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Regulation of immune system gene expression in cSCC treated with immunotherapy: real life data of responders/non responders patients.

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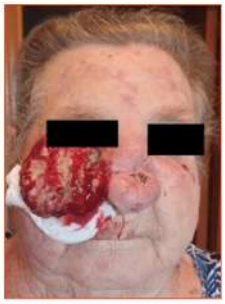
Background

Cemiplimab significantly modified outcomes of patients with Metastatic (McSCC) or Locally Advanced cutaneous Squamous Cell Carcinoma (LAcSCC)no longer amenable to radiotherapy or curative surgery. Real-life data confirms the good results demonstrated in the pivotal Empower cSCC1 clinical trial. However 1/3 of patients did not respond to treatment and progressed rapidly.

Methods

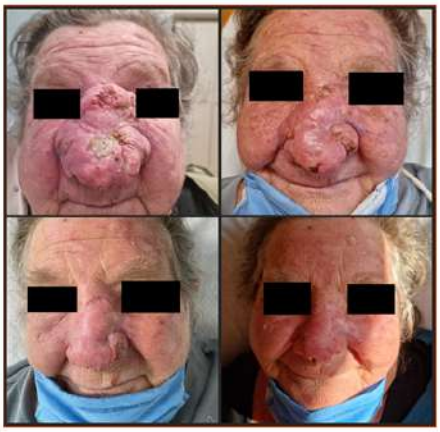
Our retrospective analysis enrolled 81 patients >18yr with LAcSCC or McSCC, who received at least one cycle with Cemiplimab (Table). To understand the possible link between treatment response and an alteration in the expression of genes regulating immune system, we selected 20 pre-treatment tissue samples, of which 9 responders, 11 non-responders and 3 healthy controls. The paraffin-coated tissues were processed for gene expression profiling using Nanostring Technologies, measuring 770 cancer and immune system-related genes to identify specific genetic signatures associated with treatment response or resistance.

Variables	Enrolled patients N = 81
Male sex	58 (71.6%)
Median age at diagnosis	82 (IQR 48-97)
Primary site	
Head/neck	62 (76.5%)
Trunk	4 (4.9%)
Upper limbs	4 (4.9%)
Lower limbs	11 (13.6%)
N. of previous surgery	
No previous surgery	37 (45.7)
1	21 (25.9)
≥2	23 (28.4)
Previous RT	27 (33.3)
T4 status	50 (61.7)
N+ status	30 (37)
M1 status	9 (11.1)



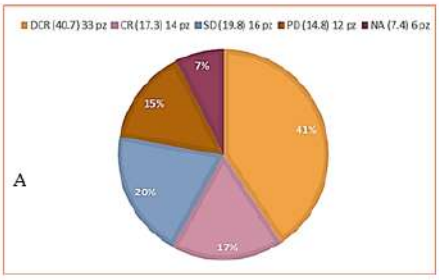
Case presentation
- Female patient
- 73 years old
- two cSCC sites, nose and cheek
- Bleeding lesion at baseline.

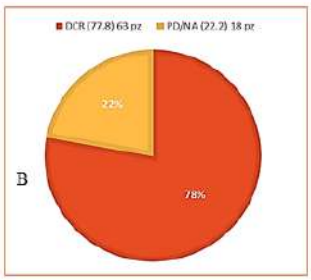
Cemiplimab treatment
- Cheek lesion responded rapidly
- Nose lesion was in progression disease, therefore treated with radiotherapy
- Cemiplimab restarted obtaining partial response in the nose lesion.



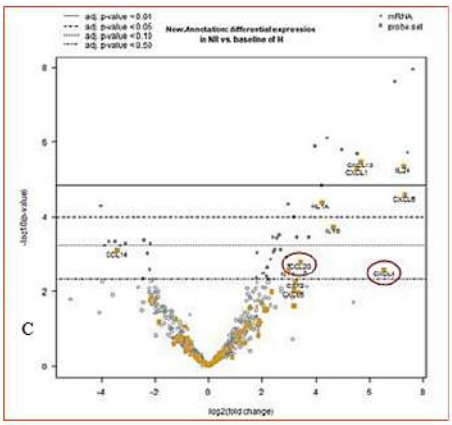
Results

Data cut-off for analysis was 31/12/2022, 41 patients progressed or died, 33 were still on treatment. Progression free survival (PFS) at 24 months was 42%. Overall response rate (ORR) was 58% (figures A-B), of which 14 complete response (CR). Median duration of response (DOR) was not reached. Median time to response was 3 months. Disease control rate (DCR) was 77.8%. Overall survival (OS) at 24 months was 61%.





Analysis of 770 mRNA levels identified a different immune system activation status between responders and non-responders/healty control and overexpression of chemokines CCL20 and CXCL8 in non-responder patients promoting invasion, migration, epithelial–mesenchymal transition (EMT), recruitment and migration of Tregs (Figure C).



Volcano plot showing top up-regulated genes encoding for cytokines and chemokines in non-responders samples compared to healthy donors.

Conclusions

Our Real Life results confirm efficacy and good safety profile of Cemiplimab demonstrated by the pivotal trial Empower CSCC 1. The peculiar gene expression highlighted in non-responders patients could explain the heterogeneity in treatment response and lay the foundation for future analysis to overcome primary resistance to immunotherapy.