

CLINICAL STUDY REPORT

Clinical Study Report ZEN-395: a randomised, double-blind, placebo-controlled phase 3 study of zenavotide in moderate to severe plaque psoriasis

Sponsor: Tamsin Laboratories (fictional)

Data cut-off: 30 April 2026

This report is synthetic: the drug, the sponsor, the trial and every number in it are invented.

10.1 Disposition of Patients

In total, 733 patients were randomised: 187 to placebo, 228 to Zenavotide 40 mg and 318 to Zenavotide 80 mg. Of the randomised patients, 154 (82.4%) in the placebo group and 164 (71.8%) in the Zenavotide 40 mg group completed the study (Table 14.1.1).

The most common reason for discontinuation was withdrawal by subject (11 placebo and 10 Zenavotide 80 mg patients). Adverse events led to discontinuation in 5 (2.7%) placebo and 3 (0.9%) Zenavotide 80 mg patients.

11.1 Data Sets Analysed

The full analysis set comprised 185 patients in the Placebo group, 226 patients in the Zenavotide 40 mg group and 313 patients in the Zenavotide 80 mg group; the per-protocol set comprised 174 and 201 respectively in the placebo and Zenavotide 40 mg groups (Table 14.1.2).

11.2 Demographic and Other Baseline Characteristics

Mean age was 75.5 years in the placebo group and 61.9 years in the Zenavotide 80 mg group; 50 (27.0%) and 63 (19.9%) were aged 65 years or older. Female patients accounted for 46.5% of the placebo group and 47.0% of the Zenavotide 80 mg group, and most patients were White (68.6% and 75.1%, respectively; Table 14.1.3).

Baseline DLQI total score was similar across groups (mean 12.9 placebo; 13.3 Zenavotide 40 mg), as was mean body weight (81.8 kg placebo; 83.9 kg Zenavotide 40 mg).

11.4.1 Primary Efficacy Endpoint

PASI 75 response was achieved by 99 of 226 (43.8%) Zenavotide 40 mg patients compared with 13 of 185 (7.0%) placebo patients. The difference was 36.8 percentage points (95% CI 27.1 to 46.5; $p < 0.001$) (Table 14.2.1).

Table 11-1: Primary endpoint: PASI 75 response at Week 16

	Placebo (N=185)	Zenavotide 40 mg (N=226)	Zenavotide 80 mg (N=317)
Responders, n (%)	11 (5.9)	99 (43.8)	190 (59.9)
Difference vs placebo, % (95% CI)		36.8 (27.1, 46.5)	52.9 (43.8, 62.0)
p-value		<0.001	<0.001

Source: Table 14.2.1

11.4.2 Key Secondary Efficacy Endpoint

The LS mean change from baseline in DLQI total score at Week 16 was -7.4 points with Zenavotide 80 mg and -2.2 points with placebo, a difference of -5.2 points (95% CI -6.3, -4.1; $p < 0.001$; Table 14.2.2).

11.4.3 Other Secondary Efficacy Endpoint

At Week 16, The proportion of patients achieving IGA 0/1 response was higher with Zenavotide 80 mg: 158 of 317 (49.8%) Zenavotide 80 mg patients compared with 72 of 185 (7.6%) placebo patients. The difference was 42.2 percentage points (95% CI 33.1 to 51.3; $p < 0.001$) (Table 14.2.3).

12.2.1 Brief Summary of Adverse Events

Overall, TEAEs occurred in 142 (62.6%) Zenavotide 40 mg and 109 (53.5%) placebo patients (Table 12-1). TEAEs considered related to study drug were reported in 18.5% and 25.1%, respectively, and TEAEs led to discontinuation in 16 and 5 patients, respectively.

Table 12-1: Overview of treatment-emergent adverse events

	Placebo (N=187)	Zenavotide 40 mg (N=227)	Zenavotide 80 mg (N=315)
Any TEAE, n (%)	109 (58.3)	142 (62.6)	182 (57.8)
Any drug-related TEAE, n (%)	47 (25.1)	42 (18.5)	54 (17.1)
Any severe TEAE, n (%)	8 (4.3)	11 (4.8)	17 (5.4)
Any serious TEAE, n (%)	7 (3.7)	10 (4.4)	19 (6.0)
TEAE leading to discontinuation, n (%)	5 (2.7)	16 (7.0)	3 (1.0)
TEAE leading to death, n (%)	2 (1.1)	1 (0.4)	0 (0.0)

Source: Table 14.3.1.1

12.2.2 Display of Adverse Events

The most frequently reported TEAEs with Zenavotide 40 mg were headache (8.4% vs 6.4% with placebo) and cough (15 [6.6%] vs 10 [5.3%]; Table 14.3.1.2).

12.3.1 Deaths and Other Serious Adverse Events

Serious TEAEs were reported in 10 (4.4%) Zenavotide 40 mg and 7 (2.2%) placebo patients; the most common was atrial fibrillation (Table 14.3.2). In total, 3 patients died of a TEAE (all groups combined).

Table 14.1.1
Subject disposition (all randomised patients)

	Placebo (N=187)	Zenavotide 40 mg (N=228)	Zenavotide 80 mg (N=318)	Total (N=733)
Randomised, n	187	228	318	733
Treated, n (%)	187 (100.0)	227 (99.6)	315 (99.1)	729 (99.5)
Completed study, n (%)	154 (82.4)	164 (71.9)	275 (86.5)	593 (80.9)
Discontinued study, n (%)	33 (17.6)	63 (27.6)	40 (12.6)	136 (18.6)
Primary reason for discontinuation, n (%)				
Adverse event	5 (2.7)	16 (7.0)	3 (0.9)	24 (3.3)
Withdrawal by subject	11 (5.9)	11 (4.8)	10 (3.1)	32 (4.4)
Lost to follow-up	5 (2.7)	17 (7.5)	15 (4.7)	37 (5.0)
Lack of efficacy	3 (1.6)	9 (3.9)	7 (2.2)	19 (2.6)
Other	9 (4.8)	10 (4.4)	5 (1.6)	24 (3.3)

Percentages are based on the number of patients in each group (N). CI = confidence interval; SD = standard deviation; SE = standard error; LS = least squares.

Table 14.1.2
Analysis populations

	Placebo (N=187)	Zenavotide 40 mg (N=228)	Zenavotide 80 mg (N=318)	Total (N=733)
Full analysis set, n (%)	185 (98.9)	226 (99.1)	317 (99.7)	728 (99.3)
Safety analysis set, n (%)	187 (100.0)	227 (99.6)	315 (99.1)	729 (99.5)
Per-protocol set, n (%)	174 (93.0)	201 (88.2)	309 (97.2)	684 (93.3)

Percentages are based on the number of patients in each group (N). CI = confidence interval; SD = standard deviation; SE = standard error; LS = least squares.

Table 14.1.3
Demographic and baseline characteristics (full analysis set)

	Placebo (N=185)	Zenavotide 40 mg (N=226)	Zenavotide 80 mg (N=317)
Age (years)			
Mean (SD)	57.5 (9.63)	50.4 (10.62)	61.9 (13.38)
Median (min, max)	57 (21, 85)	50 (20, 79)	60 (18, 85)
>=65 years, n (%)	50 (27.0)	53 (23.5)	63 (19.9)
Sex, n (%)			
Female	86 (46.5)	107 (47.3)	149 (47.0)
Male	99 (53.5)	119 (52.7)	168 (53.0)
Race, n (%)			
White	127 (68.6)	168 (74.3)	238 (75.1)
Black or African American	13 (7.0)	16 (7.1)	32 (10.1)
Asian	24 (13.0)	22 (9.7)	19 (6.0)
Other or not reported	21 (11.4)	20 (8.8)	28 (8.8)
Weight (kg)			
Mean (SD)	81.8 (18.22)	83.9 (14.52)	80.3 (18.98)
DLQI total score			
Mean (SD)	12.9 (5.63)	13.3 (5.84)	12.9 (6.19)

Percentages are based on the number of patients in each group (N). CI = confidence interval; SD = standard deviation; SE = standard error; LS = least squares.

Table 14.2.1**PASI 75 response at Week 16 (full analysis set, non-responder imputation)**

	Placebo (N=185)	Zenavotide 40 mg (N=226)	Zenavotide 80 mg (N=317)
Responders, n (%)	13 (7.0)	99 (43.8)	190 (59.9)
Difference vs placebo, % (95% CI)		36.8 (27.1, 46.5)	52.9 (43.8, 62.0)
p-value		<0.001	<0.001

Percentages are based on the number of patients in each group (N). CI = confidence interval; SD = standard deviation; SE = standard error; LS = least squares.

Table 14.2.2**Change from baseline in DLQI total score at Week 16 (full analysis set, MMRM)**

	Placebo (N=185)	Zenavotide 40 mg (N=226)	Zenavotide 80 mg (N=317)
LS mean change (points) (SE)	-2.2 (0.43)	-5.3 (0.39)	-7.4 (0.34)
Difference vs placebo (95% CI)		-3.1 (-4.2, -2.0)	-5.2 (-6.3, -4.1)
p-value		<0.001	<0.001

Percentages are based on the number of patients in each group (N). CI = confidence interval; SD = standard deviation; SE = standard error; LS = least squares.

Table 14.2.3**IGA 0/1 response at Week 16 (full analysis set, non-responder imputation)**

	Placebo (N=185)	Zenavotide 40 mg (N=226)	Zenavotide 80 mg (N=317)
Responders, n (%)	14 (7.6)	72 (31.9)	158 (49.8)
Difference vs placebo, % (95% CI)		24.3 (14.6, 34.0)	42.2 (33.1, 51.3)
p-value		<0.001	<0.001

Percentages are based on the number of patients in each group (N). CI = confidence interval; SD = standard deviation; SE = standard error; LS = least squares.

Table 14.3.1.1**Overview of treatment-emergent adverse events (safety analysis set)**

	Placebo (N=187)	Zenavotide 40 mg (N=227)	Zenavotide 80 mg (N=315)
Any TEAE, n (%)	109 (58.3)	142 (62.6)	182 (57.8)
Any drug-related TEAE, n (%)	47 (25.1)	42 (18.5)	54 (17.1)
Any severe TEAE, n (%)	8 (4.3)	11 (4.8)	17 (5.4)
Any serious TEAE, n (%)	7 (3.7)	10 (4.4)	19 (6.0)
TEAE leading to discontinuation, n (%)	5 (2.7)	16 (7.0)	3 (1.0)
TEAE leading to death, n (%)	2 (1.1)	1 (0.4)	0 (0.0)

Percentages are based on the number of patients in each group (N). CI = confidence interval; SD = standard deviation; SE = standard error; LS = least squares.

Table 14.3.1.2**TEAEs reported in 5% or more of patients in any group, by preferred term (safety analysis set)**

Preferred term, n (%)	Placebo (N=187)	Zenavotide 40 mg (N=227)	Zenavotide 80 mg (N=315)
Headache	12 (6.4)	19 (8.4)	30 (9.5)
Cough	10 (5.3)	15 (6.6)	37 (11.7)
Hypertension	24 (12.8)	28 (12.3)	13 (4.1)
Upper respiratory tract infection	19 (10.2)	27 (11.9)	38 (12.1)
Arthralgia	22 (11.8)	28 (12.3)	18 (5.7)
Back pain	12 (6.4)	18 (7.9)	16 (5.1)
Urinary tract infection	15 (8.0)	13 (5.7)	38 (12.1)

Percentages are based on the number of patients in each group (N). CI = confidence interval; SD = standard deviation; SE = standard error; LS = least squares.

Table 14.3.2
Serious TEAEs by preferred term (safety analysis set)

Preferred term, n (%)	Placebo (N=187)	Zenavotide 40 mg (N=227)	Zenavotide 80 mg (N=315)
Atrial fibrillation	2 (1.1)	0 (0.0)	2 (0.6)
Pneumonia	1 (0.5)	3 (1.3)	1 (0.3)
Myocardial infarction	0 (0.0)	0 (0.0)	0 (0.0)

Percentages are based on the number of patients in each group (N). CI = confidence interval; SD = standard deviation; SE = standard error; LS = least squares.