

EFFECTS OF CANAKINUMAB DOSE ADJUSTMENTS ON DISEASE CONTROL OF PERIODIC FEVER SYNDROMES – INTERIM RESULTS OF THE RELIANCE NIS

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Introduction

Treatment of periodic fever syndromes (PFS) with the interleukin-1 β inhibitor canakinumab (CAN) has been shown to be safe and effective in controlled clinical trials and real-world setting.

Objectives:

The RELIANCE is a prospective non-interventional study investigating long-term safety and effectiveness of Canakinumab (CAN) in the treatment of patients with cryopyrin-associated periodic syndromes (CAPS), familial Mediterranean fever (FMF), hyper-IgD syndrome/mevalonate kinase deficiency (HIDS/MKD) or tumor necrosis factor receptor-associated periodic syndrome (TRAPS) in routine clinical practice. This interim analysis examines dose adjustments of CAN with regards to a treat-to-target strategy.

Methods:

RELIANCE is a prospective, non-interventional study (NIS) in Germany, which enrolled patients with confirmed diagnosis of PFS, routinely receiving CAN. Efficacy and safety parameters were assessed at baseline and at 6-month intervals.

The recommended starting dose (SD) of canakinumab was dependent on the age, body weight and indication as described in the product information (1).

Results

In the present interim analysis, data from N=268 (265 with baseline visit) patients with PFS enrolled in the RELIANCE between September 2017 and December 2023 were included. The median age of the total study cohort was 19.5 years (2–80 years [45.1% < 18 years]; N=137 female patients [51.5%]) and the median duration of CAN treatment before study entry was 2 years (0–15 years). Over the course of the study, the proportion of patients receiving higher than the recommended SD (>SD) increased from 33.6% at baseline to 54.8% at month 30 and 80.0% at month 60 (Fig. 2, Table 1). Furthermore, 18.7% of the study participants had at least one injection with more than twice the recommended SD (> 200% of SD).

Effectiveness as indicated by control of disease activity was comparable across all three dosing categories over the course of the study. More than 90% of patients had no or mild/moderate disease activity in all dose categories at baseline and month 30 as assessed by investigators (PGA) (Figure 3, Table 1; data for month 60 not yet available). In addition, patients' assessment of disease activity (VAS score 0-10) was similarly low with median VAS scores between 1.0 and 3.0 across all dose categories at baseline, month 30 and month 60 (Figure 4, Table 1).

The percentage of patients in the >SD dosing group experiencing non-serious adverse drug reactions (nsADR) was higher than in the <SD or SD dosing group (44.2% of patients in >SD compared to 24.6% and 20.5% of patients in the <SD and SD dosing groups, respectively). While no patients in the SD dosing group experienced serious adverse drug reactions (SADR), 7.2% and 8.4% of patients in the <SD and >SD dosing groups experienced SADR, with no statistically significant difference between SADR rates in the two dosing groups (<SD and >SD) (p=0.783; chi-square test) (Table 1).

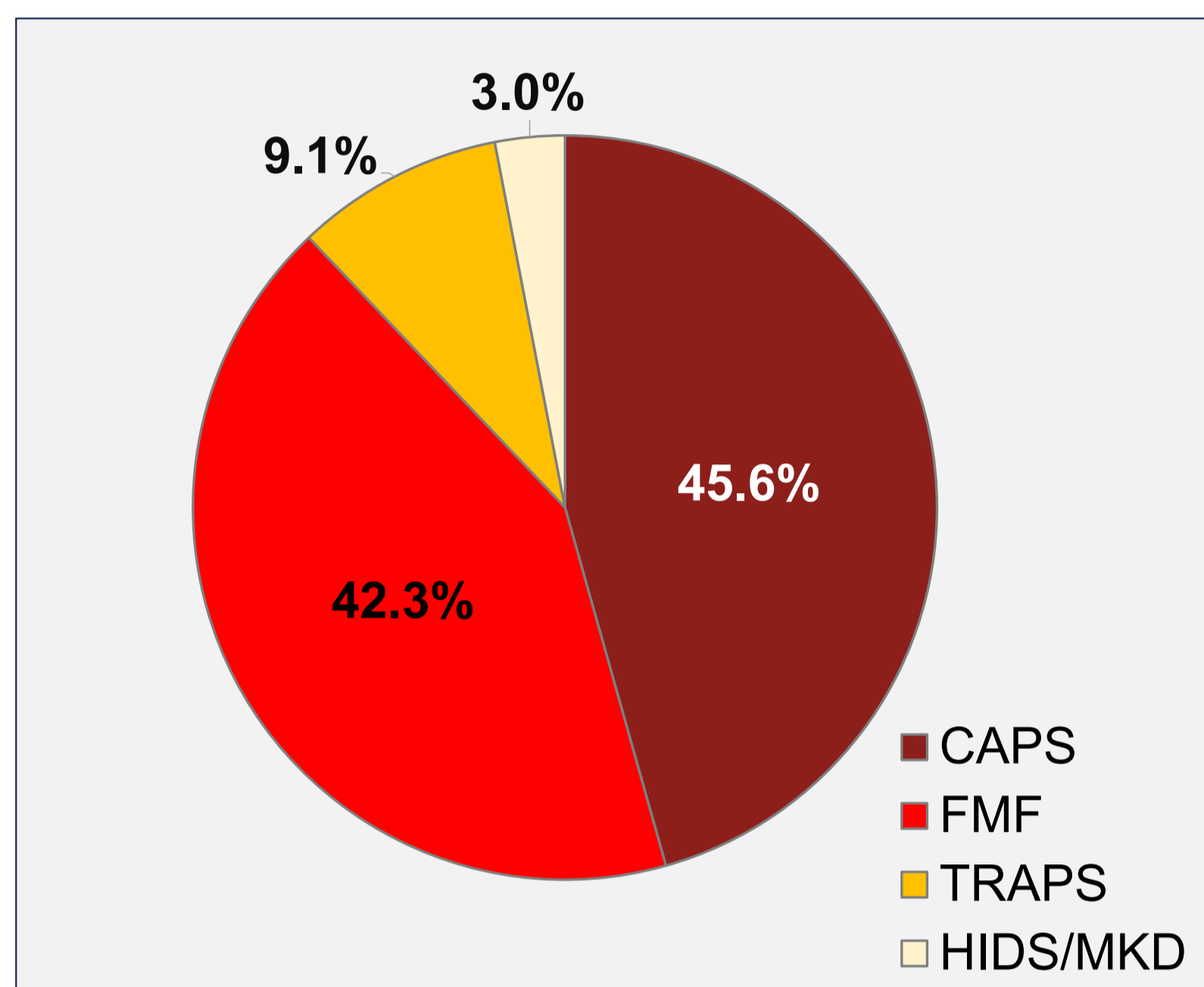


Figure 1: Patient population in this interim analysis
Total number of patients with baseline visit: 265. Distribution of diagnoses is depicted

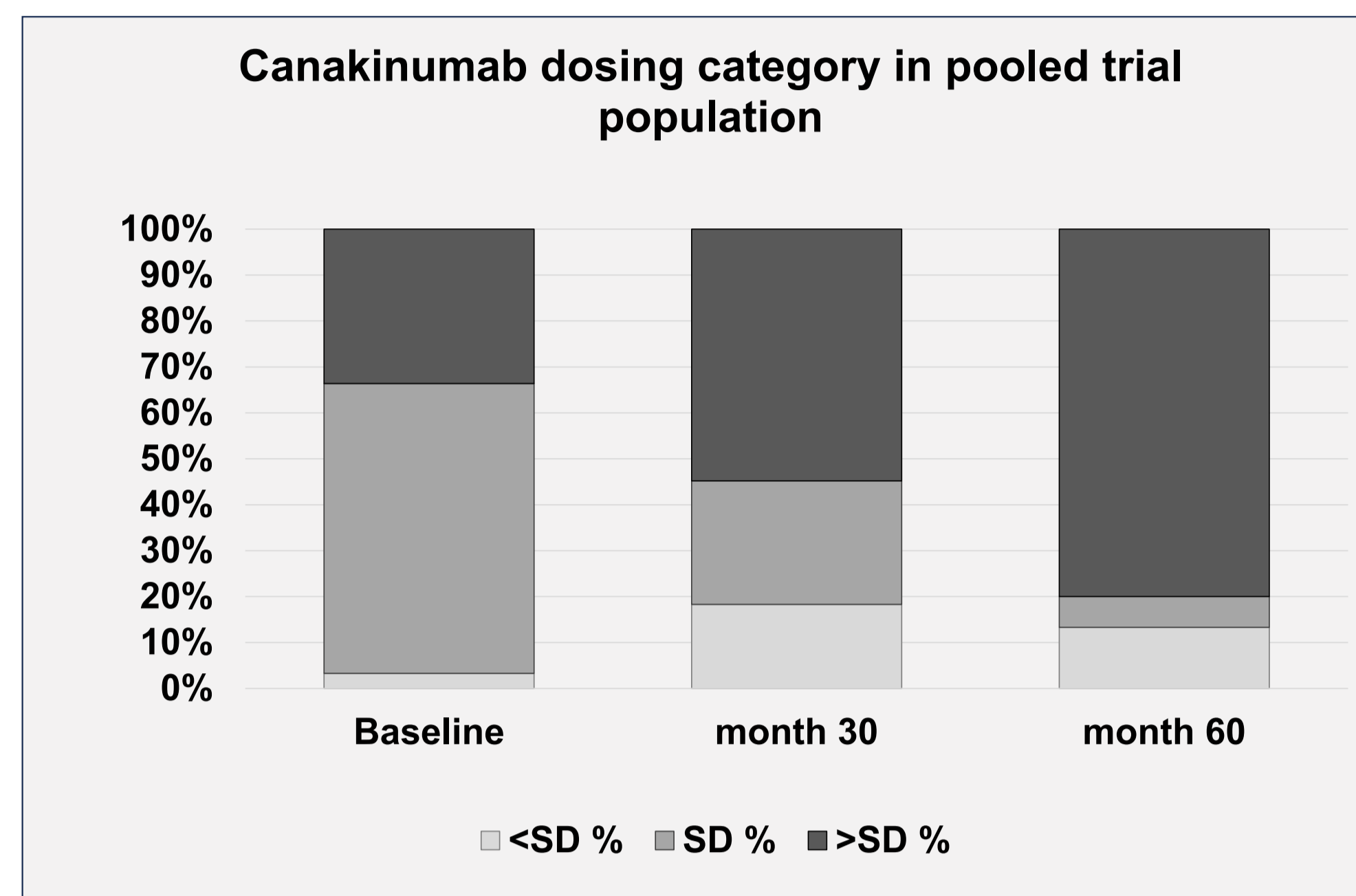


Figure 2: Adjustment of CAN dose with time of treatment.
Available information on recommended starting dosage (SD) according to SmPC and dose adjustments at baseline (n=241), month 30 (n=104) and month 60 (n=15).

	Baseline (n=265)*			Month 30 (n=120)*			Month 60 (n=17)*		
	< SD	SD	> SD	< SD	SD	> SD	< SD	SD	> SD
CAN dose category, n (% of patients)**	8 (3.3)	152 (63.1)	81 (33.6)	19 (18.3)	28 (26.9)	57 (54.8)	2 (13.3)	1 (6.7)	12 (80.0)
Investigator's assessment of disease activity (PGA), n (% of patients)									
Absent	29 (59.2)	9 (25.7)	28 (37.8)	13 (76.5)	4 (66.7)	22 (62.9)			
Mild/moderate	15 (30.6)	25 (71.4)	40 (54.1)	4 (23.5)	2 (33.3)	13 (37.1)			
Severe	3 (6.1)	0 (0.0)	4 (5.4)	0 (0.0)	0 (0.0)	0 (0.0)	n.a.	n.a.	n.a.
Not done	2 (4.1)	1 (2.9)	2 (2.7)	0 (0.0)	0 (0.0)	0 (0.0)			
Missing	20	38	21	12	22	23			
Patient's assessment of disease activity (VAS score 0-10), median (min.; max.), n	2.0 (0.0; 10.0), n=66	2.0 (0.0; 10.0), n=71	3.0 (0.0; 10.0), n=93	1.0 (0.0; 9.0), n=27	2.0 (0.0; 6.0), n=26	1.0 (0.0; 8.0), n=49	2.0 (0.0; 5.0), n=3	n.a.	1.0 (0.0; 4.0), n=12
Safety (interim analysis cut-off date December 2023), all patients (N=268)									
	< SD (n=69)			SD (n=73)			> SD (n=95)		Dose missing (n=31)
Patients with nsADR, n (%)	17 (24.6)			15 (20.5)			42 (44.2)		8 (25.8)
Patients with SADR, n (%)	5 (7.2)#			0 (0.0)			8 (8.4)#		1 (3.2)

Table 1: *Patients with baseline, month 30 and 60 visits yet documented. **Standard dose (SD) according to SmPC (1). Less than SD (<SD) defined as <87.5% of SD and greater than SD (>SD) defined as >112.5% of SD. #Comparison of SADR rates between <SD and >SD groups showed no statistically significant difference (p=0.783; chi-square test). n.a.: not annotated (data not yet available); nsADR: non-serious adverse drug reactions; PGA: physician global assessment; SADR: serious adverse drug reactions; SD: recommended starting dose; VAS: visual analogue scale

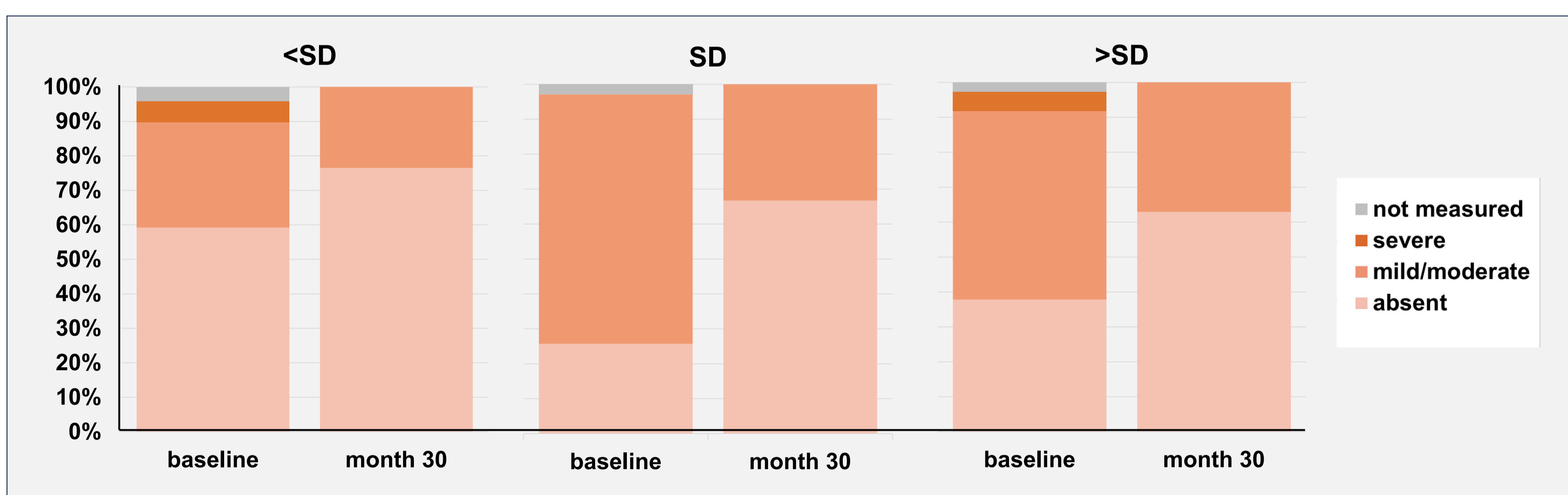


Figure 3: Investigator's assessment of disease activity (PGA)
<SD, baseline: n=8; <SD, month 30: n=19; SD, baseline: n=152; SD, month 30: 28; >SD, baseline: 81; >SD, month 30: n=5; data from month 60 not yet available

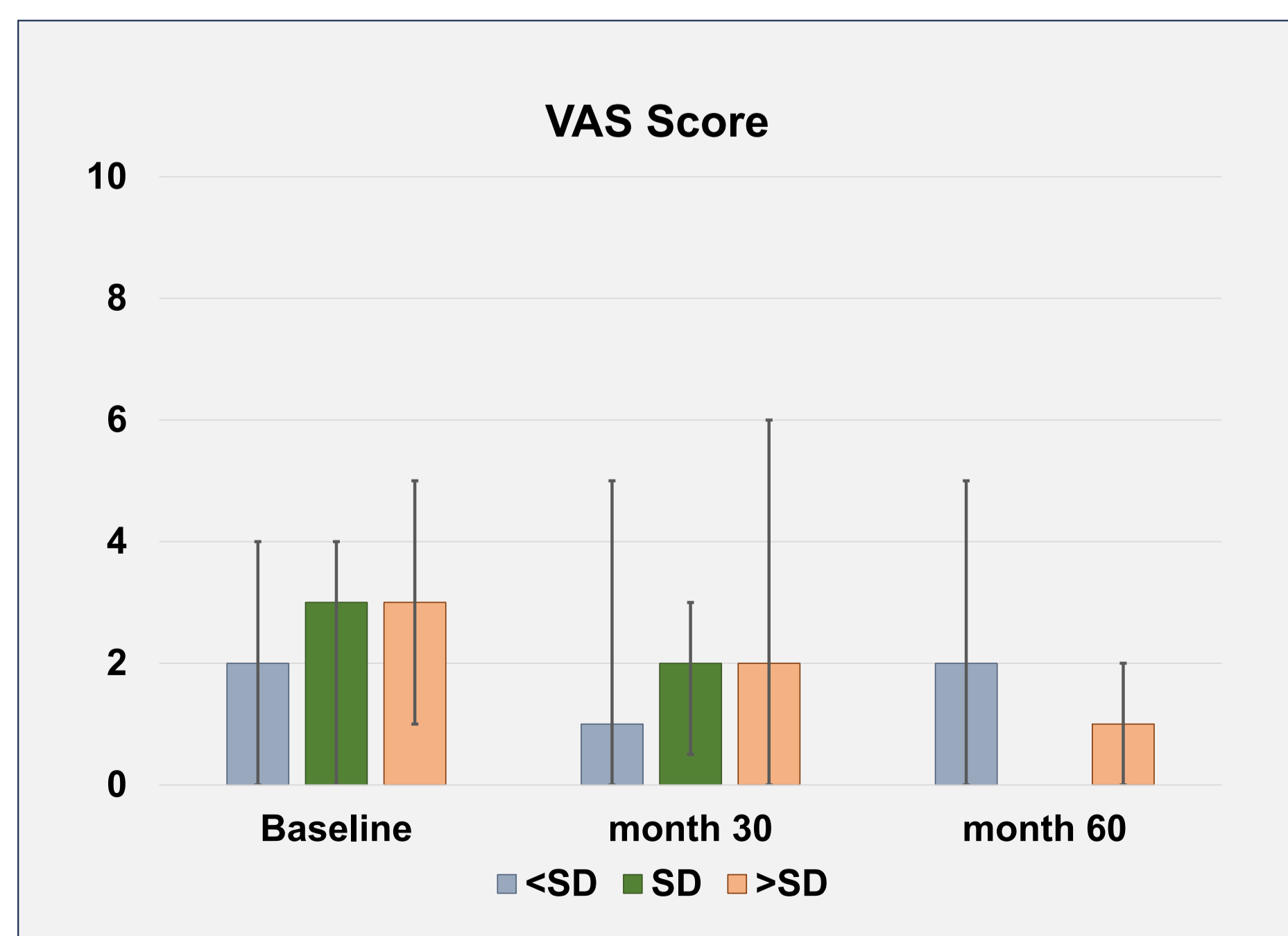


Figure 4: Patient's assessment of disease activity
Disease activity in relation to dosing category was assessed by patients using the visual analogue scale score (1-10). For patient counts please consult table 1. Columns indicate median VAS Score, error bars show 25 and 75 percentiles.

Conclusions

The present interim analysis of the RELIANCE study confirms the overall safety and effectiveness of long-term treatment with canakinumab. An increasing proportion of patients received dose adjustments towards higher doses over the course of the study, reflecting the increased implementation of a treat-to-target strategy.

Reference:

(1) European Medicines Agency (EMA). Canakinumab (Ilaris) Summary of Product Characteristics, 11 Dec 2024: https://www.ema.europa.eu/en/documents/product-information/ilaris-epar-product-information_en.pdf

Acknowledgement:

This work has been supported by Novartis Pharma GmbH, Germany