PSOPET2: A randomised, double-blind, placebo-controlled, trial to evaluate the efficacy of brodalumab monotherapy on vascular and systemic inflammation by 18F-FDG-PET/CT in subjects with moderate-to-severe plaque-type psoriasis who are candidates for systemic therapy.

Introduction

Psoriasis is a chronic inflammatory skin disease with a prevalence of 4-6% in the Danish population and 2-3% worldwide. Approximately 30% of patients with psoriasis also suffer from psoriatic arthritis.The onset of psoriasis often occurs before the age of 40, and several population-based studies indicate an increased risk of developing psoriasis in patients with a family history of the disease, suggestive of a genetic predisposition.

Recent research has illustrated that psoriasis is not only a chronic inflammatory skin disease but also a chronic systemic inflammatory disease associated with an increased risk of cardiovascular comorbidity. Various meta-analyses and systematic reviews have demonstrated that the cardiovascular risk increases with earlier onset and more severe psoriasis.

AIM

The hypothesis of this study is that brodalumab can reduce vascular inflammation in the aorta in patients with moderate-to-severe psoriasis. The primary aim of this study is to investigate the change in vascular inflammation using the maximum target-to-background ratio (TBRmax) of the entire aorta from baseline to week 16.

The secondary aim of this study is to investigate the changes in TBRmax of the ascending aorta, aortic arch, and descending aorta from baseline to week 16. Thirdly, we examine the association between the change in Psoriasis Area and Severity Index (PASI) and change in TBRmax for the entire aorta and the spleen.

Methods

Trial design and patients

This study was randomized, double-blinded, and placebo-controlled, where patients with moderate-to-severe plaque psoriasis were randomly assigned in two groups, matched by age and sex: an active group receiving brodalumab treatment and a placebo group receiving a placebo.

Brodalumab treatment was administered through subcutaneous injection at a dose of 210 mg at weeks 0, 1, and 2, followed by 210 mg every other week until week 16. Placebo was administered using the same method and intervals as the brodalumab treatment. All patients provided written consent prior to participating in the study. The study included patients aged 40 or older, with moderate-to-severe chronic plaque-type psoriasis confirmed by a dermatologist and a PASI of ≥ 10.

18F-fluorodeoxyglucose (FDG)positron emission tomography (PET) computed tomography (CT) was performed at baseline and after 16 weeks of brodalumab or placebo treatment.

Results

From December 2018 to September 2022, a total of 37 patients were enrolled in the study. Nine patients were excluded because they did not meet the inclusion criteria's or were rescreened. 28 patients fulfilled the inclusion criteria's and were randomly assigned to two groups: one group was allocated to brodalumab and the other group to placebo treatment. In the placebo group, two patients discontinued the intervention, one due to the development of an abdominal haematoma and the other due to hospitalization for pneumonia. No patients discontinued the intervention in the brodalumab group.

Brodalumab was not more effective than placebo in reducing aortic inflammation. No statistically significant difference in the change of TBRmax between the brodalumab and placebo groups was observed.

Brodalumab was not more effective than placebo in reducing inflammation in aortic subsegments. Since no change in TBRmax was observed in the brodalumab and placebo groups, aorta was separated into the ascending aorta, aortic arch, and descending aorta. However, no statistically significant difference between the brodalumab and placebo groups in TBRmax at baseline and after 16 weeks in the different subsegments of the aorta was observed.

Brodalumab was more effective than placebo in reducing PASI.
The reduction in PASI was statistically significantly greater in the brodalumab group compared to the placebo group.

No correlation was observed between PASI and the inflammation in the aorta and spleen.
Since brodalumab reduced PASI, confirming its efficacy in treating the cutaneous manifestation of psoriasis, we then assessed whether the change in PASI was correlated with decreased inflammation in the aorta.
Correlation analysis revealed no significant correlation between the change in PASI and the change in TBRmax in either group. This suggests that clinical changes in the disease do not correlate with inflammation in the aorta.
In the brodalumab group, we found a surprisingly significant correlation between the decrease in PASI and an increase in splenic inflammation. No significant correlation was found in the placebo group.

Conclusion

In conclusion, this study indicates that brodalumab does not reduce vascular inflammation in the entire aorta and in the aortic subsegments more than placebo in patients with moderate-to-severe psoriasis as assessed by FDG-PET/CT. Although no significant correlation was observed between PASI and aortic inflammation in either the brodalumab or placebo groups, an unexpected correlation was found between reduced PASI and increased splenic inflammation in the brodalumab group, but not in the placebo group. Given the small study population, the clinical significance of this correlation remains uncertain and require further investigation. This study is also limited by its short duration of 16 weeks, which may have influenced the findings. Nevertheless, this study confirms that brodalumab treatment significantly reduces PASI compared to placebo.