

INFLIXIMAB SERUM CONCENTRATIONS, ANTIBODY FORMATION AND CLINICAL RESPONSE IN PSORIATIC PATIENTS

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BACKGROUND

Therapy with biopharmaceuticals has revolutionized therapy in patients with immune diseases such as psoriasis. Despite therapeutic efficacy of these agents, a variable percentage of patients lose response over time.

Monitoring of Infliximab (IFX) trough concentrations (C_{min}) and presence of anti-IFX antibodies (ATI) together with clinical response has been recommended to guide dosing decisions but the optimal therapeutic C_{min} for IFX in psoriasis needs to be established.

OBJECTIVES

- ✓ The primary endpoint was to evaluate the IFX immunogenicity-exposure-response correlation in psoriasis.
- ✓ Secondary endpoint was to identify patient's characteristics that could affect IFX C_{min} and clinical response.

RESULTS

Study population

33 patients, of whom 33.3% were women, were included in the study and the total number of samples analyzed was 155. Patients characteristics are shown in Table 1.

Age, years	46.5 (14.6)
Weight, kg	88.2 (23.5)
Gender (Women/Men)	11 (33.3%) / 22 (66.7%)
Psoriatic arthritis, n (%)	14 (42.4%)
BMI (kg/(m ²))	31.0 (6.8)
Overweight (BMI (kg/m ²)= 25 – 30)	13 (39.4%)
Obese (BMI (kg/m ²)> 30)	15 (45.5%)
PASI (coinciding with C_{min})	2.2 (3.2)
PASI (before IFX induction)	12.8 (10.3)
Previous biological treatment, n (%)*	22 (66.7 %)
Immunosuppressant therapy, n (%)	23 (69.7%)

Table 1. Patients characteristics. Results are shown as a mean (SD). BMI: body mass index. PASI: Psoriasis area severity index. IFX: infliximab. * Patients received more than one previous biological treatment regimen.

Median IFX dose was 5mg/kg/8w (range, 3mg/kg/12s-5 mg/kg/6w). All patients with dose-intensified regimen presented IMC > 27mg/m².

IFX exposure and ATI

Mean IFX C_{min} was 2.4 mg/L (2.2). 6 patients tested ATI positive. IFX C_{min} (mg/ml) distribution is shown in Table 2.

IFX C_{min} (mg/ml)	% samples
Undetectable (<0.035)	6%
< 2.5	60%
2.5-4.9	18%
5-7.4	10%
7.5-10	4%
>10	2%

Table 2. IFX C_{min} distribution.

Variables influencing IFX exposure

ATI

C_{min} was significantly lower in positive ATI vs negative ATI samples (0.1 vs 2.7 mg/L; $p < 0.0005$) (see Figure 1)

BMI

Overweight and obese patients presented a higher IFX C_{min} than those with normal weight (2.68mg/L vs 1.64 mg/L; $p = 0.134$).

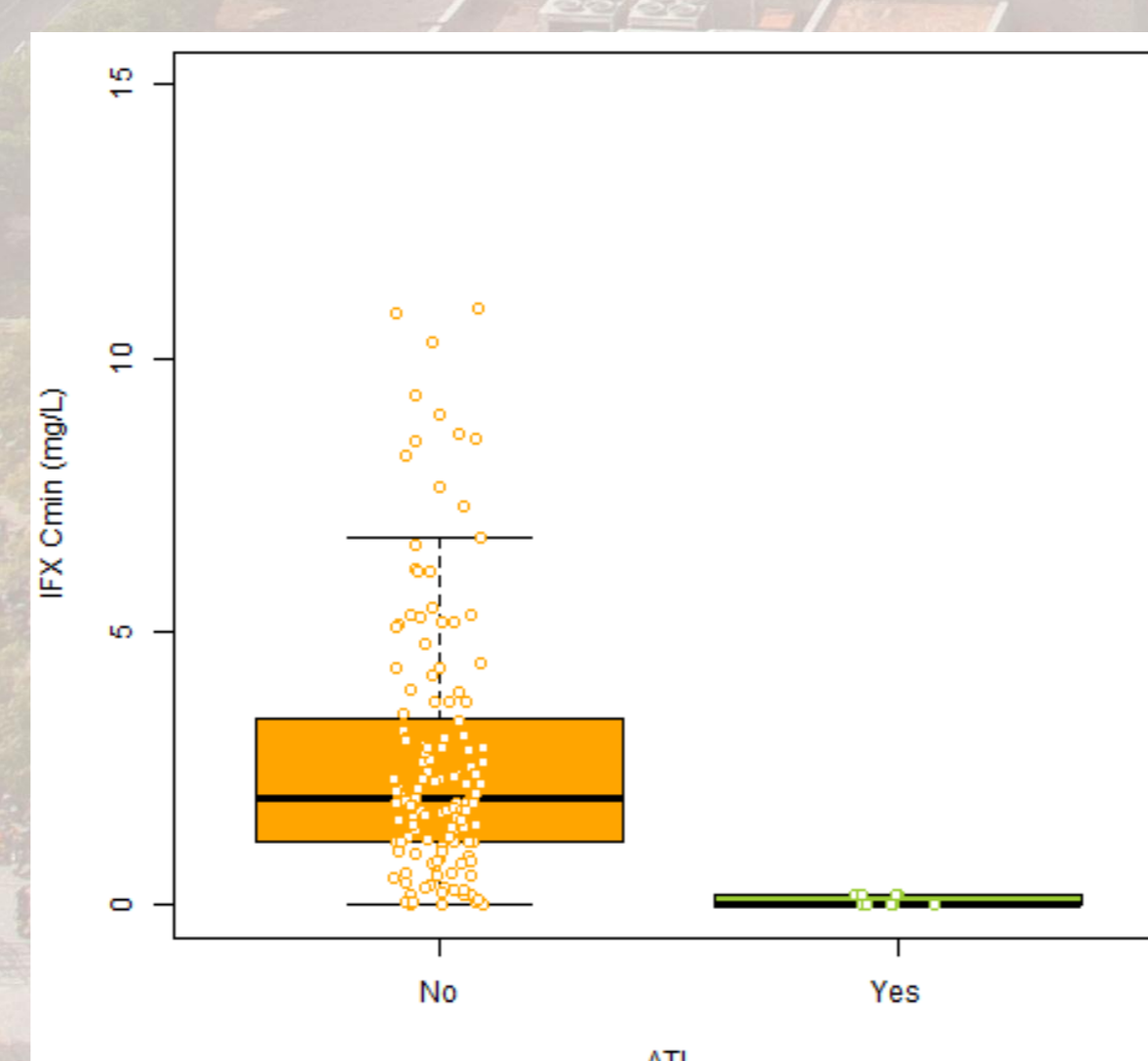


Figure 1. Boxplot of IFX C_{min} depending on ATI presence

MATERIAL AND METHODS

Study design and population: Prospective study in psoriatic adult patients receiving maintenance IFX between October 2013-November 2016.

Evaluations: Blood samples were collected under steady-state conditions before starting the intravenous infusion.

-We measured C_{min} and ATI using a validated enzyme-linked immunosorbent assay (ELISA) kit (Promonitor®).

-Data on demographic, analytical and pharmacological variables and Psoriasis Area Severity Index (PASI) were recorded.

Statistical analysis: Mixed models were estimated to evaluate the association between C_{min} and IFX response. Continuous variables were expressed as mean (standard deviation (SD)). Statistical analysis was carried out using R.

Treatment response

The percentage of patients achieving PASI 50, 75, 90 and 100 response was 85%, 73%, 59% and 48%. Patients achieving PASI 75/90/100 had a significantly higher C_{min} than non-responders (Figure 2).

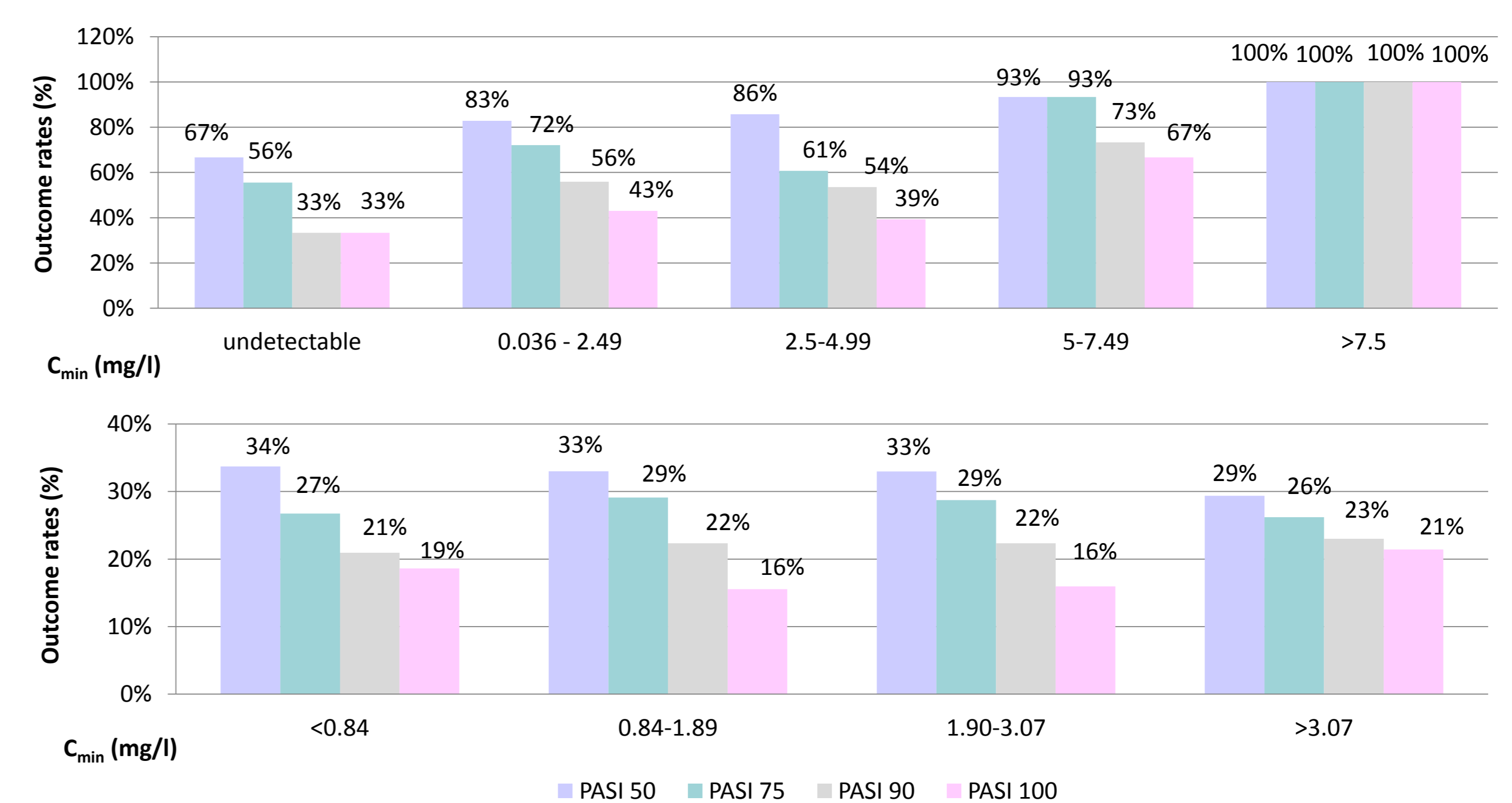


Figure 2. Relationship between IFX C_{min} and PASI response

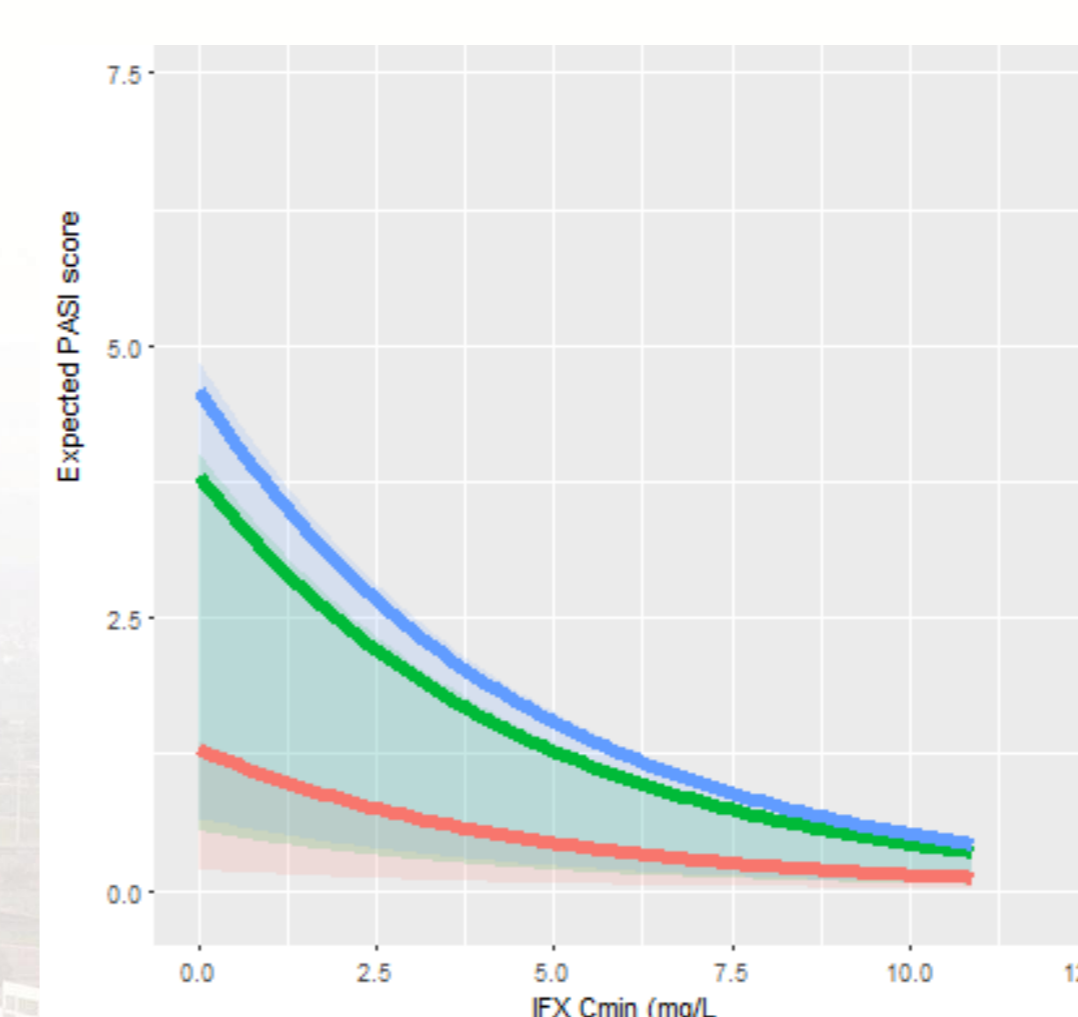


Figure 3 IFX C_{min} vs PASI expected response by BMI strata.

PASI score was significantly influenced by C_{min} (IRR:0.79, IC95%:0.69-0.91). This remained significant when adjusting by gender, BMI, diagnose, baseline PASI, leukocyte count, ATI status and immunomodulator treatment (IRR:0.8, IC95%:0.70-0.93). (Figure 3).

Similar results were obtained for PASI90/100 responses (Table 3):

PASI response	OR	IC95%
PASI 90	1.79	1.14-2.81
PASI 100	1.79	1.18-2.71

Table 3. Association between PASI 90/100 response and IFX C_{min} .

CONCLUSIONS

- ✓ PASI score and achievement of PASI 90 response or higher were significantly influenced by IFX C_{min} .
- ✓ The percentage of patients achieving PASI 75 or higher decreased with BMI, while C_{min} values increased.
- ✓ IFX C_{min} was significantly influenced by BMI and ATI presence.
- ✓ More studies are needed to define target serum levels and to evaluate the relationship between inflammation markers and PASI in overweight and obese patients.

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