

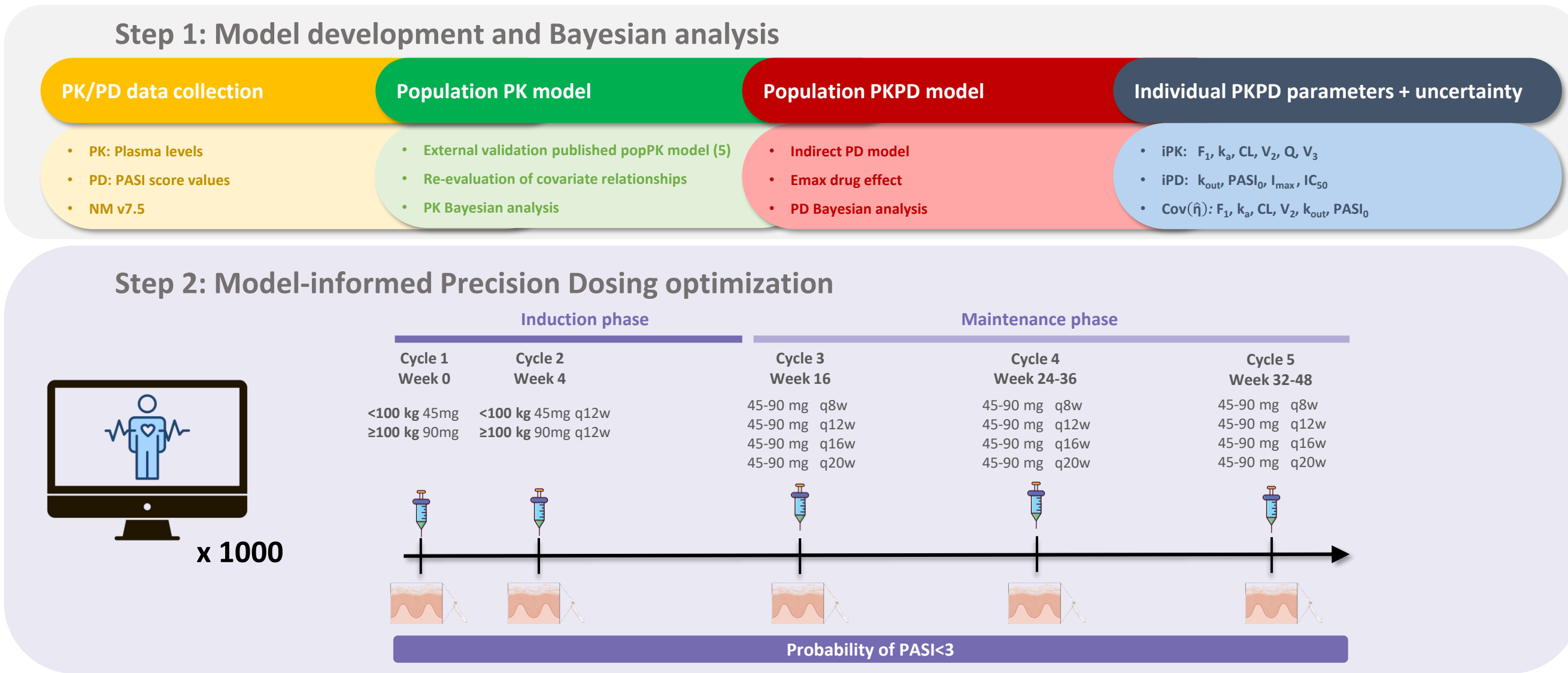
INTRODUCTION AND OBJECTIVES

Ustekinumab inhibits IL-12 and IL-23 (1), showing efficacy on the major pharmacodynamic (PD) outcome: Psoriasis Area and Sensitivity Index (**PASI**) (2,3). Ustekinumab is approved for subcutaneous administration at initial doses of 45 or 90 mg in weeks 0 and 4, following additional doses of 45 or 90 mg every 12 weeks (4). Ustekinumab requires **dosage individualization based on clinical response**, although this individualization is not reflected in summary of product characteristics (SmPC). The pharmacokinetic (PK) properties of ustekinumab have been characterized by a two-compartment model in patients with psoriasis (5). The aims of this study are:

- to develop a **population PK/PD model of ustekinumab** in patients with psoriasis
- to evaluate **individualized dosing regimens** accounting for the **individual parameter uncertainty** using a model-informed precision dosing strategy.

MATERIALS AND METHODS

A post-authorization, prospective, multicenter (national), and observational clinical practice follow-up study was conducted in psoriatic patients from the Manises Hospital in Valencia, Spain. Patients were following treatment subcutaneous 45/90 mg of ustekinumab (**Table 1**). Plasma levels and PASI score values were obtained in steady state. A summary of the modelling workflow is presented in **Figure 1**. A probability ≥80% of PASI level <3 was considered as the success criteria for schedule selection.



RESULTS

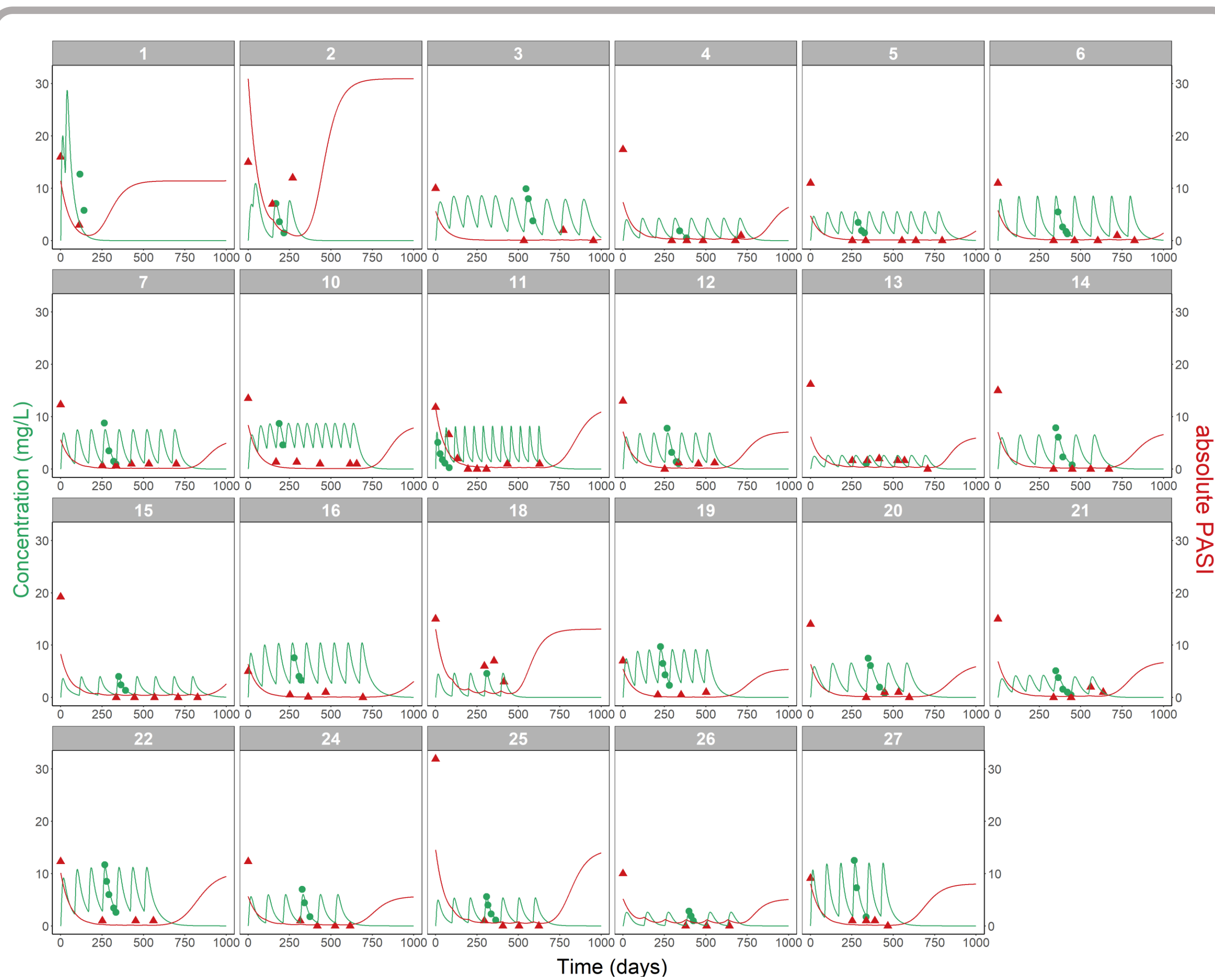
Table 2 and 3 show the description of the ustekinumab levels and PASI score collected, and the characteristics of the patients included in the study, respectively.

Dose	Patients, n (%)	Mean ± standard deviation [range]
45 mg	6 (26)	23
90mg	17 (74)	4.1 ± 3.06 [0.27-12.7]
Frequency	Patients, n (%)	
q8W	2 (9)	75
q10W	1 (4)	1.096 ± 2.13 [0-12]
q12W	9 (40)	117
q14W	3 (13)	14.4 ± 6.23 [5-32]
q15W	2 (9)	
q16W	5 (22)	
q18W	1 (4)	

Table 2. Description of the PK/PD observational data of ustekinumab collected in psoriasis disease

Measure	Age (years)	Body weight (kg)	Height (cm)	Treatment (years)	Gender (n,%)	SmPC dose regimen (n,%)	Biological “naïve” (n,%)
Mean	62	92	167	2	Male (14, 61)	Yes (9, 40)	Yes (3, 13)
SD	8.19	18.4	0.06	1.7			
Min	45	70	154	0.304	Female (9, 39)	No (14, 60)	No (20, 87)
Max	76	135	183	11.4			

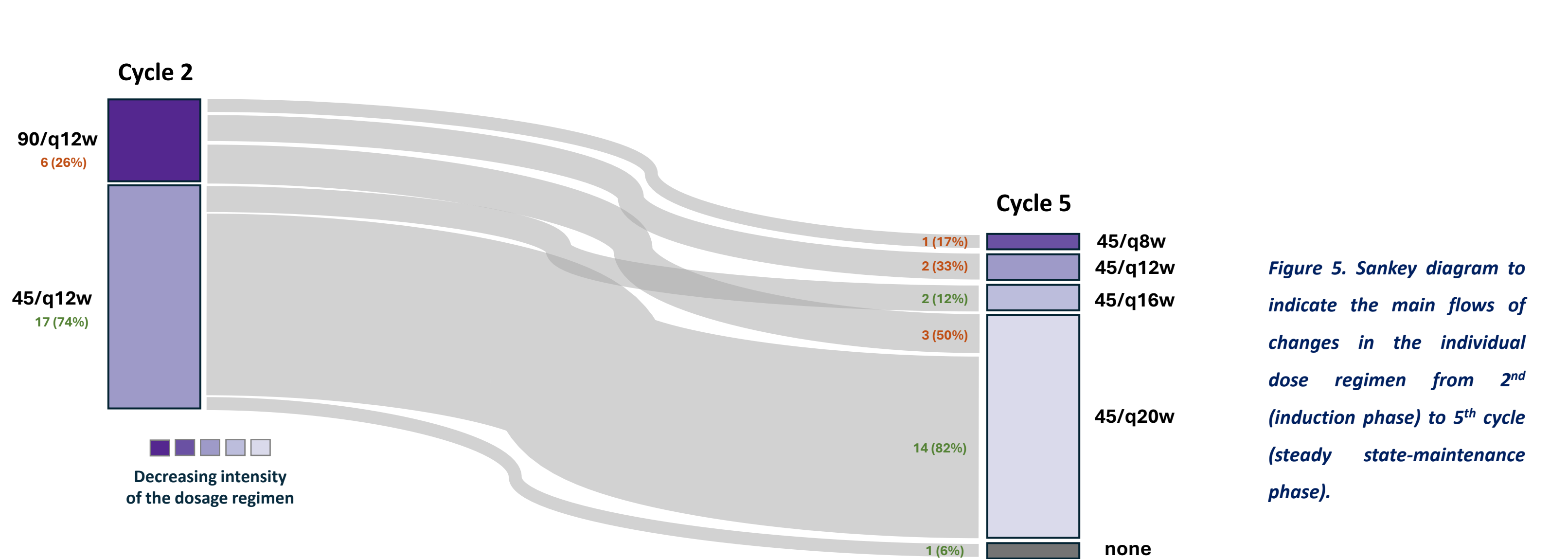
Table 3. Summary of the demographic and biochemical characteristics of the patients.



PK/PD model



Figure 3. Bar plot of 1000 simulated absolute PASI for each patient after ustekinumab administration at cycle 2 and 5, using the individual parameters and their uncertainties. In green it is represented the probability ≥ 80% of PASI level <3.



Individual schedule optimization

DISCUSSION AND CONCLUSION

- A population PK/PD model of ustekinumab has been developed to characterize sparse and clinical routine data in patients with psoriasis.
- In 22/23 (96%) patients a satisfactory PASI response would be achieved with a greater than 80% probability with **less intensive dosing regimens**.
- This analysis has demonstrated its usefulness as a tool for the selection of individualized dosing regimens in clinical practice to optimize the **efficiency for the use of ustekinumab in patients with psoriasis**.
- Although more prospective, follow-up, and observational studies of clinical practice are required, it would be appropriate to extrapolate the proposed model-informed precision dosing optimization strategy into clinical practice to **demonstrate its suitability and application**.

References

- Greenzaid J, Feldman S. Clin Pharmacokinet. 2024 Feb 27;63(2):137–53.
- Bai F, Li GG, Liu Q, Niu X, Li R, Ma H. J Immunol Res. 2019.
- McInnes IB, Kavanaugh A, Gottlieb AB, Puig L, Rahman P, Ritchlin C, et al. Lancet. 2013;382(9894):780–9.
- Stelara | European Medicines Agency.
- Shao J, Xu Z, Xu Y. Eur J Drug Metab Pharmacokinet. 2022 Jul 1;47(4):537–48.

