

Study COMP 004

Efficacy Endpoint Results

Table 1: Primary Endpoint – Time to Depressive Events, Primary Analysis, Composite Strategy Estimand - Modified Full Analysis Set

	Statistic	COMP360 25 mg (N=79)	COMP360 10 mg (N=75)	COMP360 1 mg (N=79)
Time to any depressive event (Days)				
Median	Estimate	92.0	83.0	62.0
	95% CI	(49.0, 199.0)	(39.0, 142.0)	(28.0, - ^a)

CI=confidence interval; EudraCT=European Union Drug Regulating Authorities Clinical Trials Database.

a The upper bound of the 95% CI for the median time to event in the COMP360 1 mg treatment group could not be estimated. A value of 9999.99 was entered into the primary results table in the EudraCT system to represent this non-evaluable estimate.

Source: Table 14.2.1.1.

Table 2: Summary of MADRS Change from Baseline to Week 52 – Full Analysis Set

Time point	Statistic	COMP360 25 mg (N=22)	COMP360 10 mg (N=19)	COMP360 1 mg (N=17)	COMP360 25 mg + SSRI (N=8)
Baseline	Mean (SD)	31.6 (4.69)	31.9 (5.14)	33.7 (4.28)	32.4 (6.84)
	Median (min, max)	31.0 (25, 40)	34.0 (24, 39)	33.0 (26, 42)	34.0 (18, 39)
Change from Baseline to:					
Week 12	Mean (SD)	-12.6 (13.52)	-12.6 (13.13)	-10.2 (11.10)	-24.2 (11.20)
	95% CI	-18.6, -6.6	-18.9, -6.3	-15.9, -4.5	-35.9, -12.4
	Median (min, max)	-8.5 (-40, 3)	-7.0 (-39, 3)	-7.0 (-30, 9)	-22.5 (-38, -13)
Week 16	Mean (SD)	-12.1 (12.75)	-9.2 (11.52)	-13.9 (9.60)	-25.8 (8.89)
	95% CI	-18.4, -5.7	-16.1, -2.2	-19.3, -8.6	-35.2, -16.5
	Median (min, max)	-9.0 (-38, 7)	-9.0 (-35, 8)	-13.0 (-32, 0)	-29.0 (-35, -12)
Week 20	Mean (SD)	-12.6 (13.89)	-11.2 (14.76)	-12.1 (12.02)	-25.5 (6.16)
	95% CI	-19.5, -5.6	-20.5, -1.8	-19.3, -4.8	-32.0, -19.0
	Median (min, max)	-9.5 (-36, 5)	-4.0 (-36, 4)	-8.0 (-32, 4)	-26.0 (-34, -18)
Week 24	Mean (SD)	-13.2 (13.59)	-10.8 (14.31)	-13.4 (11.95)	-28.0 (7.11)
	95% CI	-19.9, -6.4	-19.4, -2.1	-20.3, -6.5	-36.8, -19.2
	Median (min, max)	-7.5 (-37, 4)	-9.0 (-35, 6)	-12.0 (-32, 7)	-28.0 (-38, -18)
Week 28	Mean (SD)	-11.6 (14.14)	-12.9 (12.76)	-13.4 (11.58)	-31.5 (5.69)
	95% CI	-18.9, -4.3	-20.2, -5.5	-20.4, -6.4	-40.5, -22.5
	Median (min, max)	-6.0 (-39, 6)	-11.0 (-34, 5)	-13.0 (-32, 4)	-31.5 (-38, -25)
Week 40	Mean (SD)	-5.7 (10.81)	-14.6 (14.19)	-16.4 (12.26)	-25.3 (6.40)
	95% CI	-11.7, 0.3	-22.8, -6.5	-23.4, -9.3	-35.4, -15.1
	Median (min, max)	-6.0 (-35, 9)	-13.0 (-34, 9)	-16.5 (-42, 7)	-25.5 (-32, -18)
Week 52	Mean (SD)	-10.8 (7.95)	-17.0 (13.82)	-12.7 (9.60)	-25.0 (6.08)
	95% CI	-15.2, -6.4	-25.0, -9.0	-18.1, -7.4	-40.1, -9.9
	Median (min, max)	-11.0 (-23, 6)	-17.5 (-38, 5)	-14.0 (-32, 5)	-28.0 (-29, -18)

CI=confidence interval; MADRS=Montgomery-Åsberg Depression Rating Scale; SD=standard deviation; SSRI=selective serotonin reuptake inhibitor.

Source: Table 14.2.2.1.1.

Table 3: Summary of MADRS Responders – Full Analysis Set

Visit	Statistic	COMP360 25 mg (N=22) n (%)	COMP360 10 mg (N=19) n (%)	COMP360 1 mg (N=17) n (%)	COMP360 25 mg + SSRI (N=8) n (%)
Week 12	n/n* (%)	9/22 (40.9)	5/19 (26.3)	6/17 (35.3)	3/6 (50.0)
	95% CI	(20.4, 61.5)	(6.5, 46.1)	(12.6, 58.0)	(10.0, 90.0)
Week 16	n/n* (%)	8/18 (44.4)	3/13 (23.1)	5/15 (33.3)	5/6 (83.3)
	95% CI	(21.5, 67.4)	(0.2, 46.0)	(9.5, 57.2)	(53.5, 100.0)
Week 20	n/n* (%)	6/18 (33.3)	4/12 (33.3)	6/13 (46.2)	6/ 6 (100.0)
	95% CI	(11.6, 55.1)	(6.7, 60.0)	(19.1, 73.3)	(100.0, 100.0)
Week 24	n/n* (%)	7/18 (38.9)	4/13 (30.8)	5/14 (35.7)	5/5 (100.0)
	95% CI	(16.4, 61.4)	(5.7, 55.9)	(10.6, 60.8)	(100.0, 100.0)
Week 28	n/n* (%)	7/17 (41.2)	5/14 (35.7)	5/13 (38.5)	4/4 (100.0)
	95% CI	(17.8, 64.6)	(10.6, 60.8)	(12.0, 64.9)	(100.0, 100.0)
Week 40	n/n* (%)	2/15 (13.3)	7/14 (50.0)	7/14 (50.0)	4/4 (100.0)
	95% CI	(0.0, 30.5)	(23.8, 76.2)	(23.8, 76.2)	(100.0, 100.0)
Week 52	n/n* (%)	4/15 (26.7)	7/14 (50.0)	5/15 (33.3)	3/ 3 (100.0)
	95% CI	(4.3, 49.0)	(23.8, 76.2)	(9.5, 57.2)	(100.0, 100.0)

CI=confidence interval; MADRS=Montgomery-Åsberg Depression Rating Scale; SSRI=selective serotonin reuptake inhibitor.

A responder is a participant with ≥50% reduction from baseline in MADRS total score at specified timepoint.

Percentages are based on the number of participants in the Full Analysis Set with non-missing observations (identified as n* in the table)

Source: Table 14.2.2.3.1.

Table 4: Summary of MADRS Remitters – Full Analysis Set

Visit	Statistic	COMP360 25 mg (N=22) n (%)	COMP360 10 mg (N=19) n (%)	COMP360 1 mg (N=17) n (%)	COMP360 25 mg + SSRI (N=8) n (%)
Week 12	n/n* (%)	7/22 (31.8)	4/19 (21.1)	3/17 (17.6)	3/6 (50.0)
	95% CI	(12.4, 51.3)	(2.7, 39.4)	(0.0, 35.8)	(10.0, 90.0)
Week 16	n/n* (%)	5/18 (27.8)	1/13 (7.7)	3/15 (20.0)	5/6 (83.3)
	95% CI	(7.1, 48.5)	(0.0, 22.2)	(0.0, 40.2)	(53.5, 100.0)
Week 20	n/n* (%)	5/18 (27.8)	4/12 (33.3)	3/13 (23.1)	4/6 (66.7)
	95% CI	(7.1, 48.5)	(6.7, 60.0)	(0.2, 46.0)	(28.9, 100.0)
Week 24	n/n* (%)	5/18 (27.8)	3/13 (23.1)	4/14 (28.6)	4/5 (80.0)
	95% CI	(7.1, 48.5)	(0.2, 46.0)	(4.9, 52.2)	(44.9, 100.0)
Week 28	n/n* (%)	4/17 (23.5)	4/14 (28.6)	3/13 (23.1)	4/4 (100.0)
	95% CI	(3.4, 43.7)	(4.9, 52.2)	(0.2, 46.0)	(100.0, 100.0)
Week 40	n/n* (%)	1/15 (6.7)	7/14 (50.0)	4/14 (28.6)	3/4 (75.0)
	95% CI	(0.0, 19.3)	(23.8, 76.2)	(4.9, 52.2)	(32.6, 100.0)
Week 52	n/n* (%)	0/15	7/14 (50.0)	2/15 (13.3)	2/3 (66.7)
	95% CI	-	(23.8, 76.2)	(0.0, 30.5)	(13.3, 100.0)

CI=confidence interval; MADRS=Montgomery-Åsberg Depression Rating Scale; SSRI=selective serotonin reuptake inhibitor.

Remitters are defined as having MADRS total score ≤10 at a specified timepoint.

Percentages are based on the number of participants in the Full Analysis Set with non-missing observations (identified as n* in the table)

Source: Table 14.2.2.4.1.

Table 5: Summary of MADRS Sustained Responders – Full Analysis Set

Visit	Statistic	COMP360 25 mg (N=22)	COMP360 10 mg (N=19)	COMP360 1 mg (N=17)	COMP360 25 mg + SSRI (N=8)
Week 12	n/n* (%)	6/22 (27.3)	4/18 (22.2)	0/17	2/6 (33.3)
	95% CI	(8.7, 45.9)	(3.0, 41.4)	-	(0.0, 71.1)
Week 16	n/n* (%)	4/18 (22.2)	2/13 (15.4)	0/15	2/5 (40.0)
	95% CI	(3.0, 41.4)	(0.0, 35.0)	-	(0.0, 82.9)
Week 20	n/n* (%)	4/18 (22.2)	1/12 (8.3)	0/13	1/5 (20.0)
	95% CI	(3.0, 41.4)	(0.0, 24.0)	-	(0.0, 55.1)
Week 24	n/n* (%)	4/18 (22.2)	1/13 (7.7)	0/14	1/4 (25.0)
	95% CI	(3.0, 41.4)	(0.0, 22.2)	-	(0.0, 67.4)
Week 28	n/n* (%)	3/17 (17.6)	1/13 (7.7)	0/13	1/4 (25.0)
	95% CI	(0.0, 35.8)	(0.0, 22.2)	-	(0.0, 67.4)
Week 40	n/n* (%)	1/15 (6.7)	1/12 (8.3)	0/14	0/3
	95% CI	(0.0, 19.3)	(0.0, 24.0)	-	-
Week 52	n/n* (%)	1/15 (6.7)	1/13 (7.7)	0/15	0/2
	95% CI	(0.0, 19.3)	(0.0, 22.2)	-	-

CI=confidence interval; MADRS=Montgomery-Åsberg Depression Rating Scale; SSRI=selective serotonin reuptake inhibitor.

Sustained responders at a visit are defined as participants meeting the MADRS response criteria (a $\geq 50\%$ reduction from baseline in MADRS total score) at any visit up to and including week 3 and also at all visits after week 3 up to and including the visit.

Percentages are based on the number of participants in the Full Analysis Set for which a sustained responder status could be uniquely defined based on their observed MADRS scores (identified with n* in the table)

Source: Table 14.2.2.5.1.1.