Experience with ustekinumab for the treatment of moderate-to-severe cutaneous psoriasis in our clinical practice setting

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Introduction

Ustekinumab is a human monoclonal antibody that reduces the expression of interleukin-12 and interleukin-23, key regulatory cytokines involved in the pathogenic mechanisms of psoriasis. Current data from clinical trials indicate ustekinumab is safe and efficacious. Recently, results from registries and clinical practice series are being reported, confirming results reported in pivotal studies.

Objectives

The aim of the study is to analyse the use of ustekinumab in our routine care setting, evaluating patterns of use, treatment response, drug survival and safety, as well as possible factors involved in ustekinumab clinical response.

Methods

We have evaluated retrospectively all cases of moderate-to-severe plaque psoriasis treated for at least 6 months with ustekinumab since 2009 in our clinical practice settings. Data regarding psoriasis history, clinical characteristics, HLA-Cw6 status, previous and concomitant treatments, ustekinumab dosage, clinical response and adverse events were recorded, among others. Survival analyses were performed using Kaplan-Meier curves and log-rank tests. Other statistical tests used to analyse all the data were T-test and Fisher's exact test.

Results

35 patients were included in the study. Their baseline characteristics are summarized in **Table 1**.

Treatment with ustekinumab reduced absolute PASI value below 3.5 after W16, and maintained along time, which is considered an optimal therapeutic goal (**Fig. 1A**). PASI-75 was achieved by 65% of patients at W16 (PASI-90: 42%) and 68% at W28 (PASI-90: 41%)(**Fig. 1B**). Ustekinumab showed a median survival time of 45 months (IC: 36.77-53.64) (**Fig. 2A**). Drug retention at 12 months was 90%, 71% at 24 months and 69% at 36 months. Ustekinumab was discontinued in 34% patients, due to inefficacy (4 patients), lost of follow-up (4 patients), neoplasia diagnosis (1 patient) and gestation (1 patient).

When comparing patients who were naïve to previously treated with biologicals, no significant differences among percentage of PASI75/90 achievement were found (data not shown). Drug survival among these two subpopulations didn't show any difference, either (**Fig. 2B**). Analysis of ustekinumab response regarding patient weight showed that a significant higher proportion of patients below 100kg archived PASI-75 at W16, but results of PASI-75 achieved at W28 were similar, probably due to drug combination strategies in subgroup of patients above 100kg (data not shown). Fifty-four percent (54%) of the patients included in the study were HLA-Cw6 positive, which has previously been associated with a better response to ustekinumab. In our series, HLA-Cw6-positive patients had a faster and significantly higher rate of response (in terms of PASI-75), which was statistically significant at W4, 16 and 54 (**Fig. 3A**). In addition, survival drug analyses between HLA-Cw6 positive and negative patients showed a trend for HLA-Cw6 patients to long-term survival (**Fig. 3B**).

Our study didn't show any differences in clinical response to ustekinumab regarding history of psoriatic arthritis, smoking or alcohol intake, or time of psoriasis evolution.

Table 1. Characteristics of patients at baseline.

N (♂/♀)	35 (21/14)
Age of inclusion	48,46 *[25-70]*
Weight (kg)	87,16 *[50-130]*
BMI	29,70 *[18,37-44,64]*
Age of psoriasis onset	27,21 *[8-61]*
Baseline PASI	13,27 *[2,4-38]*
Psoriatic arthritis	17,10%
≥2 previous classical systemic treatments	95%
Naive to biologicals	40%
Previous biological therapy	1 (22,9%), 2 (25,7%), 3 (11.4%)
Combination therapy	20% (6 MTX, 1 CsA)
Ustekinumab dosage	Standard (45%), reduced (28.6%), increased (25.7%)

*standard dosage was 45/90mg (according to weight </>100kg) every 12-14weeks.

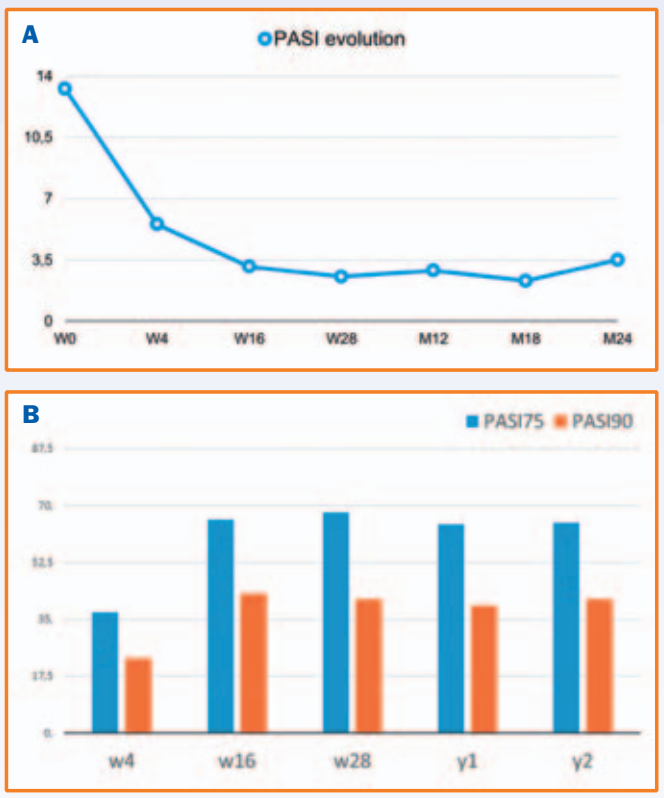

Fig. 1. Clinical response to ustekinumab.
A. Evolution of absolute PASI value along the time.
B. Proportion of patients achieving PASI-75 and PASI-90 at different endpoints.

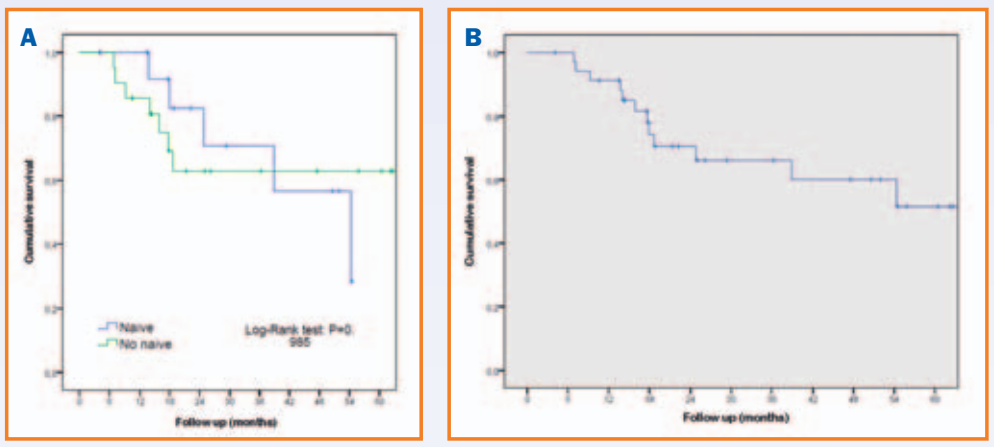

Fig. 2. Drug survival analyses.
A. Ustekinumab survival.
B. Ustekinumab survival stratified for previous biological treatment.

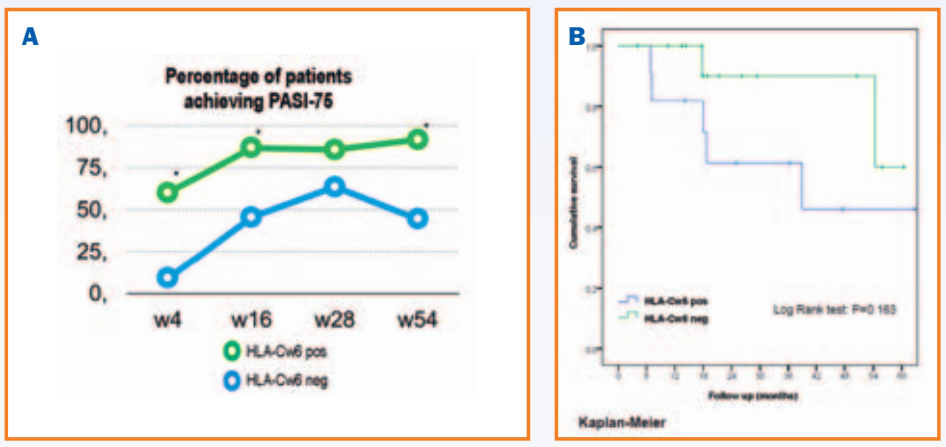

Fig. 3. Clinical response to ustekinumab and drug survival stratified for the presence of HLA-Cw6.
A. Proportion of patients achieving PASI-75 according to HLA-Cw6 status.
* p-value <0.05
B. Drug survival analysis stratified for the presence of HLA-Cw6.

Conclusions

In our series, ustekinumab seems to be an effective treatment for moderate-to-severe psoriasis, with elevated survival rates, and results comparable to clinical trials. Of note, 28% of patients (best responders) were treated with reduced doses of ustekinumab, and treatment combinations were described in 20% of the patients. Among ustekinumab response predictors, we confirm the positivity of HLA-Cw6 as an indicator of faster and higher response rates to the drug. In addition, obesity was associated to slower response. Limitations such as retrospective design and sample size must be taken into consideration.

References

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