Prospective measurements of sIL-2R concentrations in a cohort of pulmonary sarcoidosis

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INTRODUCTION

Sarcoidosis

Sarcoidosis is an immune mediated disease with unknown cause characterized by the formation of non-caseating granuloma and the influx of T-cells at the sites of active disease (fig 1). Clinical presentation varies prominently between patients with sarcoidosis and since cause is unknown therapy is aimed at suppressing the activity of the immune system.

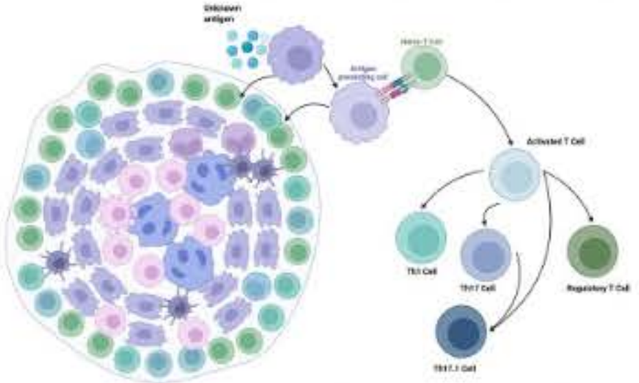


Figure 1. Graphical representation of a non-caseating sarcoid granuloma including the T-cell activation cascade leading to sIL-2R secretion

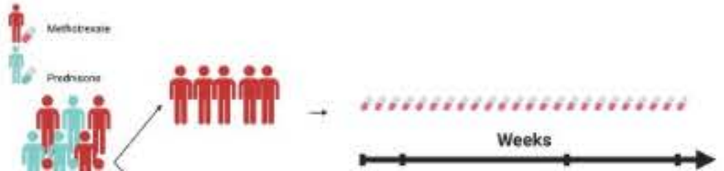
sIL-2R

Soluble Interleukin-2 receptor (sIL-2R) is secreted mainly by activated T-cells and widely used as a biomarker for disease activity in patients with sarcoidosis. Therefore peripheral sIL-2R levels are a surrogate marker for T-cell activity and effectiveness of immunosuppressive therapy.

METHODS

Study cohort

Patients (n= 137) were randomized to be treated with either prednisone or methotrexate (MTX), study visits were scheduled at 0, 4, 16 and 24 weeks after initiation of treatment. At each study visit there was blood withdrawal and lung function testing (fig 2.)



Treatment schedule

After randomisation prednisone or MTX treatment was started according to a standardized schedule (fig 3).

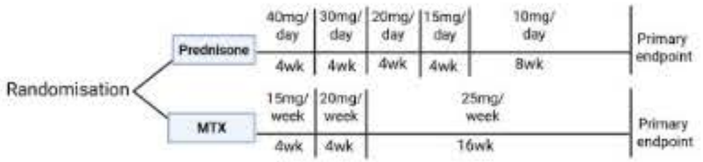


Figure 3. Standardized treatment schedule PREDMETH trial

RESULTS

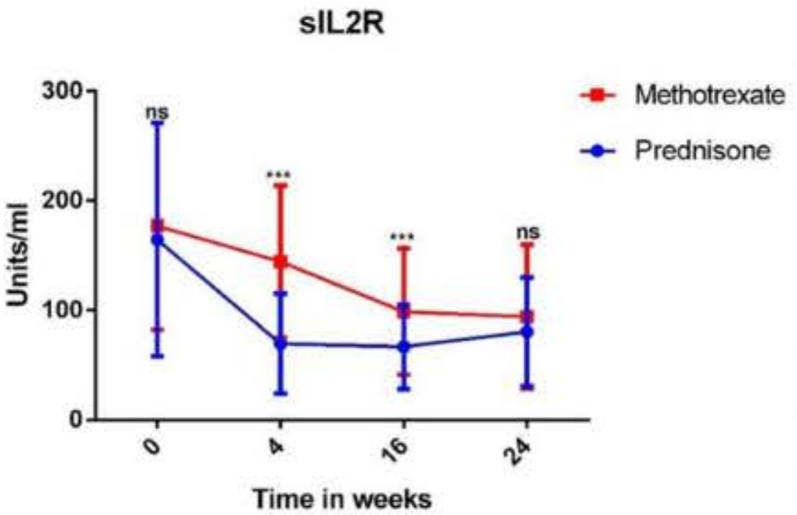


*Figure 4. Mean concentration of sIL-2R over time in MTX (red) and prednisone (blue) treated groups, error bars (SD) *** p<0,001*

In the MTX treated group the sIL-2R levels decreased gradually over the course of 24 weeks. While in the prednisone group we observe a substantial decrease in sIL-2R levels after 4 weeks which thereafter remained stable or slightly increased between 16 and 24 weeks.

At baseline and after 24 weeks of treatment there is no significant difference in the sIL-2R levels between both treatment groups. After 4 and 16 weeks sIL-2R levels were significantly lower in the prednisone group compared to the MTX group (fig. 4).

CONCLUSION

The immunosuppressive effect, depicted as a decrease in sIL-2R levels, is more pronounced during the first 4 weeks of prednisone treatment compared to the gradual change in sIL-2R levels during MTX treatment.

This effect is in line with the gradually increasing dose of MTX and the tapering schedule of prednisone.

CONTACT

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Background

Soluble Interleukin-2 receptor (sIL2R) is mainly secreted by activated T-cells and widely used as a biomarker for disease activity in sarcoidosis. Prospective studies on clinical value of sIL2R levels during immunosuppressive treatment are lacking. We studied sIL2R levels during treatment with prednisone or methotrexate (MTX) in treatment naïve patients with pulmonary sarcoidosis, exploratory endpoint of the PREDMETH trial (NCT04314193).

Methods

Serum concentrations of sIL2R were quantitatively determined, at baseline and at 4, 16 and 24 weeks, with enzyme immunoassays. Mann-Whitney U tests were used to test for differences between treatment groups.

Results

After 24 weeks of treatment sIL2R levels decreased significantly in both groups. After 4 and 16 weeks sIl2R levels were significantly lower in the prednisone group compared to the MTX group (fig. 1).

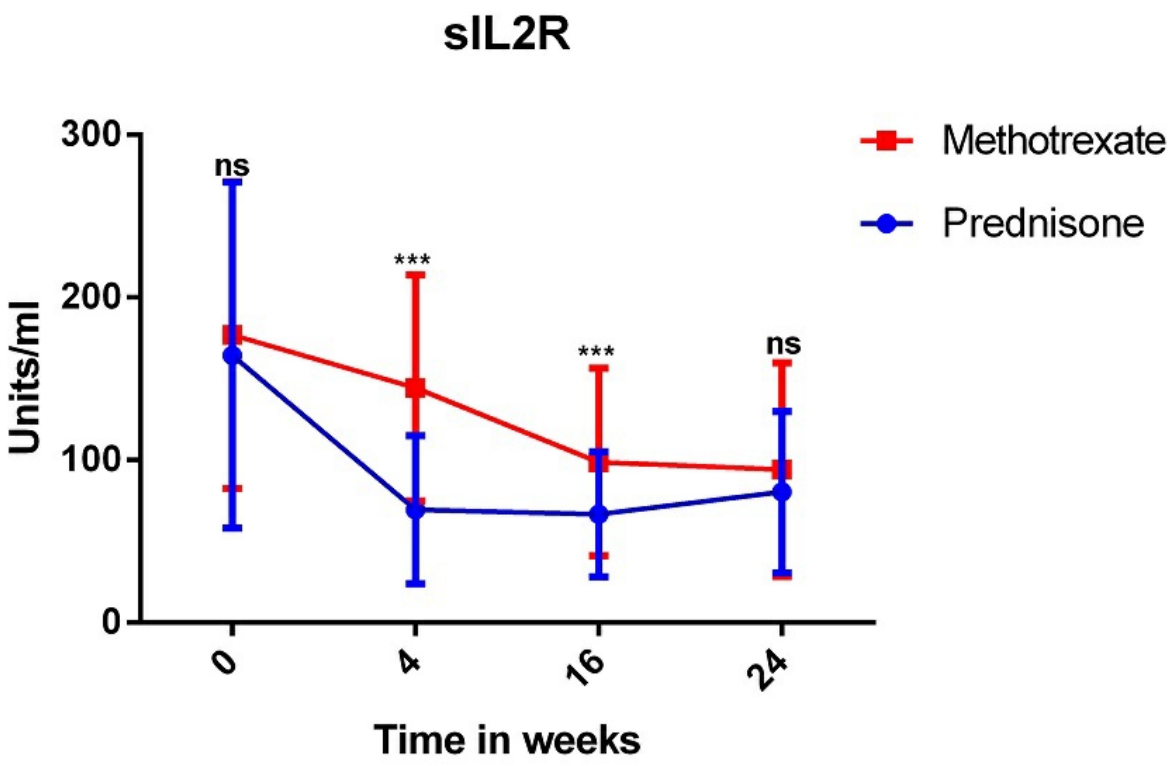

Figure 1 Mean concentration of sIL2R over time in MTX (red) and prednisone (blue) treated groups.

*** p<0.001

Conclusion

The immunosuppressive effect, measured by decrease in sIL2R levels, sets in much faster during prednisone treatment compared to MTX. While in the MTX treated group sIL2R levels steadily decreased over 24 weeks, in the prednisone group an increasing trend was observed after 16 weeks of treatment, probably due to the tapering regime. Our data suggests that sIL2R can be used as biomarker for monitoring of inflammation in patients with pulmonary sarcoidosis.