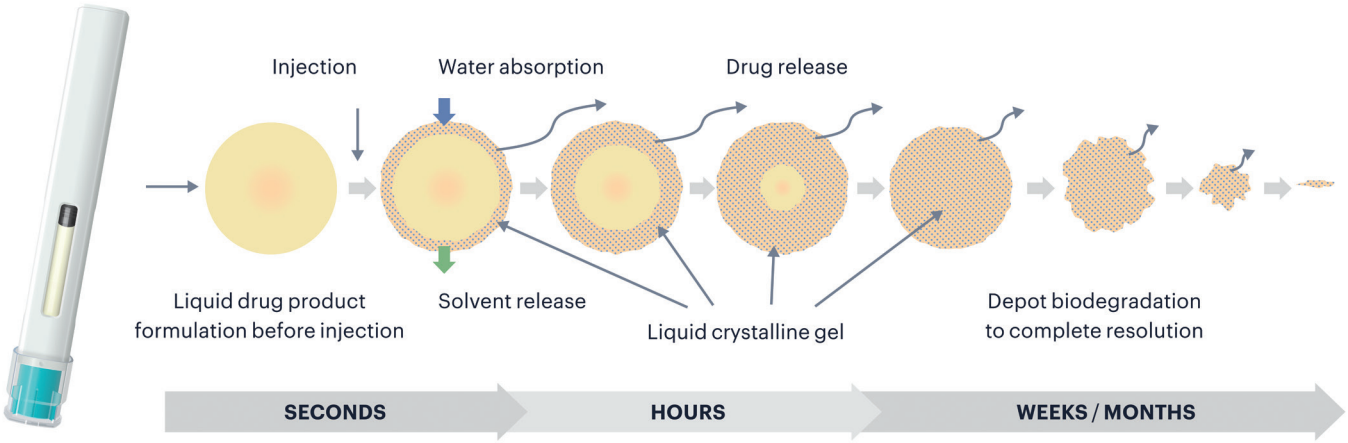
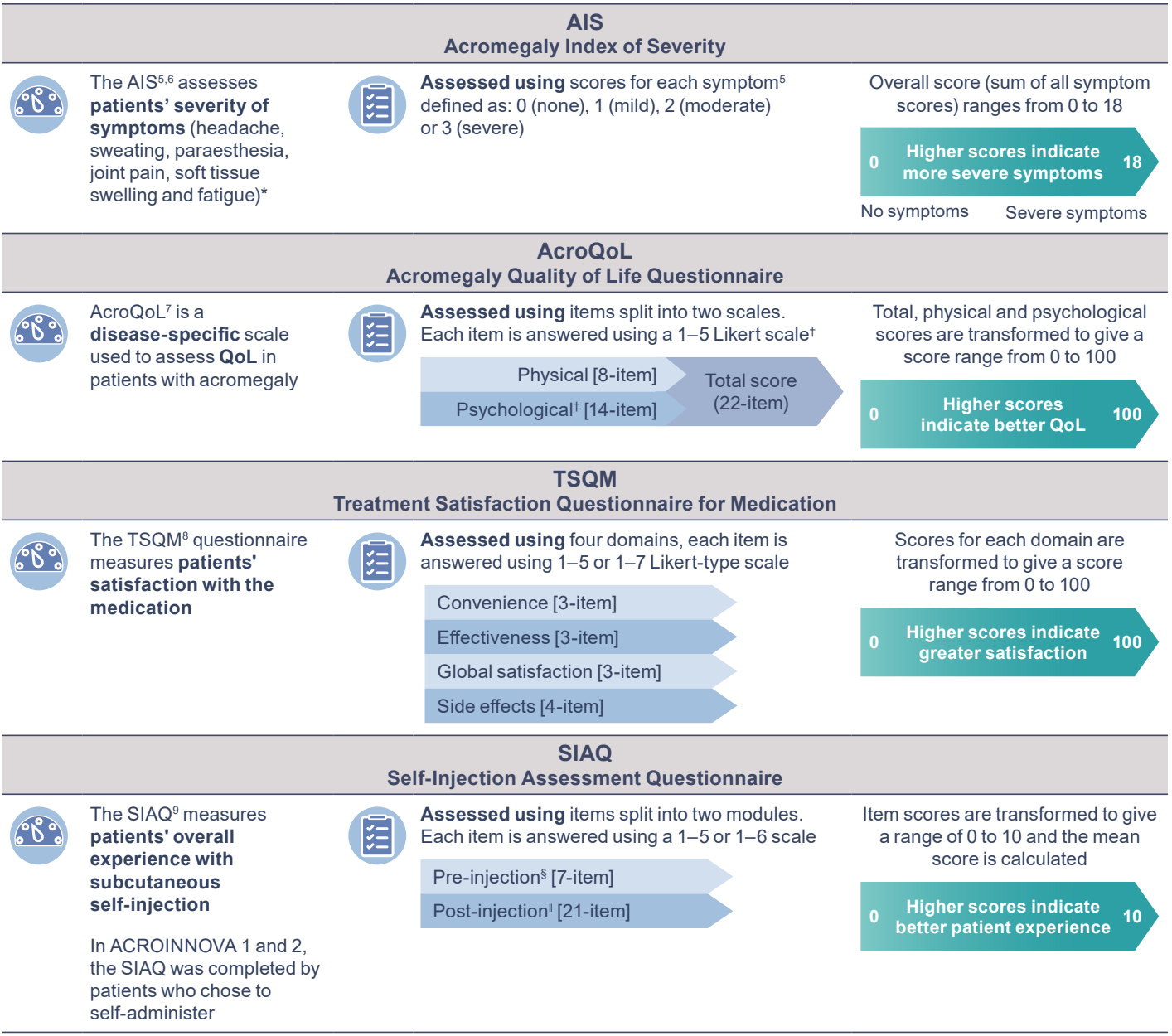
Supplementary material

Supplementary Figure 1: The FluidCrystal® drug delivery system[1–4]

CAM2029 pre-filled pen (autoinjector)

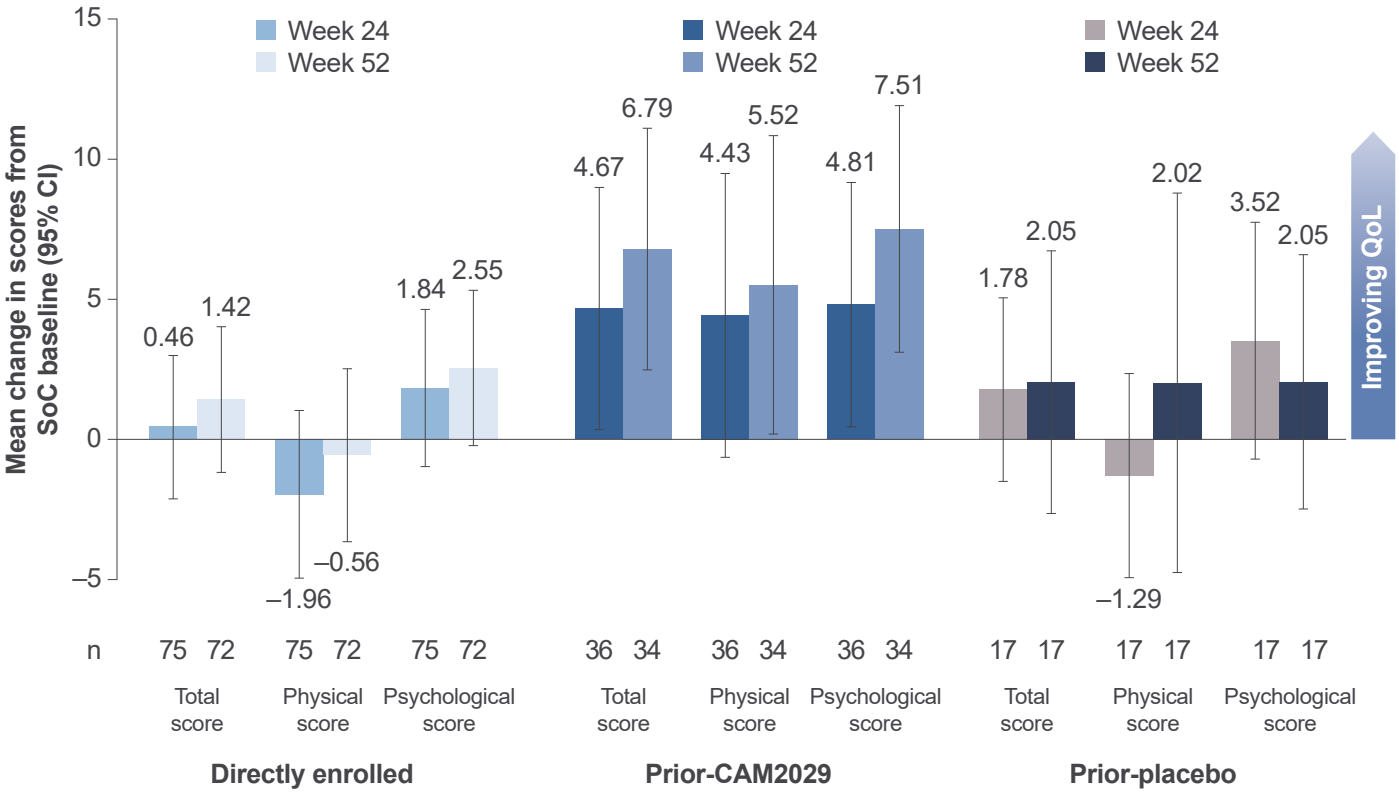


Supplementary Figure 2: Overview of AIS, AcroQoL, TSQM and SIAQ



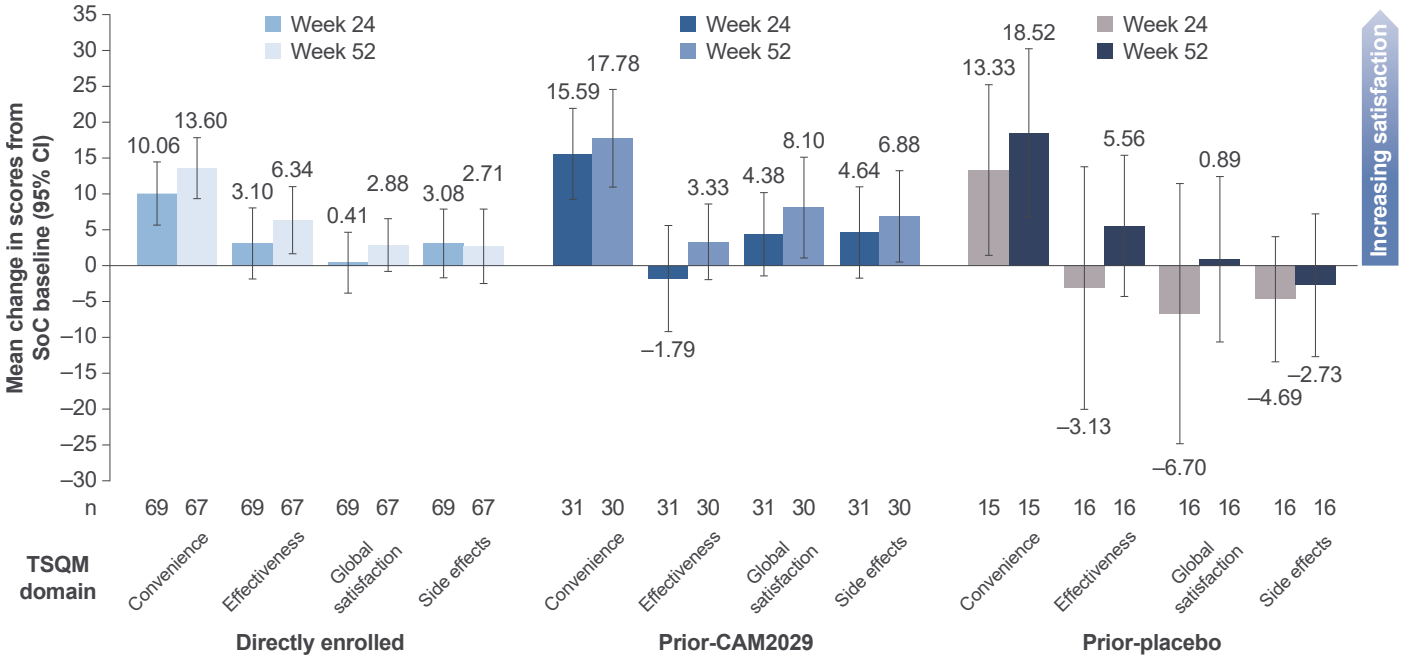
ACROINNOVA 1 and ACROINNOVA 2 were not powered to assess changes in acromegaly symptom severity using the AIS, AcroQoL, TSQM or SIAQ. *In ACROINNOVA 1 and 2, paraesthesia was included in addition to the five symptoms assessed with the AIS in Fleseriu *et al.*[5] †A 1–5 Likert scale measuring the frequency of occurrence (always, most of the time, sometimes, rarely, or never) or the degree of agreement with the items (completely agree, moderately agree, neither agree nor disagree, moderately disagree, or completely disagree); ‡The psychological domain is subdivided into physical appearance and impact of the disease on personal relationships; §The pre-injection module contains the following domains: general feelings about injections; self-confidence about giving self-injections; and satisfaction with the current way of taking medication; ‖The post-injection module contains the pre-injection module domains and the following additional domains: self-image; injection site reactions; ease of use of the self-injection device; and satisfaction with self-injection. ATG, Autogel; LAR, long-acting repeatable; QoL, quality of life.

Supplementary Figure 3: AcroQoL* scores change from baseline to week 24 and week 52 in the directly enrolled, prior-CAM2029 and prior-placebo subgroups



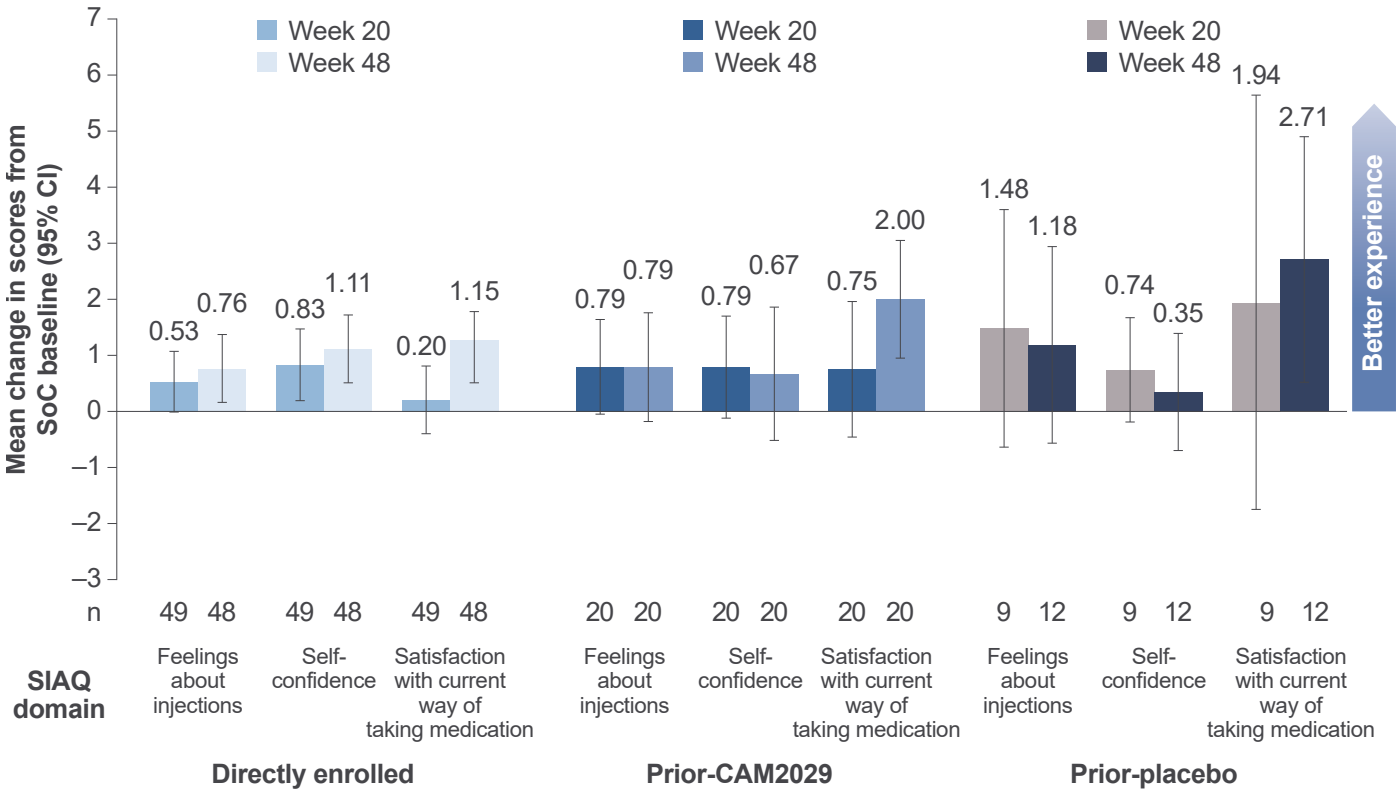
Data include the 24-week placebo period before the prior-placebo group switched to CAM2029; the group is also included in the overall population.
*Score range: 0–100.[7] CI, confidence interval.

Supplementary Figure 4: TSQM* scores change from baseline to week 24 and week 52 in the directly enrolled, prior-CAM2029 and prior-placebo subgroups



Data include the 24-week placebo period before the prior-placebo group switched to CAM2029; the group is also included in the overall population.
*Score range: 0–100.[8]

Supplementary Figure 5: SIAQ* scores change from baseline to week 20 and week 48 in the directly enrolled, prior-CAM2029 and prior-placebo subgroups



Patients assessed at week 48 or closest visit. Data include the 24-week placebo period before the prior-placebo group switched to CAM2029; the group is also included in the overall population. Baseline is defined as the last pre-treatment values before the first self-administration.
*Score range: 0–10.[9]

Supplementary Table 1: Patient demographics and medical histories at screening

	Directly enrolled (N=81)	Prior-CAM2029 (N=36)	Prior-placebo (N=18)	Overall (N=135)
Mean age, years (SD)	51.8 (11.4)	56.6 (10.5)	50.3 (15.4)	52.9 (11.9)
Sex, n (%)				
Female	48 (59.3)	18 (50.0)	10 (55.6)	76 (56.3)
Male	33 (40.7)	18 (50.0)	8 (44.4)	59 (43.7)
Mean time since diagnosis, years (SD)	10.7 (7.4)	11.1 (7.2)	12.3 (10.9)	11.1 (7.9)
Prior pituitary surgery, n (%)	70 (86.4)	32 (88.9)	17 (94.4)	119 (88.1)
Prior medications,* n (%)	81 (100)	36 (100)	18 (100)	135 (100)
Octreotide	64 (79.0)	21 (58.3)	12 (66.7)	97 (71.9)
Lanreotide	25 (30.9)	18 (50.0)	7 (38.9)	50 (37.0)
Cabergoline	4 (4.9)	4 (11.1)	1 (5.6)	9 (6.7)
Bromocriptine	2 (2.5)	0	1 (5.6)	3 (2.2)
Pegvisomant	1 (1.2)	1 (2.8)	1 (5.6)	3 (2.2)
Pasireotide	1 (1.2)	1 (2.8)	0	2 (1.5)
IGF-I ≤ULN,† n (%)	12 (14.8)	33 (91.7)	17 (94.4)	62 (45.9)

*At any time prior to enrolment; †At SoC baseline. IGF-I, insulin-like growth factor I; SD, standard deviation; SoC, standard of care; ULN, upper limit of normal per age and sex.

Supplementary Table 2: Summary of adverse events (AEs) reported in ACROINNOVA 2

n (%)	Directly enrolled (N=81)	Prior-CAM2029 (N=36)	Prior-placebo (N=18)	Overall (N=135)
Any AE	56 (69.1)	34 (94.4)	12 (66.7)	102 (75.6)
Any CAM2029-related AE	39 (48.1)	23 (63.9)	12 (66.7)	74 (54.8)
Any AE of Grade				
1	51 (63.0)	32 (88.9)	11 (61.1)	94 (69.6)
2	22 (27.2)	19 (52.8)	6 (33.3)	47 (34.8)
3	9 (11.1)	7 (19.4)	1 (5.6)	17 (12.6)
Any SAE	6 (7.4)	8 (22.2)	1 (5.6)	15 (11.1)
Any CAM2029-related SAE	0	0	1 (5.6)*	1 (0.7)
Any AE leading to discontinuation of CAM2029	2 (2.5)	0	0	2 (1.5)
Any AE leading to dose reduction	0	0	1 (5.6)	1 (0.7)
Any injection-site AE†	32 (39.5)	19 (52.8)	9 (50.0)	60 (44.4)

AEs refer to TEAEs. Only TEAEs and SAEs reported from the first administration of CAM2029 until week 52 are included. *Cholelithiasis (Grade 2; resolved); †AEs included injection site bruising, dermatitis, discomfort, erythema, extravasation, haematoma, haemorrhage, hypertrophy, inflammation, induration, mass, nodule, oedema, pain, pruritus, reaction and swelling. SAE, serious adverse event; TEAE, treatment-emergent adverse event.

Supplementary Table 3: AEs by preferred term reported in ACROINNOVA 2

AE by preferred term reported in **≥5% of patients** in any group and **≥3 patients** overall, n (%)	Directly enrolled (N=81)	Prior-CAM2029 (N=36)	Prior-placebo (N=18)	Overall (N=135)
Injection site AE*	32 (39.5)	19 (52.8)	9 (50.0)	60 (44.4)
COVID-19	9 (11.1)	9 (25.0)	2 (11.1)	20 (14.8)
Headache	12 (14.8)	7 (19.4)	0	19 (14.1)
Arthralgia	7 (8.6)	10 (27.8)	0	17 (12.6)
Diarrhoea	8 (9.9)	2 (5.6)	2 (11.1)	12 (8.9)
Cholelithiasis	3 (3.7)	0	4 (22.2)	7 (5.2)
Abdominal pain	3 (3.7)	2 (5.6)	1 (5.6)	6 (4.4)
Abdominal pain upper	2 (2.5)	3 (8.3)	1 (5.6)	6 (4.4)
Glucose tolerance impaired	5 (6.2)	1 (2.8)	0	6 (4.4)
Back pain	1 (1.2)	3 (8.3)	0	4 (3.0)
Influenza	0	3 (8.3)	1 (5.6)	4 (3.0)
Nausea	2 (2.5)	2 (5.6)	0	4 (3.0)
Pruritus	1 (1.2)	3 (8.3)	0	4 (3.0)
Haemangioma of liver	0	3 (8.3)	0	3 (2.2)
Sinusitis	1 (1.2)	2 (5.6)	0	3 (2.2)

Table shows treatment-emergent AEs. AEs refer to all events from first CAM2029 administration in ACROINNOVA 1 or 2 until week 52. *In directly enrolled patients, injection site AEs reported included bruising, dermatitis, erythema, extravasation, haematoma, haemorrhage, hypertrophy, induration, mass, nodule, oedema, pain, pruritus and swelling. In prior-CAM2029 patients, injection site AEs included bruising, discomfort, erythema, induration, mass, nodule, pain, pruritus, reaction and swelling. In prior-placebo patients, injection site AEs reported included bruising, erythema, haematoma, hypertrophy, inflammation, mass, nodule, pain and pruritus.

References

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