

Table 15.12.2.1: Analysis of Response Rate in TSS at Week 24 and at Week 12
Randomized Treatment Phase
Intent-to-Treat Analysis Set

	MMB (N=104)	BAT (N=52)	Total (N=156)
All Strata Combined			
Total Symptom Score Status			
Missing TSS at baseline (excluded from rate calculation)	0	0	0
TSS = 0 at baseline	1 (1.0%)	3 (5.8%)	4 (2.6%)
TSS > 0 at baseline	103 (99.0%)	49 (94.2%)	152 (97.4%)
Response Rate of Total Symptom Score at Week 24			
Subjects Evaluable at Week 24, n	103	51	154
TSS = 0 at baseline and TSS >0 or missing at Week 24	0	2 (3.9%)	2 (1.3%)
Responder, n(%)	27 (26.2%)	3 (5.9%)	30 (19.5%)
95% Exact CI	0.1804, 0.3580	0.0123, 0.1624	0.1355, 0.2663
Proportion Difference - Stratified CMH Method (95% CI)	0.20 (0.09, 0.32)		
p-value	<0.001		
Proportion Difference - Unstratified CMH Method (95% CI)	0.20 (0.09, 0.31)		
p-value	<0.001		
Proportion Difference - Unstratified Exact Method (95% CI)	0.20 (0.04, 0.36)		
p-value	0.002		
Non-Responder, n(%)	76 (73.8%)	48 (94.1%)	124 (80.5%)
Last participation date < Day 162 in RT phase	28 (27.2%)	10 (19.6%)	38 (24.7%)
Last participation date >= Day 162 and TSS at Week 24 not available	3 (2.9%)	3 (5.9%)	6 (3.9%)
>0% increase from baseline at Week 24	25 (24.3%)	23 (45.1%)	48 (31.2%)
<50% reduction from baseline week 24	45 (43.7%)	34 (66.7%)	79 (51.3%)

95% Exact CI is based on Clopper-Pearson method without stratification

TSS rate analysis at one visit only include subjects with TSS >0 at baseline or with TSS =0 at baseline but with TSS > 0 or missing at that visit.

TSS = Total Symptom Score; CMH = Cochran-Mantel-Haenszel;

Source: Listing 16.3.2.1

Data Extracted: CRF data: 25JUN2019

Source: ...\\version4\prog\t-tss24.sas v9.4 Output file: t-tss24.out 27AUG2020:21:10

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	MMB (N=104)	BAT (N=52)	Total (N=156)
Response Rate of Total Symptom Score at Week 12			
Subjects Evaluable at Week 12, n	103	51	154
TSS = 0 at baseline and TSS >0 or missing at Week 12	0	2 (3.9%)	2 (1.3%)
Responder, n(%)	26 (25.2%)	4 (7.8%)	30 (19.5%)
95% Exact CI	0.1720, 0.3476	0.0218, 0.1888	0.1355, 0.2663
Proportion Difference - Stratified CMH Method (95% CI)	0.17 (0.05, 0.29)		
p-value	0.007		
Proportion Difference - Unstratified CMH Method (95% CI)	0.17 (0.06, 0.29)		
p-value	0.003		
Proportion Difference - Unstratified Exact Method (95% CI)	0.17 (0.01, 0.34)		
p-value	0.010		
Non-Responder, n(%)	77 (74.8%)	47 (92.2%)	124 (80.5%)
Last participation date < Day 78 in RT phase	14 (13.6%)	9 (17.6%)	23 (14.9%)
Last participation date >= Day 78 and TSS at Week 12 not available	2 (1.9%)	0	2 (1.3%)
>0% increase from baseline at Week 12	33 (32.0%)	22 (43.1%)	55 (35.7%)
<50% reduction from baseline at week 12	61 (59.2%)	36 (70.6%)	97 (63.0%)

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TSS = Total Symptom Score; CMH = Cochran-Mantel-Haenszel;

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Strata 1			
Transfusion Dependence Yes and Baseline TSS <18	37	15	52
Total Symptom Score Status			
Missing TSS at baseline (excluded from rate calculation)	0	0	0
TSS = 0 at baseline	0	2 (13.3%)	2 (3.8%)
TSS > 0 at baseline	37 (100.0%)	13 (86.7%)	50 (96.2%)
Response Rate of Total Symptom Score at Week 24			
Subjects Evaluable at Week 24, n	37	15	52
TSS = 0 at baseline and TSS >0 or missing at Week 24	0	2 (13.3%)	2 (3.8%)
Responder, n(%)	12 (32.4%)	0	12 (23.1%)
95% Exact CI	0.1801, 0.4979	0.0000, 0.2180	0.1253, 0.3684
Proportion Difference - Unstratified CMH Method (95% CI)	0.32 (0.15, 0.50)		
Proportion Difference - Unstratified Exact Method (95% CI)	0.32 (0.02, 0.59)		
Non-Responder, n(%)	25 (67.6%)	15 (100.0%)	40 (76.9%)
Last participation date < Day 162 in RT phase	7 (18.9%)	3 (20.0%)	10 (19.2%)
Last participation date >= Day 162 and TSS at Week 24 not available	2 (5.4%)	2 (13.3%)	4 (7.7%)
>0% increase from baseline at Week 24	11 (29.7%)	7 (46.7%)	18 (34.6%)
<50% reduction from baseline week 24	16 (43.2%)	9 (60.0%)	25 (48.1%)

95% Exact CI is based on Clopper-Pearson method without stratification

TSS rate analysis at one visit only include subjects with TSS >0 at baseline or with TSS =0 at baseline but with TSS > 0 or missing at that visit.

TSS = Total Symptom Score; CMH = Cochran-Mantel-Haenszel;

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Response Rate of Total Symptom Score at Week 12			
Subjects Evaluable at Week 12, n	37	14	51
TSS = 0 at baseline and TSS >0 or missing at Week 12	0	1 (7.1%)	1 (2.0%)
Responder, n(%)	11 (29.7%)	1 (7.1%)	12 (23.5%)
95% Exact CI	0.1587, 0.4698	0.0018, 0.3387	0.1279, 0.3749
Proportion Difference - Unstratified CMH Method (95% CI)	0.23 (0.00, 0.45)		
Proportion Difference - Unstratified Exact Method (95% CI)	0.23 (-0.09, 0.51)		
Non-Responder, n(%)	26 (70.3%)	13 (92.9%)	39 (76.5%)
Last participation date < Day 78 in RT phase	1 (2.7%)	3 (21.4%)	4 (7.8%)
Last participation date >= Day 78 and TSS at Week 12 not available	1 (2.7%)	0	1 (2.0%)
>0% increase from baseline at Week 12	12 (32.4%)	6 (42.9%)	18 (35.3%)
<50% reduction from baseline at week 12	24 (64.9%)	9 (64.3%)	33 (64.7%)

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TSS = Total Symptom Score; CMH = Cochran-Mantel-Haenszel;

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	MMB (N=104)	BAT (N=52)	Total (N=156)
Strata 2			
Transfusion Dependence Yes and Baseline TSS >=18	21	12	33
Total Symptom Score Status			
Missing TSS at baseline (excluded from rate calculation)	0	0	0
TSS = 0 at baseline	0	0	0
TSS > 0 at baseline	21 (100.0%)	12 (100.0%)	33 (100.0%)
Response Rate of Total Symptom Score at Week 24			
Subjects Evaluable at Week 24, n	21	12	33
TSS = 0 at baseline and TSS >0 or missing at Week 24	0	0	0
Responder, n(%)	6 (28.6%)	0	6 (18.2%)
95% Exact CI	0.1128, 0.5218	0.0000, 0.2646	0.0698, 0.3546
Proportion Difference - Unstratified CMH Method (95% CI)	0.29 (0.06, 0.52)		
Proportion Difference - Unstratified Exact Method (95% CI)	0.29 (-0.08, 0.60)		
Non-Responder, n(%)	15 (71.4%)	12 (100.0%)	27 (81.8%)
Last participation date < Day 162 in RT phase	8 (38.1%)	3 (25.0%)	11 (33.3%)
Last participation date >= Day 162 and TSS at Week 24 not available	0	1 (8.3%)	1 (3.0%)
>0% increase from baseline at Week 24	3 (14.3%)	7 (58.3%)	10 (30.3%)
<50% reduction from baseline week 24	7 (33.3%)	8 (66.7%)	15 (45.5%)

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TSS = Total Symptom Score; CMH = Cochran-Mantel-Haenszel;

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	MMB (N=104)	BAT (N=52)	Total (N=156)
Response Rate of Total Symptom Score at Week 12			
Subjects Evaluable at Week 12, n	21	12	33
TSS = 0 at baseline and TSS >0 or missing at Week 12	0	0	0
Responder, n(%)	4 (19.0%)	1 (8.3%)	5 (15.2%)
95% Exact CI	0.0545, 0.4191	0.0021, 0.3848	0.0511, 0.3190
Proportion Difference - Unstratified CMH Method (95% CI)	0.11 (-0.15, 0.37)		
Proportion Difference - Unstratified Exact Method (95% CI)	0.11 (-0.25, 0.44)		
Non-Responder, n(%)	17 (81.0%)	11 (91.7%)	28 (84.8%)
Last participation date < Day 78 in RT phase	5 (23.8%)	3 (25.0%)	8 (24.2%)
Last participation date >= Day 78 and TSS at Week 12 not available	0	0	0
>0% increase from baseline at Week 12	5 (23.8%)	6 (50.0%)	11 (33.3%)
<50% reduction from baseline at week 12	12 (57.1%)	8 (66.7%)	20 (60.6%)

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TSS = Total Symptom Score; CMH = Cochran-Mantel-Haenszel;

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	MMB (N=104)	BAT (N=52)	Total (N=156)
Strata 3			
Transfusion Dependence No and Baseline TSS <18	24	13	37
Total Symptom Score Status			
Missing TSS at baseline (excluded from rate calculation)	0	0	0
TSS = 0 at baseline	1 (4.2%)	1 (7.7%)	2 (5.4%)
TSS > 0 at baseline	23 (95.8%)	12 (92.3%)	35 (94.6%)
Response Rate of Total Symptom Score at Week 24			
Subjects Evaluable at Week 24, n	23	12	35
TSS = 0 at baseline and TSS >0 or missing at Week 24	0	0	0
Responder, n(%)	4 (17.4%)	0	4 (11.4%)
95% Exact CI	0.0495, 0.3878	0.0000, 0.2646	0.0320, 0.2674
Proportion Difference - Unstratified CMH Method (95% CI)	0.17 (-0.02, 0.37)		
Proportion Difference - Unstratified Exact Method (95% CI)	0.17 (-0.18, 0.50)		
Non-Responder, n(%)	19 (82.6%)	12 (100.0%)	31 (88.6%)
Last participation date < Day 162 in RT phase	5 (21.7%)	1 (8.3%)	6 (17.1%)
Last participation date >= Day 162 and TSS at Week 24 not available	0	0	0
>0% increase from baseline at Week 24	8 (34.8%)	6 (50.0%)	14 (40.0%)
<50% reduction from baseline week 24	14 (60.9%)	11 (91.7%)	25 (71.4%)

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	MMB (N=104)	BAT (N=52)	Total (N=156)
Response Rate of Total Symptom Score at Week 12			
Subjects Evaluable at Week 12, n	23	13	36
TSS = 0 at baseline and TSS >0 or missing at Week 12	0	1 (7.7%)	1 (2.8%)
Responder, n(%)	5 (21.7%)	0	5 (13.9%)
95% Exact CI	0.0746, 0.4370	0.0000, 0.2471	0.0467, 0.2950
Proportion Difference - Unstratified CMH Method (95% CI)	0.22 (0.01, 0.42)		
Proportion Difference - Unstratified Exact Method (95% CI)	0.22 (-0.12, 0.53)		
Non-Responder, n(%)	18 (78.3%)	13 (100.0%)	31 (86.1%)
Last participation date < Day 78 in RT phase	3 (13.0%)	0	3 (8.3%)
Last participation date >= Day 78 and TSS at Week 12 not available	0	0	0
>0% increase from baseline at Week 12	12 (52.2%)	7 (53.8%)	19 (52.8%)
<50% reduction from baseline at week 12	15 (65.2%)	12 (92.3%)	27 (75.0%)

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	MMB (N=104)	BAT (N=52)	Total (N=156)
Strata 4			
Transfusion Dependence No and Baseline TSS >=18	22	12	34
Total Symptom Score Status			
Missing TSS at baseline (excluded from rate calculation)	0	0	0
TSS = 0 at baseline	0	0	0
TSS > 0 at baseline	22 (100.0%)	12 (100.0%)	34 (100.0%)
Response Rate of Total Symptom Score at Week 24			
Subjects Evaluable at Week 24, n	22	12	34
TSS = 0 at baseline and TSS >0 or missing at Week 24	0	0	0
Responder, n(%)	5 (22.7%)	3 (25.0%)	8 (23.5%)
95% Exact CI	0.0782, 0.4537	0.0549, 0.5719	0.1075, 0.4117
Proportion Difference - Unstratified CMH Method (95% CI)	-0.02 (-0.34, 0.30)		
Proportion Difference - Unstratified Exact Method (95% CI)	-0.02 (-0.37, 0.33)		
Non-Responder, n(%)	17 (77.3%)	9 (75.0%)	26 (76.5%)
Last participation date < Day 162 in RT phase	8 (36.4%)	3 (25.0%)	11 (32.4%)
Last participation date >= Day 162 and TSS at Week 24 not available	1 (4.5%)	0	1 (2.9%)
>0% increase from baseline at Week 24	3 (13.6%)	3 (25.0%)	6 (17.6%)
<50% reduction from baseline week 24	8 (36.4%)	6 (50.0%)	14 (41.2%)

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	MMB (N=104)	BAT (N=52)	Total (N=156)
Response Rate of Total Symptom Score at Week 12			
Subjects Evaluable at Week 12, n	22	12	34
TSS = 0 at baseline and TSS >0 or missing at Week 12	0	0	0
Responder, n(%)	6 (27.3%)	2 (16.7%)	8 (23.5%)
95% Exact CI	0.1073, 0.5022	0.0209, 0.4841	0.1075, 0.4117
Proportion Difference - Unstratified CMH Method (95% CI)	0.11 (-0.20, 0.41)		
Proportion Difference - Unstratified Exact Method (95% CI)	0.11 (-0.25, 0.45)		
Non-Responder, n(%)	16 (72.7%)	10 (83.3%)	26 (76.5%)
Last participation date < Day 78 in RT phase	5 (22.7%)	3 (25.0%)	8 (23.5%)
Last participation date >= Day 78 and TSS at Week 12 not available	1 (4.5%)	0	1 (2.9%)
>0% increase from baseline at Week 12	4 (18.2%)	3 (25.0%)	7 (20.6%)
<50% reduction from baseline at week 12	10 (45.5%)	7 (58.3%)	17 (50.0%)

95% Exact CI is based on Clopper-Pearson method without stratification

TSS rate analysis at one visit only include subjects with TSS >0 at baseline or with TSS =0 at baseline but with TSS > 0 or missing at that visit.

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