostic role in cSCC patients submitted to cemiplimab immunotherapy.

Methods: Clinical records of 25 cSCC patients receiving cemiplimab, submitted to [18F]FDG PET/CT at baseline and after approximately 12 weeks, were retrospectively reviewed. The Kaplan-Meier (KM) method was applied to analyze differences in event-free survival (EFS) and Cox regression analysis was employed to identify prognostic factors.

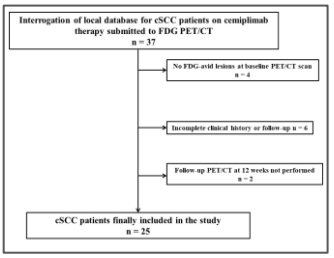
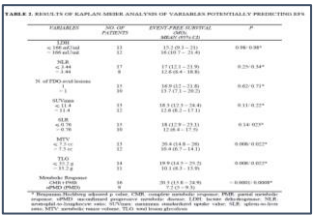


Figure 1. Diagnostic flow-chart of patient selection.

Results: at the 12-week PET/CT evaluation, 16 patients (64%) were classified as responders (complete or partial response) and 9 (36%) as non-responders ("unconfirmed progressive disease") according to immune PET Response Criteria in Solid Tumors (iPERCIST). By KM analysis, baseline metabolic tumor volume (MTV) and total lesion glycolysis (TLG) significantly correlated with EFS ($p < 0.05$). Furthermore, KM analysis showed that lack of metabolic response at 12 weeks was associated with meaningfully shorter EFS (7.2 ± 1 months in non-responders vs. 20.3 ± 2.3 months in responders). In Cox multivariate analysis, metabolic response at 12 weeks remained the only predictor of EFS ($p < 0.05$).



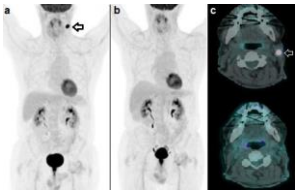


Figure 2. A 62-year-old man affected by nodular cSCC in the left laterocervical region, showing ncreased [18F]FDG incorporation on baseline PET/CT scan (a, Maximum Intensity Projection/MIP,arrow, MTV = 1.1 cc, TLG = 15.5 g). A complete metabolic response was evident on follow-up PET/CT carried out 12 weeks after cemiplimab start (b, MIP). Complete response is also well depicted by the fused axial PET/CT images (c) at baseline (upper row, arrow) and at 12 weeks (lower row). The patient is still alive, under follow-up, with an event-free survival of 29 months.

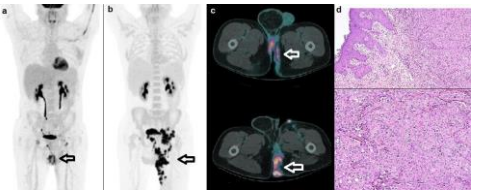


Figure 2. A 62-year-old man affected by nodular cSCC in the left laterocervical region, showing increased [18F]FDG incorporation on baseline PET/CT scan (a, Maximum Intensity Projection/MIP,arrow, MTV = 1.1 cc, TLG = 15.5 g). A complete metabolic response was evident on follow-up PET/CT carried out 12 weeks after cemiplimab start (b, MIP). Complete response is also well depicted by the fused axial PET/CT images (c) at baseline (upper row, arrow) and at 12 weeks (lower row). The patient is still alive, under follow-up, with an event-free survival of 29 months

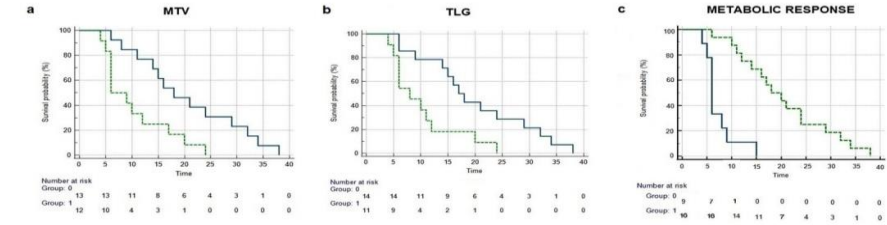


Figure 4. Kaplan-Meier analysis depicts event-free survival (months) as a function of MTV (a),TLG (b) and metabolic response (c). Graph a shows that patients with MTV > 7.5 cc (group 1, green/dotted line) had significantly shorter EFS than those with MTV ⩽ 7.5 cc (group 0, blue/solid line). Graph b demonstrates that subjects with TLG > 35.2 g (group 1, green/dotted line) had shorter EFS than those with TLG ⩽ 35.2 g (group 0, blue/solid line). Graph c shows that patients classified as non-responders at 12-week PET/CT evaluation (group 0, blue/solid line) had meaningfully shorter EFS than responders (group 1, green/dotted line).

Conclusions

Our results point out the predictive role of [18F]FDG PET in cSCC patients undergoing cemiplimab immunotherapy. In particular, high baseline tumor load (MTV and TLG) and the lack of metabolic response at 12 weeks may help identify subjects who are less likely to benefit of cemiplimab.Further studies, ideally prospective and including larger patient cohorts, are needed to confirm our preliminary findings and fully assess the potential of PET-imaging in this specific setting.

References

1. Mallardo D, Simeone E, Festino L, et al. IL-6 as new prognostic factor in patients with advanced cutaneous squamous cell carcinoma treated with cemiplimab. J Transl Med 2023;21(1):140; doi: 10.1186/s12967-023-03971-5.
2. Blach J, Wojas-Krawczyk K, Nicoś M, et al. Failure of Immunotherapy—The Molecular and Immunological Origin of Immunotherapy Resistance in Lung Cancer. IJMS 2021;22(16):9030
3. Wu X, Huang Y, Zhao Q, et al. PD-L1 expression correlation with metabolic parameters of FDG PET/CT and clinicopathological characteristics in non-small cell lung cancer. EJNMMI Res 2020;10(1):51
4. Liao X, Liu M, Li S, et al. The value on SUV-derived parameters assessed on 18F-FDG PET/CT for predicting mediastinal lymph node metastasis in non-small cell lung cancer. BMC Med Imaging 2023;23(1):49; doi: 10.1186/s12880-023-01004-7.