

Table 15.12.1.1: Analysis of Splenic Response Rate 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			
Splenic Repsonse Rate at Week 24			
Responder, n(%)	7 (6.7%)	3 (5.8%)	10 (6.4%)
95% Exact CI	0.0275, 0.1338	0.0121, 0.1595	0.0312, 0.1147
Proportion Difference - Stratified CMH Method (95% CI)	0.01 (-0.09, 0.10)		
p-value	0.90		
Proportion Difference - Unstratified CMH Method (95% CI)	0.01 (-0.07, 0.09)		
p-value	0.82		
Proportion Difference - Unstratified Exact Method (95% CI)	0.01 (-0.16, 0.18)		
p-value	1.00		
Non-Responder, n(%)	97 (93.3%)	49 (94.2%)	146 (93.6%)
Baseline spleen volume not available	0	0	0
Spleen volume at week 24 not available	34 (32.7%)	13 (25.0%)	47 (30.1%)
>0% spleen volume increase at Week 24	34 (32.7%)	19 (36.5%)	53 (34.0%)
<35% spleen volume reduction at week 24	63 (60.6%)	36 (69.2%)	99 (63.5%)
Last participation date < Day 141 in RT phase	23 (22.1%)	10 (19.2%)	33 (21.2%)

95% Exact CI is based on Clopper-Pearson method without stratification
CMH = Cochran-Mantel-Haenszel;
Source: Listing 16.3.1.1

Data Extracted: CRF data: 25JUN2019

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	MMB (N=104)	BAT (N=52)	Total (N=156)
Splenic Repsonse Rate at Week 12			
Responder, n(%)	4 (3.8%)	0	4 (2.6%)
95% Exact CI	0.0106, 0.0956	0.0000, 0.0685	0.0070, 0.0643
Proportion Difference - Stratified CMH Method (95% CI)	0.04 (-0.03, 0.11)		
p-value	0.29		
Proportion Difference - Unstratified CMH Method (95% CI)	0.04 (-0.01, 0.09)		
p-value	0.11		
Proportion Difference - Unstratified Exact Method (95% CI)	0.04 (-0.13, 0.21)		
p-value	0.30		
Non-Responder, n(%)	100 (96.2%)	52 (100.0%)	152 (97.4%)
Baseline spleen volume not available	0	0	0
Spleen volume at week 12 not available	23 (22.1%)	11 (21.2%)	34 (21.8%)
>0% spleen volume increase at Week 12	40 (38.5%)	19 (36.5%)	59 (37.8%)
<35% spleen volume reduction at week 12	77 (74.0%)	41 (78.8%)	118 (75.6%)
Last participation date < Day 57 in RT phase	12 (11.5%)	5 (9.6%)	17 (10.9%)
Splenic Repsonse Rate at Any Timepoint in RT Phase			
Responder, n(%)	8 (7.7%)	3 (5.8%)	11 (7.1%)
95% Exact CI	0.0338, 0.1460	0.0121, 0.1595	0.0357, 0.1227

95% Exact CI is based on Clopper-Pearson method without stratification
CMH = Cochran-Mantel-Haenszel;
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	MMB (N=104)	BAT (N=52)	Total (N=156)
Stratum 1			
Transfusion Dependence Yes and Baseline TSS <18	37	15	52
Splenic Response Rate at Week 24			
Responder, n(%)	4 (10.8%)	1 (6.7%)	5 (9.6%)
95% Exact CI	0.0303, 0.2542	0.0017, 0.3195	0.0320, 0.2103
Proportion Difference (95% CI)	0.04 (-0.14, 0.23)		
Proportion Difference using Exact Method (95% CI)	0.04 (-0.26, 0.33)		
Non-Responder, n(%)	33 (89.2%)	14 (93.3%)	47 (90.4%)
Baseline spleen volume not available	0	0	0
Spleen volume at week 24 not available	10 (27.0%)	4 (26.7%)	14 (26.9%)
>0% spleen volume increase at Week 24	15 (40.5%)	6 (40.0%)	21 (40.4%)
<35% spleen volume reduction at week 24	23 (62.2%)	10 (66.7%)	33 (63.5%)
Last participation date < Day 141 in RT phase	5 (13.5%)	3 (20.0%)	8 (15.4%)

95% Exact CI is based on Clopper-Pearson method without stratification
CMH = Cochran-Mantel-Haenszel;
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Splenic Repsonse Rate at Week 12			
Responder, n(%)	2 (5.4%)	0	2 (3.8%)
95% Exact CI	0.0066, 0.1819	0.0000, 0.2180	0.0047, 0.1321
Proportion Difference (95% CI)	0.05 (-0.07, 0.18)		
Proportion Difference using Exact Method (95% CI)	0.05 (-0.24, 0.35)		
Non-Responder, n(%)	35 (94.6%)	15 (100.0%)	50 (96.2%)
Baseline spleen volume not available	0	0	0
Spleen volume at week 12 not available	4 (10.8%)	3 (20.0%)	7 (13.5%)
>0% spleen volume increase at Week 12	17 (45.9%)	7 (46.7%)	24 (46.2%)
<35% spleen volume reduction at week 12	31 (83.8%)	12 (80.0%)	43 (82.7%)
Last participation date < Day 57 in RT phase	0	2 (13.3%)	2 (3.8%)
Splenic Repsonse Rate at Any Timepoint in RT Phase			
Responder, n(%)	4 (10.8%)	1 (6.7%)	5 (9.6%)
95% Exact CI	0.0303, 0.2542	0.0017, 0.3195	0.0320, 0.2103

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

CMH = Cochran-Mantel-Haenszel;

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	MMB (N=104)	BAT (N=52)	Total (N=156)
Stratum 2			
Transfusion Dependence Yes and Baseline TSS >=18	21	12	33
Splenic Response Rate at Week 24			
Responder, n(%)	1 (4.8%)	0	1 (3.0%)
95% Exact CI	0.0012, 0.2382	0.0000, 0.2646	0.0008, 0.1576
Proportion Difference (95% CI)	0.05 (-0.11, 0.21)		
Proportion Difference using Exact Method (95% CI)	0.05 (-0.31, 0.40)		
Non-Responder, n(%)	20 (95.2%)	12 (100.0%)	32 (97.0%)
Baseline spleen volume not available	0	0	0
Spleen volume at week 24 not available	9 (42.9%)	4 (33.3%)	13 (39.4%)
>0% spleen volume increase at Week 24	3 (14.3%)	4 (33.3%)	7 (21.2%)
<35% spleen volume reduction at week 24	11 (52.4%)	8 (66.7%)	19 (57.6%)
Last participation date < Day 141 in RT phase	6 (28.6%)	3 (25.0%)	9 (27.3%)

95% Exact CI is based on Clopper-Pearson method without stratification
CMH = Cochran-Mantel-Haenszel;
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	MMB (N=104)	BAT (N=52)	Total (N=156)
Splenic Repsonse Rate at Week 12			
Responder, n(%)	1 (4.8%)	0	1 (3.0%)
95% Exact CI	0.0012, 0.2382	0.0000, 0.2646	0.0008, 0.1576
Proportion Difference (95% CI)	0.05 (-0.11, 0.21)		
Proportion Difference using Exact Method (95% CI)	0.05 (-0.31, 0.40)		
Non-Responder, n(%)	20 (95.2%)	12 (100.0%)	32 (97.0%)
Baseline spleen volume not available	0	0	0
Spleen volume at week 12 not available	6 (28.6%)	3 (25.0%)	9 (27.3%)
>0% spleen volume increase at Week 12	5 (23.8%)	4 (33.3%)	9 (27.3%)
<35% spleen volume reduction at week 12	14 (66.7%)	9 (75.0%)	23 (69.7%)
Last participation date < Day 57 in RT phase	4 (19.0%)	2 (16.7%)	6 (18.2%)
Splenic Repsonse Rate at Any Timepoint in RT Phase			
Responder, n(%)	1 (4.8%)	0	1 (3.0%)
95% Exact CI	0.0012, 0.2382	0.0000, 0.2646	0.0008, 0.1576

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

CMH = Cochran-Mantel-Haenszel;

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	MMB (N=104)	BAT (N=52)	Total (N=156)
Stratum 3			
Transfusion Dependence No and Baseline TSS <18	24	13	37
Splenic Response Rate at Week 24			
Responder, n(%)	1 (4.2%)	2 (15.4%)	3 (8.1%)
95% Exact CI	0.0011, 0.2112	0.0192, 0.4545	0.0170, 0.2191
Proportion Difference (95% CI)	-0.11 (-0.35, 0.13)		
Proportion Difference using Exact Method (95% CI)	-0.11 (-0.43, 0.23)		
Non-Responder, n(%)	23 (95.8%)	11 (84.6%)	34 (91.9%)
Baseline spleen volume not available	0	0	0
Spleen volume at week 24 not available	6 (25.0%)	2 (15.4%)	8 (21.6%)
>0% spleen volume increase at Week 24	8 (33.3%)	5 (38.5%)	13 (35.1%)
<35% spleen volume reduction at week 24	17 (70.8%)	9 (69.2%)	26 (70.3%)
Last participation date < Day 141 in RT phase	4 (16.7%)	1 (7.7%)	5 (13.5%)

95% Exact CI is based on Clopper-Pearson method without stratification
CMH = Cochran-Mantel-Haenszel;
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Splenic Repsonse Rate at Week 12			
Responder, n(%)	0	0	0
95% Exact CI	0.0000, 0.1425	0.0000, 0.2471	0.0000, 0.0949
Proportion Difference (95% CI)	0.00 (-0.12, 0.12)		
Proportion Difference using Exact Method (95% CI)			
Non-Responder, n(%)	24 (100.0%)	13 (100.0%)	37 (100.0%)
Baseline spleen volume not available	0	0	0
Spleen volume at week 12 not available	5 (20.8%)	1 (7.7%)	6 (16.2%)
>0% spleen volume increase at Week 12	11 (45.8%)	4 (30.8%)	15 (40.5%)
<35% spleen volume reduction at week 12	19 (79.2%)	12 (92.3%)	31 (83.8%)
Last participation date < Day 57 in RT phase	3 (12.5%)	0	3 (8.1%)
Splenic Repsonse Rate at Any Timepoint in RT Phase			
Responder, n(%)	1 (4.2%)	2 (15.4%)	3 (8.1%)
95% Exact CI	0.0011, 0.2112	0.0192, 0.4545	0.0170, 0.2191

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

CMH = Cochran-Mantel-Haenszel;

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	MMB (N=104)	BAT (N=52)	Total (N=156)
Stratum 4			
Transfusion Dependence No and Baseline TSS >=18	22	12	34
Splenic Repsonse Rate at Week 24			
Responder, n(%)	1 (4.5%)	0	1 (2.9%)
95% Exact CI	0.0012, 0.2284	0.0000, 0.2646	0.0007, 0.1533
Proportion Difference (95% CI)	0.05 (-0.11, 0.20)		
Proportion Difference using Exact Method (95% CI)	0.05 (-0.30, 0.39)		
Non-Responder, n(%)	21 (95.5%)	12 (100.0%)	33 (97.1%)
Baseline spleen volume not available	0	0	0
Spleen volume at week 24 not available	9 (40.9%)	3 (25.0%)	12 (35.3%)
>0% spleen volume increase at Week 24	8 (36.4%)	4 (33.3%)	12 (35.3%)
<35% spleen volume reduction at week 24	12 (54.5%)	9 (75.0%)	21 (61.8%)
Last participation date < Day 141 in RT phase	8 (36.4%)	3 (25.0%)	11 (32.4%)

95% Exact CI is based on Clopper-Pearson method without stratification
CMH = Cochran-Mantel-Haenszel;
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Splenic Repsonse Rate at Week 12			
Responder, n(%)	1 (4.5%)	0	1 (2.9%)
95% Exact CI	0.0012, 0.2284	0.0000, 0.2646	0.0007, 0.1533
Proportion Difference (95% CI)	0.05 (-0.11, 0.20)		
Proportion Difference using Exact Method (95% CI)	0.05 (-0.30, 0.39)		
Non-Responder, n(%)	21 (95.5%)	12 (100.0%)	33 (97.1%)
Baseline spleen volume not available	0	0	0
Spleen volume at week 12 not available	8 (36.4%)	4 (33.3%)	12 (35.3%)
>0% spleen volume increase at Week 12	7 (31.8%)	4 (33.3%)	11 (32.4%)
<35% spleen volume reduction at week 12	13 (59.1%)	8 (66.7%)	21 (61.8%)
Last participation date < Day 57 in RT phase	5 (22.7%)	1 (8.3%)	6 (17.6%)
Splenic Repsonse Rate at Any Timepoint in RT Phase			
Responder, n(%)	2 (9.1%)	0	2 (5.9%)
95% Exact CI	0.0112, 0.2916	0.0000, 0.2646	0.0072, 0.1968

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

CMH = Cochran-Mantel-Haenszel;

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