

# Time to Event Analysis: Efficacy Endpoints

## List of Figures

## List of Tables

1	Annualized Relapse Rate: Parameter = Duration of Confirmed Response (mITT Population)	2
2	Annualized Relapse Rate: Parameter = Duration of Confirmed Response (mITT Population)	4
3	Annualized Relapse Rate: Parameter = Event Free Survival (mITT Population)	6
4	Annualized Relapse Rate: Parameter = Event Free Survival (mITT Population)	8
5	Annualized Relapse Rate: Parameter = Overall Survival (mITT Population)	10
6	Annualized Relapse Rate: Parameter = Overall Survival (mITT Population)	12
7	Annualized Relapse Rate: Parameter = Progression Free Survival (mITT Population)	14
8	Annualized Relapse Rate: Parameter = Progression Free Survival (mITT Population)	16
9	Annualized Relapse Rate: Parameter = Total Number of Exacerbations (mITT Population)	18
10	Annualized Relapse Rate: Parameter = Total Number of Exacerbations (mITT Population)	20

Table 1: Annualized Relapse Rate: Parameter = Duration of Confirmed Response (mITT Population)

Parameter	Statistics	Fakemethaline 50 mg	Placebo	Comparison	P-Value
Duration of treatment (years)	n	134	134		
	Mean	2.633 (0.571)	2.6 (0.612)		
	(SD)				
	Median	3.001	3.001		
	Q1/Q3	2.36/3	2.14/3		
	Min/Max	1.08/3	1.06/3		
Duration of Confirmed Response	n	134	134		
	Mean	143.233 (40.095)	146.908 (38.743)		
	(SD)				
	Median	148.947	149.859		
	Q1/Q3	117.11/176.29	121/180.82		
	Min/Max	15.05/199.63	27.98/198.65		
Cumulative treatment time (subject years)		352.87	348.45		
Cumulative number of Duration of Confirmed Response		19193.26	19685.65		
Raw Annualized Relapse Rate		54.39	56.49		
Rate Ratio				0.963	
Difference				-2.1	
Least square means (95% CI)		141.175(132.731, 150.157)	144.814(135.911, 154.3)		
Difference				-3.639(-14.398, 7.121)	
Rate Ratio				0.975(0.902, 1.048)	0.5072

Duration of Confirmed Response Least Square means (95% CI)  
(mITT Set)

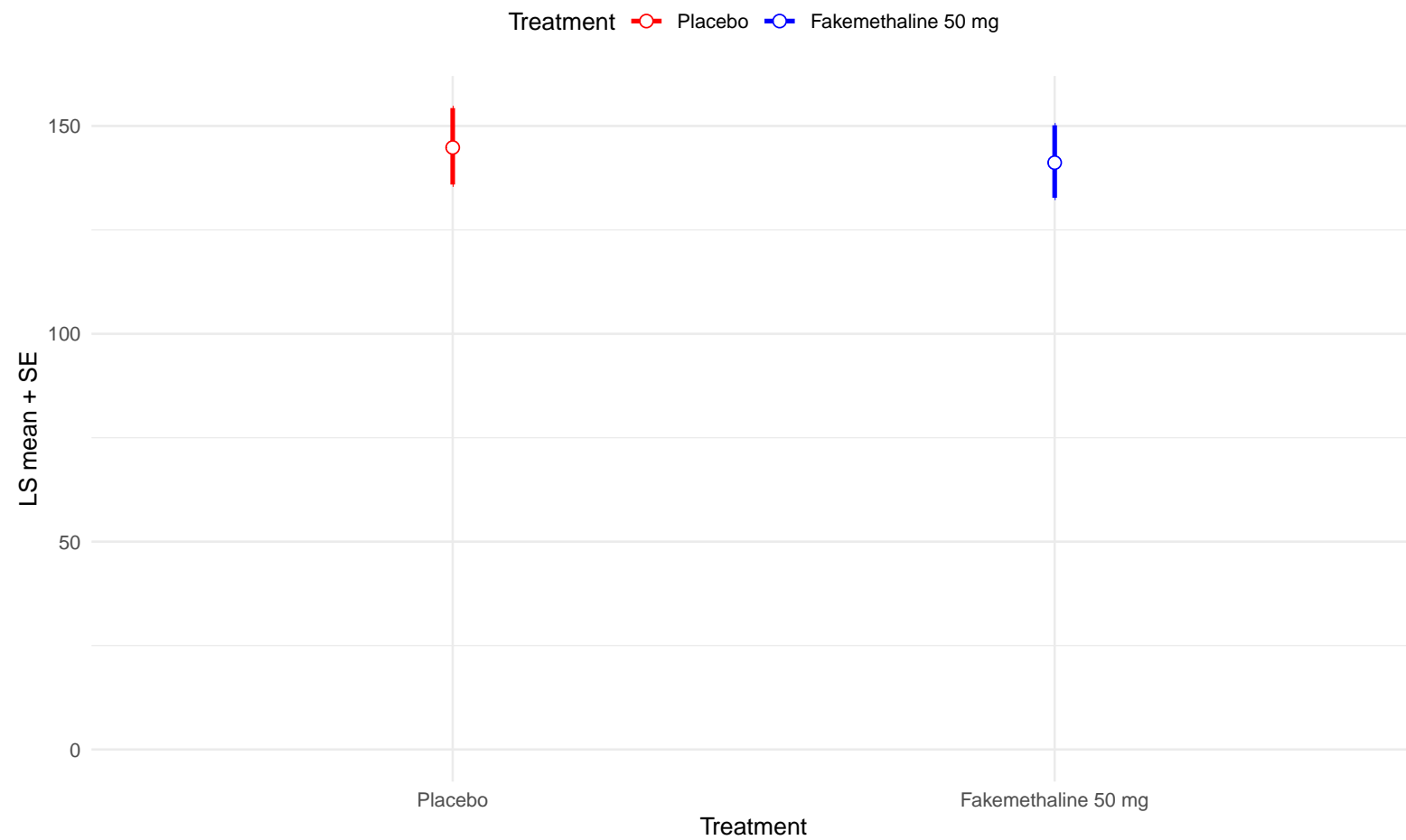


Table 2: Annualized Relapse Rate: Parameter = Duration of Confirmed Response (mITT Population)

Parameter	Statistics	Fakemethaline 150 mg	Placebo	Comparison	P- Value
Duration of treatment (years)	n	132	134		
	Mean	2.697 (0.548)	2.6 (0.612)		
	(SD)				
	Median	3.001	3.001		
	Q1/Q3	2.63/3	2.14/3		
	Min/Max	1.01/3	1.06/3		
Duration of Confirmed Response	n	132	134		
	Mean	133.902 (41.365)	146.908 (38.743)		
	(SD)				
	Median	134.582	149.859		
	Q1/Q3	110.86/165.93	121/180.82		
	Min/Max	16.21/199.85	27.98/198.65		
Cumulative treatment time (subject years)		355.99	348.45		
Cumulative number of Duration of Confirmed Response		17675.04	19685.65		
Raw Annualized Relapse Rate		49.65	56.49		
Rate Ratio				0.879	
Difference				-6.84	
Least square means (95% CI)		115.531(82.726, 161.345)	126.877(90.426, 178.023)		
Difference				-11.347(-22.026, -0.667)	
Rate Ratio				0.911(0.837, 0.984)	0.0227

Duration of Confirmed Response Least Square means (95% CI)  
(mITT Set)

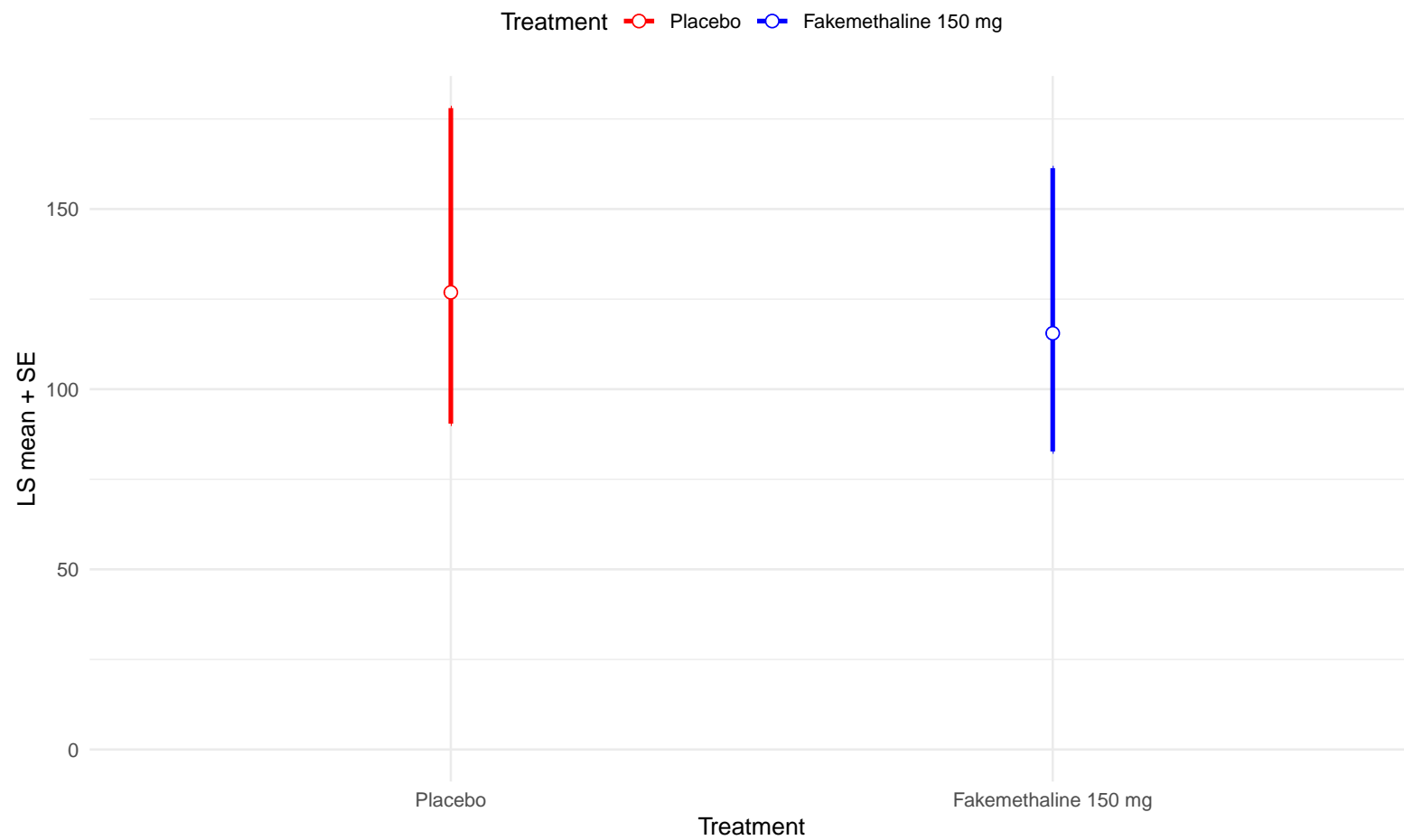


Table 3: Annualized Relapse Rate: Parameter = Event Free Survival (mITT Population)

Parameter	Statistics	Fakemethaline 50 mg	Placebo	Comparison	P-Value
Duration of treatment (years)	n	134	134		
	Mean (SD)	2.633 (0.571)	2.6 (0.612)		
	Median	3.001	3.001		
	Q1/Q3	2.36/3	2.14/3		
	Min/Max	1.08/3	1.06/3		
Event Free Survival	n	134	134		
	Mean (SD)	55.757 (24.431)	56.532 (25.9)		
	Median	55.643	55.038		
	Q1/Q3	35.47/75.47	34.04/78.82		
	Min/Max	15.05/98.16	15.67/99.9		
Cumulative treatment time (subject years)		352.87	348.45		
Cumulative number of Event Free Survival		7471.4	7575.32		
Raw Annualized Relapse Rate		21.17	21.74		
Rate Ratio				0.974	
Difference				-0.569999999999997	
Least square means (95% CI)		55.889(50.888, 61.381)	56.683(51.47, 62.423)		
Difference				-0.794(-7.234, 5.647)	
Rate Ratio				0.986(0.873, 1.099)	0.809

Event Free Survival Least Square means (95% CI)  
(mITT Set)

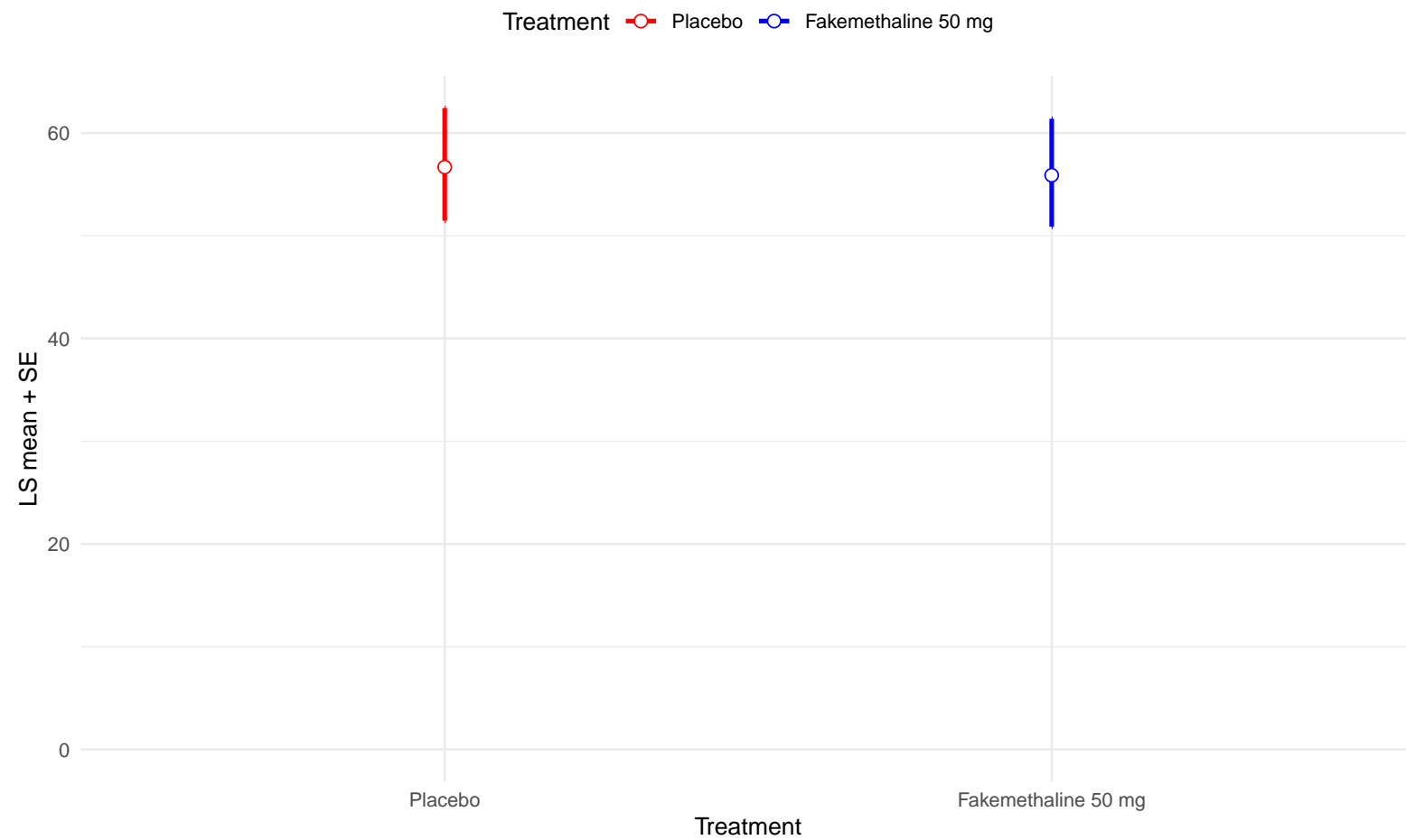


Table 4: Annualized Relapse Rate: Parameter = Event Free Survival (mITT Population)

Parameter	Statistics	Fakemethaline 150 mg	Placebo	Comparison	P-Value
Duration of treatment (years)	n	132	134		
	Mean (SD)	2.697 (0.548)	2.6 (0.612)		
	Median	3.001	3.001		
	Q1/Q3	2.63/3	2.14/3		
	Min/Max	1.01/3	1.06/3		
Event Free Survival	n	132	134		
	Mean (SD)	54.239 (26.405)	56.532 (25.9)		
	Median	52.365	55.038		
	Q1/Q3	30.45/78.45	34.04/78.82		
	Min/Max	15.09/99.33	15.67/99.9		
Cumulative treatment time (subject years)		355.99	348.45		
Cumulative number of Event Free Survival		7159.49	7575.32		
Raw Annualized Relapse Rate		20.11	21.74		
Rate Ratio				0.925	
Difference				-1.63	
Least square means (95% CI)		45.52(27.379, 75.683)	47.214(28.198, 79.053)		
Difference				-1.694(-7.457, 4.069)	
Rate Ratio				0.964(0.847, 1.082)	0.5567



Event Free Survival Least Square means (95% CI)  
(mITT Set)

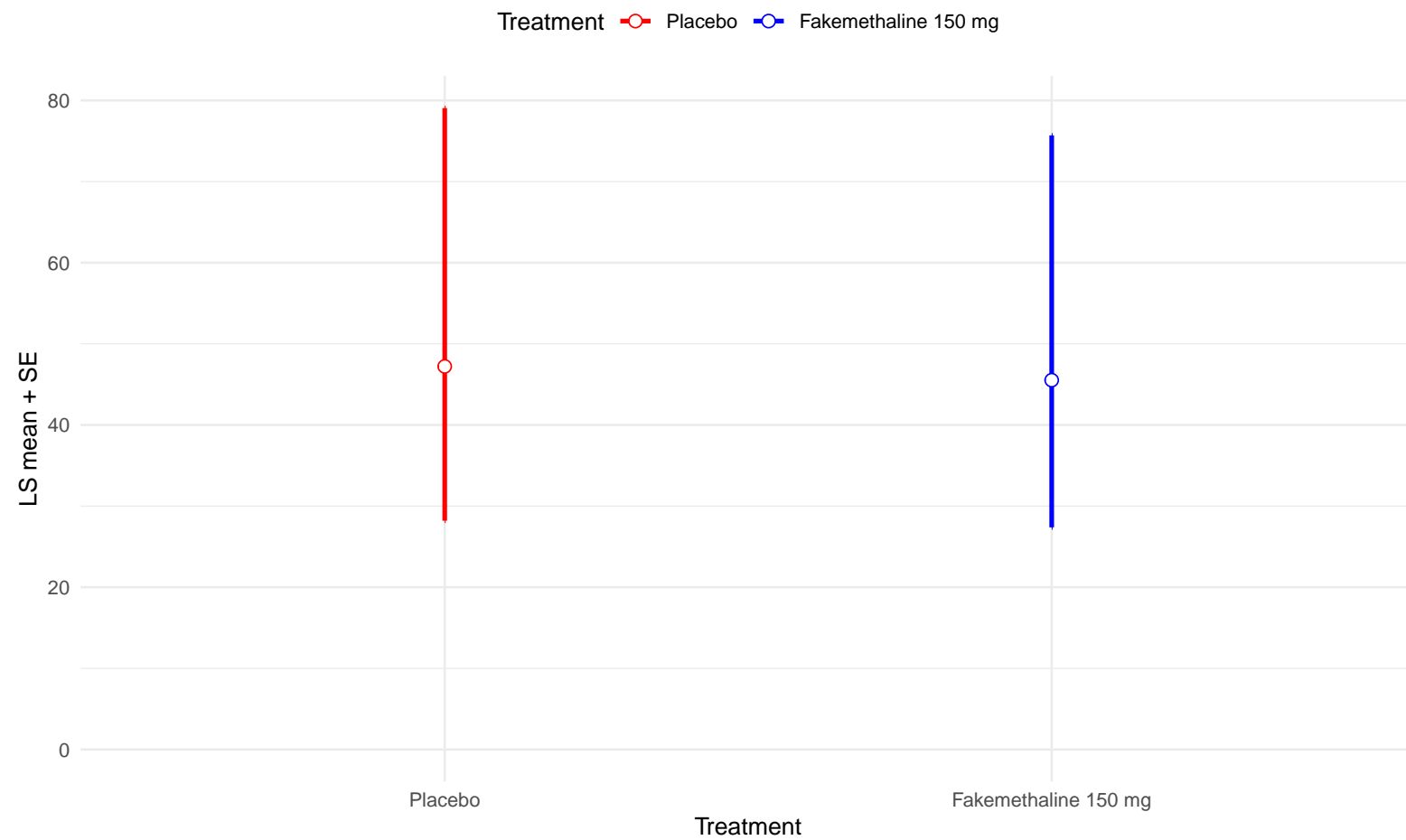


Table 5: Annualized Relapse Rate: Parameter = Overall Survival (mITT Population)

Parameter	Statistics	Fakemethaline 50 mg	Placebo	Comparison	P-Value
Duration of treatment (years)	n	134	134		
	Mean (SD)	2.633 (0.571)	2.6 (0.612)		
	Median	3.001	3.001		
	Q1/Q3	2.36/3	2.14/3		
	Min/Max	1.08/3	1.06/3		
Overall Survival	n	134	134		
	Mean (SD)	292.725 (135.173)	290.311 (129.9)		
	Median	309.611	316.349		
	Q1/Q3	169.18/408.97	173.32/388.9		
	Min/Max	15.05/499.27	27.98/495.23		
Cumulative treatment time (subject years)		352.87	348.45		
Cumulative number of Overall Survival		39225.16	38901.68		
Raw Annualized Relapse Rate		111.16	111.64		
Rate Ratio				0.996	
Difference				-0.4800000000000004	
Least square means (95% CI)		292.926(263.217, 325.989)	291.269(260.904, 325.168)		
Difference				1.657(-36.459, 39.773)	
Rate Ratio				1.006(0.874, 1.137)	0.9321

Overall Survival Least Square means (95% CI)  
(mITT Set)

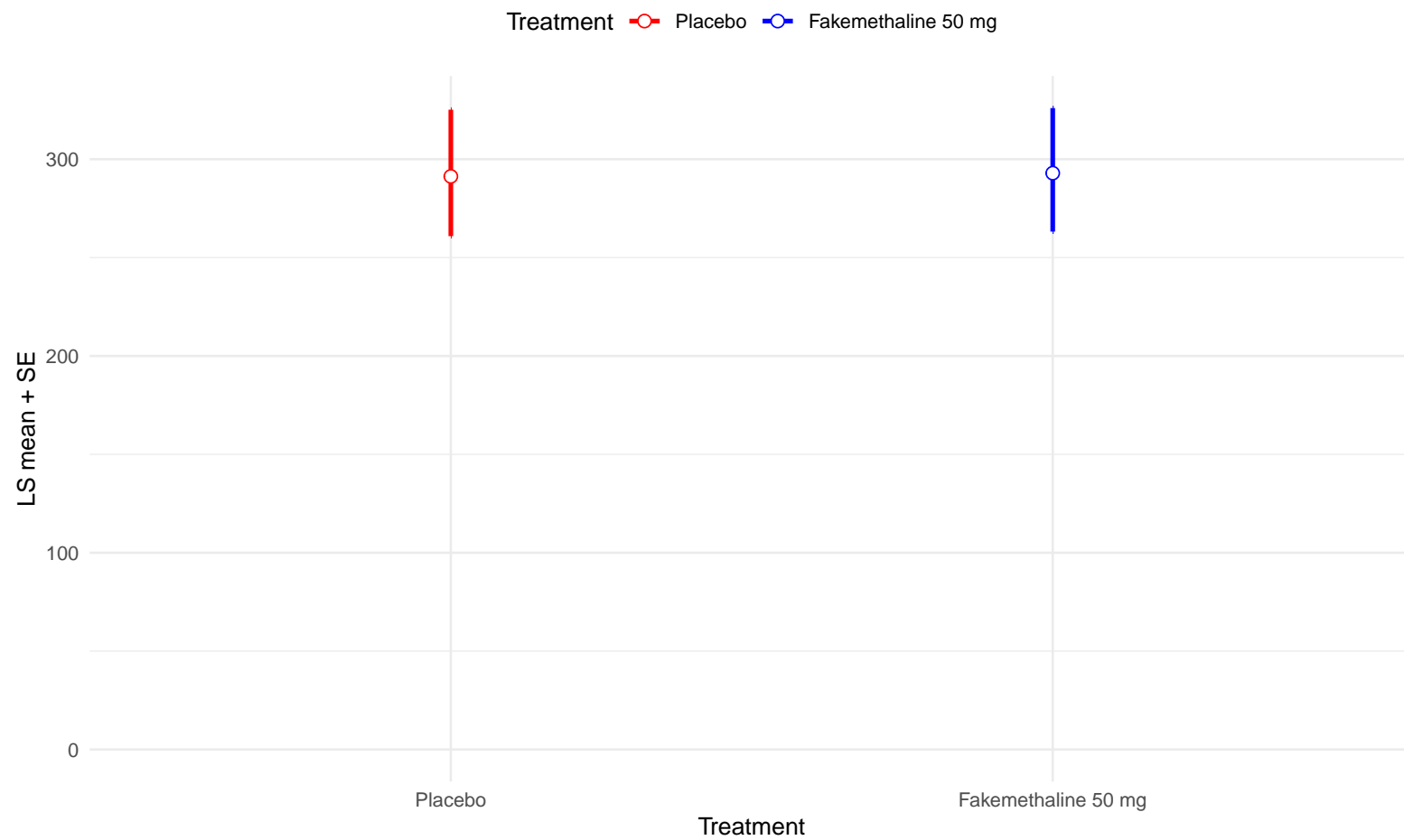


Table 6: Annualized Relapse Rate: Parameter = Overall Survival (mITT Population)

Parameter	Statistics	Fakemethaline 150 mg	Placebo	Comparison	P-Value
Duration of treatment (years)	n	132	134		
	Mean	2.697 (0.548)	2.6 (0.612)		
	(SD)				
	Median	3.001	3.001		
	Q1/Q3	2.63/3	2.14/3		
	Min/Max	1.01/3	1.06/3		
Overall Survival	n	132	134		
	Mean	270.94 (135.875)	290.311 (129.9)		
	(SD)				
	Median	286.629	316.349		
	Q1/Q3	154.95/387.42	173.32/388.9		
	Min/Max	16.21/495.71	27.98/495.23		
Cumulative treatment time (subject years)		355.99	348.45		
Cumulative number of Overall Survival		35764.1	38901.68		
Raw Annualized Relapse Rate		100.46	111.64		
Rate Ratio				0.9	
Difference				-11.18	
Least square means (95% CI)		248.903(141.912, 436.556)	269.156(152.225, 475.905)		
Difference				-20.253(-58.173, 17.667)	
Rate Ratio				0.925(0.798, 1.052)	0.2633

Overall Survival Least Square means (95% CI)  
(mITT Set)

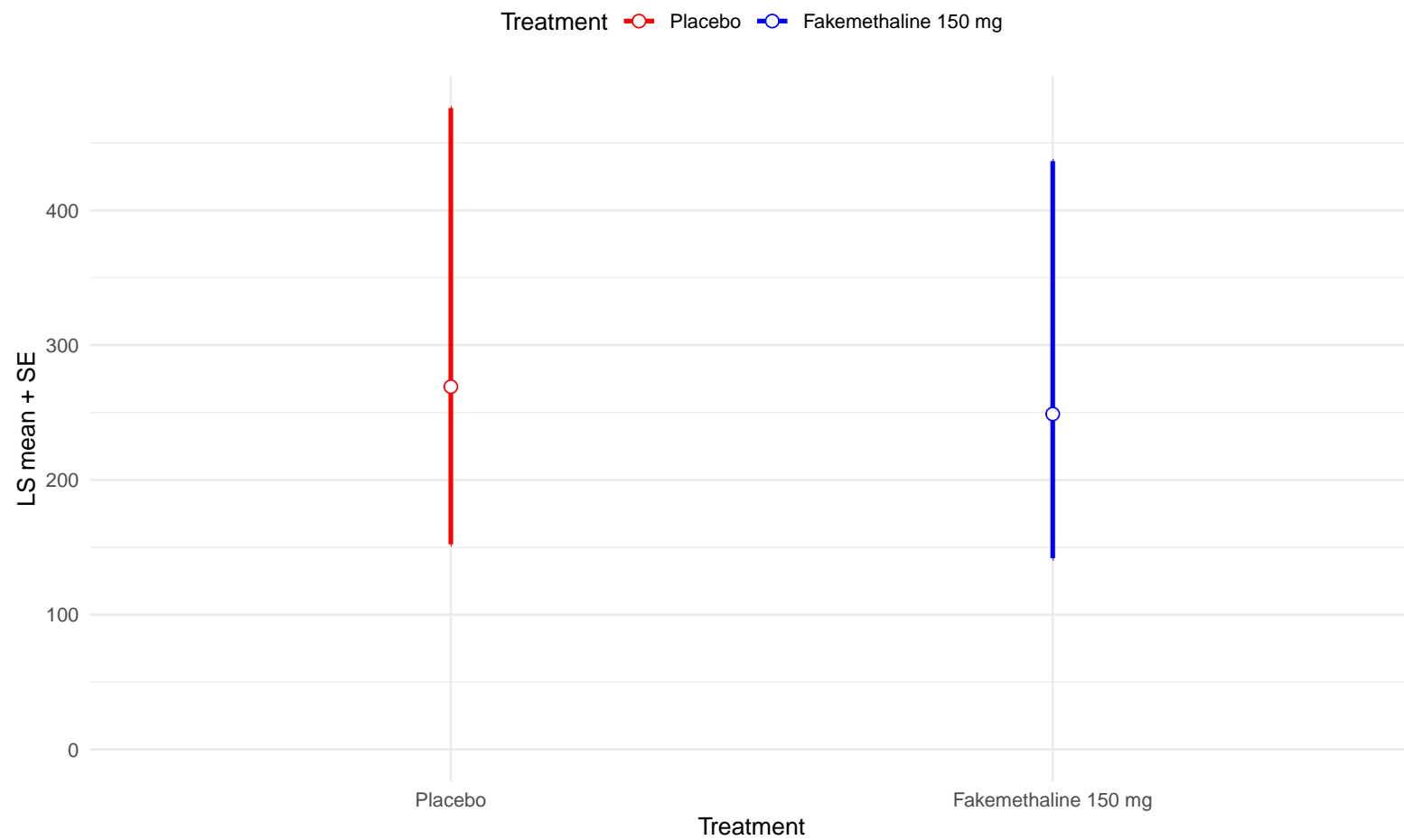


Table 7: Annualized Relapse Rate: Parameter = Progression Free Survival (mITT Population)

Parameter	Statistics	Fakemethaline 50 mg	Placebo	Comparison	P-Value
Duration of treatment (years)	n	134	134		
	Mean (SD)	2.633 (0.571)	2.6 (0.612)		
	Median	3.001	3.001		
	Q1/Q3	2.36/3	2.14/3		
	Min/Max	1.08/3	1.06/3		
Progression Free Survival	n	134	134		
	Mean (SD)	211.946 (71.098)	210.394 (67.746)		
	Median	230.33	225.776		
	Q1/Q3	169.18/268.36	173.32/264.61		
	Min/Max	15.05/299.48	27.98/299.53		
Cumulative treatment time (subject years)		352.87	348.45		
Cumulative number of Progression Free Survival		28400.7	28192.83		
Raw Annualized Relapse Rate		80.48	80.91		
Rate Ratio				0.995	
Difference				-0.4299999999999993	
Least square means (95% CI)		210.198(194.134, 227.59)	209.489(193.027, 227.355)		
Difference				0.709(-19.645, 21.063)	
Rate Ratio				1.003(0.906, 1.101)	0.9456

Progression Free Survival Least Square means (95% CI)  
(mITT Set)

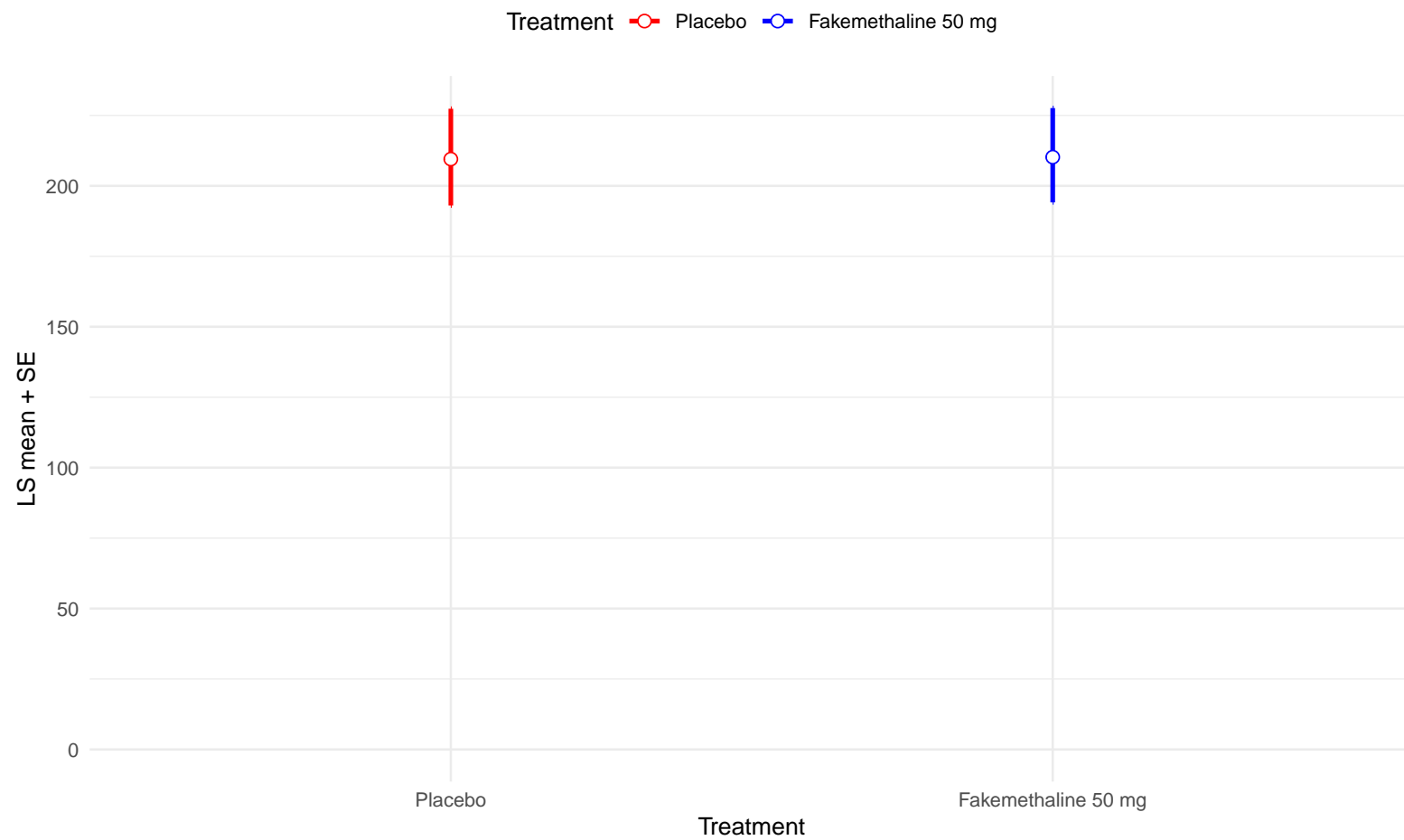


Table 8: Annualized Relapse Rate: Parameter = Progression Free Survival (mITT Population)

Parameter	Statistics	Fakemethaline 150 mg	Placebo	Comparison	P-Value
Duration of treatment (years)	n	132	134		
	Mean (SD)	2.697 (0.548)	2.6 (0.612)		
	Median	3.001	3.001		
	Q1/Q3	2.63/3	2.14/3		
	Min/Max	1.01/3	1.06/3		
Progression Free Survival	n	132	134		
	Mean (SD)	201.179 (73.689)	210.394 (67.746)		
	Median	220.978	225.776		
	Q1/Q3	154.95/256.17	173.32/264.61		
	Min/Max	16.21/297.87	27.98/299.53		
Cumulative treatment time (subject years)		355.99	348.45		
Cumulative number of Progression Free Survival		26555.6	28192.83		
Raw Annualized Relapse Rate		74.6	80.91		
Rate Ratio				0.922	
Difference				-6.31	
Least square means (95% CI)		215.707(141.212, 329.501)	228.119(148.426, 350.6)		
Difference				-12.412(-36.309, 11.485)	
Rate Ratio				0.946(0.848, 1.044)	0.2901



Progression Free Survival Least Square means (95% CI)  
(mITT Set)

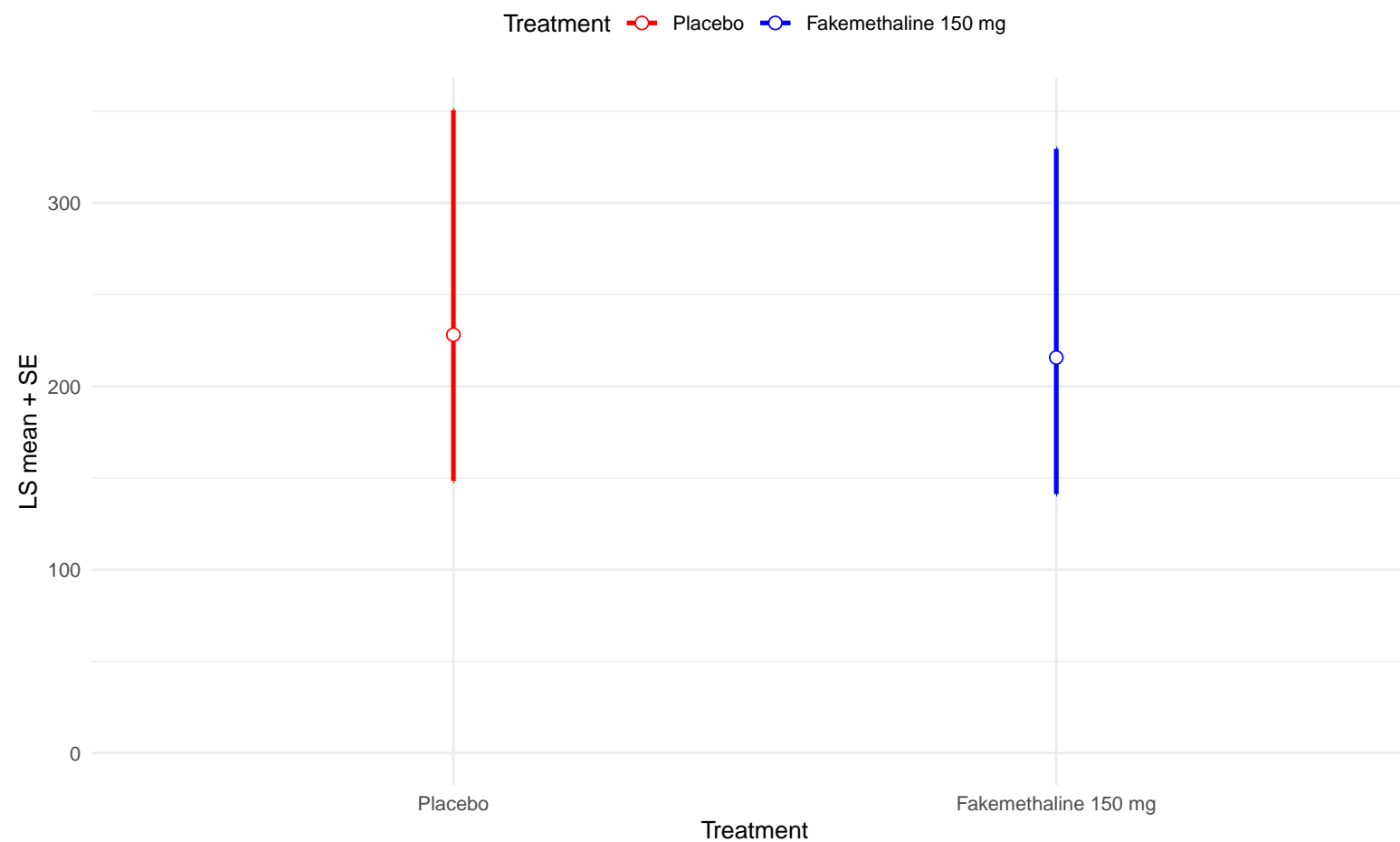


Table 9: Annualized Relapse Rate: Parameter = Total Number of Exacerbations (mITT Population)

Parameter	Statistics	Fakemethaline 50 mg	Placebo	Comparison	P-Value
Duration of treatment (years)	n	134	134		
	Mean (SD)	2.633 (0.571)	2.6 (0.612)		
	Median	3.001	3.001		
	Q1/Q3	2.36/3	2.14/3		
	Min/Max	1.08/3	1.06/3		
Total Number of Exacerbations	n	134	134		
	Mean (SD)	2.843 (1.703)	2.776 (1.894)		
	Median	2	2		
	Q1/Q3	2/4	1/4		
	Min/Max	0/8	0/9		
Cumulative treatment time (subject years)		352.87	348.45		
Cumulative number of Total Number of Exacerbations		381	372		
Raw Annualized Relapse Rate		1.08	1.07		
Rate Ratio				1.009	
Difference				0.01	
Least square means (95% CI)		2.763(2.435, 3.134)	2.684(2.355, 3.059)		
Difference				0.078(-0.337, 0.494)	
Rate Ratio				1.029(0.872, 1.186)	0.7121

Total Number of Exacerbations Least Square means (95% CI)  
(mITT Set)

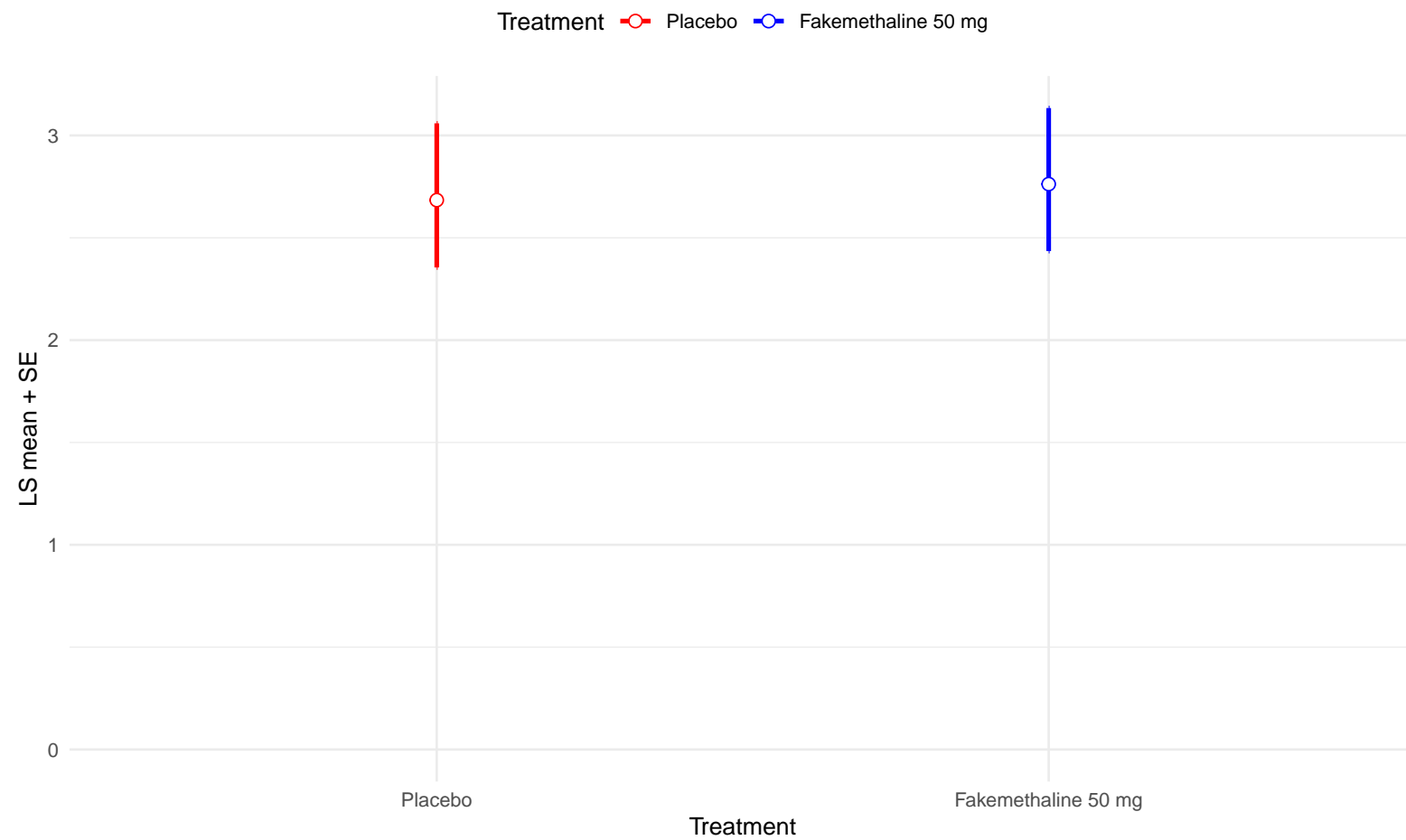


Table 10: Annualized Relapse Rate: Parameter = Total Number of Exacerbations (mITT Population)

Parameter	Statistics	Fakemethaline 150 mg	Placebo	Comparison	P-Value
Duration of treatment (years)	n	132	134		
	Mean (SD)	2.697 (0.548)	2.6 (0.612)		
	Median	3.001	3.001		
	Q1/Q3	2.63/3	2.14/3		
	Min/Max	1.01/3	1.06/3		
Total Number of Exacerbations	n	132	134		
	Mean (SD)	2.985 (1.752)	2.776 (1.894)		
	Median	3	2		
	Q1/Q3	2/4	1/4		
	Min/Max	0/8	0/9		
Cumulative treatment time (subject years)		355.99	348.45		
Cumulative number of Total Number of Exacerbations		394	372		
Raw Annualized Relapse Rate		1.11	1.07		
Rate Ratio				1.037	
Difference				0.04	
Least square means (95% CI)		2.335(1.121, 4.861)	2.166(1.032, 4.545)		
Difference				0.169(-0.19, 0.527)	
Rate Ratio				1.078(0.913, 1.242)	0.3352

Total Number of Exacerbations Least Square means (95% CI)  
(mITT Set)

