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Research Article

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Ixekizumab in the Management of Non-Selected Out Patients with Moderate to Severe Psoriasis -New Data and Personal Clinical Experience

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Abstract

Introduction: *Too many patients with moderate to severe psoriasis do not receive adequate treatment. This means a vast undersupply in the treatment of patients with psoriasis. Only biologics fulfill the whole range of the treatment of psoriasis – psoriasis does not affect only skin but the whole organism: It is a systemic disease! Between the biologics are evident differences concerning the effect.*

Discussion: *Based on broad personal experience in the management of patients with moderate to severe psoriasis new data from clinical studies with ixekizumab are examined. This contains new data on long-term-efficacy of ixekizumab, effectiveness in special localizations (scalp psoriasis, nail psoriasis, palmoplantar psoriasis, genital psoriasis) as well as safely data and experience on patients switched to ixekizumab from other biologics. Personal clinical experience is based on >300 non-selected outpatients with moderate to severe psoriasis, >250 patients on biological therapies, > 50 patients with ixekizumab.*

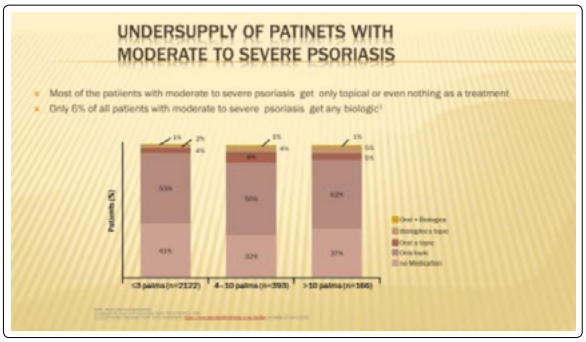
Conclusions: *Focusing on a relevant number of patients switched from secukinumab to ixekizumab due to first or secondary loss of efficacy significant differences between both IL-17A-inhibitors mainly in terms of efficacy and speed of therapeutic response are shown. Finally the correlation between PASI-90-/PASI-100 response and significant changes in DLQI are highlighted.*

Keywords: Psoriasis, Undersupply, Biologics, Ixekizumab

Introduction

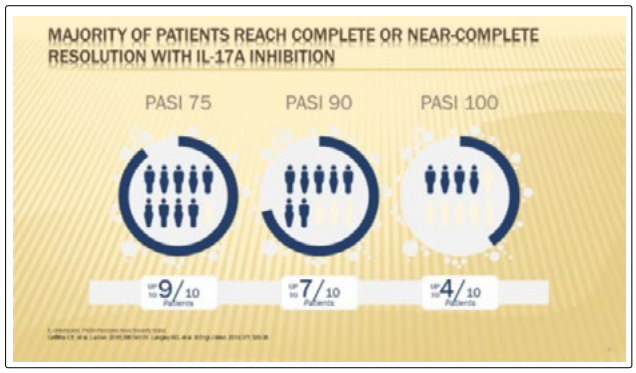
Even among the patients with severe to moderate psoriasis only 7 to 13% due to the expansion receive a systemic therapy [1-2] (Table 1). Only 3-6% of all patients with moderate to severe psoriasis receive a biological therapy.

Table 1



Although the biological therapies are proved for their effectiveness for many years, it is still a giant undersupply. For example the majority of patients reach complete or near-complete resolution with IL-17A inhibition.

Table 2

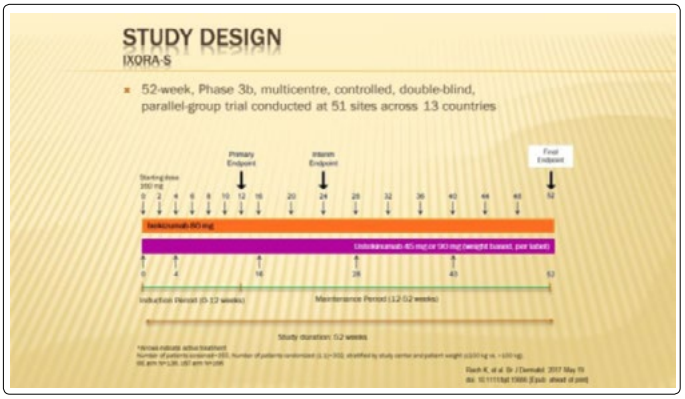


The IL-23/IL-17 axis is a key signaling pathway in psoriasis pathogenesis [1-7].

In previous studies, UST, an IL-12/IL-23 inhibitor, achieved PASI 90 in 40–50% of patients after 12 weeks of treatment [8]. (9-10) IXE, a high-affinity monoclonal antibody that selectively targets IL-17A, has shown greater efficacy than TNF alpha-inhibitor, ETN, in two Phase 3 studies [11-13].

Review and Results

The present study (IXORA-S) aims to compare safety and efficacy of IXE vs. UST over 52 weeks in patients with moderate-to-severe psoriasis (ETN= etanercept; IL=interleukin; IXE=ixekizumab; PASI=Psoriasis Area and Severity Index; TNF=Tissue Necrosis factor; UST= ustekinumab) Here, the safety and efficacy for up to week 24 are presented.



Key Inclusion Criteria

Males and females of 18 years of age or older Diagnosis of chronic plaque psoriasis for ≥6 months PASI score ≥10 Failure, contraindication, or intolerability to at least one systemic therapy (including cyclosporine, methotrexate or phototherapy).

Key Exclusion Criteria

Predominant pattern of pustular, erythrodermic, and/or guttate forms of psoriasis Contraindication for UST. Prior treatment with UST, IXE, or any other IL-17 or IL-12/23 antagonists sample size. Response rates used for sample size calculation were estimated using a Bayesian logistic regression model based on literature data from 19 studies reporting the PASI 90 data for ETN, Infliximab, Adalimumab, UST, Secukinumab, Brodalumab, and using Lilly in-house data for IXE.

A response rate of 70% was assumed for IXE, and of 43% for UST 90 mg for the PASI 90 Using the method for sample size calculation for a Chi-squared test on the 5% level (2-sided) for 2 proportions, a sample size of 150 patients per group will provide a power of at least 95%.

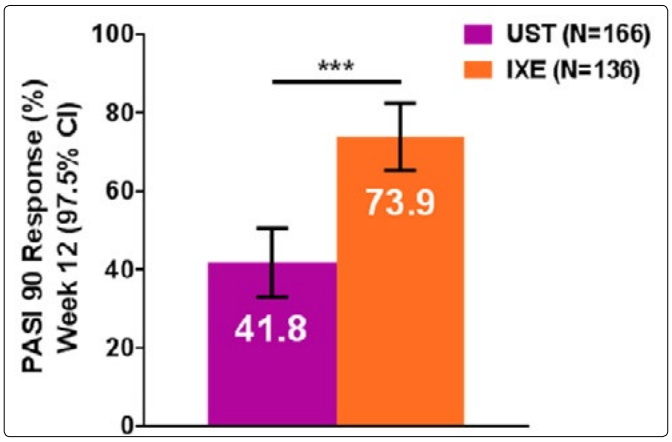
Therefore, the total sample size was 300 patients to be randomized to account for a 25% screen-failure rate, approximately 400 patients were planned to be screened

These are the Results

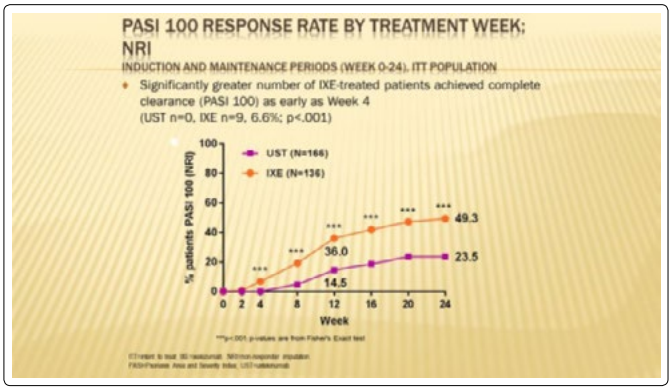
IXE was superior over UST in achieving PASI 90 at Week 12 UST: 41.8% (97.5% CI: 33.0% - 50.6%) IXE: 73.9% (97.5% CI: 65.3%- 82.5%)

Response Difference: 32.1% (97.5% CI: 19.8% - 44.5%; p<.001) ***p<.001

Logistic regression model with terms for treatment group, weight, and geographic region was used to estimate a 97.5% CI for the difference between the proportions between IXE and UST CI=confidence interval, ITT=intent to treat; IXE=ixekizumab; NRI=non-responder imputation, PASI=Psoriasis Area and Severity Index, UST= ustekinumab.



Reich K, et al. Br J Dermatol. 2017 May 19. doi: 10.1111/bjd.15666.



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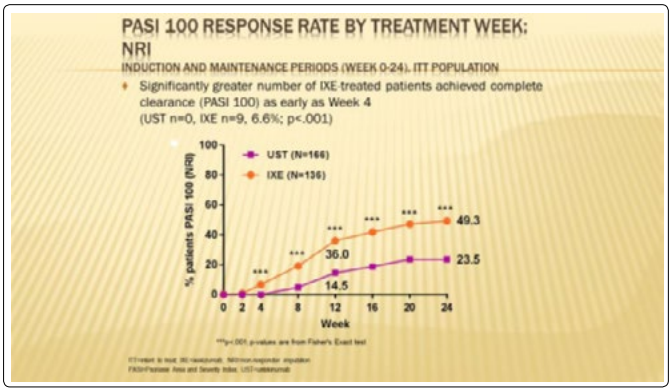

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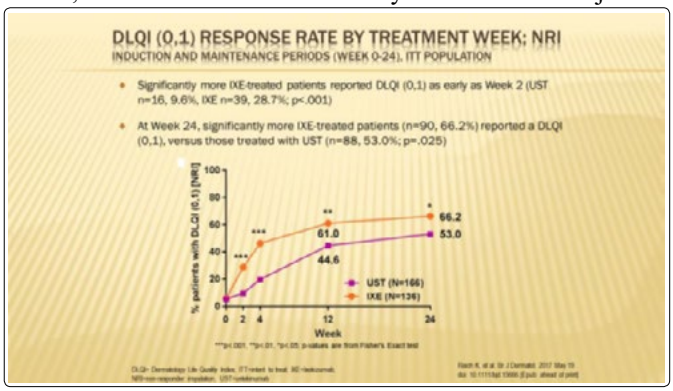

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Discussion and Conclusions

The present study (IXORA-S) demonstrated that IXE has superior efficacy over UST, at Week 12, as assessed by PASI 90, which was maintained through Week 24 results showed that IXE can provide a faster and greater level of improvement than UST in patients with plaque psoriasis.

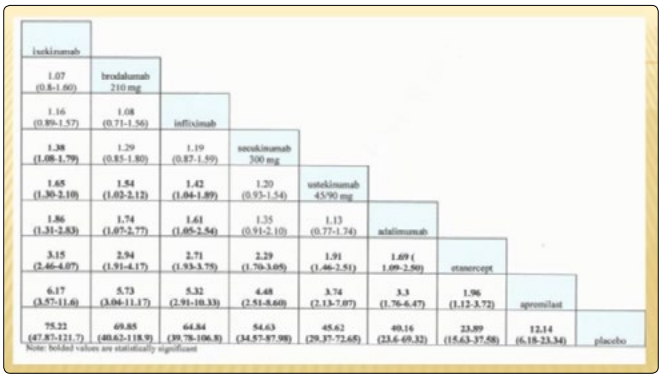
Concurrent DLQI improvement provides evidence that IXE treatment allows patients to reach a better quality of life IXE was well tolerated through 24 weeks of treatment, while maintaining a safety profile consistent with previous reports.

Personal clinical experience

Based on 50 outpatients: of these 15 patients with secondary loss of efficacy on therapy with secukinumab. These 15 patients were switched to ixekizumab of that 13 patients with very fast (median 2 weeks) and very good response. All 13 patients achieved PASI 90 and remain on PASI 90 until now.

This personal experience is confident with newest meta analysis data on the efficacy of the different biologics in the treatment of moderate to severe psoriasis probability to reach PASI 90.

Comparison between different systemic biologics plus apremilast. It shows e.g. that the probability to reach a PASI 90 is about 38 percent higher under therapy with ixekizumab than under the rapier with secukinumab.



(Modified after Loos AM et al., J Am Acad Dermatol. 2018 Feb 10 (Epub ahead of print)

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