

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(%)			
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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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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<b>Strata 1</b>			
Transfusion Dependence Yes and Baseline TSS <18	37	15	52
<b>Total Symptom Score Status</b>			
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%)
<b>Response Rate of Total Symptom Score at Week 24</b>			
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

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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 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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	MMB (N=104)	BAT (N=52)	Total (N=156)
<b>Strata 2</b>			
Transfusion Dependence Yes and Baseline TSS >=18	21	12	33
<b>Total Symptom Score Status</b>			
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%)
<b>Response Rate of Total Symptom Score at Week 24</b>			
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%)

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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	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 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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	MMB (N=104)	BAT (N=52)	Total (N=156)
<b>Strata 3</b>			
Transfusion Dependence No and Baseline TSS <18	24	13	37
<b>Total Symptom Score Status</b>			
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%)
<b>Response Rate of Total Symptom Score at Week 24</b>			
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)		
<b>Non-Responder, n(%)</b>			
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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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%)

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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	MMB (N=104)	BAT (N=52)	Total (N=156)
<b>Strata 4</b>			
Transfusion Dependence No and Baseline TSS >=18	22	12	34
<b>Total Symptom Score Status</b>			
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%)
<b>Response Rate of Total Symptom Score at Week 24</b>			
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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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%)

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