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PROPRIETARY DRUG NAME®/GENERIC DRUG NAME: Enbrel® / Etanercept

PROTOCOL NO.: 0881A6-3326 (B1801009)

PROTOCOL TITLE: A 3 Month, Randomized, Open Label, Parallel Group, Descriptive Study to Explore and Compare Perceptions and Satisfaction for Two Different Delivery Mechanisms for Etanercept (Etanercept Auto-Injector and the Etanercept Prefilled Syringe) in Patients With Psoriasis

Study Centers: A total of 71 centers took part in the study and randomized subjects; 3 each in Finland, Norway and Netherlands, 2 in Denmark, 4 in Sweden, 5 in Greece, 6 in Belgium, 7 in Spain, 10 in France and 28 in Germany.

Study Initiation Date and Primary Completion Date: 18 July 2007 to 22 April 2009.

Phase of Development: Phase 3

Study Objectives:

Primary Objective: The primary objective of the study was to compare subject satisfaction with 2 different delivery devices for etanercept (ETN) (prefilled syringe [PFS] and auto injector [AI]) after 12 weeks of use in subjects with psoriasis, using a 10-point scale from totally dissatisfied to totally satisfied.

Secondary Objectives: The secondary objectives of the study were:

- To compare subject satisfaction with the 2 different delivery devices by asking "Are you satisfied with your injection device?" using a dichotomous "yes" or "no".
- To identify subject and device attributes associated with subject satisfaction.
- To compare device attributes and subject perceptions with 2 different delivery devices for ETN after 4 and 12 weeks of use.
- To identify subject attributes associated with subject perceptions.

METHODS

Study Design: This was a multicenter, open-label, randomized, 2-arm parallel-design Phase 3 study. Eligible subjects were randomized to receive treatment with ETN 50 mg

twice-weekly subcutaneous (SC) either as PFS or AI. Subjects participated in the study for approximately 5 months (20 weeks). This included the screening period of up to 6 weeks, the treatment period of 12 weeks, and the 2 weeks follow-up telephone call to assess for adverse events (AEs).

The study flowchart is described in further detail in Table 1.

Table 1. Study Flowchart

Study Procedures	Week -6/-1	Week 1	Week 4	Week 12/ET	
	Day -42/-1	Day 1	Day 28	Day 84	Day 99
			±4 Days	±7 Days	±3 Days
	Screening	Treatment			Phone Call
Visit ID (For Sponsor Use Only)	**0**	**1**	**2**	**3**	
Informed consent	X				
Demographics, educational status	X				
Injection and self-injection experience	X				
Medical and psoriasis history, prior medication, weight	X				
Physical examination, vital signs[a]	X	X		X	
Joint symptoms - co morbidities	X				
TB test[b]	X				
Blood test, urinalysis (safety baseline)	X				
Pregnancy test[c]	X	X[c]		X	
Randomization		X			
Instruction[d]		X			
DLQI		X	X	X	
Psoriasis efficacy assessments	X[e]	X[e]	X[e]	X[e]	
General health (VAS)	X	X	X	X	
Patient Activation Measure short form		X			
Hospital Anxiety Depression Scale		X			
Subject satisfaction[f]		X[f]	X	X	
Device attributes and subject perceptions[f]		X[f]	X	X	
Anxiety measure (SF-STAI)[f]		X[f]	X	X	
Administer etanercept[g]		X[g]----------X			
Device query monitoring		X----------X			
Compliance		X----------X			
Concomitant medications	X	X	X	X	
Adverse events[h]	X	X	X	X	X[h]

DLQI = Dermatology Life Quality Index; SF-STAI = Short form State-Trait Anxiety Inventory; TB = tuberculosis; VAS = visual analog scale.

a. Sitting blood pressure and pulse rate.
b. Required according to local license and guidelines.
c. Serum test at screening. Urine test at Baseline, if positive serum test.

Table 1. Study Flowchart

d. Includes recording of time required for instruction.
e. PASI, plus Subject Global Assessment of Psoriasis (VAS) and Physician Global Assessment (PGA).
f. Via subject questionnaire. At Visit 1, the questionnaires had to be filled after the instruction in the device and the first administration.
g. First administration by subject.
h. Investigators were requested to contact each subject via telephone for the assessment of adverse events approximately 15 days after the last intake of study medication.

Number of Subjects (Planned and Analyzed): The number of subjects planned for this study was 448. Of the 473 screened subjects, 421 subjects were randomized to receive test article, including 207 subjects in the AI group and 214 subjects in the PFS group.

Diagnosis and Main Criteria for Inclusion: Subjects eligible to participate in this study were 18 years old or older, with moderate to severe plaque psoriasis who failed to respond, or who had a contraindication to, or were intolerant to other systemic therapy including cyclosporine, methotrexate or psoralen plus ultraviolet A therapy (PUVA). They had to be eligible for treatment with ETN according to Summary of Product Characteristics and applicable local guidelines and to be willing and able to self-inject ETN or have a carer to perform the injections. All women of childbearing potential had to have a negative serum β-human chorionic gonadotropin (β-HCG) pregnancy test at screening. Sexually active men and women had to use a reliable form of contraception during the study. Subjects with prior experience of biologics and anti-tumor necrosis factor (TNF) treatment for their psoriasis including ETN, subjects with sepsis or at risk of sepsis, subjects with current or recent infections (including chronic or localized), subjects with sensitivity to latex and subjects vaccinated with live vaccine in the previous 4 weeks, or expected to require such vaccination during the course of the study, were excluded from the study.

Study Treatment: ETN was supplied by the Sponsor as a sterile solution in either a PFS or an AI containing 50 mg of ETN. All subjects received 2 SC injections per week at approximately the same time of day (±4 hours) and on the same day of the week. Injections could be administered in the abdomen, thigh, or upper arm. The location of injections had to be rotated with each dose. The duration of treatment was 12 weeks.

Efficacy Endpoints:

Primary Efficacy Endpoint: The primary efficacy endpoint was subject satisfaction at Visit 3 (Week 12). This endpoint was measured by asking subjects: "How satisfied are you with your injection device?" using a 0-10 point scale from totally dissatisfied to totally satisfied. If there was no evaluation available after the first administration of test agent, the subject was not considered for the analysis of the primary endpoint.

Secondary Efficacy Endpoints:

- Subject satisfaction was also determined by asking "Are you satisfied with your injection device?" using a dichotomous Yes or No.

- Subject attributes associated with subject satisfaction. The influence of the following attributes on subject satisfaction was investigated:

  Subject Characteristics:

  - Age, sex, and social-educational status as recorded in the case report form (CRF).

  - Psychological status as determined by the Hospital Anxiety Depression (HAD) Scale.

  - Willingness to self-manage as determined by the Patient Activation Measure (PAM) Short Form.

  - Prior self-injection experience as recorded in the CRF.

  Psoriasis Characteristics:

  - Duration of disease as calculated from the date of diagnosis, as recorded in the CRF.

  - Disease activity as determined by the Physician Global Assessment (PGA) of psoriasis (0= clear, 1= almost clear, 2= mild, 3= moderate, 4= marked, or 5= severe) and by calculating the Psoriasis Area and Severity Index (PASI).

  - Subject's assessment of general health as measured on a visual analogue scale (VAS) of 100 mm.

  - Subject Global Assessment of Psoriasis as measured on a VAS of 100 mm.

  - Dermatology Life Quality Index (DLQI).

  - Co-morbidities as recorded in the CRF.

  - Prior systemic treatment for psoriasis.

  - Prior injection experience as recorded on the CRF.

- Device attributes and subject perceptions measured by asking subjects the following concepts and questions and evaluating them with a Likert scale:

  - Ease of use and convenience of injection device operation.

  - Confidence in the device.

- Presence or absence of fear of the device.
- Device characteristics.
- Side effects related to administration.
- The Short Form State-Trait Anxiety Inventory (SF STAI)

- Subject attributes associated with subject perception. The same attributes as listed above for their influence on subject satisfaction were also investigated for their influence on subject perception.

Safety Evaluations: The safety of ETN was determined using the following assessments: monitoring of AEs, vital signs, physical examinations and premature withdrawal.

Statistical Methods:

Analysis Populations: There were 3 populations analyzed for this study:

- The modified Intent-To-Treat (mITT) set included all randomized subjects who received at least 1 injection of test article and who had at least 1 available evaluation after the first administration of test article.
- The Per-Protocol (PP) set included subjects from mITT who completed the study with no major protocol violation.
- The Safety set included all randomized subjects who received at least 1 injection of test article.

The efficacy assessments were done according to the randomization group regardless of the device actually used. Missing or incomplete data were not replaced, except in case of last observation carried forward (LOCF) analysis where missing values on Day 84 were replaced by the last values obtained during the on-therapy study interval.

Non-inferiority of AI over PFS was assessed on the subject satisfaction after 12 weeks of use in the PP and mITT sets. The lower limit of the 95% confidence interval (CI) of the difference between AI and PFS groups, derived from a repeated-measures analysis of variance (ANOVA) using a mixed linear model, was compared to a non-inferiority margin of -1. In case of non-inferiority of AI, superiority of AI over PFS was investigated.

Generalized estimating equations (GEE) models were used to analyze the proportion of satisfied subjects as well as the subject perception. A multiple correspondence analysis (MCA) and ascending hierarchical classification (AHC) were performed to identify subject attributes that are associated with subject perceptions.

RESULTS

Subject Disposition and Demographic Characteristics: A total of 473 subjects were screened and 421 subjects were randomly assigned on a 1 to 1 basis to receive test article, including 207 subjects in the AI group and 214 subjects in the PFS group. One (1) subject used AI instead of PFS as assigned by the randomization. This subject was therefore analyzed in the PFS group for efficacy and in the AI group for safety. As 3 subjects were withdrawn from the study just after randomization because of protocol deviation without receiving any injection, the safety population included 418 subjects, of whom 207 subjects used AI and 211 subjects used PFS. One (1) subject who received at least 1 injection of test article was withdrawn from the study because of AE 7 days after randomization and had no evaluation after the first injection. Thus, the mITT population included 417 subjects (ie, 206 and 211 subjects in the AI and PFS groups, respectively), and the PP population included 380 subjects who completed the study with no major protocol deviation, 190 in each randomization group (Table 2).

Table 2. Analysis Populations

	AI	PFS	Total
All screened subjects			473
All randomized subjects	207	214	421
mITT	206	211	417
PP set	190	190	380
Safety set	207	211	418

AI = auto injector; mITT = Modified intent to treat; PFS = pre filled syringe; PP = per protocol.

Table 3 summarizes the subject disposition for the study. Among the 35 subjects prematurely withdrawn from the study, 19 subjects withdrew because of an AE, 7 subjects withdrew on their own request, and 5 subjects had a protocol deviation.

Table 3. Subject Disposition, All Randomized Subjects

Conclusion Status Reason	AI N=207	PFS N=214	Total N=421
Completed	192 (92.8%)	194 (90.7%)	386 (91.7%)
Prematurely withdrawn	15 (7.2%)	20 (9.3%)	35 (8.3%)
Adverse event	5 (2.4%)	14 (6.5%)	19 (4.5%)
Subject request	6 (2.9%)	1 (0.5%)	7 (1.7%)
Protocol deviation	2 (1.0%)	3 (1.4%)	5 (1.2%)
Lost to follow-up	2 (1.0%)	-	2 (0.5%)
Other	-	2 (0.9%)	2 (0.5%)

AI = auto injector; PFS = pre filled syringe; N = total number of subjects.

The summary of the subject demography and Baseline characteristics is presented in Table 4. For the mITT population, the demographic and other baseline characteristics were comparable between the 2 groups. Age of subjects ranged from 19 to 81 years, with a mean age at baseline of 46 years. The gender distribution was 67% men and 33% women.

Table 4. Demographic and Baseline Characteristics, mITT Population

Characteristics	AI N=206	PFS N=211	Total N=417
Age (years)			
n	206	211	417
Mean (SD)	46.1 (13.2)	46.1 (13.4)	46.1 (13.3)
Median	47.0	44.0	45.0
Gender			
n	206	211	417
Men	135 (65.5%)	146 (69.2%)	281 (67.4%)
Women	71 (34.5%)	65 (30.8%)	136 (32.6%)
Socio-educational level			
n	206	211	417
Reading/writing capacity	65 (31.6%)	70 (33.2%)	135 (32.4%)
High school/baccalaureate level	104 (50.5%)	99 (46.9%)	203 (48.7%)
University level	37 (18.0%)	42 (19.9%)	79 (18.9%)

AI = auto injector; mITT = modified Intent-to-Treat; N = total number of subjects; n = number of evaluable subjects; PFS = pre filled syringe; SD = standard deviation.

Efficacy Results:

Primary Endpoint: The subject satisfaction with the injection device evaluated on a 0 (totally dissatisfied) to 10 point (totally satisfied) scale is described for the mITT and PP populations at Week 12 (Day 84) in Table 5.

Table 5. Subject Satisfaction at Week 12 (Day 84), mITT and PP Populations

	AI N=206	PFs N=211
mITT population		
n	198	197
Mean (SD)	8.9 (1.9)	7.6 (2.6)
Median	10.0	9.0
Min, max	0.0, 10.0	0.0, 10.0
PP population		
n	189	186
Mean (SD)	9.0 (1.9)	7.5 (2.6)
Median	10.0	8.5
Min, max	0.0, 10.0	0.0, 10.0

AI = auto injector; mITT = modified Intent-to-Treat; N = total number of subjects; n = number of evaluable subjects; PFS = pre filled syringe; PP = per protocol; SD = standard deviation.

In the mITT population, the estimate of the mean difference between the 2 groups was quite stable throughout the study, with better satisfaction for AI group of subjects than PFS group of subjects. This difference (2-sided 95% CI) was 1.32 (0.87; 1.77) at Week 12 (Day 84). The lower bound of the 2-sided 95% CI on the mean difference in subject satisfaction on Day 84 was greater than the pre-defined clinically relevant non-inferiority margin of -1. Therefore, the difference between the 2 groups was statistically significantly higher than -1. Results were similar in the PP population (Table 6).

Table 6. Subject Satisfaction-Estimated Mean Differences, mITT and PP Set

	Difference (AI-PFS)		
	Mean (SE)	**95%CI**	**p-Value**
mITT set			
Day 84	1.32 (0.23)	(0.87; 1.77)	<0.001
PP Set			
Day 84	1.41 (0.23)	(0.95; 1.87)	<0.001

AI = auto injector; CI = confidence interval; mITT = modified Intent-to-Treat; PFS = pre filled syringe; PP = per protocol; SE = standard error.

Secondary Endpoints**:**

Proportion of Satisfied Subjects: The proportion of subjects satisfied with their injection device (Table 7) remained quite stable between baseline and Day 84. In the AI group, 99.5% of the subjects were satisfied at baseline after the training and this proportion was 98.4% on Day 84. In the PFS group, 92.5% of the subjects were satisfied at baseline after the training and this proportion was 88.8% on Day 84.

In the mITT population, the estimate of the odds ratio (2-sided 95% CI) between the 2 groups at Week 12 (Day 84) was 7.88 (2.26; 27.44); thus, the probability of being satisfied with the device was greater in the AI group than in the PFS group. The same conclusions were obtained for the other time-points (Table 8).

Table 7. Proportion of Satisfied Subjects – Observed Data - mITT Set

Visit	AI N=206	PFS N=211
Baseline (after the training)		
n	198	199
Yes	197 (99.5%)	184 (92.5%)
No	1 (0.5%)	15 (7.5%)
Missing data	8	12
Baseline (after the first injection)		
n	196	196
Yes	193 (98.5%)	177 (90.3%)
No	3 (1.5%)	19 (9.7%)
Missing data	10	15
Day 28		
n	190	190
Yes	188 (98.9%)	171 (90.0%)
No	2 (1.1%)	19 (10.0%)
Missing data	16	21
Day 84		
n	188	179
Yes	185 (98.4%)	159 (88.8%)
No	3 (1.6%)	20 (11.2%)
Missing data	18	32
Last observation		
n	206	210
Yes	203 (98.5%)	186 (88.6%)
No	3 (1.5%)	24 (11.4%)
Missing data	0	1

AI = auto injector; mITT = modified Intent-to-Treat; N = total number of subjects; n = number of evaluable subjects; PFS = pre filled syringe.

Table 8. Proportion of Satisfied Subjects-Estimated Odds Ratios, mITT Set

	Odds Ratio AI/PFS		
	Estimate	95% CI	p-Value
Baseline (after the training)	16.12	(2.05; 126.9)	0.008
Baseline (after the first injection)	6.80	(1.94; 23.82)	0.003
Day 28	11.25	(2.44; 51.83)	0.002
Day 84	7.88	(2.26; 27.44)	0.001
Last observation	8.73	(2.59; 29.47)	<0.001

AI = auto injector; mITT = modified Intent-to-Treat; N = total number of subjects; n = number of evaluable subjects; PFS = pre filled syringe; PP = per protocol; SD = standard deviation

Influence of Subject Attributes on Satisfaction: Mean satisfaction according to subject attributes is summarized in Table 9. The results of the statistical analysis of the influence of subject attributes on satisfaction is summarized in Table 10.

Table 9. Influence of Subject Attributes on the Mean (SD) Satisfaction at Week 12 (Day 84) – mITT Set

	AI N=206	PFS N=211
Age		
≤36 years	8.94 (1.95)	7.18 (2.62)
>36 years to 45 years	8.91 (1.52)	7.41 (2.39)
>45 years to 55 years	9.06 (1.89)	7.93 (2.90)
>55 years	8.82 (2.12)	8.07 (2.49)
Gender		
Male	9.07 (1.59)	7.60 (2.57)
Female	8.70 (2.31)	7.68 (2.66)
Socio-educational level		
Reading/writing capacity	9.22 (1.62)	7.96 (2.49)
High school/Baccalaureate level	8.80 (1.97)	7.55 (2.73)
University level	8.89 (2.01)	7.24 (2.39)
HAD anxiety subscale score at baseline		
≤4	8.98 (1.77)	7.83 (2.42)
>4 to 7	9.17 (1.48)	7.49 (2.65)
>7 to 10	8.89 (2.27)	7.42 (2.88)
>10	8.73 (1.92)	7.74 (2.44)
HAD depression subscale score at baseline		
≤3	8.68 (2.19)	7.93 (2.39)
>3 to 5	9.15 (2.04)	7.57 (2.42)
>5 to 8	9.20 (1.02)	7.50 (2.50)
>8	8.90 (1.92)	7.31 (3.09)
PAM at baseline		
≤47.4	8.73 (1.90)	7.05 (2.76)
>47.4 to 56.4	9.41 (1.14)	7.94 (2.17)
>56.4 to 68.5	8.28 (2.68)	7.94 (2.70)
>68.5	9.11 (1.73)	7.93 (2.49)
Prior injection experience		
Yes	9.05 (1.66)	7.70 (2.58)
No	8.88 (2.01)	7.56 (2.61)
Prior self-injection experience		
Yes	8.89 (1.92)	7.53 (2.74)
No	8.96 (1.87)	7.66 (2.53)
Duration of psoriasis at screening		
≤11 years	9.09 (1.56)	7.90 (2.22)
>11 years to 19 years	8.74 (1.99)	7.17 (2.67)
>19 years to 28 years	9.12 (1.65)	7.72 (2.76)
>28 years	8.82 (2.29)	7.76 (2.66)
PGA of psoriasis at screening (0-5)		
≤3	8.87 (1.91)	7.51 (2.48)
>3 to 4	8.96 (1.97)	7.79 (2.79)
>4	9.62 (0.51)	7.83 (3.06)

Table 9. Influence of Subject Attributes on the Mean (SD) Satisfaction at Week 12 (Day 84) – mITT Set

	AI N=206	PFS N=211
PASI at screening (0-72)		
≤11.2	8.41 (2.26)	7.45 (2.33)
>11.2 to 16.2	9.17 (1.97)	7.81 (2.78)
>16.2 to 21.9	9.11 (1.66)	7.67 (2.49)
>21.9	9.00 (1.57)	7.67 (2.79)
Subject's global assessment of psoriasis activity at screening		
≤63	8.79 (1.54)	7.96 (2.18)
>63 to 76	9.02 (1.91)	7.51 (2.80)
>76 to 88	8.71 (2.19)	7.70 (2.55)
>88	9.20 (1.90)	7.33 (2.78)
Subject's global assessment of general health at screening		
≤48	8.54 (2.36)	7.06 (3.26)
>48 to 67.25	9.15 (1.24)	7.79 (2.61)
>67.25 to 84	8.70 (2.22)	7.72 (2.06)
>84	9.42 (1.20)	7.85 (2.44)
DLQI at baseline (0-30)		
≤8	8.82 (2.18)	7.82 (2.23)
>8 to 13	8.94 (1.70)	7.71 (2.53)
>13 to 18	8.81 (2.04)	7.37 (2.72)
>18	9.14 (1.67)	7.55 (2.87)
Current tobacco usage		
Yes	8.94 (2.11)	7.40 (2.60)
No	8.95 (1.70)	7.76 (2.58)
Current use of alcoholic beverages		
Yes	8.96 (1.93)	8.06 (2.06)
No	8.94 (1.84)	7.33 (2.86)
Prior systemic and/or topical medication for psoriasis		
Yes	8.95 (1.87)	7.61 (2.59)
No	NE	9.00 (NE)

AI = auto injector; DLQI = Dermatology Life Quality Index; HAD = Hospital Anxiety Depression; mITT = modified Intent-to-Treat; N = total number of subjects; NE = not evaluable; PAM = Patient Activation Measure; PASI = Psoriasis Area and Severity Index; PFS = pre filled syringe; PGA = Physician Global Assessment; SD = standard deviation.

Table 10. Influence of Subject Attributes on Satisfaction at Endpoint – Univariate Analysis – mITT Set

Explanatory Variable Interpretation	Estimate (95% CI)	p-Value
Randomization group		<0.001
AI	1.33 (0.89; 1.76)	
PFS (reference)	0.00	
Age		0.045
By 10 unit increment	0.17 (0.00; 0.34)	
Subject's global assessment of general health at Screening		0.045
By 10 unit increment	0.09 (0.00; 0.18)	
Current use of alcoholic beverages		0.061
Yes	0.44 (-0.02; 0.90)	
No (reference)	0.00	
PAM at baseline		0.123
By 10 unit increment	0.13 (-0.04; 0.30)	
PGA of psoriasis at screening (0-5)		0.170
By 1 unit increment	0.22 (-0.09; 0.53)	
Socio-educational level		0.195
Reading/writing capacity (reference)	0.00	
High school/baccalaureate level	-0.38 (0.89; 0.14)	
University level	-0.55 (-1.21; 0.11)	
PASI at screening (0-72)		0.211
By 1 unit increment	0.02 (-0.01; 0.04)	
HAD depression subscale score at Baseline		0.287
By 5 unit increment	-0.16 (0.46; 0.14)	
Prior self-injection experience		0.359
Yes	-0.24 (-0.76; 0.28)	
No (reference)	0.00	
HAD anxiety subscale score at Baseline		0.493
By 5 unit increment	-0.09 (0.36; 0.17)	
Current tobacco usage		0.531
Yes	-0.15 (0.61; 0.32)	
No (reference)	0.00	
Duration of psoriasis at screening		0.693
By 5 unit increment	0.02 (-0.08; 0.12)	
Gender		0.707
Male (reference)	0.00	
Female	-0.09 (-0.58; 0.39)	
Prior injection experience		0.713
Yes	0.09 (-0.37; 0.55)	
No (reference)	0.00	
Prior systemic and/or topical medication for psoriasis		0.759
Yes	-0.73 (-5.37; 3.92)	
No (reference)	0.00	
Who performed the injection at endpoint		0.811
Subject (reference)	0.00	
Other	-0.12 (-1.09; 0.85)	
Subject's global assessment of psoriasis activity at screening		0.913
By 10 unit increment	-0.01 (-0.12; 0.11)	
Educational or professional activity in the health area		0.923
No (reference)	0.00	
Yes	0.06 (-1.16; 1.28)	
DLQI at Baseline (0-30)		0.968
By 5 unit increment	-0.00 (-0.17; 0.17)	

Table 10. Influence of Subject Attributes on Satisfaction at Endpoint – Univariate Analysis – mITT Set

AI = auto injector; CI = confidence interval; DLQI = Dermatology Life Quality Index; HAD = Hospital Anxiety Depression; mITT = modified Intent-to-Treat; PAM = Patient Activation Measure; PASI = Psoriasis Area and Severity Index; PFS = pre filled syringe; PGA = Physician Global Assessment.

Device Attributes and Subject Perceptions Questionnaire: Device attributes and subject perceptions were evaluated with 0 to 4 Likert scales, scales numbers interpretation varying between questions.

Ease of Use of Injection Device: Results of the device attributes and subject perceptions questionnaire for Q1 to Q5, Q6 and Q7 are summarized by visit in Table 11, Table 12 and Table 13, respectively. In both groups, evaluation of perceptions of subjects concerning easiness of use of the device was slightly better for Q1 and Q4 on Day 84 compared to baseline after the training, and it was quite stable for Q2, Q5, Q6 and Q7. For Q3, evaluation was slightly better in the PFS group and slightly worse in the AI group on Day 84 than after the training. Odds ratios of the 2 subject groups (AI/PFS; Table 14) were statistically significantly different from 1 at all time-points for Q2, Q5 and Q6; at all time-points except after the first injection for Q1; only after the training for Q3; and were never significant for Q4 and Q7. All odds-ratios significantly different from 1 indicated that group of subjects using AI found their device easier to use than group of subjects using PFS, except the odds-ratio of Q2 after the first injection, which indicated a greater easiness to learn to use within the group of subjects using PFS compared to the group of subjects using AI.

Table 11. Device Attributes and Subject Perceptions Questionnaire Questions 1 to 5: Observed Data – mITT Set

Visit	Question 1		Question 2		Question 3		Question 4		Question 5	
	AI N=206	PFS N=211	AI N=206	PFS N=211	AI N=206	PFS N=211	AI N=206	PFS N=211	AI N=206	PFS N=211
Baseline-after the training										
n	202	208	201	208	198	205	201	207	199	206
Very easy	134 (66.3%)	92 (44.2%)	154 (76.6%)	132 (63.5%)	158 (79.8%)	141 (68.8%)	140 (69.7%)	129 (62.3%)	134 (67.3%)	100 (48.5%)
1	50 (24.8%)	72 (34.6%)	39 (19.4%)	57 (27.4%)	25 (12.6%)	47 (22.9%)	44 (21.9%)	62 (30.0%)	48 (24.1%)	72 (35.0%)
2	15 (7.4%)	33 (15.9%)	7 (3.5%)	13 (6.3%)	12 (6.1%)	9 (4.4%)	13 (6.5%)	10 (4.8%)	15 (7.5%)	24 (11.7%)
3	3 (1.5%)	7 (3.4%)	1 (0.5%)	5 (2.4%)	3 (1.5%)	2 (1.0%)	3 (1.5%)	4 (1.9%)	2 (1.0%)	8 (3.9%)
Very difficult	0 (0.0%)	4 (1.9%)	0 (0.0%)	1 (0.5%)	0 (0.0%)	6 (2.9%)	1 (0.5%)	2 (1.0%)	0 (0.0%)	2 (1.0%)
Day 28										
n	180	190	179	189	173	189	175	189	179	190
Very easy	126 (70.0%)	94 (49.5%)	137 (76.5%)	122 (64.6%)	131 (75.7%)	142 (75.1%)	124 (70.9%)	123 (65.1%)	114 (63.7%)	83 (43.7%)
1	42 (23.3%)	62 (32.6%)	32 (17.9%)	54 (28.6%)	29 (16.8%)	34 (18.0%)	40 (22.9%)	50 (26.5%)	45 (25.1%)	59 (31.1%)
2	6 (3.3%)	20 (10.5%)	4 (2.2%)	6 (3.2%)	5 (2.9%)	5 (2.6%)	5 (2.9%)	8 (4.2%)	14 (7.8%)	33 (17.4%)
3	2 (1.1%)	12 (6.3%)	1 (0.6%)	4 (2.1%)	4 (2.3%)	5 (2.6%)	2 (1.1%)	5 (2.6%)	3 (1.7%)	12 (6.3%)
Very difficult	4 (2.2%)	2 (1.1%)	5 (2.8%)	3 (1.6%)	4 (2.3%)	3 (1.6%)	4 (2.3%)	3 (1.6%)	3 (1.7%)	3 (1.6%)
Day 84										
n	194	195	189	195	187	195	194	192	193	196
Very easy	149 (76.8%)	109 (55.9%)	154 (81.5%)	126 (64.6%)	150 (80.2%)	148 (75.9%)	147 (75.8%)	137 (71.4%)	133 (68.9%)	101 (51.5%)
1	35 (18.0%)	54 (27.7%)	26 (13.8%)	54 (27.7%)	21 (11.2%)	34 (17.4%)	40 (20.6%)	38 (19.8%)	51 (26.4%)	55 (28.1%)
2	4 (2.1%)	18 (9.2%)	4 (2.1%)	9 (4.6%)	6 (3.2%)	9 (4.6%)	4 (2.1%)	9 (4.7%)	4 (2.1%)	27 (13.8%)
3	4 (2.1%)	9 (4.6%)	2 (1.1%)	2 (1.0%)	4 (2.1%)	2 (1.0%)	0 (0.0%)	6 (3.1%)	1 (0.5%)	10 (5.1%)
Very difficult	2 (1.0%)	5 (2.6%)	3 (1.6%)	4 (2.1%)	6 (3.2%)	2 (1.0%)	3 (1.5%)	2 (1.0%)	4 (2.1%)	3 (1.5%)
Last observation										
n	202	207	201	207	202	210	204	210	203	209
Very easy	153 (75.7%)	115 (55.6%)	161 (80.1%)	134 (64.7%)	161 (79.7%)	161 (76.7%)	155 (76.0%)	151 (71.9%)	140 (69.0%)	105 (50.2%)
1	36 (17.8%)	58 (28.0%)	26 (12.9%)	57 (27.5%)	23 (11.4%)	36 (17.1%)	42 (20.6%)	42 (20.0%)	52 (25.6%)	61 (29.2%)
2	4 (2.0%)	19 (9.2%)	6 (3.0%)	10 (4.8%)	6 (3.0%)	9 (4.3%)	4 (2.0%)	9 (4.3%)	6 (3.0%)	29 (13.9%)
3	5 (2.5%)	9 (4.3%)	5 (2.5%)	2 (1.0%)	5 (2.5%)	2 (1.0%)	0 (0.0%)	6 (2.9%)	1 (0.5%)	11 (5.3%)
Very difficult	4 (2.0%)	6 (2.9%)	3 (1.5%)	4 (1.9%)	7 (3.5%)	2 (1.0%)	3 (1.5%)	2 (1.0%)	4 (2.0%)	3 (1.4%)

Table 11. Device Attributes and Subject Perceptions Questionnaire Questions 1 to 5: Observed Data – mITT Set

Q1: Overall, how easy was it to perform an injection with this device?
Q2: How easy was it to learn how to use the device?
Q3: How easy is it to dispose of the device?
Q4: How easy is it to know when the injection is complete?
Q5: How easy is it to hold the device whilst injecting?
AI = auto injector; mITT = modified Intent-to-Treat; N = total number of subjects; n = number of evaluable subjects; PFS = pre filled syringe.

Table 12. Device Attributes and Subject Perceptions Questionnaire Question 6: Observed Data – mITT Set

Visit	Question 6	
	AI N=206	PFS N=211
Baseline-after the training		
n	197	208
None	158 (80.2%)	131 (63.0%)
1	26 (13.2%)	44 (21.2%)
2	6 (3.0%)	20 (9.6%)
3	3 (1.5%)	10 (4.8%)
Extreme	4 (2.0%)	3 (1.4%)
Day 28		
n	176	188
None	144 (81.8%)	114 (60.6%)
1	18 (10.2%)	37 (19.7%)
2	7 (4.0%)	26 (13.8%)
3	7 (4.0%)	8 (4.3%)
Extreme	0 (0.0%)	3 (1.6%)
Day 84		
n	193	195
None	159 (82.4%)	125 (64.1%)
1	24 (12.4%)	45 (23.1%)
2	7 (3.6%)	15 (7.7%)
3	2 (1.0%)	7 (3.6%)
Extreme	1 (0.5%)	3 (1.5%)
Last observation		
n	204	210
None	168 (82.4%)	138 (65.7%)
1	25 (12.3%)	46 (21.9%)
2	8 (3.9%)	15 (7.1%)
3	2 (1.0%)	8 (3.8%)
Extreme	1 (0.5%)	3 (1.4%)

Q6: Did you feel any hand discomfort whilst using the device?
AI = auto injector; mITT = modified Intent-to-Treat; N = total number of subjects; n = number of evaluable subjects; PFS = pre filled syringe.

Table 13. Device Attributes and Subject Perceptions Questionnaire Question 7: Observed Data – mITT Set

Visit	Question 7	
	AI N=206	PFS N=211
Baseline-after the training		
n	200	206
<5	132 (66.0%)	129 (62.6%)
5-10	43 (21.5%)	56 (27.2%)
11-20	12 (6.0%)	14 (6.8%)
21-30	9 (4.5%)	7 (3.4%)
>30	4 (2.0%)	0 (0.0%)
Day 28		
n	180	189
<5	117 (65.0%)	121 (64.0%)
5-10	36 (20.0%)	41 (21.7%)
11-20	14 (7.8%)	16 (8.5%)
21-30	8 (4.4%)	10 (5.3%)
>30	5 (2.8%)	1 (0.5%)
Day 84		
n	192	196
<5	124 (64.6%)	132 (67.3%)
5-10	44 (22.9%)	40 (20.4%)
11-20	12 (6.3%)	12 (6.1%)
21-30	6 (3.1%)	7 (3.6%)
>30	6 (3.1%)	5 (2.6%)
Last observation		
n	204	210
<5	131 (64.2%)	143 (68.1%)
5-10	48 (23.5%)	43 (20.5%)
11-20	12 (5.9%)	12 (5.7%)
21-30	7 (3.4%)	7 (3.3%)
>30	6 (2.9%)	5 (2.4%)

Q7: How long does it take to perform the injection, including any preparation and disposal?
AI = auto injector; mITT = modified Intent-to-Treat; N = total number of subjects; n = number of evaluable subjects; PFS = pre filled syringe.

Table 14. Device Attributes and Subject Questionnaire Questions 1 to 7 -Estimated Odds Ratios, mITT Set

	Odds Ratio AI/PFS		p-Value
	Estimate	95% CI	
Question 1			
Baseline (after the training)	2.39	(1.63; 3.49)	<0.001
Day 28	2.43	(1.61; 3.67)	<0.001
Day 84	2.74	(1.78; 4.21)	<0.001
Last observation	2.51	(1.66; 3.80)	<0.001
Question 2			
Baseline (after the training)	1.88	(1.22; 2.89)	0.004
Day 28	1.73	(1.10; 2.72)	0.017
Day 84	2.34	(1.47; 3.73)	<0.001
Last observation	2.06	(1.32; 3.21)	0.001
Question 3			
Baseline (after the training)	1.68	(1.07; 2.64)	0.025
Day 28	1.02	(0.63; 1.64)	0.936
Day 84	1.22	(0.75; 1.99)	0.420
Last observation	1.12	(0.71; 1.79)	0.625
Question 4			
Baseline (after the training)	1.30	(0.86; 1.94)	0.210
Day 28	1.31	(0.85; 2.03)	0.227
Day 84	1.33	(0.84; 2.08)	0.220
Last observation	1.29	(0.84; 2.00)	0.249
Question 5			
Baseline (after the training)	2.18	(1.48; 3.21)	<0.001
Day 28	2.42	(1.62; 3.62)	<0.001
Day 84	2.35	(1.58; 3.51)	<0.001
Last observation	2.42	(1.64; 3.59)	<0.001
Question 6			
Baseline (after the training)	2.34	(1.50; 3.65)	<0.001
Day 28	2.96	(1.83; 4.77)	<0.001
Day 84	2.58	(1.62; 4.12)	<0.001
Last observation	2.45	(1.55; 3.86)	<0.001
Question 7			
Baseline (after the training)	1.09	(0.73; 1.62)	0.681
Day 28	1.01	(0.67; 1.54)	0.947
Day 84	0.90	(0.59; 1.36)	0.604
Last observation	0.85	(0.57; 1.27)	0.430

Q1: Overall, how easy was it to perform an injection with this device?
Q2: How easy was it to learn how to use the device?
Q3: How easy is it to dispose of the device?
Q4: How easy is it to know when the injection is complete?
Q5: How easy is it to hold the device whilst injecting?
Q6: Did you feel any hand discomfort whilst using the device?
Q7: How long does it take to perform the injection, including any preparation and disposal?
AI = auto injector; CI = confidence interval; mITT = modified Intent-to-Treat; PFS = pre filled syringe.

Convenience of Use of Injection Device: In both groups, evaluation of perceptions of subjects concerning convenience of use of devices was slightly better for Q8, Q9 and Q10 on Day 84 compared with baseline after the training. Results of the device attributes and subject perceptions questionnaire for Q8 to Q10 are summarized by visit in Table 15. Odds ratios for the 2 subjects groups (AI/PFS; Table 16) for these 3 questions were statistically not

significantly different from 1, indicating that group of subjects using AI found their device no more convenient to use than group of subjects using PFS.

Table 15. Device Attributes and Subject Perceptions Questionnaire Questions 8 to 10: Observed Data – mITT Set

Visit	Question 8		Question 9		Question 10	
	AI N=206	PFS N=211	AI N=206	PFS N=211	AI N=206	PFS N=211
Baseline-after the training						
n	203	208	202	208	203	208
Not at all	116 (57.1%)	134 (64.4%)	134 (66.3%)	137 (65.9%)	105 (51.7%)	98 (47.1%)
1	34 (16.7%)	37 (17.8%)	45 (22.3%)	45 (21.6%)	48 (23.6%)	55 (26.4%)
2	30 (14.8%)	20 (9.6%)	14 (6.9%)	16 (7.7%)	34 (16.7%)	32 (15.4%)
3	11 (5.4%)	8 (3.8%)	6 (3.0%)	5 (2.4%)	13 (6.4%)	20 (9.6%)
Very much	12 (5.9%)	9 (4.3%)	3 (1.5%)	5 (2.4%)	3 (1.5%)	3 (1.4%)
Day 28						
n	196	201	194	201	193	199
Not at all	145 (74.0%)	138 (68.7%)	150 (77.3%)	145 (72.1%)	101 (52.3%)	107 (53.8%)
1	32 (16.3%)	34 (16.9%)	35 (18.0%)	37 (18.4%)	46 (23.8%)	37 (18.6%)
2	6 (3.1%)	14 (7.0%)	4 (2.1%)	8 (4.0%)	34 (17.6%)	33 (16.6%)
3	8 (4.1%)	8 (4.0%)	3 (1.5%)	7 (3.5%)	9 (4.7%)	12 (6.0%)
Very much	5 (2.6%)	7 (3.5%)	2 (1.0%)	4 (2.0%)	3 (1.6%)	10 (5.0%)
Day 84						
n	195	197	195	198	195	197
Not at all	133 (68.2%)	131 (66.5%)	147 (75.4%)	137 (69.2%)	109 (55.9%)	101 (51.3%)
1	44 (22.6%)	33 (16.8%)	40 (20.5%)	39 (19.7%)	44 (22.6%)	40 (20.3%)
2	8 (4.1%)	17 (8.6%)	6 (3.1%)	13 (6.6%)	33 (16.9%)	36 (18.3%)
3	4 (2.1%)	7 (3.6%)	0 (0.0%)	4 (2.0%)	5 (2.6%)	12 (6.1%)
Very much	6 (3.1%)	9 (4.6%)	2 (1.0%)	5 (2.5%)	4 (2.1%)	8 (4.1%)
Last observation						
n	206	211	206	210	206	211
Not at all	139 (67.5%)	144 (68.2%)	155 (75.2%)	148 (70.5%)	115 (55.8%)	111 (52.6%)
1	46 (22.3%)	34 (16.1%)	42 (20.4%)	40 (19.0%)	46 (22.3%)	43 (20.4%)
2	8 (3.9%)	17 (8.1%)	7 (3.4%)	13 (6.2%)	34 (16.5%)	37 (17.5%)
3	5 (2.4%)	7 (3.3%)	0 (0.0%)	4 (1.9%)	7 (3.4%)	12 (5.7%)
Very much	8 (3.9%)	9 (4.3%)	2 (1.0%)	5 (2.4%)	4 (1.9%)	8 (3.8%)

Q8: How much do you think injecting etanercept will interfere with your ability to enjoy social or leisure activities?
Q9: Do you think injecting etanercept will interfere with your usual daily activities?
Q10: How much do you think injecting etanercept will interfere with traveling on holidays / business / visiting?
AI = auto injector; mITT = modified Intent-to-Treat; N = total number of subjects; n = number of evaluable subjects; PFS = pre filled syringe.

Table 16. Device Attributes and Subject Questionnaire Questions 8 to 10 -Estimated Odds Ratios, mITT Set

	Odds Ratio AI/PFS		p-Value
	Estimate	95% CI	
Question 8			
Baseline (after the training)	0.70	(0.48; 1.03)	0.072
Day 28	1.32	(0.86; 2.03)	0.205
Day 84	1.18	(0.78; 1.78)	0.434
Last observation	1.04	(0.69; 1.55)	0.857
Question 9			
Baseline (after the training)	1.04	(0.70; 1.56)	0.837
Day 28	1.37	(0.87; 2.15)	0.172
Day 84	1.45	(0.94; 2.24)	0.096
Last observation	1.36	(0.88; 2.08)	0.164
Question 10			
Baseline (after the training)	1.18	(0.83; 1.69)	0.356
Day 28	1.07	(0.73; 1.56)	0.737
Day 84	1.31	(0.90; 1.91)	0.156
Last observation	1.22	(0.85; 1.76)	0.290

Q8: How much do you think injecting etanercept will interfere with your ability to enjoy social or leisure activities?
Q9: Do you think injecting etanercept will interfere with your usual daily activities?
Q10: How much do you think injecting etanercept will interfere with traveling on holidays / business / visiting?
AI = auto injector; CI = confidence interval; mITT = modified Intent-to-Treat; PFS = pre filled syringe.

Confidence in the Device: In both groups, evaluation of perceptions of subjects concerning confidence when using the device was a little better for questions Q11 to Q15 on Day 84 compared with baseline after the training. Results of the device attributes and subject perceptions questionnaire for Q11 to Q15 are summarized by visit in Table 17. Overall, odds ratios for the 2 subject groups (AI/PFS; Table 18) for these 5 questions were statistically not significantly different from 1, indicating that the subject group using AI was no more confident than the subject group using PFS when using their device. Only the odds-ratio on Day 28 for Q13 indicated that the subject group using AI was statistically significantly more confident that they can inject themselves properly than the subject group using PFS.

Table 17. Device Attributes and Subject Perceptions Questionnaire Questions 11 to 15: Observed Data – mITT Set

Visit	Question 11		Question 12		Question 13		Question 14		Question 15	
	AI N=206	PFS N=211	AI N=206	PFS N=211	AI N=206	PFS N=211	AI N=206	PFS N=211	AI N=206	PFS N=211
Baseline-After the training										
n	206	207	206	207	206	205	202	206	205	207
Not at all	6 (2.9%)	11 (5.3%)	5 (2.4%)	2 (1.0%)	4 (1.9%)	2 (1.0%)	4 (2.0%)	2 (1.0%)	3 (1.5%)	1 (0.5%)
1	13 (6.3%)	20 (9.7%)	4 (1.9%)	7 (3.4%)	3 (1.5%)	7 (3.4%)	2 (1.0%)	10 (4.9%)	2 (1.0%)	8 (3.9%)
2	30 (14.6%)	31 (15.0%)	19 (9.2%)	15 (7.2%)	12 (5.8%)	27 (13.2%)	11 (5.4%)	21 (10.2%)	16 (7.8%)	22 (10.6%)
3	76 (36.9%)	78 (37.7%)	67 (32.5%)	54 (26.1%)	70 (34.0%)	53 (25.9%)	72 (35.6%)	56 (27.2%)	69 (33.7%)	54 (26.1%)
Very much	81 (39.3%)	67 (32.4%)	111 (53.9%)	129 (62.3%)	117 (56.8%)	116 (56.6%)	113 (55.9%)	117 (56.8%)	115 (56.1%)	122 (58.9%)
Day 28										
n	196	201	195	201	195	201	194	200	195	201
Not at all	4 (2.0%)	3 (1.5%)	5 (2.6%)	3 (1.5%)	6 (3.1%)	3 (1.5%)	3 (1.5%)	3 (1.5%)	3 (1.5%)	2 (1.0%)
1	9 (4.6%)	8 (4.0%)	3 (1.5%)	6 (3.0%)	0 (0.0%)	5 (2.5%)	3 (1.5%)	4 (2.0%)	3 (1.5%)	3 (1.5%)
2	6 (3.1%)	10 (5.0%)	8 (4.1%)	3 (1.5%)	7 (3.6%)	10 (5.0%)	8 (4.1%)	9 (4.5%)	5 (2.6%)	12 (6.0%)
3	56 (28.6%)	75 (37.3%)	53 (27.2%)	50 (24.9%)	47 (24.1%)	65 (32.3%)	49 (25.3%)	62 (31.0%)	60 (30.8%)	52 (25.9%)
Very much	121 (61.7%)	105 (52.2%)	126 (64.6%)	139 (69.2%)	135 (69.2%)	118 (58.7%)	131 (67.5%)	122 (61.0%)	124 (63.6%)	132 (65.7%)
Day 84										
n	199	197	198	197	199	196	199	196	199	197
Not at all	9 (4.5%)	1 (0.5%)	7 (3.5%)	2 (1.0%)	9 (4.5%)	1 (0.5%)	6 (3.0%)	2 (1.0%)	5 (2.5%)	2 (1.0%)
1	5 (2.5%)	7 (3.6%)	4 (2.0%)	6 (3.0%)	1 (0.5%)	6 (3.1%)	3 (1.5%)	5 (2.6%)	3 (1.5%)	4 (2.0%)
2	7 (3.5%)	12 (6.1%)	7 (3.5%)	7 (3.6%)	4 (2.0%)	12 (6.1%)	6 (3.0%)	10 (5.1%)	1 (0.5%)	10 (5.1%)
3	47 (23.6%)	60 (30.5%)	48 (24.2%)	43 (21.8%)	43 (21.6%)	54 (27.6%)	43 (21.6%)	52 (26.5%)	55 (27.6%)	49 (24.9%)
Very much	131 (65.8%)	117 (59.4%)	132 (66.7%)	139 (70.6%)	142 (71.4%)	123 (62.8%)	141 (70.9%)	127 (64.8%)	135 (67.8%)	132 (67.0%)
Last observation										
n	206	211	206	211	206	211	206	211	206	211
Not at all	9 (4.4%)	2 (0.9%)	7 (3.4%)	3 (1.4%)	9 (4.4%)	2 (0.9%)	6 (2.9%)	2 (0.9%)	5 (2.4%)	2 (0.9%)
1	5 (2.4%)	7 (3.3%)	4 (1.9%)	6 (2.8%)	1 (0.5%)	6 (2.8%)	3 (1.5%)	5 (2.4%)	3 (1.5%)	4 (1.9%)
2	7 (3.4%)	13 (6.2%)	8 (3.9%)	7 (3.3%)	4 (1.9%)	13 (6.2%)	8 (3.9%)	10 (4.7%)	2 (1.0%)	12 (5.7%)
3	49 (23.8%)	67 (31.8%)	52 (25.2%)	47 (22.3%)	47 (22.8%)	60 (28.4%)	45 (21.8%)	59 (28.0%)	58 (28.2%)	53 (25.1%)
Very much	136 (66.0%)	122 (57.8%)	135 (65.5%)	148 (70.1%)	145 (70.4%)	130 (61.6%)	144 (69.9%)	135 (64.0%)	138 (67.0%)	140 (66.4%)

Q11: Overall, how confident are you in your management of your injections?
Q12: How confident are you that you inject the right amount of medicine every time?
Q13: How confident are you that you can inject yourself properly with the device?
Q14: Are you confident that you have good control over the injection process?
Q15: How confident are you that you injected yourself successfully?
AI = auto injector; mITT = modified Intent-to-Treat; N = total number of subjects; n = number of evaluable subjects; PFS = pre filled syringe.

Table 18. Device Attributes and Subject Questionnaire Questions 11 to 15 -Estimated Odds Ratios, mITT Set

	Odds Ratio AI/PFS		p-Value
	Estimate	95% CI	
Question 11			
Baseline (after the training)	0.72	(0.50; 1.02)	0.065
Day 28	0.73	(0.50; 1.06)	0.100
Day 84	0.81	(0.54; 1.21)	0.298
Last observation	0.75	(0.51; 1.11)	0.148
Question 12			
Baseline (after the training)	1.38	(0.94; 2.03)	0.098
Day 28	1.24	(0.82; 1.87)	0.311
Day 84	1.21	(0.79; 1.85)	0.376
Last observation	1.24	(0.83; 1.86)	0.299
Question 13			
Baseline (after the training)	0.88	(0.60; 1.28)	0.494
Day 28	0.65	(0.44; 0.97)	0.036
Day 84	0.69	(0.45; 1.04)	0.079
Last observation	0.68	(0.46; 1.02)	0.063
Question 14			
Baseline (after the training)	0.91	(0.62 ;1.33)	0.628
Day 28	0.77	(0.51; 1.15)	0.203
Day 84	0.77	(0.51; 1.17)	0.222
Last observation	0.79	(0.53; 1.19)	0.263
Question 15			
Baseline (after the training)	1.02	(0.70; 1.50)	0.914
Day 28	1.05	(0.70; 1.57)	0.827
Day 84	0.93	(0.61; 1.40)	0.712
Last observation	0.93	(0.62; 1.39)	0.733

Q11: Overall, how confident are you in your management of your injections?
Q12: How confident are you that you inject the right amount of medicine every time?
Q13: How confident are you that you can inject yourself properly with the device?
Q14: Are you confident that you have good control over the injection process?
Q15: How confident are you that you injected yourself successfully?
AI = auto injector; CI = confidence interval; mITT = modified Intent-to-Treat; PFS = pre filled syringe.

Presence or Absence of Fear of the Device: In both groups, evaluation of perceptions of subjects concerning feeling when using the device was better for questions Q16 to Q19 on Day 84 compared to baseline after the training. Results of the device attributes and subject perceptions questionnaire for Q16 to Q19 are summarized by visit in Table 19. Odds ratios for the 2 subject groups (AI/PFS Table 20) were statistically significantly different from 1 at all time-points for Q18; at all time-points except Day 84 for Q17; and were only significant on Day 84 and at last observation for Q16 and Q19. All odds-ratios significantly different from 1 indicated that subject group using AI was less nervous when using their device than subject group using PFS.

Table 19. Device Attributes and Subject Perceptions Questionnaire Questions 16 to 19: Observed Data – mITT Set

Visit	Question 16		Question 17		Question 18		Question 19	
	AI N=206	PFS N=211	AI N=206	PFS N=211	AI N=206	PFS N=211	AI N=206	PFS N=211
Baseline-after the training								
n	206	207	205	207	206	206	206	206
Not at all	92 (44.7%)	80 (38.6%)	102 (49.8%)	82 (39.6%)	129 (62.6%)	103 (50.0%)	124 (60.2%)	105 (51.0%)
1	59 (28.6%)	54 (26.1%)	44 (21.5%)	49 (23.7%)	43 (20.9%)	40 (19.4%)	45 (21.8%)	57 (27.7%)
2	29 (14.1%)	39 (18.8%)	32 (15.6%)	38 (18.4%)	22 (10.7%)	29 (14.1%)	28 (13.6%)	26 (12.6%)
3	16 (7.8%)	24 (11.6%)	17 (8.3%)	22 (10.6%)	10 (4.9%)	22 (10.7%)	7 (3.4%)	11 (5.3%)
Very much	10 (4.9%)	10 (4.8%)	10 (4.9%)	16 (7.7%)	2 (1.0%)	12 (5.8%)	2 (1.0%)	7 (3.4%)
Day 28								
n	196	201	195	201	194	201	195	201
Not at all	110 (56.1%)	103 (51.2%)	110 (56.4%)	93 (46.3%)	135 (69.6%)	96 (47.8%)	124 (63.6%)	119 (59.2%)
1	54 (27.6%)	51 (25.4%)	61 (31.3%)	54 (26.9%)	42 (21.6%)	52 (25.9%)	57 (29.2%)	50 (24.9%)
2	22 (11.2%)	27 (13.4%)	13 (6.7%)	29 (14.4%)	15 (7.7%)	33 (16.4%)	11 (5.6%)	21 (10.4%)
3	7 (3.6%)	15 (7.5%)	10 (5.1%)	18 (9.0%)	0 (0.0%)	11 (5.5%)	2 (1.0%)	9 (4.5%)
Very much	3 (1.5%)	5 (2.5%)	1 (0.5%)	7 (3.5%)	2 (1.0%)	9 (4.5%)	1 (0.5%)	2 (1.0%)
Day 84								
n	199	198	199	197	199	197	198	198
Not at all	125 (62.8%)	111 (56.1%)	115 (57.8%)	105 (53.3%)	143 (71.9%)	112 (56.9%)	143 (72.7%)	125 (63.1%)
1	53 (26.6%)	46 (23.2%)	59 (29.6%)	47 (23.9%)	39 (19.6%)	39 (19.8%)	41 (20.7%)	42 (21.2%)
2	17 (8.5%)	19 (9.6%)	19 (9.5%)	19 (9.6%)	13 (6.5%)	28 (14.2%)	12 (6.1%)	24 (12.1%)
3	4 (2.0%)	15 (7.6%)	6 (3.0%)	19 (9.6%)	1 (0.5%)	11 (5.6%)	1 (0.5%)	5 (2.5%)
Very much	0 (0.0%)	7 (3.5%)	0 (0.0%)	7 (3.6%)	3 (1.5%)	7 (3.6%)	1 (0.5%)	2 (1.0%)
Last observation								
n	206	211	206	211	206	211	206	211
Not at all	131 (63.6%)	119 (56.4%)	121 (58.7%)	112 (53.1%)	150 (72.8%)	119 (56.4%)	149 (72.3%)	134 (63.5%)
1	53 (25.7%)	48 (22.7%)	59 (28.6%)	52 (24.6%)	39 (18.9%)	43 (20.4%)	42 (20.4%)	45 (21.3%)
2	18 (8.7%)	22 (10.4%)	20 (9.7%)	20 (9.5%)	13 (6.3%)	30 (14.2%)	13 (6.3%)	25 (11.8%)
3	4 (1.9%)	15 (7.1%)	6 (2.9%)	20 (9.5%)	1 (0.5%)	12 (5.7%)	1 (0.5%)	5 (2.4%)
Very much	0 (0.0%)	7 (3.3%)	0 (0.0%)	7 (3.3%)	3 (1.5%)	7 (3.3%)	1 (0.5%)	2 (0.9%)

Q16: Overall, how nervous do you feel about your injections?
Q17: Overall, how nervous do you feel about inserting the needle into your skin?
Q18: Do you dislike injecting yourself with this device?
Q19: Overall, are you emotionally distressed or anxious about your injections?
AI = auto injector; mITT = modified Intent-to-Treat; N = total number of subjects; n = number of evaluable subjects; PFS = pre filled syringe.

Table 20. Device Attributes and Subject Questionnaire Questions 16 to 19 -Estimated Odds Ratios, mITT Set

	Odds Ratio AI/PFS		p-Value
	Estimate	95% CI	
Question 16			
Baseline (after the training)	1.36	(0.95; 1.95)	0.090
Day 28	1.31	(0.90; 1.91)	0.154
Day 84	1.51	(1.02; 2.22)	0.037
Last observation	1.53	(1.05; 2.24)	0.028
Question 17			
Baseline (after the training)	1.53	(1.06; 2.21)	0.022
Day 28	1.68	(1.17; 2.41)	0.005
Day 84	1.40	(0.97; 2.03)	0.076
Last observation	1.45	(1.00; 2.11)	0.049
Question 18			
Baseline (after the training)	1.93	(1.32; 2.83)	<0.001
Day 28	2.63	(1.78; 3.87)	<0.001
Day 84	2.13	(1.42; 3.19)	<0.001
Last observation	2.27	(1.52; 3.39)	<0.001
Question 19			
Baseline (after the training)	1.44	(0.99; 2.11)	0.057
Day 28	1.33	(0.90; 1.96)	0.151
Day 84	1.61	(1.06; 2.44)	0.024
Last observation	1.59	(1.06; 2.39)	0.025

Q16: Overall, how nervous do you feel about your injections?
Q17: Overall, how nervous do you feel about inserting the needle into your skin?
Q18: Do you dislike injecting yourself with this device?
Q19: Overall, are you emotionally distressed or anxious about your injections?
AI = auto injector; CI = confidence interval; mITT = modified Intent-to-Treat; PFS = pre filled syringe.

Device Characteristics: In both groups, evaluation of perceptions of subjects concerning the characteristics of the device was slightly better for questions Q20 to Q22 on Day 84 compared with baseline after the training. Results of the device attributes and subject perceptions questionnaire for Q20 to Q22 on Day 84 are summarized by visit in Table 21. Odds ratios for the 2 subject groups (AI/PFS; Table 22) were statistically significantly different from 1 at all time-points for these 3 questions, indicating that the subject group using AI appreciated more the characteristics (look, feel and comfort to use) of their device than the subject group using PFS.

Table 21. Device Attributes and Subject Perceptions Questionnaire Questions 20 to 22: Observed Data – mITT Set

Visit	Question 20		Question 21		Question 22	
	AI N=206	PFS N=211	AI N=206	PFS N=211	AI N=206	PFS N=211
Baseline-after the training						
n	206	205	206	204	206	205
Not at all	4 (1.9%)	18 (8.8%)	1 (0.5%)	9 (4.4%)	7 (3.4%)	32 (15.6%)
1	10 (4.9%)	21 (10.2%)	9 (4.4%)	24 (11.8%)	11 (5.3%)	26 (12.7%)
2	62 (30.1%)	90 (43.9%)	69 (33.5%)	92 (45.1%)	68 (33.0%)	76 (37.1%)
3	81 (39.3%)	56 (27.3%)	78 (37.9%)	60 (29.4%)	67 (32.5%)	55 (26.8%)
Very much	49 (23.8%)	20 (9.8%)	49 (23.8%)	19 (9.3%)	53 (25.7%)	16 (7.8%)
Day 28						
n	193	201	193	201	193	201
Not at all	3 (1.6%)	14 (7.0%)	2 (1.0%)	15 (7.5%)	6 (3.1%)	28 (13.9%)
1	2 (1.0%)	22 (10.9%)	7 (3.6%)	21 (10.4%)	8 (4.1%)	22 (10.9%)
2	51 (26.4%)	92 (45.8%)	58 (30.1%)	90 (44.8%)	51 (26.4%)	74 (36.8%)
3	79 (40.9%)	46 (22.9%)	71 (36.8%)	45 (22.4%)	69 (35.8%)	45 (22.4%)
Very much	58 (30.1%)	27 (13.4%)	55 (28.5%)	30 (14.9%)	59 (30.6%)	32 (15.9%)
Day 84						
n	199	198	199	198	199	198
Not at all	1 (0.5%)	13 (6.6%)	4 (2.0%)	7 (3.5%)	7 (3.5%)	27 (13.6%)
1	11 (5.5%)	20 (10.1%)	9 (4.5%)	19 (9.6%)	15 (7.5%)	21 (10.6%)
2	43 (21.6%)	77 (38.9%)	46 (23.1%)	87 (43.9%)	47 (23.6%)	62 (31.3%)
3	78 (39.2%)	59 (29.8%)	76 (38.2%)	54 (27.3%)	65 (32.7%)	54 (27.3%)
Very much	66 (33.2%)	29 (14.6%)	64 (32.2%)	31 (15.7%)	65 (32.7%)	34 (17.2%)
Last observation						
n	206	211	206	211	206	211
Not at all	1 (0.5%)	14 (6.6%)	4 (1.9%)	7 (3.3%)	7 (3.4%)	27 (12.8%)
1	11 (5.3%)	21 (10.0%)	9 (4.4%)	20 (9.5%)	16 (7.8%)	22 (10.4%)
2	46 (22.3%)	82 (38.9%)	49 (23.8%)	94 (44.5%)	47 (22.8%)	68 (32.2%)
3	79 (38.3%)	62 (29.4%)	77 (37.4%)	58 (27.5%)	67 (32.5%)	58 (27.5%)
Very much	69 (33.5%)	32 (15.2%)	67 (32.5%)	32 (15.2%)	69 (33.5%)	36 (17.1%)

Q20: How much do you like the look of the device?
Q21: How much do you like the feel of the device?
Q22: How much does the device look like something you would feel comfortable to use?
AI = auto injector; mITT = modified Intent-to-Treat; N = total number of subjects; n = number of evaluable subjects; PFS = pre filled syringe.

Table 22. Device Attributes and Subject Questionnaire Questions 20 to 22 -Estimated Odds Ratios, mITT Set

	Odds Ratio AI/PFS		p-Value
	Estimate	95% CI	
Question 20			
Baseline (after the training)	0.34	(0.24; 0.49)	<0.001
Day 28	0.26	(0.18; 0.37)	<0.001
Day 84	0.31	(0.21; 0.45)	<0.001
Last observation	0.32	(0.23; 0.47)	<0.001
Question 21			
Baseline (after the training)	0.38	(0.27; 0.54)	<0.001
Day 28	0.31	(0.21; 0.46)	<0.001
Day 84	0.34	(0.24; 0.50)	<0.001
Last observation	0.35	(0.24; 0.50)	<0.001
Question 22			
Baseline (after the training)	0.33	(0.24; 0.46)	<0.001
Day 28	0.32	(0.22; 0.46)	<0.001
Day 84	0.38	(0.26; 0.56)	<0.001
Last observation	0.41	(0.28; 0.58)	<0.001

Q20: How much do you like the look of the device?
Q21: How much do you like the feel of the device?
Q22: How much does the device look like something you would feel comfortable to use?
AI = auto injector; CI = confidence interval; mITT = modified Intent-to-Treat; PFS = pre filled syringe.

Side Effects Related to Administration: In both groups, evaluation of perceptions of subjects concerning the pain experienced during or immediately after the injection was worse on Day 84 compared to baseline after the training, with lower percentages of subjects reporting no pain at all: 38.2% compared to 49.2% in the AI group and 42.4% compared to 54.0% in the PFS group. Results of the device attributes and subject perceptions questionnaire for Q23 are summarized by visit in Table 23. Odds ratios for the 2 subject groups (AI/PFS; Table 24) for this question were statistically not significantly different from 1, indicating that there was no statistical difference between the subject group using AI and the subject group using PFS regarding experience of side effects.

Table 23. Device Attributes and Subject Perceptions Questionnaire Question 23: Observed Data – mITT Set

Visit	Question 23	
	AI N=206	PFS N=211
Baseline-after the first injection		
n	199	202
None	98 (49.2%)	109 (54.0%)
1	65 (32.7%)	54 (26.7%)
2	24 (12.1%)	31 (15.3%)
3	9 (4.5%)	8 (4.0%)
Severe	3 (1.5%)	0 (0.0%)
Day 28		
n	195	201
None	77 (39.5%)	88 (43.8%)
1	60 (30.8%)	60 (29.9%)
2	33 (16.9%)	31 (15.4%)
3	22 (11.3%)	21 (10.4%)
Severe	3 (1.5%)	1 (0.5%)
Day 84		
n	199	198
None	76 (38.2%)	84 (42.4%)
1	68 (34.2%)	70 (35.4%)
2	30 (15.1%)	28 (14.1%)
3	21 (10.6%)	15 (7.6%)
Severe	4 (2.0%)	1 (0.5%)
Last observation		
n	206	211
None	79 (38.3%)	90 (42.7%)
1	70 (34.0%)	72 (34.1%)
2	31 (15.0%)	32 (15.2%)
3	22 (10.7%)	16 (7.6%)
Severe	4 (1.9%)	1 (0.5%)

Q23: Do you experience pain DURING or immediately AFTER the injection?
AI = auto injector; mITT = modified Intent-to-Treat; N = total number of subjects; n = number of evaluable subjects; PFS = pre filled syringe.

Table 24. Device Attributes and Subject Questionnaire Question 23 -Estimated Odds Ratios, mITT Set

	Odds Ratio AI/PFS		p-Value
	Estimate	95% CI	
Question 23			
Baseline after the first injection	0.87	(0.60; 1.26)	0.470
Day 28	0.83	(0.57; 1.20)	0.325
Day 84	0.79	(0.55; 1.13)	0.197
Last observation	0.80	(0.56; 1.14)	0.212

Q23: Do you experience pain DURING or immediately AFTER the injection?
AI = auto injector; CI = confidence interval; mITT = modified Intent-to-Treat; PFS = pre filled syringe.

Likeliness to Use the Device Again: In both groups, evaluation of perceptions of subjects concerning the likeliness to use the device again was better for questions Q24 (Table 25) and Q25 (Table 26) on Day 84 compared with baseline after the training (Q26 [Table 27] was only measured on Day 84). Odds ratios or the 2 subject groups (AI/PFS; Table 28) were statistically significantly different from 1 at all time-points for the 3 questions Q24 to Q26, indicating that the group of subjects using AI would be significantly less likely to consider an alternative device than the group of subjects using PFS, and the subject group using AI would more be likely to recommend or continue injecting with the AI than the group of subjects using PFS would be to recommend or continue injecting with the PFS.

Table 25. Device Attributes and Subject Perceptions Questionnaire Question 24: Observed Data – mITT Set

Visit	Question 24	
	AI N=206	PFS N=211
Baseline-After the training		
n	159	167
Very little	84 (52.8%)	34 (20.4%)
1	27 (17.0%)	22 (13.2%)
2	23 (14.5%)	57 (34.1%)
3	13 (8.2%)	32 (19.2%)
Very much	12 (7.5%)	22 (13.2%)
Day 28		
n	156	165
Very little	85 (54.5%)	39 (23.6%)
1	29 (18.6%)	33 (20.0%)
2	18 (11.5%)	50 (30.3%)
3	7 (4.5%)	25 (15.2%)
Very much	17 (10.9%)	18 (10.9%)
Day 84		
n	160	162
Very little	87 (54.4%)	43 (26.5%)
1	29 (18.1%)	31 (19.1%)
2	17 (10.6%)	43 (26.5%)
3	7 (4.4%)	20 (12.3%)
Very much	20 (12.5%)	25 (15.4%)
Last observation		
n	165	171
Very little	89 (53.9%)	44 (25.7%)
1	30 (18.2%)	33 (19.3%)
2	18 (10.9%)	47 (27.5%)
3	8 (4.8%)	22 (12.9%)
Very much	20 (12.1%)	25 (14.6%)

Q24: To what extent would you consider alternative devices if you were to continue on etanercept?
AI = auto injector; mITT = modified Intent-to-Treat; N = total number of subjects; n = number of evaluable subjects; PFS = pre filled syringe.

Table 26. Device Attributes and Subject Perceptions Questionnaire Question 25: Observed Data – mITT Set

Visit	Question 25	
	AI N=206	PFS N=211
Baseline-after the training		
n	199	203
Not at all	5 (2.5%)	7 (3.4%)
1	1 (0.5%)	17 (8.4%)
2	17 (8.5%)	63 (31.0%)
3	39 (19.6%)	39 (19.2%)
Yes definitely	137 (68.8%)	77 (37.9%)
Day 28		
n	194	201
Not at all	2 (1.0%)	9 (4.5%)
1	3 (1.5%)	14 (7.0%)
2	2 (1.0%)	49 (24.4%)
3	39 (20.1%)	45 (22.4%)
Yes definitely	148 (76.3%)	84 (41.8%)
Day 84		
n	199	198
Not at all	3 (1.5%)	8 (4.0%)
1	2 (1.0%)	10 (5.1%)
2	11 (5.5%)	43 (21.7%)
3	31 (15.6%)	42 (21.2%)
Yes definitely	152 (76.4%)	95 (48.0%)
Last observation		
n	206	211
Not at all	3 (1.5%)	9 (4.3%)
1	2 (1.0%)	11 (5.2%)
2	11 (5.3%)	44 (20.9%)
3	34 (16.5%)	46 (21.8%)
Yes definitely	156 (75.7%)	101 (47.9%)

Q25: Would you recommend this device to someone else who needed to self-inject?
AI = auto injector; mITT = modified Intent-to-Treat; N = total number of subjects; n = number of evaluable subjects; PFS = pre filled syringe.

Table 27. Device Attributes and Subject Perceptions Questionnaire Question 26: Observed Data – mITT Set

Visit	Question 26	
	AI N=206	PFS N=211
Day 84		
n	198	198
Not at all	4 (2.0%)	1 (0.5%)
1	5 (2.5%)	14 (7.1%)
2	20 (10.1%)	26 (13.1%)
3	24 (12.1%)	37 (18.7%)
Very likely	145 (73.2%)	120 (60.6%)

Q26: If your doctor advised you to, how likely would you to be continue injecting regularly with this device?
AI = auto injector; mITT = modified Intent-to-Treat; N = total number of subjects; n = number of evaluable subjects; PFS = pre filled syringe.

Table 28. Device Attributes and Subject Questionnaire Questions 24 to 26 -Estimated Odds Ratios, mITT Set

	Odds Ratio AI/PFS		p-Value
	Estimate	95% CI	
Question 24			
Baseline-after the training	3.67	(2.44; 5.52)	<0.001
Day 28	3.02	(2.01; 4.56)	<0.001
Day 84	2.92	(1.91; 4.44)	<0.001
Last observation	2.80	(1.88; 4.19)	<0.001
Question 25			
Baseline-after the training	0.25	(0.17; 0.36)	<0.001
Day 28	0.20	(0.13; 0.30)	<0.001
Day 84	0.26	(0.17; 0.40)	<0.001
Last observation	0.27	(0.18; 0.41)	<0.001
Question 26			
Day 84	0.58	(0.38; 0.88)	0.010

Q24: To what extent would you consider alternative devices if you were to continue on etanercept?
Q25: Would you recommend this device to someone else who needed to self-inject?
Q26: If your doctor advised you to, how likely would you to be continue injecting regularly with this device?
AI = auto injector; CI = confidence interval; mITT = modified Intent-to-Treat; PFS = pre filled syringe.

Short Form – State-Trait Anxiety Inventory (SF-STAI): The short form of STAI includes 6 items related to anxiety (calm, tense, upset, relaxed, content, and worried) rated on a 4-point scale from 1 to 4. The total summary score can, therefore, range from 6 to 24 with higher scores indicating more anxiety. In both groups subjects felt slightly better on Day 84 than at baseline after the training. The SF-STAI mean global score decreased from 11.0 (±3.5) at baseline after the training to 10.1 (±3.2) on Day 84 in the AI group and from 11.2 (±3.6) to 10.1 (±3.3) in the PFS group (Table 29). The difference was not statistically significant between the 2 groups on Day 84, with the estimate of the mean difference (2-sided 95% CI) of -0.03 (-0.67; 0.61). Estimated mean differences for the 2 subject groups (AI/PFS) for the SF-STAI global score are summarized in Table 30.

Table 29. SF-STAI: Global Score (6-24)[a] – Observed Data - mITT Set

Visit	AI N=206	PFS N=211
Baseline-after the training		
n	202	205
Mean (SD)	11.0 (3.5)	11.2 (3.6)
Median	11.0	11.0
Minimum, Maximum	6.0, 21.0	6.0, 21.0
Day 28		
n	194	201
Mean (SD)	9.9 (3.3)	10.0 (3.5)
Median	9.5	9.0
Minimum, Maximum	6.0, 21.0	6.0, 24.0
Day 84		
n	199	197
Mean (SD)	10.1 (3.2)	10.1 (3.3)
Median	10.0	10.0
Minimum, Maximum	6.0, 21.0	6.0, 21.0
Last observation		
n	206	211
Mean (SD)	10.1 (3.3)	10.1 (3.3)
Median	10.0	10.0
Minimum, Maximum	6.0, 21.0	6.0, 21.0

AI = auto injector; mITT = modified Intent-to-Treat; N = total number of subjects; n = number of evaluable subjects; PFS = pre filled syringe; SD = standard deviation; SF-STAI = Short form State-Trait Anxiety Inventory.
a. The higher the score is, the more anxious the subject is.

Table 30. SF – STAI: Global Score (6-24)[a] - Estimated Mean Difference, mITT Set

	Difference (AI/PFS)		p-value
	Mean (SE)	95% CI	
Baseline-after the training	-0.23 (0.35)	(-0.91; 0.46)	0.515
Day 28	-0.07 (0.34)	(-0.74; 0.60)	0.842
Day 84	-0.03 (0.33)	(-0.67; 0.61)	0.928
Last observation	0.01 (0.32)	(-0.62; 0.64)	0.974

AI = auto injector; CI = confidence interval; mITT = modified Intent-to-Treat; PFS = pre filled syringe; SF-STAI = Short form State-Trait Anxiety Inventory; SE standard error.
a. The higher the score is, the more anxious the subject is.

Subject and Psoriasis Attributes Associated With Subject Perceptions: Graphical representations following multiple correspondence analysis (MCA) and ascending hierarchical classification (AHC) showed a satisfaction gradient, represented by 3 clusters of categories: very satisfied, satisfied, and less satisfied subjects. The interpretation of this gradient was confirmed by the satisfaction level measured on the 0- to 10-point scale (primary endpoint, Table 31).

A description of the baseline characteristics statistically significantly different between these 3 clusters is provided by group in Table 32. Several baseline characteristics were statistically significantly different between these 3 clusters: very satisfied subjects were the oldest and

had a longer duration of psoriasis, while less satisfied subjects were the most anxious and depressed, as measured by Hospital Anxiety Depression (HAD) subscales scores.

Table 31. Subject and Psoriasis Attributes Associated With Subject Perceptions at Last Observation by Clusters, mITT Population

	AI			PFS		
	Very Satisfied N=119	Satisfied N=56	Less Satisfied N=20	Very Satisfied N=92	Satisfied N=65	Less Satisfied N=41
Subject satisfaction at last observation (0-10)						
n	119	56	20	92	65	41
Mean (SD)	9.5 (1.5)	8.0 (2.0)	7.9 (2.6)	8.9 (1.9)	7.1 (2.4)	5.3 (2.5)
Median	10.0[a]	9.0	9.0[b]	10.0[a]	8.0[c]	5.0[b]
Minimum, Maximum	0.0, 10.0	0.0, 10.0	3.0, 10.0	0.0, 10.0	0.0, 10.0	0.0, 10.0

AI = auto injector; mITT = modified Intent-to-Treat; N = total number of subjects; n = number of evaluable subjects; PFS = pre filled syringe; SD = standard deviation.

a. Cluster very satisfied statistically significantly different from cluster satisfied.

b. Cluster less satisfied statistically significantly different from cluster very satisfied.

c. Cluster satisfied statistically significantly different from cluster less satisfied.

Table 32. Subject / Psoriasis Attributes Associated With Subject Perceptions at Last Observation by Clusters – mITT Set

	AI				PFS			
	Very Satisfied N=119	**Satisfied N=56**	**Less satisfied N=20**	**Overall p-Value**	**Very Satisfied N=92**	**Satisfied N=65**	**Less satisfied N=41**	**Overall p-Value**
Age (years)				0.030 (A)				0.010 (A)
n	119	56	20		92	65	41	
Mean (SD)	47.9 (12.6)[a]	42.8 (12.9)	42.7 (15.4)		49.1 (12.7)[a]	43.9 (13.3)	42.5 (14.4)[b]	
Median	49.0	42.0	47.0		48.5	41.0	41.0	
Gender				0.984 (C)				0.549 (C)
n	119	56	20		92	65	41	
Male	77 (64.7%)	37 (66.1%)	13 (65.0%)		67 (72.8%)	45 (69.2%)	26 (63.4%)	
Female	42 (35.3%)	19 (33.9%)	7 (35.0%)		25 (27.2%)	20 (30.8%)	15 (36.6%)	
Socio-educational level				0.158 (F)				0.808 (C)
n	119	56	20		92	65	41	
Reading / writing capacity	41 (34.5%)	12 (21.4)	10 (50.0%)		32 (34.8%)	19 (29.2)	16 (39.0%)	
High school / Baccalaureate level	56 (47.1%)	34 (60.7%)	7 (35.0%)		43 (46.7%)	32 (49.2%)	16 (39.0%)	
University level	22 (18.5%)	10 (17.9%)	3 (15.0%)		17 (18.5%)	14 (21.5%)	9 (22.0%)	
HAD anxiety subscale score at Baseline				0.029 (KW)				0.005 (KW)
n	119	56	20		92	65	41	
Mean (SD)	7.2 (3.8)	7.7 (4.3)	9.7 (3.5)		7.0 (4.6)	7.2 (4.1)	9.7 (4.2)	
Median	7.0	7.0[c]	9.2[b]		6.0	7.0[c]	10.0[b]	
HAD depression subscale score at Baseline				0.411 (KW)				0.005 (KW)
n	119	56	20		92	65	41	
Mean (SD)	5.4 (3.7)	5.4 (4.0)	6.6 (4.2)		5.2 (3.9)	5.2 (3.3)	7.4 (4.0)	
Median	5.0	5.5	6.5		4.0	5.0[c]	8.0[b]	
PAM (%)				0.039 (A)				0.006 (A)
n	116	56	20		91	63	40	
Mean (SD)	58.0 (13.8)[a]	53.0 (11.7)[c]	60.0 (13.9)		60.5 (14.0)	57.5 (11.8)	52.4 (12.6)[b]	
Median	56.4	49.9	56.4		60.0	56.4	49.9	
Prior injection experience				0.752 (C)				0.700 (C)
n	119	56	20		92	65	41	
Yes	47 (39.5%)	20 (35.7%)	9 (45.0%)		43 (46.7%)	28 (43.1%)	16 (39.0%)	
No	72 (60.5%)	36 (64.3%)	11 (55.0%)		49 (53.3%)	37 (56.9%)	25 (61.0%)	
Prior self-injection experience				0.697 (F)				0.159 (C)
n	119	56	20		92	65	41	
Yes	23 (19.3%)	13 (23.2%)	5 (25.0%)		33 (35.9%)	16 (24.6%)	9 (22.0%)	
No	96 (80.7%)	43 (76.8%)	15 (75.0%)		59 (64.1%)	49 (75.4%)	32 (78.0%)	

Table 32. Subject / Psoriasis Attributes Associated With Subject Perceptions at Last Observation by Clusters – mITT Set

	AI				PFS			
	Very Satisfied N=119	Satisfied N=56	Less satisfied N=20	Overall p-Value	Very Satisfied N=92	Satisfied N=65	Less satisfied N=41	Overall p-Value
Psoriasis Attributes				0.004 (A)				0.024 (A)
Psoriasis duration (years)								
n	119	56	20		92	65	41	
Mean (SD)	23.2 (13.3) [a]	17.8 (10.0)	16.1 (7.4) [b]		22.9 (12.1)	20.6 (10.8)	17.1 (9.8) [b]	
Median	21.0	15.0	16.0		23.0	18.0	17.0	
PGA of psoriasis at Screening (0-5)				0.652 (KW)				0.024 (KW)
n	119	56	20		92	65	40	
Mean (SD)	3.4 (0.8)	3.3 (0.7)	3.3 (0.7)		3.4 (0.6)	3.2 (0.8)	3.1 (0.8)	
Median	3.0	3.0	3.0		3.0[a]	3.0	3.0[b]	
PASI at Screening (0-72)				0.560 (A)				0.474 (A)
n	118	56	20		92	65	39	
Mean (SD)	17.2 (7.5)	18.6 (9.8)	17.1 (8.0)		17.9 (8.5)	17.5 (7.9)	15.9 (10.2)	
Median	15.9	17.4	14.5		16.5	16.0	13.7	
Subject's global assessment of psoriasis activity at Screening				0.494 (A)				0.782 (A)
n	116	55	20		90	65	39	
Mean (SD)	73.5 (17.7)	69.9 (19.1)	72.6 (21.2)		73.4 (18.0)	73.3 (19.8)	70.8 (26.7)	
Median	74.0	73.0	77.8		76.0	78.0	77.0	
Subject's global assessment of general health at Screening				0.023 (A)				0.089 (A)
n	117	55	20		90	65	40	
Mean (SD)	64.9 (23.7)	59.3 (25.3)	48.8 (31.2) [b]		63.8 (27.9)	70.7 (21.5)	60.5 (22.7)	
Median	67.0	63.0	52.5		73.5	76.0	62.5	
DLQI at Baseline (0-30)				0.444 (A)				0.947 (A)
n	116	54	18		90	63	41	
Mean (SD)	13.4 (6.8)	12.4 (6.4)	14.6 (6.9)		13.1 (7.1)	12.8 (6.0)	13.1 (6.7)	
Median	13.0	12.0	14.0		13.0	13.0	13.0	
Current tobacco usage				0.787 (C)				0.379 (C)
n	119	56	20		92	65	41	
Yes	49 (41.2%)	20 (35.7%)	8 (40.0)		31 (33.7%)	25 (38.5%)	19 (46.3)	
No	70 (58.8%)	36 (64.3%)	12 (60.0)		61 (66.3%)	40 (61.5%)	22 (53.7)	
Current use of alcoholic beverages				0.098 (C)				0.166 (C)
n	119	56	20		92	65	41	
Yes	59 (49.6%)	20 (35.7%)	6 (30.0%)		38 (41.3%)	29 (44.6%)	11 (26.8%)	
No	60 (50.4%)	36 (64.3%)	14 (70.0%)		54 (58.7%)	36 (55.4%)	30 (73.2%)	

Table 32. Subject / Psoriasis Attributes Associated With Subject Perceptions at Last Observation by Clusters – mITT Set

	AI				PFS			
	Very Satisfied N=119	**Satisfied N=56**	**Less satisfied N=20**	**Overall p-Value**	**Very Satisfied N=92**	**Satisfied N=65**	**Less satisfied N=41**	**Overall p-Value**
Prior systemic and / or topical medication for psoriasis								0.535 (F)
n	119	56	20		92	65	41	
Yes	119 (100.0%)	56 (100.0%)	20 (100.0%)		92 (100.0%)	64 (98.5%)	41 (100.0%)	
No	0 (0.0%)	0 (0.0%)	0 (0.0%)		0 (0.0%)	1 (1.5%)	0 (0.0%)	
Subject satisfaction at endpoint				<0.001(KW)				<0.001(KW)
n	119	56	20		92	65	41	
Mean (SD)	9.5 (1.5) [a]	8.0 (2.0) [c]	7.9 (2.6)		8.9 (1.9) [a]	7.1 (2.4) [c]	5.3 (2.5) [b]	
Median	10.0	9.0	9.0		10.0	8.0	5.0	

(A) = Analysis of variance; AI = auto injector; (C) = Chi-square test; DLQI = Dermatology Life Quality Index; (F) = Fisher's Exact Test; HAD = Hospital Anxiety Depression; (KW) = Kruskal-Wallis Test; mITT = modified Intent-to-Treat; N = total number of subjects; n = number of evaluable subjects; PAM = Patient activation measure; PGA = Physician Global Assessment; PASI = Psoriasis Area and Severity Index; PFS = pre filled syringe; SD = standard deviation.

a. cluster very satisfied statistically significantly different from cluster satisfied.
b. cluster satisfied statistically significantly different from cluster less satisfied.
c. cluster less satisfied statistically significantly different from cluster very satisfied.

Safety Results: Non-serious treatment-emergent AEs (all causalities) experienced by ≥2% of subjects in either the AI and PFS group are summarized in Table 33.

Table 33. Number (%) of Subjects Reporting Treatment Emergent Non-Serious Adverse Events – Events Reported by ≥2% of Subjects in Either Treatment Group

System Organ Class Preferred Term	Treatment AI (N=207)	 PFS (N=211)	 Total (N=418)
Any Adverse Event	94 (45.4)	96 (45.5)	190 (45.5)
General disorders and administration site conditions	44 (21.3)	46 (21.8)	90 (21.5)
Injection site erythema	10 (4.8)	17 (8.1)	27 (6.5)
Injection site haematoma	10 (4.8)	3 (1.4)	13 (3.1)
Injection site irritation	6 (2.9)	9 (4.3)	15 (3.6)
Injection site pain	10 (4.8)	10 (4.7)	20 (4.8)
Injection site pruritis	3 (1.4)	5 (2.4)	8 (1.9)
Injection site reaction	18 (8.7)	17 (8.1)	35 (8.4)
Infections and infestations	36 (17.4)	38 (18.0)	74 (17.7)
Influenza	5 (2.4)	9 (4.3)	14 (3.3)
Nasopharyngitis	24 (11.6)	27 (12.8)	51 (12.2)
Upper respiratory tract infection	7 (3.4)	4 (1.9)	11 (2.6)
Musculoskeletal and connective tissue disorders	5 (2.4)	2 (0.9)	7 (1.7)
Arthralgia	5 (2.4)	2 (0.9)	7 (1.7)
Nervous system disorders	13 (6.3)	15 (7.1)	28 (6.7)
Headache	13 (6.3)	15 (7.1)	28 (6.7)
Respiratory thoracic and mediastinal disorders	4 (1.9)	5 (2.4)	9 (2.2)
Cough	4 (1.9)	5 (2.4)	9 (2.2)
Skin and subcutaneous tissue disorders	19 (9.2)	19 (9.0)	38 (9.1)
Erythema	4 (1.9)	5 (2.4)	9 (2.2)
Pruritis	13 (6.3)	6 (2.8)	19 (4.5)
Psoriasis	5 (2.4)	9 (4.3)	14 (3.3)

AI = auto injector; PFS = pre filled syringe; N = total number of subjects.

Treatment Related Adverse Events: Treatment emergent treatment related AEs are summarized in Table 34. The most frequent AEs related to study product were administration site conditions: injection site reaction, injection site erythema, injection site pain and injection site irritation.

Table 34. Number (%) of Subjects Reporting Treatment Emergent Treatment Related Adverse Events

System Organ Class Preferred Term	Treatment AI (N=207) NAE	 NS (%)	 PFS (N=211) NAE	 NS (%)	 Total (N=418) NAE	 NS (%)
All	175	63 (30.4%)	214	74 (35.1%)	389	137 (32.8%)
Cardiac disorders	1	1 (0.5%)	0	0 (0.0%)	1	1 (0.2%)
Acute myocardial infarction	1	1 (0.5%)	0	0 (0.0%)	1	1 (0.2%)
Ear and labyrinth disorders	0	0 (0.0%)	1	1 (0.5%)	1	1 (0.2%)
Vertigo	0	0 (0.0%)	1	1 (0.5%)	1	1 (0.2%)
Gastrointestinal disorders	3	2 (1.0%)	0	0 (0.0%)	3	2 (0.5%)
Abdominal wall haematoma	1	1 (0.5%)	0	0 (0.0%)	1	1 (0.2%)
Nausea	2	1 (0.5%)	0	0 (0.0%)	2	1 (0.2%)
General disorders and administration site conditions	103	46 (22.2%)	141	49 (23.2%)	244	95 (22.7%)
Asthenia	1	1 (0.5%)	2	2 (0.9%)	3	3 (0.7%)
Fatigue	1	1 (0.5%)	3	3 (1.4%)	4	4 (1.0%)
Feeling hot	0	0 (0.0%)	4	1 (0.5%)	4	1 (0.2%)
Injection site dermatitis	0	0 (0.0%)	1	1 (0.5%)	1	1 (0.2%)
Injection site erythema	14	9 (4.3%)	44	16 (7.6%)	58	25 (6.0%)
Injection site haematoma	7	6 (2.9%)	2	2 (0.9%)	9	8 (1.9%)
Injection site haemorrhage	3	2 (1.0%)	1	1 (0.5%)	4	3 (0.7%)
Injection site inflammation	0	0 (0.0%)	2	2 (0.9%)	2	2 (0.5%)
Injection site irritation	12	6 (2.9%)	14	8 (3.8%)	26	14 (3.3%)
Injection site oedema	1	1 (0.5%)	3	1 (0.5%)	4	2 (0.5%)
Injection site pain	13	9 (4.3%)	10	7 (3.3%)	23	16 (3.8%)
Injection site pruritus	4	3 (1.4%)	12	4 (1.9%)	16	7 (1.7%)
Injection site rash	0	0 (0.0%)	1	1 (0.5%)	1	1 (0.2%)
Injection site reaction	32	16 (7.7%)	33	15 (7.1%)	65	31 (7.4%)
Injection site urticaria	0	0 (0.0%)	1	1 (0.5%)	1	1 (0.2%)
Local reaction	0	0 (0.0%)	5	1 (0.5%)	5	1 (0.2%)
Oedema	12	4 (1.9%)	0	0 (0.0%)	12	4 (1.0%)
Oedema peripheral	1	1 (0.5%)	0	0 (0.0%)	1	1 (0.2%)
Pain	1	1 (0.5%)	1	1 (0.5%)	2	2 (0.5%)
Pyrexia	1	1 (0.5%)	2	2 (0.9%)	3	3 (0.7%)
Immune system disorders	0	0 (0.0%)	1	1 (0.5%)	1	1 (0.2%)
Hypersensitivity	0	0 (0.0%)	1	1 (0.5%)	1	1 (0.2%)
Infections and infestations	11	9 (4.3%)	18	15 (7.1%)	29	24 (5.7%)
Candidiasis	1	1 (0.5%)	0	0 (0.0%)	1	1 (0.2%)
Folliculitis	0	0 (0.0%)	2	2 (0.9%)	2	2 (0.5%)
Herpes simplex ophthalmic	0	0 (0.0%)	1	1 (0.5%)	1	1 (0.2%)
Influenza	1	1 (0.5%)	2	2 (0.9%)	3	3 (0.7%)
Nasopharyngitis	4	4 (1.9%)	5	5 (2.4%)	9	9 (2.2%)
Oral herpes	0	0 (0.0%)	1	1 (0.5%)	1	1 (0.2%)
Paronychia	0	0 (0.0%)	1	1 (0.5%)	1	1 (0.2%)
Pharyngitis	0	0 (0.0%)	3	3 (1.4%)	3	3 (0.7%)
Septic arthritis staphylococcal	0	0 (0.0%)	1	1 (0.5%)	1	1 (0.2%)
Sinusitis	0	0 (0.0%)	1	1 (0.5%)	1	1 (0.2%)

Table 34. Number (%) of Subjects Reporting Treatment Emergent Treatment Related Adverse Events

System Organ Class Preferred Term	Treatment AI (N=207) NAE	 NS (%)	 PFS (N=211) NAE	 NS (%)	 Total (N=418) NAE	 NS (%)
Tooth infection	2	1 (0.5%)	1	1 (0.5%)	3	2 (0.5%)
Upper respiratory tract infection	2	2 (1.0%)	0	0 (0.0%)	2	2 (0.5%)
Urinary tract infection	1	1 (0.5%)	0	0 (0.0%)	1	1 (0.2%)
Injury, poisoning and procedural complications	0	0 (0.0%)	1	1 (0.5%)	1	1 (0.2%)
Procedural nausea	0	0 (0.0%)	1	1 (0.5%)	1	1 (0.2%)
Investigations	2	2 (1.0%)	5	4 (1.9%)	7	6 (1.4%)
Aspartate aminotransferase increased	0	0 (0.0%)	1	1 (0.5%)	1	1 (0.2%)
Blood alkaline phosphatase increased	0	0 (0.0%)	1	1 (0.5%)	1	1 (0.2%)
Gamma-glutamyltransferase increased	0	0 (0.0%)	1	1 (0.5%)	1	1 (0.2%)
Hepatic enzyme increased	0	0 (0.0%)	1	1 (0.5%)	1	1 (0.2%)
Weight increased	2	2 (1.0%)	1	1 (0.5%)	3	3 (0.7%)
Musculoskeletal and connective tissue disorders	5	4 (1.9%)	0	0 (0.0%)	5	4 (1.0%)
Arthralgia	2	2 (1.0%)	0	0 (0.0%)	2	2 (0.5%)
Arthritis	1	1 (0.5%)	0	0 (0.0%)	1	1 (0.2%)
Dactylitis	1	1 (0.5%)	0	0 (0.0%)	1	1 (0.2%)
Psoriatic arthropathy	1	1 (0.5%)	0	0 (0.0%)	1	1 (0.2%)
Nervous system disorders	7	5 (2.4%)	12	7 (3.3%)	19	12 (2.9%)
Depressed level of consciousness	1	1 (0.5%)	0	0 (0.0%)	1	1 (0.2%)
Dizziness postural	1	1 (0.5%)	0	0 (0.0%)	1	1 (0.2%)
Dysaesthesia	1	1 (0.5%)	2	1 (0.5%)	3	2 (0.5%)
Headache	4	3 (1.4%)	8	4 (1.9%)	12	7 (1.7%)
Paraesthesia	0	0 (0.0%)	1	1 (0.5%)	1	1 (0.2%)
Somnolence	0	0 (0.0%)	1	1 (0.5%)	1	1 (0.2%)
Reproductive system and breast disorders	0	0 (0.0%)	1	1 (0.5%)	1	1 (0.2%)
Vulval disorder	0	0 (0.0%)	1	1 (0.5%)	1	1 (0.2%)
Respiratory, thoracic and mediastinal disorders	1	1 (0.5%)	3	3 (1.4%)	4	4 (1.0%)
Asthma	0	0 (0.0%)	1	1 (0.5%)	1	1 (0.2%)
Dyspnoea	0	0 (0.0%)	1	1 (0.5%)	1	1 (0.2%)
Oropharyngeal pain	0	0 (0.0%)	1	1 (0.5%)	1	1 (0.2%)
Sneezing	1	1 (0.5%)	0	0 (0.0%)	1	1 (0.2%)
Skin and subcutaneous tissue disorders	28	11 (5.3%)	25	16 (7.6%)	53	27 (6.5%)
Dermatitis	1	1 (0.5%)	0	0 (0.0%)	1	1 (0.2%)
Eczema	0	0 (0.0%)	1	1 (0.5%)	1	1 (0.2%)
Erythema	11	3 (1.4%)	11	5 (2.4%)	22	8 (1.9%)
Hyperhidrosis	1	1 (0.5%)	1	1 (0.5%)	2	2 (0.5%)
Livedo reticularis	1	1 (0.5%)	0	0 (0.0%)	1	1 (0.2%)
Pruritus	11	7 (3.4%)	6	5 (2.4%)	17	12 (2.9%)

Table 34. Number (%) of Subjects Reporting Treatment Emergent Treatment Related Adverse Events

System Organ Class	Treatment					
	AI (N=207)		PFS (N=211)		Total (N=418)	
Preferred Term	NAE	NS (%)	NAE	NS (%)	NAE	NS (%)
Pruritus generalised	0	0 (0.0%)	1	1 (0.5%)	1	1 (0.2%)
Psoriasis	2	2 (1.0%)	4	4 (1.9%)	6	6 (1.4%)
Purpura	1	1 (0.5%)	0	0 (0.0%)	1	1 (0.2%)
Rash papular	0	0 (0.0%)	1	1 (0.5%)	1	1 (0.2%)
Social circumstances	2	2 (1.0%)	0	0 (0.0%)	2	2 (0.5%)
Refusal of treatment by patient	2	2 (1.0%)	0	0 (0.0%)	2	2 (0.5%)
Vascular disorders	12	6 (2.9%)	6	2 (0.9%)	18	8 (1.9%)
Flushing	0	0 (0.0%)	5	1 (0.5%)	5	1 (0.2%)
Haematoma	3	3 (1.4%)	1	1 (0.5%)	4	4 (1.0%)
Haemorrhage	8	2 (1.0%)	0	0 (0.0%)	8	2 (0.5%)
Hypertension	1	1 (0.5%)	0	0 (0.0%)	1	1 (0.2%)

AEs and SAEs are not separated out.
AI = auto injector; AEs = adverse events; PFS = pre filled syringe; N = total number of subjects; NAE = number of adverse events; NS = number of subjects with adverse events; SAEs = serious adverse events.

Serious Adverse Events: Treatment emergent serious adverse events (SAEs) are summarized in Table 35. Nine (9, 2.2%) subjects reported SAEs during this study from the day of the first injection of ETN, 4 subjects in the PFS group and 5 subjects in the AI group. Only 2 of these SAEs, reported for the same subject, were considered related to the study product: acute myocardial infarction and peripheral edema. Both events resolved within 2 weeks and the subject was withdrawn from the study.

Table 35. Description of Treatment Emergent Serious Adverse Events, Safety Population

Serial number	Event (Preferred Term)	Start Date	Stop Date	Severity	Outcome	Related to Study Product
AI Group						
1	Acute myocardial infarction	15/12/2008	29/12/2008	Life threatening	Recovered	Yes
	Oedema peripheral	15/12/2008	29/12/2008	Severe	Recovered	Yes
2	Brusitis infective	22/02/2008	17/03/2008	Moderate	Recovered	No
3	Cerebrovascular accident	05/04/2008	-	Life threatening	Persisting	No
4	Retinal operation	21/08/2008	-	Severe	Persisting	No
5	Dermatitis exfoliative	31/12/2008	13/01/2009	Severe	Recovered	No
PFS Group						
1	Urinary calculus removal	09/07/2008	11/07/2008	Moderate	Recovered	No
2	Joint abscess	24/12/2007	22/01/2008	Severe	Recovered	No
3	Vertigo	17/11/2008	20/11/2008	Mild	Recovered	No
4	Prostatic operation	23/02/2009	03/03/2009	Moderate	Recovered	No

AI = auto injector; PFS = pre-filled syringe

Withdrawals due to Adverse Events: AEs leading to study withdrawal are summarized in Table 36. A total of 13 subjects (3.1%) experienced AEs that led to study withdrawal: 5 (2.4%) in the AI group and 8 (3.8%) in the PFS group. These AEs were mostly infections and infestations or skin and subcutaneous tissue disorders.

AEs leading to test article permanent discontinuation are summarized in Table 37. Six (6) subjects experienced AEs leading to test article permanent discontinuation: 1 in the AI group and 5 in the PFS group. There was no statistically significant difference between the 2 groups concerning the AEs leading to study withdrawal (p=0.575) or the AEs leading to test article permanent discontinuation (p=0.215).

Table 36. Adverse Events Leading to Study Withdrawal From the Day of the First Injection of Etanercept, Safety Population

System Organ Class Preferred Term	Treatment					
	AI (N=207)		PFS (N=211)		Total (N=418)	
	NAE	NS (%)	NAE	NS (%)	NAE	NS (%)
All	6	5 (2.4%)	8	8 (3.8%)	14	13 (3.1%)
Cardiac disorders	1	1 (0.5%)	-	-	1	1 (0.2%)
Acute myocardial infarction	1	1 (0.5%)	-	-	1	1 (0.2%)
General disorders and administration site conditions	-	-	2	2 (0.9%)	2	2 (0.5%)
Injection site haematoma	-	-	1	1 (0.5%)	1	1 (0.2%)
Injection site pain	-	-	1	1 (0.5%)	1	1 (0.2%)
Infections and infestations	1	1 (0.5%)	3	3 (1.4%)	4	4 (1.0%)
Bronchitis			1	1 (0.5%)	1	1 (0.2%)
Brusitis infective	1	1 (0.5%)	-	-	1	1 (0.2%)
Rhinitis	-	-	1	1 (0.5%)	1	1 (0.2%)
Septic arthiritis staphylococcal	-	-	1	1 (0.5%)	1	1 (0.2%)
Musculoskeletal and connective tissue disorders	1	1 (0.5%)	-	-	1	1 (0.2%)
Psoriatic arthropathy	1	1 (0.5%)	-	-	1	1 (0.2%)
Nervous system disorders	2	2 (1.0%)	-	-	2	2 (0.5%)
Cerebrovascular accident	1	1 (0.5%)	-	-	1	1 (0.2%)
Headache	1	1 (0.5%)	-	-	1	1 (0.2%)
Skin and subcutaneous tissue disorders	1	1 (0.5%)	3	3 (1.4%)	4	4 (1.0%)
Eczema	-	-	1	1 (0.5%)	1	1 (0.2%)
Erythema	-	-	1	1 (0.5%)	1	1 (0.2%)
Psoriasis	1	1 (0.5%)	1	1 (0.5%)	2	2 (0.5%)

AI = auto injector; PFS = pre filled syringe; N = total number of subjects; NAE = number of adverse events; NS = number of subjects with adverse events

Table 37. Adverse Events Leading to Test Article Permanent Discontinuation From the Day of the First Injection of Etanercept, Safety Population

System Organ Class Preferred Term	Treatment					
	AI (N=207)		PFS (N=211)		Total (N=418)	
	NAE	NS (%)	NAE	NS (%)	NAE	NS (%)
All	1	1 (0.5%)	7	5 (2.4%)	8	6 (1.4%)
Gastrointestinal disorders	-	-	1	1 (0.5%)	1	1 (0.2%)
Gastritis	-	-	1	1 (0.5%)	1	1 (0.2%)
General disorders and administration site conditions	1	1 (0.5%)	-	-	1	1 (0.2%)
Oedema peripheral	1	1 (0.5%)	-	-	1	1 (0.2%)
Infections and infestations	-	-	1	1 (0.5%)	1	1 (0.2%)
Pharyngitis	-	-	1	1 (0.5%)	1	1 (0.2%)
Nervous system disorders	-	-	2	2 (0.9%)	2	2 (0.5%)
Paraesthesia	-	-	1	1 (0.5%)	1	1 (0.2%)
Peripheral sensory neuropathy	-	-	1	1 (0.5%)	1	1 (0.2%)
Respiratory, thoracic and mediastinal disorders	-	-	1	1 (0.5%)	1	1 (0.2%)
Asthma	-	-	1	1 (0.5%)	1	1 (0.2%)
Skin and subcutaneous tissue disorders	-	-	1	1 (0.5%)	1	1 (0.2%)
Pruritus	-	-	1	1 (0.5%)	1	1 (0.2%)
Surgical and medical procedures	-	-	1	1 (0.5%)	1	1 (0.2%)
Prostatic operation	-	-	1	1 (0.5%)	1	1 (0.2%)

AI = auto injector; PFS = pre filled syringe; N = total number of subjects; NAE = number of adverse events; NS = number of subjects with adverse event

Laboratory Evaluations: Only baseline clinical laboratory parameters were measured. No on treatment data have been analyzed for the scope of this study. Vital signs results were similar in both groups, and mean values remained stable during the course of the study.

Deaths: No deaths were reported during the study.

CONCLUSION:

In conclusion, this study showed high subject satisfaction when injecting etanercept either as a pre-filled syringe or in the auto-injector, with satisfaction being even higher in the subject group the auto-injector. Profiles could be identified regarding the subject's perceptions, with the oldest subjects and those who had had psoriasis for a longer duration showing higher percentages of subjects who were 'very satisfied', while subjects who were more anxious and depressed, as measured by HAD subscales scores, were more often into the 'less satisfied' category.

Whatever the device, the beneficial effect on health status and psoriasis activity of etanercept could be observed after 12 weeks of treatment with the 50 mg twice weekly regimen. The overall safety profile was comparable for both devices and in keeping with the profile as understood to date, with no new signals.