Additional file 3. Severity of adverse events and incidence of Grade 3 and 4 adverse events in the integrated safety analysis of SP-C-003-05, SP-C-007-07, and WANECAM (SP-C-013-11) comparing PA and AL. Results for the PA observational study CANTAM (SP-C-021-15) are also shown.

Severity grade	Integrated safety analysis					SP-C-021-15 (N=2599)	
	PA (N=667)		AL (N=358)		*P* value[a]		
	N	% (95%CI)	N	% (95%CI)		N	% (95%CI)
Total	426	63.9 (60.2, 67.4)	222	62.0 (56.9, 66.9)	0.59	460	17.7 (16.3, 19.2)
Grade 1	299	44.8 (41.1, 48.6)	178	49.7 (44.6, 54.9)	0.15	244	9.4 (8.3, 10.6)
Grade 2	117	17.5 (14.8, 20.6)	40	11.2 (8.3, 14.9)	0.008[b]	203	7.8 (6.8, 8.9)
Grade 3	7	1.0 (0.5, 2.2)	4	1.1 (0.4, 2.8)	>0.99	8	0.3 (0.2, 0.6)
Grade 4	3	0.4 (0.1, 1.3)	0	0 (0, 1.1)	0.6	0	0 (0, 0.1)
Missing	0	0 (0, 0.6)	0	0 (0, 1.1)	NA	5	0.2 (0.1, 0.4)

[a] Pyronaridine-artesunate (PA) versus artemether-lumefantrine (AL).

[b] Relative risk 1.6 (95%CI 1.3, 2.2); NC, not applicable.

Grade 3 Adverse Events

Primary system class and preferred term	Integrated safety analysis		SP-C-021-15 (N=2599)
	PA (N=667)	AL (N=358)	
Transaminases increased	2 (0.3)	0	0
Anaemia	1 (0.1)	0	2 (0.1)
Neutropenia	1 (0.1)	0	0
Thrombocytopenia	1 (0.1)	0	0
Multi-organ failure	1 (0.1)	0	0
Malaria	1 (0.1)	0	3 (0.1)
ALT increased	1 (0.1)	1 (0.3)	0
AST increased	1 (0.1)	1 (0.3)	0
Acarodermatitis	0	1 (0.3)	0
Vomiting	0	1 (0.3)	1 (<0.1)
Dermatosis	0	1 (0.3)	0
Toxic epidermial necrolysis	0	1 (0.3)	0
Asthenia	0	0	1 (<0.1)
Pyrexia	0	0	1 (<0.1)
Sepsis	0	0	1 (<0.1)
Seizure	0	0	1 (<0.1)

Values are n (%). Patients may have had more than one Grade 3 adverse event.

Grade 4 Adverse Events

Primary system class and preferred term	Integrated safety analysis	
	PA (N=667)	AL (N=358)
Drug-induced liver failure	1 (0.1)	0
Malaria	3 (0.4)	0

Values are n (%).