

BODY SURFACE AREA, CIGARRETE SMOKING AND INFLIXIMAB RESPONSE IN PSORIASIS PATIENTS

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BACKGROUND

Infliximab (IFX) is a chimeric anti-tumour necrosis factor- α monoclonal antibody authorized for psoriasis treatment. Loss of response occurs in approximately 25% of the patients.

Due to the large interindividual variability of IFX, measurement of serum concentrations and correlate it with disease activity and covariables that could be useful for psoriasis management.

PURPOSE

• **Primary endpoint:** Assess the relation between IFX trough levels (C_{min}) and treatment efficacy.

• **Secondary endpoint:** Identify variables that could affect C_{min} .

MATERIAL AND METHODS

Prospective study of patients with psoriasis treated with IFX between October 2013 and August 2015. All patients received IFX at 5 mg/kg at week (w) 0, 2 and 6 and then every 8w. Patients could have been dose-intensified according to clinical response.

C_{min} and antibodies towards IFX (ATI) were determined at steady state by enzyme-linked immunosorbent assay (ELISA) (Promonitor®). C_{min} (mg/L) and dose adjusted C_{min} (C_{min}/D) ($mgL^{-1}/mg\ kg^{-1}month^{-1}$) were statistically compared after logotransformation.

Clinical response was assessed by a dermatologist according to PASI scale.

Statistical analysis was performed using SPSS v19.

RESULTS

16 patients were included in the study. Baseline patient characteristics are shown in Table 1.

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| Age, years | 45 (38-54) |
| Weight, kg | 83.4 (65.5-93.8) |
| Gender (Women/Men) | 4/12 |
| BSA, m ² | 1.96 (1.66-1.96) Men: 2.1 (1.9-2.3). Women: 1.6 (1.5-1.9) |
| Cigarette smoking, n (%) | 4(25%) |
| PASI (coinciding with C_{min}) ATI positive vs undetectable (mean) | 1.84 (0-2.8) 5 vs 1.58* |
| PASI (before IFX induction) | 13 (9-20) |
| Previous biological treatment, n (%) | 3 (19%) |
| IFX doses | 21 (10-44) |
| Immunosuppressant therapy, n (%) | 12 (75%) |

Table 1. Patients characteristics. Results are shown as median (Q1-Q3). BSA: body surface area. PASI: Psoriasis area severity index. IFX: infliximab. *p=0.074

Median IFX dose was 5 mg/kg/8w (range, 4 mg/kg/8w-5 mg/kg/6w). 3 patients were under dose-intensified IFX treatment (Figure 1).

40 samples were available for analysis. Samples distribution according to IFX dose was: 64% 5 mg/kg/8w, 18% 4mg/kg/8w, 13% 5mg/kg/6w and 5% 5mg/kg/7w.

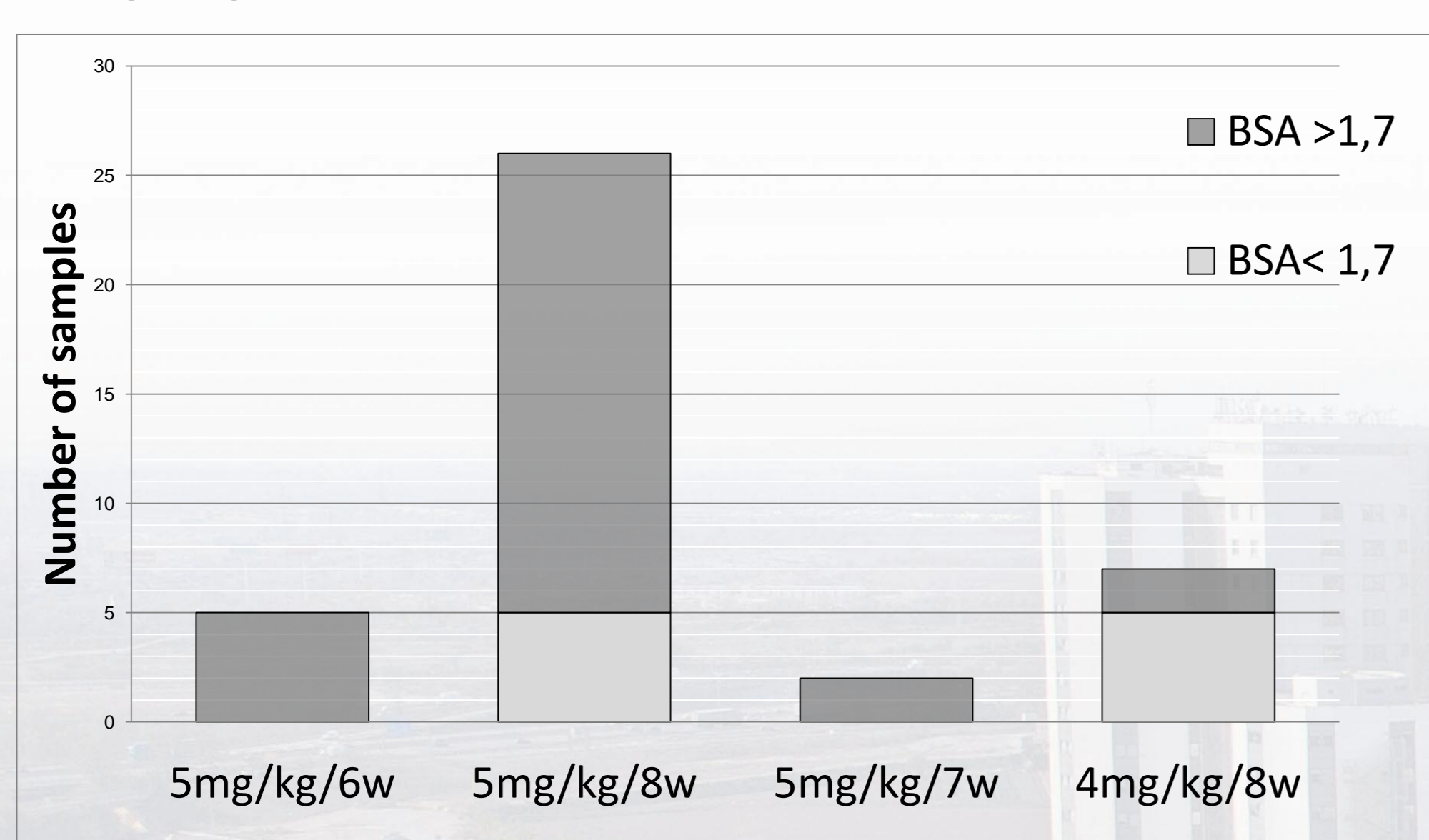


Figure 1. IFX dosing according to BSA (>1.7 m² or <1.7 m²)

Variables influencing IFX exposure

Median C_{min} and C_{min}/D were 1.59 (Q1-Q3: 0.86-2.63) and 0.66 (Q1-Q3: 0.37-1.1) respectively. 3 samples were positive for ATI. All patients who developed ATI had undetectable C_{min} . Median C_{min} was a 13.7% lower in cigarette smoking patients (1,49 mg/L vs 1,73 mg/L). C_{min} distribution is shown in Figure 2.

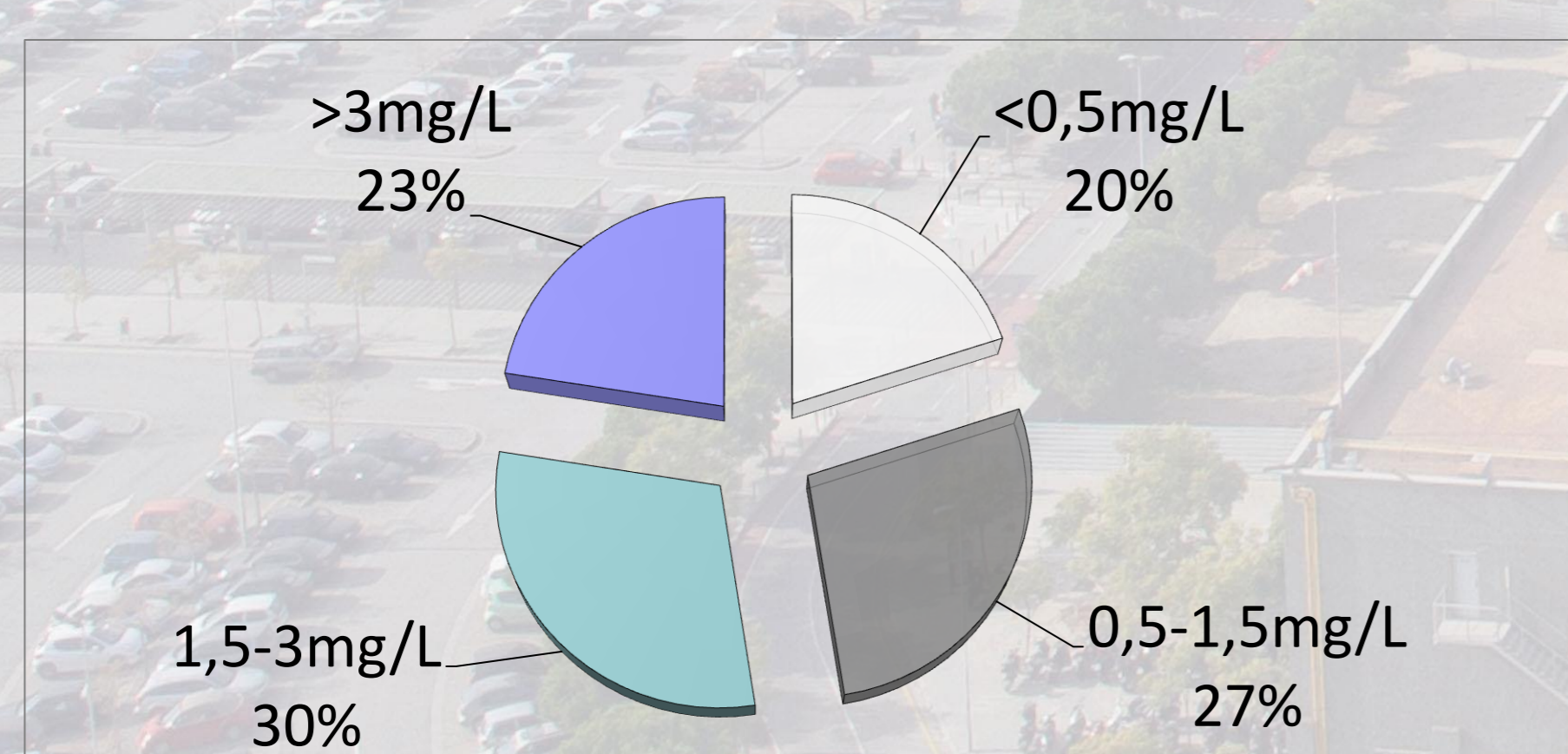


Figure 2. IFX C_{min} distribution

Multivariate analysis showed that C_{min} was significantly influenced by ATI status (p=0.028), BSA > 1.9 m² (men) (p=0.024) or 1.6 (women) (p=0.034), previous biological treatment (men: p=0.09; women: 0.053) and initial PASI (men: p= 0.006; women: p=0.008).

Treatment efficacy

All patients with BSA ≤ 1.7 m² vs 63% of patients with BSA >1.7 m² achieved PASI75 (p=0.026). Patients with BSA >1.7m², had a 45% and 15% higher median C_{min} (1.89 vs 1.30 mg/L) and C_{min}/D , respectively. However, median PASI was higher when BSA >1.7m² (2.39 vs 0.16). Patients with BSA >1.7 m² and achieving PASI75 had a 36% higher C_{min}/D compared to those not achieving PASI75.

Patients achieving PASI75 had a 23% higher C_{min}/D compared to those not achieving PASI75. Surprisingly, 50 % patients who tested ATI positive achieved PASI75. All of them had undetectable C_{min} and % had a BSA value <1.7 m².

A higher percentage of patients with C_{min} <3mg/L (67.7%) achieved PASI100 compared to patients with C_{min} >3mg/L (22.2%) (p=0.023). All patients with C_{min} >3mg/L had BSA >1.7m².

PASI in relation to IFX C_{min} is shown in Figure 4.

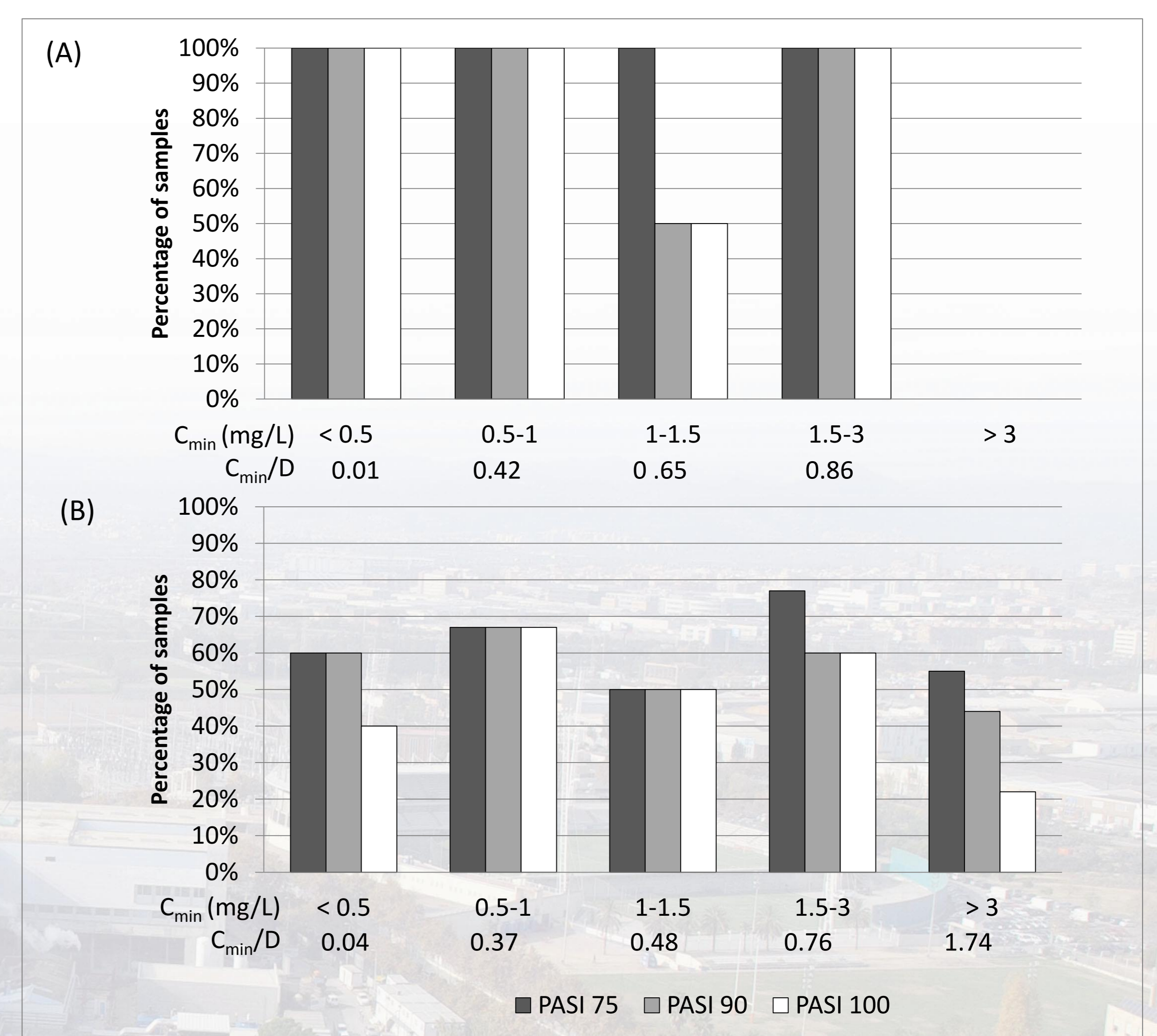


Figure 4. PASI in relation to IFX C_{min} . (A) Patients with BSA < 1.7 m². (B) Patients with BSA > 1.7 m². The 3 patients treated with dose-intensified IFX had a BSA>1.7 m² and C_{min} >1.5 mg/L. Only 1 of these patients achieved PASI75. Three patients were treated with IFX 4 mg/kg/8w. 57.1% of samples in these patients measured C_{min} <1.5mg/L. All of these patients achieved PASI 75 and two of them achieved PASI 100.

CONCLUSIONS

- Higher C_{min} and C_{min}/D values were associated with better treatment response in all patients.
- Patients with SC ≥ 1.7 m² showed a tendency to lower treatment response.
- Lower C_{min} was found in smoking patients.
- More studies with a higher number of patients are needed to define the target levels and assess the influence of covariables.