

Supplementary figures 1

Figure 1a Stage progression (PP)

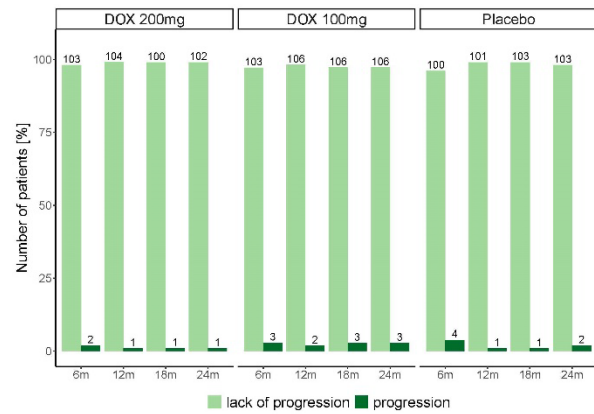


Figure 1b Stage improvement (PP)

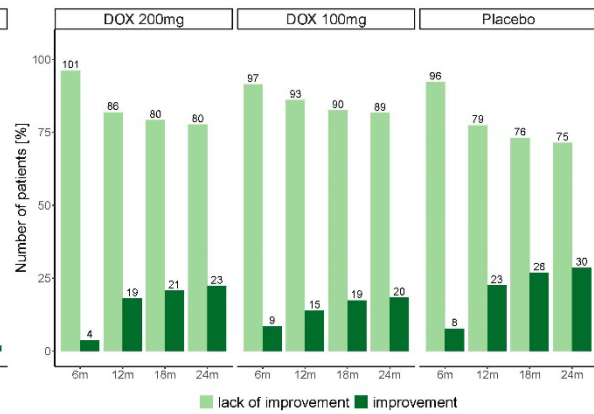


Figure 1a shows the number and percentage of participants (IPP collective) who showed LE stage progression at the different follow-up time points divided by the treatment groups. Figure 1b shows the same for the parameter LE stage improvement.

Supplementary table 1: List of study communities in Kassena Nankana East Municipal (KNEM)

Kassena Nankana East Municipal (KNEM)						
Sub-districts						
Communities	Pungu	Wuru	Manyoro	Navrongo East	Vanania/ Kapania	Biu/Sensa/Kologo
		<ol style="list-style-type: none"> 1. Lower Talania 2. Upper Talania 3. Machoro 4. Bavegnia 5. Bawiu A&B 6. Wusugu 7. Punyoro 8. Yitonia 9. Tekuru 10. Dembasenia 11. Badayoro 	<ol style="list-style-type: none"> 1. Gia-Bngania 2. Gia-Jammagisongo 3. Gia Kwosongo 4. Gia- Nangwao 5. Bonia 1 & 2 6. Lower Nangalikinia 7. Upper Nangalikinia 8. Wuru Central 9. Korania 	<ol style="list-style-type: none"> 1. Wanjanja 2. Sakonia 3. Akumbisi 4. Saabisi 5. Dambisi 6. Gumongu 7. Gerebisi 8. Natugnia-Dazongo 9. Nyogsi 10. Gware/ Chilla 	<ol style="list-style-type: none"> 1. Abepingo A & B 2. Akukongo 3. Gayingo-Doba 4. Akuka 5. Akurugu-Dabo 6. Agurum-aluku 7. Korigo-Kandango 8. Gingabnia 9. Badania 	<ol style="list-style-type: none"> 1. Janania 2. Vunania 3. Gaani 4. Kapania 5. Tampola

Supplementary table 2: List of study communities in Kassena Nankana West District (KNW)

Kassena Nankana West (KNW)							
Sub-districts							
	Mirigu	Sirigu	Kandiga	Chiana	Paga	Navio	Nakolo
Communities	<ol style="list-style-type: none"> 1. Chengo 2. Nayire 3. Kassalingo 4. Tikongo 5. Abugzidone 6. Gonum 7. Gayingo 8. Kumbusingo 9. Pungubisi 10. Alembilla 11. Kansaam 12. Woligum 13. Azinzorka 14. Aburuwasah 15. Nyongo 16. Zampengo 17. Dorsum 	<ol style="list-style-type: none"> 1. Wuingo 2. Abillateo 3. Dazongo 4. Puwellingo 5. Tangasia 6. Tidongo 7. Bugsongo 8. Basengo-Moo 9. Nyango-lingo 10. Basengo-Azuo- Done 11. Amutanga 	<ol style="list-style-type: none"> 1. Azeadoma 2. Agandaa 3. Azuredone 4. Tindongo 5. Nindongo 6. Kurugu 7. Akamo 8. Atiyorom 9. Kaase 10. Akamo 	<ol style="list-style-type: none"> 1. Gwernia 2. Gaania 3. Nyangania 4. KalvioAbulu 5. Kanania 6. Kalvio- Aboenia 7. Gugoro 8. Saboro 9. Adognia 10. Wurunia 11. Yidania 12. Asunia 13. Kafania 	<ol style="list-style-type: none"> 1. Kakungu North 2. Chaina 3. Batiu 4. Bisao 5. Baloo 6. Kajello 1 & 2 7. Nania 8. Zenga 1 & 2 9. Nabio 10. Babile 11. Gwaru 1&2 	<ol style="list-style-type: none"> 1. Bagtua 2. Kasili 3. Navio Tazika 4. Kazugu 5. Badunu 6. Sakaa 7. Tigakuri 8. Sanwo 	<ol style="list-style-type: none"> 1. Nakolo Central 2. Banyono 3. Kuliya 4. Nakolo Tazika 5. Boania 6. Buburu-yuu 7. Bugani

Supplementary table 3a

Additional baseline data – demographics

			DOX 200mg	DOX 100mg	Placebo	Total	<i>p-value</i>
Marital Status	Never married	N (%)	1 (0.9%)	2 (1.7%)	8 (6.7%)	11 (3.1%)	0.0264^a
	Currently married	N (%)	67 (57.3%)	72 (60%)	82 (68.9%)	221 (62.1%)	
	Separated	N (%)	1 (0.9%)	2 (1.7%)	0 (0%)	3 (0.8%)	
	Divorced	N (%)	5 (4.3%)	3 (2.5%)	2 (1.7%)	10 (2.8%)	
	Widowed	N (%)	43 (36.8%)	41 (34.2%)	27 (22.7%)	111 (31.2%)	
Married	no	N (%)	50 (42.7%)	48 (40%)	37 (31.1%)	135 (37.9%)	0.1557^a
	yes	N (%)	67 (57.3%)	72 (60%)	82 (68.9%)	221 (62.1%)	
Main work status	Paid work	N (%)	1 (0.9%)	2 (1.7%)	3 (2.5%)	6 (1.7%)	0.7293^a
	Self-employed	N (%)	115 (98.3%)	113 (94.2%)	113 (95%)	341 (95.8%)	
	Non-paid work	N (%)	0 (0%)	1 (0.8%)	0 (0%)	1 (0.3%)	
	Student	N (%)	0 (0%)	0 (0%)	2 (1.7%)	2 (0.6%)	
	Keeping house/ homemaker	N (%)	0 (0%)	1 (0.8%)	0 (0%)	1 (0.3%)	
	Retired	N (%)	1 (0.9%)	1 (0.8%)	0 (0%)	2 (0.6%)	
	Unemployed (health reason)	N (%)	0 (0%)	1 (0.8%)	0 (0%)	1 (0.3%)	
	Unemployed (other reasons)	N (%)	0 (0%)	1 (0.8%)	1 (0.8%)	2 (0.6%)	

^a Fishers exact test

Supplementary table 3b

Additional baseline data - Participants characteristics

			DOX 200mg	DOX 100mg	Placebo	Total	<i>p-value</i>
LE staging right leg	0 - No abnormality	N (%)	42 (35.9%)	44 (36.7%)	47 (39.5%)	133 (37.4%)	<i>n.d.</i>
	1 - Swelling is reversible	N (%)	1 (0.9%)	2 (1.7%)	2 (1.7%)	5 (1.4%)	
	2 - Swelling is not reversible	N (%)	42 (35.9%)	46 (38.3%)	35 (29.4%)	123 (34.6%)	
	3 - Presence of shallow skin folds	N (%)	31 (26.5%)	27 (22.5%)	32 (26.9%)	90 (25.3%)	
	5 - Presence of deep skin folds	N (%)	0 (0%)	0 (0%)	1 (0.8%)	1 (0.3%)	
	6 - Presence of mossy lesions	N (%)	1 (0.9%)	1 (0.8%)	2 (1.7%)	4 (1.1%)	
LE staging Left leg	0 - No abnormality	N (%)	49 (41.9%)	49 (40.8%)	51 (42.9%)	149 (41.9%)	<i>n.d.</i>
	1 - Swelling is reversible	N (%)	2 (1.7%)	1 (0.8%)	2 (1.7%)	5 (1.4%)	
	2 - Swelling is not reversible	N (%)	43 (36.8%)	51 (42.5%)	32 (26.9%)	126 (35.4%)	
	3 - Presence of shallow skin folds	N (%)	23 (19.7%)	17 (14.2%)	34 (28.6%)	74 (20.8%)	
	6 - Presence of mossy lesions	N (%)	0 (0%)	2 (1.7%)	0 (0%)	2 (0.6%)	
Last ADL attack^e (months before V1)	N		112	119	118	349	<i>0.4815^c</i>
	median, iqr		14; 11	14; 12	15; 12	14; 12	
	95% CI median		[14; 15]	[14; 15]	[14; 15]	[14; 15]	
	min - max		2-89	2-76	2-64	2-89	
Number of attacks within the last year (all patients)	N		101	103	108	312	<i>0.9847^c</i>
	median, iqr		1; 1	1; 1	1; 1	1; 1	
	95% CI median		[1; 1]	[1; 1]	[1; 1]	[1; 1]	
	min - max		0-6	0-6	0-9	0-9	
Duration of attacks (average within the last year (days)) (all patients)	N		114	119	118	351	<i>0.5065^c</i>
	median, iqr		5; 7	5; 5	5; 4	5; 5	
	95% CI median		[4; 7]	[4; 7]	[4; 7]	[5; 6]	
	min - max		0-90	0-30	0-90	0-90	
Duration of attacks (average within the last year (days)) (only patients who had attacks)	N		85	90	98	273	<i>0.9906^c</i>
	median, iqr		7; 4	7; 6	7; 5	7; 5	
	95% CI median		[5; 7]	[6; 7]	[5; 7]	[7; 7]	
	min - max		1-90	2-30	1-90	1-90	
Observer Assessed Cleanliness Score^f	N		117	120	119	356	<i>0.6799^c</i>
	median, iqr		1; 0.2	1; 0.2	1; 0.3	1; 0.3	
	95% CI median		[0.8; 1]	[1; 1]	[0.9; 1]	[1; 1]	
	min - max		0.3-1	0.3-1	0.3-1	0.3-1	

		DOX 200mg	DOX 100mg	Placebo	Total	<i>p-value</i>
Observer Assessed Skin Score^f	N	117	120	119	356	<i>0.4262^c</i>
	median, iqr	0.9; 0.2	0.9; 0.2	0.9; 0.2	0.9; 0.2	
	95% CI median	[0.9; 0.9]	[0.9; 0.9]	[0.8; 0.9]	[0.9; 0.9]	
	min - max	0.7-1	0.6-1	0.4-1	0.4-1	
Self Assessed Hygiene Score^f	N	103	101	102	306	<i>0.0133^c</i>
	median, iqr	0.57; 0.05	0.57; 0.05	0.57; 0.05	0.57; 0.05	
	95% CI median	[0.57; 0.57]	[0.57; 0.62]	[0.57; 0.57]	[0.57; 0.57]	
	min - max	0.52-0.81	0.52-0.90	0.43-0.76	0.43-0.90	
WHODAS 2.0 Physical LF Sub-score (Items S1, S7-S9)	N	117	120	119	356	<i>0.6116^c</i>
	median, iqr	8.3; 10.4	6.3; 9.4	6.3; 8.3	6.3; 9.4	
	95% CI median	[6.25; 8.34]	[6.25; 8.34]	[6.25; 8.34]	[6.25; 8.34]	
	min - max	0-33.3	0-31.2	0-25	0-33.3	
WHODAS 2.0 Not Physical LF Sub-Score (Items S2-S6, S10-S12)	N	117	120	119	356	<i>0.88^c</i>
	median, iqr	16.7; 16.7	14.6; 18.8	14.6; 16.7	14.6; 18.8	
	95% CI median	[12.5; 20.8]	[12.5; 16.7]	[12.5; 18.7]	[12.5; 16.7]	
	min - max	0-66.6	0-52.1	0-54.2	0-66.6	
H1: Overall, in the past 30 days, how many days were these difficulties present?	N	117	120	119	356	<i>0.8318^c</i>
	median, iqr	21; 26	24; 25	30; 24	22.5; 25	
	95% CI median	[11; 30]	[16; 30]	[14; 30]	[16; 30]	
	min - max	0-30	0-30	0-30	0-30	
H2: In the past 30 days, for how many days were you totally unable to carry out your usual activities or work because of any health condition?	N	117	120	119	356	<i>0.4095^c</i>
	median, iqr	0; 3	0; 3	0; 2	0; 2	
	95% CI median	[0; 0]	[0; 0]	[0; 0]	[0; 0]	
	min - max	0-15	0-14	0-14	0-15	
H3: In the past 30 days, not counting the days that you were totally unable, for how many days did you cut back or reduce your usual activities or work because of any health condition?	N	117	120	119	356	<i>0.7443^c</i>
	median, iqr	21; 27	18; 27	20; 26	20; 27	
	95% CI median	[7; 27]	[14; 27]	[10; 30]	[14; 26]	
	min - max	0-30	0-30	0-30	0-30	

^a Fishers exact test ^b ANOVA ^c Kruskal-Wallis test ^d Chi-square test

^e For some participants it was very difficult to recall the history of ADL attacks. Therefore, some questions were not answered.

^f For “overall hygiene” did the assessor evaluate whether the legs were generally well washed and cared for. To answer this question, the assessor had several other questions available within the questionnaire, which have been summarized as scores in this table.

Supplementary table 4

AEs reported between treatment end and 4 month follow-up

Adverse event (MedDRA "Preferred Terms")	DOX 200	DOX 100	Placebo	Total
Headache	23 (42.6%)	21 (38.9%)	10 (18.5)	54
Pain	16 (31.4%)	18 (35.3%)	17 (33.3%)	51
Malaria	17 (43.6%)	9 (23.1%)	13 (33.3%)	39
Pain in extremity	10 (26.3%)	9 (23.7%)	19 (50%)	38
Back pain	14 (58.3%)	3 (12.5%)	7 (29.2%)	24
Diarrhoea	8 (40%)	5 (25%)	7 (35%)	20
Abdominal discomfort/pain	9 (60%)	2 (13.3%)	4 (26.7%)	15
Arthralgia	7 (63.6%)	1 (9.1%)	3 (27.3%)	11
Cough	4 (36.4%)	6 (64.5%)	1 (9.1%)	11
Chest pain	3 (37.5%)	3 (37.5%)	2 (25%)	8
Hypertension	2 (33.3%)	3 (50%)	1 (16.7%)	6
Influenza	2 (33.3%)	1 (16.7%)	3 (50%)	6
Pruritus	2 (40%)	2 (40%)	1 (20%)	5
Dizziness	2 (50%)	1 (25%)	1 (25%)	4
Gastroenteritis	2 (50%)	2 (50%)	0	4
Pyrexia	2 (66.7%)	0	1 (33.3%)	3
Other*	12 (33.3%)	13 (36.1%)	11 (30.6%)	36
Total	135 (40.3%)	99 (29.6%)	101 (30.1%)	335

*Other – occurrence < 3 (Candida infection, Catarrh, Decreased appetite, Eye pain, Gastritis, Peripheral swelling, Skin ulcer, Asthenia, Carbuncle, Cerebrovascular accident, Chills, Contusion, Face injury, Flank pain, Furuncle, Hypoaesthesia, Infection, Limb injury, Lymphangitis, Migraine, Muscle spasms, Musculoskeletal stiffness, Pain in jaw, Rash, Stress, Toothache, Upper limb fracture, Varicella, Wound)