Table 1. Cohort characteristics, numbers in count (%) unless specified

	voxelotor (N=1049)	hydroxyurea (N=1681)	crizanlizumab-tmca (N=778)	L-glutamine (N=460)	Total (N=3968)
Age					
0-11	0 (0%)	616 (36.6%)	1 (0.1%)	63 (13.7%)	680 (17.1%)
12-19	313 (29.8%)	333 (19.8%)	118 (15.2%)	84 (18.3%)	848 (21.4%)
20-29	253 (24.1%)	278 (16.5%)	292 (37.5%)	133 (28.9%)	956 (24.1%)
30-49	387 (36.9%)	345 (20.5%)	314 (40.4%)	144 (31.3%)	1190 (30.0%)
50+	96 (9.2%)	109 (6.5%)	53 (6.8%)	36 (7.8%)	294 (7.4%)
Gender					
Female	646 (61.6%)	952 (56.6%)	463 (59.5%)	258 (56.1%)	2319 (58.4%)
Male	403 (38.4%)	729 (43.4%)	315 (40.5%)	202 (43.9%)	1649 (41.6%)
Region					
Northeast	215 (20.5%)	289 (17.2%)	172 (22.1%)	110 (23.9%)	786 (19.8%)
Midwest	122 (11.6%)	359 (21.4%)	133 (17.1%)	96 (20.9%)	710 (17.9%)
South	629 (60.0%)	931 (55.4%)	420 (54.0%)	221 (48.0%)	2201 (55.5%)
West	83 (7.9%)	102 (6.1%)	53 (6.8%)	33 (7.2%)	271 (6.8%)
CCI					
0	341 (32.5%)	975 (58.0%)	233 (29.9%)	186 (40.4%)	1735 (43.7%)
1-3	562 (53.6%)	583 (34.7%)	436 (56.0%)	224 (48.7%)	1805 (45.5%)
4+	146 (13.9%)	123 (7.3%)	109 (14.0%)	50 (10.9%)	428 (10.8%)
Transfusion					
Yes	359 (34.2%)	303 (18.0%)	254 (32.6%)	99 (21.5%)	1015 (25.6%)
No	690 (65.8%)	1378 (82.0%)	524 (67.4%)	361 (78.5%)	2953 (74.4%)
VOC (Inpatient)					
0	340 (32.4%)	891 (53.0%)	118 (15.2%)	149 (32.4%)	1498 (37.8%)
1	189 (18.0%)	365 (21.7%)	116 (14.9%)	85 (18.5%)	755 (19.0%)
2	126 (12.0%)	158 (9.4%)	82 (10.5%)	59 (12.8%)	425 (10.7%)
3+	394 (37.6%)	267 (15.9%)	462 (59.4%)	167 (36.3%)	1290 (32.5%)
VOC (Emergency Room)					
0	472 (45.0%)	1066 (63.4%)	232 (29.8%)	203 (44.1%)	1973 (49.7%)
1	177 (16.9%)	265 (15.8%)	122 (15.7%)	78 (17.0%)	642 (16.2%)
2	110 (10.5%)	128 (7.6%)	69 (8.9%)	51 (11.1%)	358 (9.0%)
3+	290 (27.6%)	222 (13.2%)	355 (45.6%)	128 (27.8%)	995 (25.1%)
Number of Prescriptions					
Mean (SD)	7.07 (5.49)	6.05 (4.76)	7.54 (4.77)	5.40 (4.66)	6.54 (5.01)
PDC					
Mean (SD)	0.446 (0.299)	0.437 (0.290)	0.461 (0.292)	0.334 (0.269)	0.432 (0.293)

CCI - Charlson Comorbidity Index
VOC - Vaso-Occlusive Crisis
PDC - Proportion of Days Covered

Table 2. Linear regression analysis results for all-medication bundle effects

Covariate	Estimate (95% CI)	p-Value
Intercept	0.491 (0.459, 0.523)	<0.001
Age		
0-11	(Reference)	
12-19	-0.034 (-0.064, -0.004)	0.026
20-29	-0.104 (-0.134, -0.073)	<0.001
30-49	-0.099 (-0.128, -0.070)	<0.001
50+	-0.054 (-0.100, -0.009)	0.018
Gender		
Female	(Reference)	
Male	0.008 (-0.010, 0.027)	0.371
Region		
Northeast	(Reference)	
Midwest	0.008 (-0.022, 0.037)	0.616
South	0.012 (-0.012, 0.036)	0.347
West	-0.067 (-0.107, -0.027)	<0.001
CCI		
0	(Reference)	
1-3	0.010 (-0.010, 0.031)	0.333
4+	0.024 (-0.012, 0.060)	0.193
Transfusion		
No	(Reference)	
Yes	0.045 (0.023, 0.066)	<0.001
VOC (Inpatient)		
0	(Reference)	
1	-0.004 (-0.030, 0.022)	0.775
2	-0.013 (-0.045, 0.020)	0.447
3+	-0.001 (-0.028, 0.027)	0.968
VOC (Emergency Room)		
0	(Reference)	
1	-0.007 (-0.034, 0.020)	0.620
2	0.001 (-0.034, 0.035)	0.970
3+	-0.058 (-0.086, -0.030)	<0.001

CCI - Charlson Comorbidity Index
VOC - Vaso-Occlusive Crisis