EA DV CONGRESS
BERLIN 11-14 OCTOBER 2023
EUROPEAN ACADEMY OF DERMATOLOGY AND VENEREOLOGY

Abstract N°: 6544

Topical chlormethine induces tumor micro-environment shift in early-stage mycosis fungoides by interstitial fluid immunophenotyping.

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Introduction & Objectives:

Early stages of Mycosis fungoides (MF) can be treated effectively with topical chlormethine. However, insight into changes in the tumor-micro environment (TME) during treatment and how these changes contribute to therapeutic success is limited. In this study we aimed to characterize TME of MF on a cellular level by suction blister fluid analysis.

Materials & Methods:

In this exploratory, open-label, deep phenotyping trial a total of 21 early-stage (IA – IIA) MF patients were treated with chlormethine gel 160µg/g QD for 16 weeks. Suction blister exudates were collected pre-treatment from lesional (LS) and non-lesional skin (NL) and after 16 weeks of treatment from LS and analyzed with flow cytometry. For all statistical analyses a Wilcoxon signed-rank test was used.**

Results:

In blister exudate pre-treatment, statistically significant more absolute cells were observed in LS compared to NL ($p<0.0001$). Exudates from LS contained statistically significant more CD3+ cells ($p<0.001$), CD3+4+ T-lymphocytes ($p<0.0001$), activated CD4+HLA-DR+ effector T-lymphocytes ($p=0.0001$), CD3+8+ T-lymphocytes ($p<0.0001$), activated CD8+HLA-DR+ cytotoxic T-lymphocytes ($p<0.001$), CD14-CD16- dendritic cells ($p<0.01$) and CD68+ macrophages ($p<0.01$). After 16W chlormethine gel treatment significantly less aberrant T-cells ($p<0.05$), CD3+8+ T-lymphocytes ($p<0.05$), activated CD8+HLA-DR+ cytotoxic T-lymphocytes ($p<0.01$) and Tregs ($p<0.05$) were observed compared to LS baseline.

Conclusion:

We show for the first time the feasibility of suction blister fluid analysis to investigate TME in MF patients. These results suggest that CD8+HLA-DR+ cytotoxic and regulatory T-lymphocytes have a prominent role in disease improvement with chlormethine therapy in MF.