

A PHASE II DOSE-INCREASING STUDY OF SITAMAQUINE FOR THE TREATMENT OF VISCERAL LEISHMANIASIS IN KENYA

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Abstract. Sitamaquine (WR6026) is an 8-aminoquinoline in development for the oral treatment of visceral leishmaniasis (VL). This was an open-label, dose-increasing study to determine the dose-response and safety profile for sitamaquine in Kenyan patients with VL caused by *Leishmania donovani*. Patients (mean age 15.9 [range = 5–47] years) received sitamaquine daily for 28 days at one of four doses: 1.75 (n = 12), 2.0 (n = 61), 2.5 (n = 12), or 3.0 (n = 12) mg/kg/day. The primary efficacy outcome was cure (absence of parasites on splenic aspirate) in the intent-to-treat population at day 180. Cure was achieved in 79 (83%) of 95 patients overall, and in 11 (92%) of 12, 49 (80%) of 61, 9 (82%) of 11, and 10 (91%) of 11 patients at sitamaquine doses of 1.75, 2.0, 2.5, or 3.0 mg/kg/day, respectively. The most frequent adverse events during active treatment were abdominal pain (12 [12%] of 97) and headache (11 [11%] of 97), and one patient in each of the 2.5 mg/kg/day and 3.0 mg/kg/day dose groups had a severe renal adverse event. The effects of sitamaquine on the kidney need further investigation. Sitamaquine was efficacious and generally well tolerated in Kenyan patients with VL.

INTRODUCTION

Leishmaniasis is a protozoal infection spread by sand fly bites. The most serious form of the disease is visceral leishmaniasis (VL), which involves infection of the reticuloendothelial system. Clinical presentation typically includes fever, weight loss, hepatosplenomegaly, and lymphadenopathy.¹ In the absence of treatment, symptomatic VL is usually fatal. In Africa, VL is a particular problem in Kenya, Sudan, Ethiopia, and Eritrea. In Kenya, VL is endemic in the Baringo, Koibatek, Turkana, West Pokot, Kitui, Meru, Mwingi, and Machakos districts.

Sodium stibogluconate at a dose of 20 mg/kg/day intravenously or intramuscularly daily for 28–30 days is still the treatment of choice for VL in Africa.¹ However, the requirement for daily injections, and frequent monitoring because of the potential for toxic adverse events may be challenging in rural and resource-poor settings. In Africa, resistance to pentavalent antimonials is currently uncommon.¹ However, resistance is significant in other disease-endemic regions such as India² and is likely to be an issue in Africa in the future. Liposomal amphotericin B was an effective treatment for VL in Sudan and Kenya,^{3,4} but it is prohibitively expensive, and its use in African patients is limited.^{3,4} Standard amphotericin B is effective but toxic. Paromomycin (aminosidine) has shown good efficacy against VL in Africa,⁵ and is in phase III studies in India. However, this agent also requires parenteral administration.

Miltefosine is an oral anti-leishmanial drug recently approved for use against VL in India. Although miltefosine is not yet available in Kenya, it is currently being investigated in east African patients.⁶ Although miltefosine is an important breakthrough in the treatment of VL, it has two main limitations regarding its use in a public health setting. First, its long half-life could lead to the rapid emergence of resistance.⁷ Second, miltefosine has a narrow therapeutic window and has demonstrated teratogenicity in animal studies, leading to its

contraindication in pregnancy and recommended caution in women of child-bearing potential.⁸ Thus, there remains a need for an inexpensive oral anti-leishmanial agent with a safety profile that makes it acceptable for use in a wide range of patients.

Sitamaquine (WR6026) is an orally administered 8-aminoquinoline in development for the treatment of VL. Studies in animals and preliminary clinical studies in Kenya and Brazil have shown encouraging efficacy against various species of *Leishmania*.^{9,10} This study was conducted to determine the dose-response and safety profile for oral sitamaquine in Kenyan patients with VL caused by *Leishmania donovani*. A similar study has been conducted in India and is also reported in this issue of the journal.¹¹

PATIENTS AND METHODS

This was an open-label, increasing-dose, sequential cohort study conducted at the Kenya Medical Research Institute in Nairobi, Kenya. The study was conducted in accordance with Good Clinical Practice (ICH E6) and the Declaration of Helsinki. The protocol was reviewed and approved by the Kenya Medical Research Institute National Ethical Committee. Informed, written, or witnessed oral consent was obtained from all study subjects (or their parent or guardian for subjects less than 18 years of age).

Inclusion and exclusion criteria. Subjects eligible for inclusion had a clinical diagnosis of VL with symptomatic disease and the diagnosis confirmed by the presence of *Leishmania* amastigotes in splenic aspirates. Subjects 5–65 years of age of either sex were included in the study. Females that were pregnant or lactating were excluded. Additional exclusion criteria included known hypersensitivity to sitamaquine, use of an anti-leishmanial agent within 10 days or of an investigational compound within 30 days (or 5 half-lives) of the start of the study, subjects with marked deviations in serum chemistry or abnormal hematologic markers outside those expected to be caused by VL, patients with serious underlying disease, including human immunodeficiency virus (HIV) infection, malnutrition, or severe kala-azar, glucose-6-phosphate dehydrogenase deficiency, or previous inclusion in this study.

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Investigations and assessments. All patients recruited into the study received sitamaquine daily for 28 days at an investigational dose, with follow-up to day 180. Parasite load was determined by splenic aspirate at baseline and at days 42, 90, and 180. Spleen tissue samples were stained using Giemsa (Dade International Inc., Miami, FL) and parasite load was quantified using the *Leishmania* index¹² with the assessor blinded to study treatment. Patients were assessed clinically at baseline and at days 7, 14, 21, 28, 42, 90, and 180. Spleen size was evaluated by palpation and ultrasound.

The study was initiated with two cohorts; cohort 1 received sitamaquine, 1.75 mg/kg/day and cohort 2 received sitamaquine, 2.0 mg/kg/day. Six patients were randomized to cohort 1 and 12 patients to cohort 2. These patients were treated in an observer-blind fashion and followed-up for 42 days, after which efficacy and safety assessments were used to determine study progression. The remainder of the study was conducted on an open-label (non-blinded) basis. In cohort 1, acceptable efficacy (85% of the patients with no evidence of amastigotes in a splenic sample at day 42) led to the recruitment of an additional six patients to this cohort. Additional cohorts were recruited sequentially, with no dose escalation for individual patients. Dose escalation in cohort 3 (2.5 mg/kg/day of sitamaquine) occurred if less than 4 of 12 patients in cohort 2 had dose-limiting toxicity at day 42. Dose escalation in cohort 4 (3.0 mg/kg/day of sitamaquine) was initiated if in cohort 3 at day 28 less than 4 of 12 patients had dose-limiting toxicity. After 12 patients had been recruited, treated, and assessed at day 42 for each cohort, the protocol allowed for the recruitment of at least 49 additional subjects into the cohort that appeared to offer the most promising efficacy-safety profile as assessed by the investigators and study sponsor.

Efficacy assessment. The primary efficacy outcome was cure (absence of amastigotes in splenic aspirate [*Leishmania* index = 0]) at day 180 in the intent-to-treat (ITT) population. Cure was also evaluated at days 90 and 42. Failure was reported as a *Leishmania* index ≥ 1 , a reappearance of the signs and symptoms of VL after previous cure or no effect or worsening of the signs and symptoms of VL, or withdrawal because of a lack of efficacy at any time during the study. Patients who withdrew because of adverse events were followed-up for the remainder of the study and their final outcome was determined at day 180. Observed data at day 180 and known failures because of a lack of efficacy were included in the efficacy analysis, with a sensitivity analysis planned to determine the effect of any missing data.

Safety assessment. All adverse events, regardless of their relationship to study medication, were noted. Their cause or relationship to drug treatment was recorded by the investigator, based on their clinical judgment, as not related, unlikely, suspected or probable. Dose-limiting toxicity included any adverse event with a probable relationship to drug treatment and a positive temporal relationship. Clinical laboratory evaluations were conducted at baseline and on days 7, 14, 21, 28, 42, 56, 70, 90, and 180 of the study. The following variables were measured: hemoglobin, hematocrit, methemoglobin, white blood cell count, platelets, liver enzyme activity, urea, serum creatinine, albumin globulin, prothrombin time, and partial thromboplastin time. At screening, additional measurements included glucose-6-phosphate dehydrogenase and in women of child-bearing potential serum β -human chorionic gonadotrophin.

Statistical assessment. As the study was designed to estimate the dose-response and safety of sitamaquine and not to make any formal comparisons between cohorts, a sample size calculation relating to this objective was not performed. However, in the original protocol a sample size calculation was performed to ensure the accurate estimation of efficacy for the dose believed to be most efficacious. Assuming a true response rate of 85%, this calculation showed that 61 patients would be required to detect within 9% of the true response rate at a confidence level of 95%, assuming that the binomial distribution can be approximated by a normal curve. It was subsequently decided to present exact 95% confidence intervals for the primary efficacy outcome calculated using the Clopper Pearson method. With 61 patients and assuming a true response rate of 85%, this method would detect within -11% to +8% of the true response rate at a two-sided confidence level of 95%. All other data were summarized using descriptive statistics only. The efficacy and safety analyses were carried out on the ITT and safety populations, respectively. The ITT population included all patients that had a valid baseline assessment and received at least one dose of study medication, and the safety population included all patients who received at least one dose of study medication.

RESULTS

Patient characteristics. A total of 97 patients were recruited, all of whom received at least one dose of sitamaquine (ITT and safety population). Cohort 2 (2.0 mg/kg/day of sitamaquine) was chosen for further evaluation and included 61 patients, compared with 12 patients for each of the other three cohorts. Allowing for the low numbers in cohorts 1, 3, and 4, and the higher recruitment to cohort 2, baseline demographics and clinical characteristics for the ITT population were broadly similar between the cohorts (Table 1 and Figure 1). All subjects were black Africans. Sixteen patients withdrew prematurely from the study. One patient withdrew consent after four days of treatment with sitamaquine and before completing any of the planned clinical evaluations; the remaining 15 patients withdrew because of a lack of efficacy (treatment failure).

Efficacy. At day 180 in the ITT population, cure was achieved in 79 (83%) of 95 patients (primary efficacy outcome, Table 2). In cohort 2, 49 (80%) of 61 were cured at day 180. Similar results were seen at day 90 and day 42 (Table 2).

Results of a splenic aspirate were missing for two patients at day 180: one had withdrawn consent after four days of

TABLE 1
Baseline characteristics for the intent-to-treat population*

Characteristic	Sitamaquine dose			
	1.75 mg/kg/day Cohort 1 n = 12	2.0 mg/kg/day Cohort 2 n = 61	2.5 mg/kg/day Cohort 3 n = 12	3.0 mg/kg/day Cohort 4 n = 12
Age, years†	21.5 (13.0) [9–47]	14.5 (7.0) [6–32]	14.8 (8.4) [5–32]	18.3 (11.8) [7–39]
Weight, kg	37.6 (15.5) [15–54]	33.3 (15.1) [15–58]	31.2 (13.9) [12–55]	35.9 (13.0) [11–55]
Male, %	75	77	67	58

* Values are mean (SD) [range] unless stated otherwise.

† For many subjects, the day and month of birth were not known and following standard convention these were recorded as January 1.

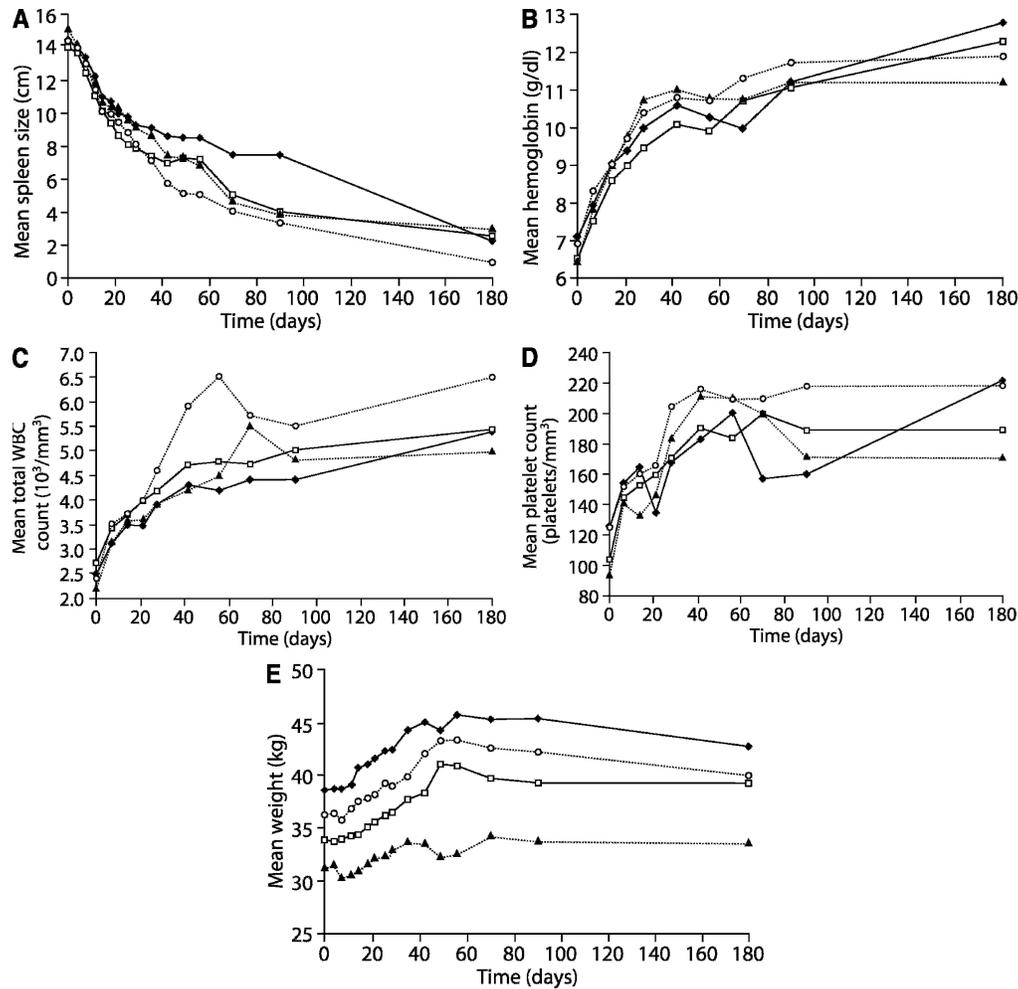


FIGURE 1. Changes in clinical assessments during the study for **A**, mean spleen size, **B**, mean hemoglobin level, **C**, mean total white blood cell (WBC) count, **D**, mean platelet count, and **E**, mean weight in the four cohorts.

treatment with sitamaquine (cohort 3) and one withdrew consent prior to the day 180 assessment and was considered missing for this assessment (cohort 4). All 16 failures were due to a lack of efficacy, either determined by parasitologic findings or based on the clinical signs and symptoms of VL.

Improvements were seen in all of the key clinical assessments of spleen size, hemoglobin, white blood cell count, platelets, and weight over the course of the study (Figure 1). In particular, there was a rapid reduction in spleen size after the initiation of sitamaquine therapy (Figure 1A). This reduction was more rapid than seen with standard therapy, although not as rapid as with liposomal amphotericin B.

Safety and tolerability. Adverse events due to any cause were observed in 72 (74%) of 97 subjects during active treatment. The most common adverse events during active treatment were abdominal pain (12 [12%] of 97), headache (11 [11%] of 97), hematuria (9 [9%] of 97), epistaxis (8 [8%] of 97), and increased levels of aspartate aminotransferase (AST) (8 [8%] of 97). Six of the eight patients who had an elevated AST level also had an elevated AST level before the start of therapy. At least one adverse event was recorded for 10 (83%) of 11, 41 (67%) of 61, 11 (92%) of 12, and 10 (83%) of 12 patients in cohorts, 1, 2, 3, and 4, respectively. However, there were no consistent or clear differences between the

cohorts in the frequency or incidence of individual adverse events.

During follow-up, after active treatment, 79 (81%) of 97 patients experienced at least one adverse event due to any cause. The most common adverse events during follow-up were fungal dermatitis (19 [20%] of 97), coughing (14 [14%] of 97), and infection (13 [13%] of 97). There were no clear differences between the cohorts for individual adverse events: 10 (83%) of 12, 50 (82%) of 61, 10 (83%) of 12, and 9 (75%) of 12 patients experienced at least one adverse event during follow up in cohorts, 1, 2, 3, and 4, respectively.

Adverse events having a suspected or probable relationship to study medication occurred in 30 (31%) of 97 patients during active drug therapy and are summarized in Table 3. Hematuria, an increased AST level, and abdominal pain were the most common drug-related adverse events. There was no increase in the frequency of adverse events at the higher sitamaquine doses. During follow-up, 17 (18%) of 97 patients had adverse events of suspected or probable relationship to study medication: 2 (17%) patients each in cohorts 1, 3 and 4, and 11 (18%) patients in cohort 2. There was no substantial difference in the nature or frequency of these adverse events between the cohorts.

There were no deaths and no withdrawals due to adverse

TABLE 2

Efficacy outcomes with sitamaquine in the intent-to-treat population at day 180 (primary efficacy outcome), day 90, and day 42

	Sitamaquine dose			
	1.75 mg/kg/day Cohort 1 n = 12	2.0 mg/kg/day Cohort 2 n = 61	2.5 mg/kg/day Cohort 3 n = 12	3.0 mg/kg/day Cohort 4 n = 12
Outcome at day 180				
Cure, no. (%)	11 (91.7)	49 (80.3)	9 (81.8)	10 (90.9)
95% CI, %	61.5, 99.8	68.2, 89.4	48.2, 97.7	58.7, 99.8
Failure, no. (%)	1 (8.3)	12 (19.7)	2 (18.2)	1 (9.1)
Missing,†,* no.	0	0	1	1
Outcome at day 90				
Cure, no. (%)	11 (91.7)	50 (83.3)	9 (81.8)	11 (91.7)
95% CI, %	61.5, 99.8	71.5, 91.7	48.2, 97.7	61.5, 99.8
Failure, no. (%)	1 (8.3)	10 (16.7)	2 (18.2)	1 (8.3)
Missing,† no.	0	1	1	0
Outcome at day 42				
Cure, no. (%)	12 (100)	53 (86.9)	10 (90.9)	12 (100)
95% CI, %	73.5, 100	75.8, 94.2	58.7, 99.8	73.5, 100
Failure, no. (%)	0	8 (13.1)	1 (9.1)	0
Missing, no.	0	0	1	0

* Two patients withdrew consent, one in cohort 3 on day 4 and one in cohort 4 before the day 180 assessment.

† One patient in cohort 2 did not attend the day 90 assessment.

events during the study period. Three patients had adverse events determined by the investigators as serious, all of which were of suspected or probable relationship to study medication. The first of these, in cohort 2, had an overdose of their initial dose of sitamaquine, having been given an additional 10 mg of study medication by mistake. There were no sequelae and the patient continued in the study. The second patient, in cohort 3, had a serious adverse event of glomerulonephritis recorded during active treatment (day 23) and was treated with intravenous frusemide and completed sitamaquine therapy (day 28). This patient had a serious adverse event of renal failure at day 32 and was withdrawn at day 56 due to a lack of efficacy after immunosuppressive therapy was given (azathioprine and prednisone) for acute glomerulonephritis. Urea and creatinine levels were elevated in this patient at day 28, but laboratory values had normalized by study withdrawal at day 56. The third patient, in cohort 4, had serious adverse events of glomerulonephritis and renal failure at day 25 and was treated with intravenous frusemide and completed sitamaquine therapy. This patient had elevated creatinine and urea levels at day 21 that continued to increase until day 56 and which remained elevated until the end of the study. A serious adverse event of chronic renal failure was recorded at

day 180. This patient completed the study, but died seven months later; the primary cause of death was pulmonary arteriole thromboembolism, secondary to chronic renal failure. There were no grade 3 or 4 laboratory abnormalities (National Cancer Institute Common Terminology Criteria for Adverse Events¹³) for creatinine or urea levels other than those recorded for the two patients described in this report.

DISCUSSION

This study demonstrated the efficacy and tolerability of sitamaquine as treatment for VL in Kenyan patients. Overall, 83% of the patients achieved cure based on an absence of parasites at day 180, with 92%, 80%, 82%, and 91% of the patients achieving cure at sitamaquine doses of 1.75, 2.0, 2.5, or 3.0 mg/kg/day, respectively. There did not appear to be a significant dose-response relationship, although it should be remembered that the highest dose is only 1.7 times the lowest dose.

The primary efficacy outcome measure in this study was defined prospectively as the derived parasitologic outcome at day 180. A successful outcome was defined as parasitologic cure (*Leishmania* index = 0) or in the absence of a splenic

TABLE 3

Most frequently reported adverse events (> 2 subjects overall) commencing during the active treatment phase and recorded by the investigator as suspected or probably related to drug therapy

Adverse event, no. (%)	Sitamaquine dose			
	1.75 mg/kg/day Cohort 1 n = 12	2.0 mg/kg/day Cohort 2 n = 61	2.5 mg/kg/day Cohort 3 n = 12	3.0 mg/kg/day Cohort 4 n = 12
At least one adverse event	3 (25)	21 (34)	4 (33)	2 (17)
Hematuria	0	8 (13)	0	1 (8)
Elevated aspartate aminotransferase level	2 (17)	6 (10)	0	0
Abdominal pain	1 (8)	4 (7)	1 (8)	0
Elevated blood urea nitrogen level	0	3 (5)	1 (8)	1 (8)
Headache	1 (8)	3 (5)	1 (8)	0
Elevated creatinine level	0	1 (2)	1 (8)	1 (8)
Nausea	1 (8)	1 (2)	1 (8)	0

aspirate at day 180, this outcome could be carried forward from the last available parasitologic assessment if the patient remained clinically well. Parasitologic assessment was mandatory in this study at days 42, 90, and 180. In fact, a parasitologic assessment was available at day 180 for all patients remaining in the study at this time point. Data were missing for two patients who had withdrawn consent prior to the day 180 assessment.

In the original protocol, all subjects were to have been followed to day 180 even if they had withdrawn from the study. As a consequence, any subject who had no day 180 data was considered missing and was to be excluded from the efficacy analysis. However, when analyzing the data, it was realized that this approach risked ignoring those patients who were withdrawn due to lack of efficacy and who were not followed-up for whatever reason. As a result, in the analysis presented in this report, all patients who withdrew due to a lack of efficacy had their outcomes carried forward to day 180. This amendment did not materially affect the conclusions of this study but was believed to be a more conservative approach to the data analysis.

Parasitologic assessment was not scheduled before day 42 in this study, and the efficacy results based on parasitologic data were very similar from day 42 through to day 180. Clinical evaluation indicated rapid improvement in key clinical measures of disease severity, such as spleen size and hematologic parameters. For hemoglobin levels, white blood cell counts, and platelet counts, most of the improvement had been achieved by the end of therapy (day 28). However, for spleen size, further improvements were achieved out to day 180.

The results presented for this study are similar to those reported elsewhere in this journal issue for sitamaquine efficacy against VL in Indian patients, with 87% efficacy overall and 81%, 89%, 100%, and 80% efficacy at sitamaquine doses of 1.5, 1.75, 2.0, or 2.5 mg/kg/day, respectively.¹¹ However, in the Indian study, cure was based mainly on clinical evaluation at day 180 with parasitologic assessment carried forward from day 14. A previous study in Kenyan patients included 8 patients treated with 0.75–1.0 mg/kg/day of sitamaquine for 14 days and 8 treated with 1.0 mg/kg/day of sitamaquine for 28 days with no additional follow-up.¹⁴ Overall, 5 patients were cured and 11 showed clinical improvement.¹⁴ Another study was conducted in 22 Brazilian patients, although these patients were infected with *L. chagasi*.⁹ Cure rates were 0 of 4 for 1 mg/kg/day of sitamaquine for 28 days, 1 of 6 for 1.5 mg/kg/day, 4 of 6 for 2 mg/kg/day, 1 of 5 for 2.5 mg/kg/day, and 0 of 1 for 3.25 mg/kg/day.⁹ However, the small numbers of patients in these trials and lack of follow-up does not allow reasonable comparison with the current, more extensive, study.

Sitamaquine was generally well tolerated in this study, with abdominal pain and headache the most frequently reported adverse events. There was no clear relationship between the nature and incidence of adverse events and sitamaquine dose, which is probably due to the small number of patients in cohorts, 1, 3, and 4. Although methemoglobinemia is associated with 8-aminoquinolines,¹⁴ and was observed in Indian patients,¹¹ it was not reported by investigators as an adverse event in this study. A single subject (2 mg/kg cohort) had a single elevated methemoglobin concentration (21.6% on day 21). The difference between the Kenyan and Indian studies in

this respect is puzzling and will continue to be monitored in future studies.

Two patients in this study experienced glomerulonephritis and renal failure in cohorts 3 and 4, i.e., at sitamaquine doses of 2.5 and 3.0 mg/kg/day. These adverse events were attributed to drug therapy. In a previous study in 23 Brazilian subjects,⁹ reversible elevations in serum creatinine levels occurred in two subjects receiving a sitamaquine dose of 2.0 mg/kg/day and in one subject receiving a sitamaquine dose of 3.25 mg/kg/day. The two subjects receiving 2.0 mg/kg/day of sitamaquine had concomitant infections with varicella virus, which was suggested may have contributed to this adverse event.⁹ In an earlier Kenyan study, formal renal monitoring was not conducted, but urinalysis in the 16 subjects included in the study showed no significant abnormalities with sitamaquine doses up to 1 mg/kg/day.¹⁰ Renal adverse events were also observed in the recent Indian study in 9 of 120 patients receiving sitamaquine at doses of 2.0 or 2.5 mg/kg/day (plus one patient who also received amphotericin B).¹¹ Of these nine patients, two had glomerulonephritis, three had nephrotic syndrome, two had proteinuria, one had an elevated serum creatinine level, and one had acute renal failure, although only two patients had creatinine levels greater than or equal to twice the upper limit of normal.¹¹

Nephrotoxicity is not a documented side effect with drugs of the primaquine family. However, as renal adverse events were only seen for sitamaquine doses ≥ 2 mg/kg/day, it is possible that this represents a dose-related toxicity. As renal impairment has been seen as an adverse event in three previous studies with sitamaquine,^{15–17} it is clearly something that requires better understanding. Renal involvement is well described in VL,^{15–17} and may lead to renal failure.¹⁸ Given the high mortality of untreated VL, it is impossible to evaluate new therapies against placebo. Thus, adverse events due to drug therapy cannot easily be separated from the sequelae of the infection. It has been postulated that immune complexes generated as a result of parasite lysis during therapy may be responsible for the renal damage.¹⁹ Renal adverse events are often seen in clinical studies with anti-leishmanial drugs, several of which are nephrotoxins. As this is an important development issue for sitamaquine, further preclinical studies are planned and renal adverse events will be monitored closely in subsequent clinical trials.

The sponsors and investigators acted conservatively, and selected cohort 2 for additional patient recruitment. This decision was based on the lack of serious adverse events in cohort 2 and the equivalent efficacy of 2.0 mg/kg/day of sitamaquine compared with the higher sitamaquine doses after 12 patients had been enrolled in each cohort.

Sixteen (17%) of 95 patients failed sitamaquine therapy. Possible resistance to sitamaquine was not evaluated in this study, but is unlikely given the limited use of this agent in Kenya. A competent immune system assists in elimination of the infection and immunosuppression may explain some of the failures. One patient, who was responding well to sitamaquine therapy, subsequently failed after receiving immunosuppressive therapy.

Patients were tested by an HIV enzyme-linked immunosorbent assay before enrollment, and those who were HIV+ were excluded from this study. The overall prevalence of HIV in Kenya is estimated to be 6.7%, although it varies regionally; the highest prevalence is in Nyanza (15%), followed by

Nairobi (10%), and the lowest prevalence is in the North Eastern province (<1%).²⁰ The patients in this study were recruited in the Rift Valley province in northwestern Kenya on the border with Sudan where HIV prevalence is reported to be between 4% and 6%.²⁰ Sitamaquine at a dosage of 120 mg a day for 28 days has been used in one patient coinfecting with HIV and VL on a compassionate basis with encouraging results.²¹

Overall, oral sitamaquine for 28 days was efficacious and well tolerated in the treatment of VL, with a dose of 2.0 mg/kg/day evaluated in 61 Kenyan patients. Further studies are required to define the optimal dose and duration of sitamaquine in a larger number of African patients and to better understand its effects on the kidney. Thus, sitamaquine is a promising oral agent for the treatment of VL in Africa.

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