Appendix F: Characteristics and outcomes of studies included in the network meta-analysis*

Author/Year/Country Ref/Enrolment/NCT registry	Design Total N of PT (N of female); N of arm Follow-ups	Interventions	Crisis	All-cause Hospitalization days	Adverse events (AE)	Serious adverse events (SAE)
Glassberg 2017[47] USA	RCT, triple-blind	1. Mometasone furoate 220mcg OD inhale (n=35)		Rate hospitalization days: 2.67	Total number of AE: 32	
	Adults and adolescents	In addition to standard SCD care				
Feb 2014 to Oct 2016 NCT02061202	Single centre	2. Placebo (n=17)		Rate of hospitalization days: 4.09	Total number of AE: 9	
	54 (23); 2	In addition to standard SCD care				
	16 weeks					
Ataga 2017[15]	RCT, double-blind	1. Crizanlizumab 5 mg/kg IV	Median annual	Annual rate of days		
Brazil, Jamaica, USA		(n=67)	rate of crisis 1.63	hospitalized 4.00	Number of patients with ≥1 AE: 57	Number of patients with ≥1 SAE: 17
	Adults and adolescents	Two doses 2 weeks apart (loading dose) and then every 4 weeks. A				
Aug 2013 to Jan 2015		total of 14 doses for 50 weeks				
NCT01895361	Multicentre					
	198 (109); 3	2. Crizanlizumab 2.5 mg/kg IV (n=66)	Median annual rate of crisis 2.01	Annual rate of days hospitalized 6.87	Number of patients with ≥1 AE: 56	Number of patients with ≥1 SAE: 21
	52 weeks	Two doses 2 weeks apart (loading dose) and then every 4 weeks. A				
		total of 14 doses for 50 weeks				
		3. Placebo (n=65)	Median annual rate of crisis 2.98	Annual rate of days hospitalized 6.87	Number of patients with ≥1 AE: 55	Number of patients with ≥1 SAE: 17
Sins 2017[48] Netherlands, Belgium, UK	RCT, double-blind	1. NAC 600mg BID oral (n=27)		Total hospital admission days: 9	Total number of AE: 39	Total number of SAE: 8
	Adults					
	Multicentre	2. Placebo (n=40)		Total hospital admission days: 53	Total number of AE: 36	Total number of SAE: 2
Apr 2013 to Nov 2015 NCT01849016	96 (40); 2					
	6 months					
Niihara 2018[12] US	RCT, double-blind (phase 3)	1. L-glutamine 0.3 g/kg BID oral (n=152)	Mean number pain crises: 3.2	Total hospitalization days: 12.1	Percentage with ≥1 AE: 0.98	Percentage with ≥1 SAE: 0.782
		Maximum dose: 30mg				

Jun 2010 to Dec 2013 NCT01179217	Adults and children Multicentre 230 (124); 2 48 weeks	2. placebo (n=78)	Mean number pain crises: 3.9	Total hospitalization days: 18.1	Percentage with ≥1 AE: 1.00	Percentage with ≥1 SAE: 0.871	
Ataga 2011[56] United States, Jamaica, Brazil, France, Trinidad and the United Kingdom. Feb 2005 to Apr 2007 NCT00102791	RCT, double-blind (phase 3, terminated early) Adults and adolescents Multicentre 297 (160); 2 52 weeks	1. Senicapoc 20mg/d BID (loading) and then 10mg/dOD oral (n=145)		Total number of crises: 89		Total number of AE: 127	
		2. Placebo (n=144)		Total number of crises: 106		Total number of AE: 119	
Ataga 2008[52] US Feb 2002 and Jan 2004 NCT00040677	RCT, double-blind (phase 2) Adults Multicentre 90 (45); 3 12 weeks	1. Senicapoc (high-dose): 150 mg (loading dose); 10 mg/d (maintenance) oral OD (n=31)		Total number of crises: 5			
		2. Senicapoc (low-dose): 100 mg (loading dose); 6 mg/d(maintenance) oral OD (n=29)		Total number of crises: 5			
		3. Placebo (n=30)		Total number of crises: 5			
Pace 2003[51] USA	RCT, double-blind Adults and Adolescents Single centre 21 (10); 4 7 months	1. NAC (high-dose) 2400mg/day (n=6) All doses were divided by 3 to be taken		Total number of crises: 5			
		2. NAC (mid-dose) 1200mg/day (n=5) All doses were divided by 3 to be taken		Total number of crises: 5			
		3. NAC (low-dose) 600 mg/day (n=5) All doses were divided by 3 to be taken		Total number of crises: 4			
		4. Placebo (n=5)		Total number of crises: 3			
NCT02482298[55] USA, Egypt, France, Italy, Kenya, Lebanon, UK, Turkey	RCT, double-blind Adults	1. Ticagrelor 45mg BID oral (n=30)					Total number of SAE: 5
		2. Ticagrelor 10MG BID oral (n=27)					Total number of SAE: 6

	Multicentre	3. Placebo (n =30)	Total number of SAE: 6
Jul 2015 to Nov 2016	87 (47); 3		
	12 weeks		
Wun 2013[46]	RCT, double-blind (phase 2)	1. Prasugrel 5 mg/day oral (n=41)	Total number of SAE: 8
United States and Canada	Adults		
		2. placebo (n=19)	Total number of SAE: 4
	Multicentre		
26 Aug 2010 to 13 Jun 2011	62 (30); 2		
NCT01167023			

*ACS: Acute chest syndrome; ALT: Alanine transaminase; CA: Conference abstract; Cr: creatinine; CSRPM: Center for Scientific Research into Plant Medicine; CT: Clinical trial registry; DDCF: Doris Duke Charitable Foundation; ED: emergency department; HbSS: Homozygous sickle haemoglobin (HbS); HbSC: sickle haemoglobin S and haemoglobin C; HbSβ: sickle beta thalassemia, type '0' or '+'; HU: hydroxyurea; JA: Journal article; MTX: Methotrexate; NAD: N-acetylcysteine ;NCATS: National Center for Advancing Translational Sciences; NCRR: National Center for Research Resources; NHLBI: National Heart Lung and Blood Institute; NSAID: Nonsteroidal anti-inflammatory drugs; NR: Not reported; OOPD: FDA's Office of Orphan Products Development; PT: patient; SCD: sickle cell disease; TCD: transcranial Doppler; ZonMw: The Netherlands Organisation for Health Research and Development

** Entry is blank if no data provided for crisis, all-cause hospitalization days, adverse events, or serious adverse events. See appendix for relevant link function to connect different outcome summaries to network meta-analysis.