ISRCTN51184184 ABRS-P1-DOSE Phase 1 clinical trial to determine maximum tolerable dose of African Bitter Root Food Supplement

Summary of Results

Rev A0. 9th September 2026

Trial registration	ISRCTN51184184
Trial completion date	8 August 2026
Trial design	Two-centre (Europe and W. Africa), double-blind, placebo-controlled, cross-over, 3+3 dose-escalation study of a herbal food supplement
Sponsor	Deep Life Medical Ltd (UK) / Deep Life Medical Lda (Portugal)
Principal Investigator	Dr Emem Usoro

1. Participant Flow

The trial used a modified Fibonacci 3+3 dose-escalation design across four planned dose stages (12, 16, 20 and 25g/day), run from Scotland with participants from either Europe or West Africa (Nigeria). Participants were volunteers and were not remunerated, other than for actual costs (transport or other costs arising from the trial) and medical expenses pertaining to the trial. Participants with Sickle Cell Disease (SCD) were provided additional medical cover after their participation to minimise their health risks generally: this benefit was decided after the trial and was not mentioned during recruitment.

No Tolerability-Limiting Events (TLEs) were reported at any stage, so no cohort required expansion beyond 3 participants and no de-escalation was triggered. The trial completed at the highest planned dose (25g), which is reported as the Maximum Tolerable Intake (MTI) taken at a time.

Stage	Participants
Participants recruited (full trial pool)	24
Participants who underwent screening and dosing (allocated and received at least one intervention pack)	13
Participants withdrawn by the Principal Investigator following full participation, due to a protocol deviation identified after dosing was complete, and substituted.	1
Participants forming the analysis population, other than analysis for adverse events which included all participants that had received a dose (i.e. 13).	12

One participant, among the original 24 recruited, was excluded during pre-dosing screening on identification of an undisclosed medication relevant to the trial's eligibility criteria that had not been declared at recruitment. She did not proceed to dosing and was replaced within the recruited pool, which remained at 24. She is not included in the count of 13 who received a dose. At the end of the trial, there were 11 in the pool who did not proceed to dosing as the trial reached its safety conclusion without needing to draw further on those recruited.

In the A1 revision of the trial protocol, participants received both dosing packs with instructions to take Dose A and then Dose B at least seven days later while meeting with or on video call with the Principal Investigator (PI). One participant took the second dose without the Principal Investigator being present or on video. In response the participant was withdrawn by the PI and the protocol was revised to prevent recurrence (A2 Revision) by providing the participants with each dose only immediately prior to their taking it. The participant that was withdrawn did not have any adverse events or TLEs.

Stage-by-stage allocation (analysis population, n=12)

Stage	Dose (g/day)	Participants	TLEs reported
1	12	3	0
2	16	3	0
3	20	3	0
4	25	3	0

The participants were drawn from populations that traditionally use ABRS, including two with sickle cell disease (SCD) and six with symptoms consistent with osteoarthritis (OA).

All 12 participants in the analysis population completed both the ABRS and placebo arms of their allocated stage (double-blind, cross-over, minimum 7-day washout, extended where clinically indicated, see Section 4) and completed both scheduled post-dose medical examinations. No participant in the analysis population was lost to follow-up.

2. Baseline Characteristics

Standard screening for all participants comprised medical history, vital signs, ECG, full blood count and blood chemistry. Participants with a sickle cell disease additionally underwent abdominal sonography to assess major organs and spleen size. Screening did not include specific testing for infectious diseases other than white cell counts in the blood count. No participant, in any health-profile group, had an acute illness at enrolment; this was an inclusion requirement. At least three participants had peptic ulcers.

Baseline characteristics are reported for the 12 participants forming the analysis population.

Characteristic	Summary
Age (years), mean (range)	21 to 84, mean 47.
Sex, n (%) female / male	3 (25%) female / 9 (75%) male
Centre, n (%) Europe / W. Africa	1 / 11
Ethnicity, n (%) by category	8 % European, 92% Nigerian (exploratory objective data)
Health profile, n (%): SCD / OA / healthy volunteer	2 (17%) SCD / 6 (50%) OA / 4 (33%) healthy volunteer
Baseline vital signs (BP, HR, temperature, respiratory rate)	All vital signs were in the normal range.
Baseline ECG findings	All ECGs were either normal or had mild anomalies consistent with age and physical fitness.
Baseline full blood count and blood chemistry	All were normal, other than the expected anaemia of those with SCD and one in the healthy cohort with marginally low platelet count for reasons that were unable to be determined by follow up diagnostics – that participant also had Gilbert's syndrome, a hereditary condition that is generally considered either benign or beneficial.
Baseline abdominal sonography (SCD health profile only, n=2): major organs and spleen size	All were in normal range for a healthy person other than both SCD participants had a functional spleen with mild splenomegaly, typical of SCD.

The participant who was withdrawn following both doses, was a female European, age 52, healthy volunteer, and is not included in the above analysis but is included in the count and monitoring for adverse events.

3. Outcome Measures

3.1 Primary outcome measure

Establish the Maximum Tolerable Intake (MTI) of ABRS using a double-blind 3+3 dose-escalation algorithm.

Result	Value
Maximum Tolerable Intake (MTI)	25g taken at once (highest planned dose; no stopping rule triggered)
TLEs recorded (any stage)	0 of 12 participants (0%)
Dose de-escalation required	No

The participants with sickle cell disease (SCD) health profile were allocated to Stage 3 (20g) and Stage 4 (25g, the maximum planned dose), and completed dosing without a TLE.

Each participant took their full allocated daily dose at one time as intended by the trial design: dosing was not spread through the day.

3.2 Secondary outcome measure

Identify any immediate side effects or tolerability issues, by quantitative interview at pre-dose, 30 minutes, 1 hour, 1 day and 1 week after each intervention.

No side effects or tolerability issues that had any plausible causal relation to ABRS were identified by quantitative interview at any monitoring time-point, or by laboratory screening, in either the ABRS or placebo period, at any dose stage up to and including 25g. Three adverse events occurring during the trial period were assessed and judged not causally related to ABRS; these are reported in full in Section 4: all the adverse events occurred with the two SCD participants and none with any others.

No participant reported any stomach irritation or peptic ulcer response: at least three participants had active peptic ulcers and one further participant had H. Pylori eradication therapy that completed just prior to participation. Peptic ulcers are particularly common in W. Africa.

The clinical baseline characteristics were measured pre-participation and post-participation (the day after their second dose). No change with statistical significance was found of any parameter measured in the screening at any dose level.

3.3 Exploratory objective

Ethnicity data was collected for all persons recruited. One third of those recruited were European (Slavic ethnicity), two thirds were Nigerian ethnicity. Of the 13 who were dosed, 2 were European, 11 were Nigerian. In the analysis set of 12, 1 was European, the remainder were Nigerian. The reason for the difference between recruitment ethnicity ratio and dosing ratio, was due to holidays in June, July and August affecting the immediate availability of Europeans, when the Nigerian volunteers were not taking holidays during their rainy season.

3.4 Note on efficacy

This trial was designed and registered to determine tolerability and Maximum Tolerable Intake only. No analysis or claim of therapeutic efficacy is made in this report. This is consistent with the trial's registered primary and secondary objectives, and reflects three specific limitations identified during trial conduct that would affect the reliability of any exploratory efficacy signal: (i) the randomised intervention ordering resulted in more participants with osteoarthritis receiving ABRS in the first dose which may create a placebo effect for that dose; (ii) informal communication occurred between some participants during the trial, which cannot be excluded as a source of bias in any unblinded or participant-reported observation of efficacy; and (iii) ambiguity in the clinical diagnosis of osteoarthritis in two participants, identified during the trial. Any therapeutic benefit of ABRS remains unproven and is not assessed by this trial; it is intended to be examined under controlled conditions in a subsequent Phase 2 trial. Observations of ABRS use during SCD crisis outside

the trial dosing are recorded as they pertain to the maximum dose determination, with respect to their timing.

4. Harms/Adverse Events

Adverse events (AEs) are reported below for all 13 participants who received doses, regardless of causal relation to the intervention, in accordance with ISRCTN reporting requirements. Three AEs occurred during the trial, together with one incidental finding not classified as an AE (see below); all three were reported to the Data Safety Monitoring Board (DSMB) promptly. These three AEs involve two participants only, both of whom had SCD. The percentages in the table below are of events in the dosed population of 13, noting that one event is double counted as one participant had an event after each dose.

Adverse event category	ABRS period n (%)	Placebo period n (%)	Total events n (%)
All-cause mortality	0 (0%)	0 (0%)	0 (0%)
Serious adverse events	0 (0%)	0 (0%)	0 (0%)
Other adverse events (any causality)	2 (15.4%)	1 (7.7%)	3 (23.1%)

The three events were:

- Adverse Event 1: Participant (A) with SCD had a vaso-occlusive crisis seven days following an ABRS dose
- Adverse Event 2: Participant (B) with SCD had malaria/typhoid illness (Adverse Event 2) following that participant's second dose
- Adverse Event 3: Participant A, the same participant as in Event 1, had another crisis twelve days after the placebo dose (Adverse Event 3).

The PI treats all AEs as possible Adverse Reactions until proven otherwise: in each case, ruling out causality was swift and did not require emergency unblinding.

Both participants with a sickle cell disease (SCD) health profile experienced adverse event(s) during the trial; no other participant did. Each event was assessed and attributed to a distinct, unrelated cause as set out below (cold-induced vaso-occlusion in two cases; an intercurrent mosquito- and food/water-borne infection in the other), and the events are not connected to one another. Given the small number of SCD participants in the trial, the fact that events were confined to the SCD subgroup, is noted here explicitly, to avoid any impression that any relationship was overlooked.

4.1 Adverse Event 1: Vaso-occlusive (sickle cell) crisis

Participant	Stage 3 (20 g), sickle cell disease health profile (Participant A). This participant has frequent SCD crises, often two a month during cooler months, and had an active peptic ulcer. The participant has a documented history in which peptic ulcer pain has, on prior occasions, triggered SCD crises. The sponsor funded H. Pylori testing and eradication therapy, completed prior to first dosing. Eradication success was assessed by resolution of symptoms: the participant reported no ulcer pain and tolerated coffee and heavily spiced food, both previously identified triggers, without difficulty; a confirmatory microbiological retest was not performed, as this requires a gap of several months following a positive result. Participants were specifically and consistently asked about gastrointestinal and ulcer symptoms, not only general adverse events, at every monitoring contact; this participant reported none at any contact up to and including the 1-week contact for this dose, which coincided with the onset of this event.
Onset	7 days after first dose (confirmed by CT Manager, following trial completion, to have been the active ABRS dose)
Severity	Severe 10/10 pain; no directly life-threatening symptoms

Seriousness	The participant was not hospitalised and did not meet any SAE criterion under Section 9.1.2 of the protocol.
Action taken	The participant received immediate medical care, funded by the sponsor, including a haematology review. No further follow-up was advised by the haematologist. The participant took ABRS outside the trial as part of her normal process of managing sickle cell crisis. The interval between doses was extended for this participant to enable that ABRS to wash out before taking the second trial dose, and ensure the participant had fully recovered from the crisis.
Causality assessment	Judged not causally related to ABRS by both the Principal Investigator and the DSMB physician, independently. The event occurred substantially beyond ABRS's observed washout period (a matter of hours, based on prior observational use). The affected limb corresponded to the side of the participant's body directly exposed to sustained air-conditioning airflow at her workplace, consistent with cold-induced vaso-occlusion, a recognised SCD crisis trigger, and she was noted to be wearing lightweight clothing (shorts and a t-shirt) at the time. The participant's documented history of ulcer-pain-triggered SCD crises was considered as an alternative explanation. This was excluded, as no ulcer pain or related symptoms were reported at any monitoring contact up to and including onset of this event.
Regulatory reporting	Reported to the DSMB promptly. Not reported to the Food Standards Agency, as the event was assessed as having no plausible causal relation to the intervention.

4.2 Adverse Event 2: Malaria infection

Participant	Sickle cell disease health profile (Participant B, a different participant to that in Adverse Event 1)
Onset	Malaria-suspicious symptoms developed eight hours after her second dose (confirmed by CT Manager to have been ABRS). Tested the following day using the standard combined malaria/typhoid panel (see incidental finding below); malaria confirmed positive.
Seriousness	Not hospitalised, no symptoms indicating any urgent life-threatening risk.
Action taken	Treated for malaria as an outpatient at a contracted clinic. Fully resolved. Reported promptly to the DSMB.
Causality assessment	Assessed as an intercurrent infectious illness, unrelated to ABRS. The participant worked outdoors on a farm in a high malaria risk area without protective precautions against mosquito exposure. Malaria typically takes 7 to 30 days between infection and symptoms being manifest, a timeline which puts the infection date prior to trial dosing.
Outcome	Resolved fully following standard treatment regime.

4.3 Adverse Event 3: Vaso-occlusive (sickle cell) crisis

Participant	Stage 3 (20 g), sickle cell disease health profile (Participant A) Same participant as in the first adverse event. No ulcer-related symptoms were reported at that or any earlier contact, though no monitoring contact fell precisely at the time of onset.
Onset	12 days after second dose (confirmed by CT Manager, following trial completion, to have been the placebo dose)
Severity	Severe 10/10 pain; no directly life-threatening symptoms.
Seriousness	The participant was not hospitalised and did not meet any SAE criterion under

	Section 9.1.2 of the protocol.
Action taken	The participant took ABRS outside the trial as part of her normal process of managing sickle cell crisis. The pain and crisis subsided over 12 hours. The participant's crises last six to seven days typically when not treated with ABRS, which is further indicative of there being no adverse effect of ABRS on SCD crisis (no efficacy is implied).
Causality assessment	Judged not causally related to ABRS by both the Principal Investigator and the DSMB physician, independently. The event occurred substantially beyond the trial's ABRS's dosing observed washout period (a matter of hours, based on prior observational use). The trigger for this crisis was likely due to cold. As with Adverse Event 1, the participant's documented ulcer-pain trigger pathway was considered and excluded, as no ulcer-related symptoms were reported at any monitoring contact for this dose.
Regulatory reporting	Reported to the DSMB promptly. Not reported to the Food Standards Agency, as the event was assessed as having no plausible causal relation to the intervention.

4.4 Incidental finding, reported for completeness (not classified as an adverse event): Asymptomatic typhoid carrier state

Participant	Same participant as Adverse Event 2 (Participant B)
How identified	Identified through the combined malaria/typhoid test panel that is routinely used in West Africa whenever malaria is suspected, reflecting the high background prevalence of typhoid. This is standard testing practice for her presentation, not an additional or unusual investigation. The participant's presenting symptoms were assessed as attributable to malaria; she had no symptoms specifically attributable to typhoid.
Assessment	Assessed as a pre-existing, asymptomatic chronic carrier state, predating trial enrolment, rather than an infection acquired during the trial. Standard pre-participation screening (medical history, vital signs, ECG, full blood count and blood chemistry) did not include specific testing for malaria or typhoid, so no baseline result is available to directly confirm carrier status before enrolment; this assessment therefore rests on the following: the participant resided throughout her participation in sponsor-arranged accommodation with all food prepared for her, and typhoid is endemic in the rural area in which she normally resides. Her baseline full blood count, including white cell count, was normal (other than anaemia); this is consistent with an asymptomatic carrier state, which characteristically produces no haematological abnormality.
Action taken	The sponsor funded treatment of the carrier state. This was undertaken for public health reasons independent of trial participation (the participant has a one-year-old child), and was not undertaken as management of any trial-related event.
Why not classified as an adverse event	The finding reflects a pre-existing condition rather than a new or worsening change in health arising during trial participation, and caused no symptoms at any time. It is reported here in the interests of complete transparency, consistent with how incidental findings have been handled elsewhere in this trial. On the determination of the significance of the typhoid diagnosis, it is not uncommon to find asymptomatic typhoid in Nigerians. This is due to three factors: a) in Nigeria boreholes for drinking and washing water are often in close proximity to cesspits and soakaways, b) the culture of communal dining without use of implements, and c) poor awareness of the availability of a typhoid vaccine.

Reported to DSMB	Yes, promptly, notwithstanding that it is not classified as an adverse reaction

Following the trial, the sponsor noting use of ABRS during crisis, paid for a health package for both SCD participants: this was not offered or known to them prior to the completion of the trial. The package covered their consultation with a specialist haematologist, a year of treatment with Hydroxycarbamide (including regular monitoring blood analysis), and home supply of Diclofenac, Omeprazole, Paracetamol and Aspirin. The sponsor also funded typhoid vaccinations for both SCD participants post trial, and for the participant's infant.

No serious adverse events and no deaths occurred during the trial.

No participant, at any dose stage up to and including the maximum planned dose of 25g, experienced an adverse event judged to have plausible causal relation to ABRS (i.e. no TLE was recorded).

No evidence of toxicity was observed at doses up to 25g. No adverse safety signal attributable to ABRS was observed in the small numbers of participants with SCD, peptic ulcers, or OA who took part; the sample size in each of these subgroups is too small to conclude that ABRS is not contraindicated in these conditions, and this would need to be examined in a larger study.