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Report from Informal Consultation

on Albendazole Research

Findings in Lymphatic Filariasis

13-14 October 1998

Filariasis Elimination Programme (CDS/FIL)
Division of Control of Tropical Diseases
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Executive Summary

Those medical researchers responsible for the clinical trials of albendazole carried out to date in lymphatic filariasis came from **Africa, Asia and the Americas** to participate in this meeting, along with SmithKline Beecham's clinical developer of albendazole and members of the WHO* secretariat who have extensive experience in the use of albendazole and other drugs for filariasis and intestinal parasite infections. The meeting focussed on the safety and efficacy of albendazole (alone and in combination with either ivermectin or DEC) primarily in lymphatic filariasis. Conclusions and recommendations were formulated.

Safety of Albendazole and albendazole combinations

Numbers of individuals assessed: During the past 20 years it is estimated that albendazole has been given for intestinal helminth infections to 200-300 million people (mostly children) living in filariasis-endemic areas. If only 1% of these had active filarial infections [more likely to be 10-30%], still at least several million co-infected children would already have been treated. Safety experience with the drug has been excellent, and no adverse reactions have ever been attributed to concurrent filarial infections.

In the present studies (funded by WHO, SB, USAID, CDC and DBL) 2 728 men, women and children have been treated (~25% being microfilaraemic) under conditions of both clinical and laboratory safety monitoring (668 with albendazole alone, 1 850 with albendazole-plus-ivermectin and 116 with albendazole-plus-DEC). Another 1 110 children with intestinal parasites received the same regimens and were clinically monitored for safety. By the end of 1998 the total number monitored for safety will be almost 4 000. Drug dosages generally were: albendazole 400 mg, ivermectin 200 mcg/kg and DEC 6 mg/kg, given alone (albendazole) or in 2-drug combinations, but higher dosages and longer durations were used in ~100 patients.

Safety assessments: Clinically, single-dose albendazole, alone or co-administered, was extremely well tolerated. Systemic reactions of fever, headache and myalgia in microfilaraemic patients treated with albendazole were seen only when albendazole was co-administered with one of the microfilaricidal drugs DEC or ivermectin (as these reactions are caused by host responses to the dying microfilariae, and albendazole appears to be minimally or not microfilaricidal). Albendazole alone did not induce these systemic reactions and when co-administered did not increase their frequency or severity. Localized reactions (inflammatory nodules indicative of death of adult filarial worms) were seen occasionally after single-dose treatments and were generally well tolerated, but such reactions were frequent and severe in the 15 men treated with high-dose (800 mg) albendazole daily for 3 weeks. Blood chemistry, haematologic and renal indices were unaffected by albendazole (either alone or in combination), except for mild, self-limited liver transaminase elevations regularly seen in 10-20% of individuals treated with albendazole for any indication.

Efficacy of Albendazole in Lymphatic Filariasis

Numbers of individuals assessed: Completed studies have provided data for microfilaraemic patients treated with albendazole alone (n = 130), albendazole-plus-ivermectin (n = 160) and albendazole-plus-DEC (n = 45). Studies currently underway will add data from about 165, 1 070 and 211 patients to each of these three groups, respectively. Additionally, data from treated patients whose infections are defined by circulating-antigen positivity in the absence of microfilaraemia will shortly be available from ~100-400 individuals on each of these

* See overall List of abbreviations (p. 19)

single-dose treatment regimens. Drug dosages were those described above; all received only 'single-dose' regimens except for the 15 receiving high-dose albendazole daily for 3 weeks.

Efficacy assessments: Albendazole was not demonstrably microfilaricidal when administered in single-dose regimens (though it does appear to reduce microfilaraemia by inhibiting adult worms from shedding additional microfilariae into the circulation). Therefore, assessment of anti-filarial effects of albendazole alone must be based on long-term 'suppression' of microfilaraemia (after the 'natural' clearance [death] of microfilariae over 6-12 months) and on decreasing levels of circulating antigen.

In repeated high doses, albendazole appears curative for *W. bancrofti* infections. As a single dose it demonstrated a sterilizing effect on adult *W. bancrofti* (but not *B. malayi*) worms, that was either statistically significant or showed the same trend in all studies. When administered in combination with ivermectin or DEC it enhanced suppression of microfilaraemia (probably because of the activity against adult worms) for both *W. bancrofti* and *B. malayi* infections.

Overall Conclusions

1. 'Single-dose' combinations of albendazole plus either ivermectin or DEC were found to be equally safely administered to patients with lymphatic filariasis (and other individuals living in endemic communities) as single doses of ivermectin or DEC alone.

2. 'Single-dose' 2-drug combinations of albendazole plus either ivermectin or DEC are superior in efficacy to single drug treatment for decreasing microfilaraemia in lymphatic filariasis.

3. Albendazole alone has a killing or sterilizing activity on lymphatic filarial adult worms.

4. There appears to be no reason why large-scale programmes to interrupt transmission of lymphatic filariasis should not be based on single-dose treatment regimens based on albendazole plus either DEC or ivermectin.

5. Combination treatment for lymphatic filariasis creates programmatic opportunities for coordinated public health interventions.

Report from Informal Consultation on Albendazole Research Findings in Lymphatic Filariasis
13-14 October 1998, WHO, Geneva

Introduction

It is the introduction of dramatically effective treatment regimens to decrease microfilaraemia that is most responsible for the recent designation of lymphatic filariasis as a disease that can be eliminated and for the Resolution by the World Health Assembly to eliminate lymphatic filariasis as a public health problem globally[1]. The observation that single-dose ivermectin produced a rapid and sustained reduction of microfilaraemia in lymphatic filariasis[2] was followed by studies which showed that single-dose diethylcarbamazine (DEC) was equally effective in the long-term[2]. The microfilaricidal efficacy of combinations of ivermectin and DEC proved to be greater than with either of the two drugs given alone[3]. Most recently, combinations of albendazole with ivermectin or DEC have been shown to be equally effective as the combination of ivermectin with DEC in the long-term reduction of microfilaraemia[4]. Albendazole has the additional benefit of its safe use in areas endemic for onchocerciasis and loiasis and its ability to reduce prevalence and intensity of intestinal worm infections[5].

Purpose of the Consultation

The main purpose of the Informal Consultation was to examine critically all the data available on studies, both published and unpublished, carried out on the safety, tolerability and efficacy of albendazole and its combinations with ivermectin or DEC in lymphatic filariasis. It also looked at studies, both completed and ongoing, on the efficacy of albendazole combinations in the treatment of intestinal nematode infections.

Those medical researchers responsible for the clinical trials of albendazole in lymphatic filariasis came from Africa, Asia and the Americas to participate in this meeting, along with SmithKline Beecham's clinical developer of albendazole and members of the WHO secretariat who have extensive experience in the use of albendazole and other drugs for filariasis and intestinal parasite infections (see Appendix 1). The meeting focussed on the safety and efficacy of albendazole (alone and in combination with either ivermectin or DEC) primarily in lymphatic filariasis (see Appendix 2). Conclusions and recommendations were formulated (see below).

Research findings (see Table)

Macrofilaricidal activity of albendazole has been demonstrated against sub-periodic *Brugia malayi* in the leaf monkey[6] and against *Brugia pahangi* in jirds[10].

Details of studies carried out on the safety and efficacy of albendazole and its combinations in lymphatic filariasis in humans are summarized in the Table. In the first study, the comparative efficacy of high doses of albendazole (400 mg bid for 21 days) and DEC (6 mg/kg per day in divided doses given for the same period) was evaluated in asymptomatic microfilaraemic men with bancroftian filariasis[7]. Multiple high dose albendazole reduced microfilaraemia less than DEC did but appeared to have greater macrofilaricidal activity, as

11 of 15 patients treated with albendazole had "scrotal syndrome" with development of scrotal nodules (indicative of adult worm death) in the second week of treatment. The "scrotal syndrome" was self-limited in most cases, but 3 patients required some analgesic support and rest. Patients with scrotal involvement also showed systemic effects such as fever, chills, anorexia and nausea. Multiple high-dose albendazole was clearly unsuitable as a treatment regimen for bancroftian filariasis, but given the macrofilaricidal activity and microfilaraemic reductions seen with albendazole and given the remarkable microfilaricidal efficacy of other single-dose regimens, it seemed logical to investigate the antifilarial activity of *single-dose* albendazole, especially in combinations with either ivermectin or DEC.

The first of these studies was carried out in Sri Lanka in a 'blinded' trial in which the safety, tolerability and filaricidal efficacy of single-dose albendazole 600 mg (alb 600) alone or in combination with DEC 6 mg/kg (alb 600 / DEC 6) or ivermectin 400 mcg/kg (alb 600 / iver 400) were compared with a single-dose combination of DEC 6 mg/kg and ivermectin 400 mcg/kg (DEC 6 / iver 400). Prior to its commencement, however, a safety study was conducted on 10 'healthy' amicrofilaraemic volunteers (unpublished). Five were given alb600 / DEC 6 and 5 alb600 / Iver400. The drugs were well tolerated and none of the volunteers showed any clinical adverse effects during the 4 week period following treatment. A comprehensive set of laboratory safety tests was carried out pre-treatment and on days 7, 14 and 28 (where necessary). Four patients (2 in each group) showed slight elevations of liver enzymes on day 14. The interpretation was complicated, however, by concurrent consumption of alcohol by the volunteers; enzymes returned to normal levels by day 28. One patient who had pre-test electrocardiographic evidence of a Grade II A-V block continued to be clinically normal and showed no additional ECG changes after treatment. The albendazole combinations therefore appeared to be safe.

In the study on asymptomatic microfilaraemic patients[4] all 4 treatments, including alb 600 alone, significantly reduced mf counts, but alb 600 / iver 400 was the most effective regimen for clearing mf from night blood; 9 of 13 subjects (69%) were amicrofilaraemic by membrane filtration 15 months after treatment. Alb 600 / DEC 6 brought about a slow reduction of microfilaraemia initially but at the ninth month and thereafter there was no significant difference between the % pre-treatment mf levels in the alb 600 / iver 400, alb 600 / DEC 6 and DEC 6 / iver 400 treatment groups. At 15 months post-treatment the mf/ml level expressed as a % of the pre-treatment levels in these 3 combination regimens were below 1.5%. Filarial antigen tests suggested that all 4 treatments had significant activity against adult *W. bancrofti* but alb 600 / DEC 6 had the greatest activity according to this test, with antigen levels decreasing by 77%. Early clinical assessments and laboratory safety screens were hospital-based. All 4 regimens were well tolerated and clinically safe. Systemic adverse effects such as fever (in 58% of the patients), headache (in 60%), myalgia (in 48%) and weakness (in 46%) were no different from those seen in Sri Lankan patients in previous studies using ivermectin and DEC for treatment of asymptomatic microfilaraemia. These adverse effects were transient, lasting no more than 48 hours and, with one exception, required no intervention other than the administration of paracetamol in a few cases. One patient treated with alb 600 / iver 400 developed wheezing with breathlessness about 36 hours after treatment. This was controlled with a single-dose of hydrocortisone 100 mg IV. The systemic adverse effects appeared to be correlated to the pre-treatment mf level and *not* to the individual treatment groups. Mild elevation of liver enzymes were seen in 25-35% of patients in all 4 groups; levels returned to within normal limits by day 14. Three patients in the alb 600 / DEC 6 group developed small scrotal nodules by 48 hours following treatment. The nodules regressed spontaneously by 2 to 4 weeks.

All 4 treatment regimens were thus well tolerated, clinically safe and resulted in significant reduction of microfilaraemia. Both albendazole combinations were better than albendazole alone. It was possible to determine the mf levels in 34 of the 50 patients at 30 months post-treatment; the mean mf levels in all 4 groups were unchanged from to those observed at 15 months (unpublished).

In a similar ongoing study in Sri Lanka using *standard* doses of albendazole (400 mg), ivermectin (200 mcg/kg) and DEC (6 mg/kg), 47 male asymptomatic microfilaraemic patients were randomly allocated to one of 3 treatment regimens; namely, albendazole 400mg with ivermectin 200 mcg/kg, albendazole 400 mg with DEC 6 mg/kg, and albendazole 600 mg/kg with ivermectin 400 mcg/kg (for comparison). A follow-up of 21 months after treatment has shown clinical and laboratory safety and microfilaricidal efficacy to be very similar to that observed in the previous study with higher doses of albendazole and ivermectin (manuscript in preparation).

A randomised placebo-controlled comparison of ivermectin and albendazole alone and in combination with *W. bancrofti* microfilaraemia was carried out in Haitian children[8]. One hundred and thirteen microfilaraemic children (mean age 7.8 years) were randomly assigned to one of the 4 single-dose treatments; namely, placebo, ivermectin 200-400 mcg/kg, albendazole 400 mg or albendazole 400 mg with ivermectin 200-400 mcg/kg. Follow-up blood examinations for microfilariae were carried out 4 months after treatment. The post-treatment mf concentrations did not differ significantly between placebo and albendazole treatment (4 months likely being too early to detect any microfilaricidal [or microfilaraemia-reducing] effect in the albendazole treated group); however, there were significant differences between the placebo and both the ivermectin and the albendazole / ivermectin combination. The reduction in mf concentration was significantly greater for children who received the combination than for those who received ivermectin alone. Adverse reactions following treatment were generally mild and well tolerated but fever, headache, myalgia and cough were reported significantly more frequently among children who received ivermectin alone or albendazole / ivermectin combination compared to the other two groups. However, no significant differences were found in the frequency or severity of symptoms between children who were treated with ivermectin alone and those who received ivermectin with albendazole. The results thus showed that for children with *W. bancrofti* microfilaraemia, combined treatment with albendazole and ivermectin was more effective than ivermectin alone with no measurable increase in severity of adverse reactions.

In a study of *Brugia malayi* patients in India, 48 asymptomatic microfilaraemic adults and children of both sexes were randomly allocated to receive one of the following 3 treatments: ivermectin 200 mcg/kg with DEC 6 mg/kg, albendazole 400 mg with DEC 6 mg/kg, and albendazole 400 mg with ivermectin 200 mcg/kg. All patients were hospitalized for drug administration and initial safety assessments. The systemic adverse effects such as fever, headache and myalgia and laboratory screens were similar to those observed in previous studies with brugian filariasis. Local inflammatory reactions were not observed. At the end of the first year microfilarial densities showed greater than 98% reductions from pre-treatment in the DEC/ivermectin and the DEC/albendazole treatment groups. With ivermectin / albendazole the reduction was 90%. This study is now in its second year.

In a double-blind, placebo-controlled trial in a *W. bancrofti* endemic community in Ghana involving 1 246 (340 being mf positive) men, women and children over 6 years of age (pregnant women were excluded), 4 treatment regimens were used: albendazole 400 mg alone, ivermectin 150 mcg/kg alone, a combination of the two, and placebo. Both the ivermectin alone and the albendazole / ivermectin treatment groups showed profound statistically significant

reductions of microfilaraemia up to 12 months after treatment, with the reduction being significantly greater for the combined therapy only at 3 months. Albendazole alone resulted in a progressive decline in microfilarial density but which still had not reached statistical significance by 12 months. Mild adverse effects (fever, myalgia) occurred beginning at 18 hours and disappeared by 3 to 4 days without intervention.

In Tanzania an ongoing two-period crossover, double-blind, placebo-controlled trial has examined the safety and efficacy of a combination of albendazole and ivermectin treatment in 20 patients with dual infections of bancroftian filariasis and onchocerciasis and 25 patients with bancroftian filariasis alone. Twenty males between the ages of 15 and 55 years showing *W. bancrofti* mf counts of $\geq$ 100 mf/ml blood and $\geq$ 5 *O. volvulus* mf/skin snip without chronic manifestations associated with bancroftian filariasis or onchocerciasis were admitted to hospital for 14 days. They received albendazole 400 mg with ivermectin 150 mcg/kg or placebo and observed for 7 days. On day 8 a crossover of treatment regimens was effected and all patients are being followed up. The results of clinical and laboratory safety assessments on the first 10 patients were similar to those seen in other studies. The trial is still ongoing and the code remains intact. Ninety per cent of the treated individuals were amicrofilaraemic at 30 days post-treatment. A similarly designed study is also underway with 25 individuals having bancroftian filariasis alone.

In Sri Lanka a field study involving 200 asymptomatic *W. bancrofti* microfilaraemic adults and children of both sexes has commenced. These patients have been randomly allocated to receive one of 4 treatment regimens, albendazole 400 mg alone, DEC 6 mg/kg alone, albendazole 400 mg / DEC 6 mg/kg and albendazole 400 mg / ivermectin 200 mcg/kg combinations. The safety and microfilaricidal efficacy of these regimens are being monitored. So far more than a hundred patients have been treated with no significant adverse effects.

In Papua New Guinea, studies to examine the efficacy of DEC 6 mg/kg alone and DEC 6 mg/kg in combination with ivermectin 400 mcg/kg in interruption of *W. bancrofti* infections are now in their fifth year. After two annual treatments villages where DEC / ivermectin was given showed a greater reduction in mf prevalence and intensity (~90-98% reduction) than those where DEC alone was given (~80-90% reduction); with respect to transmission, the ATP in villages where DEC / ivermectin was used had reductions of ~80-95% and those where DEC alone was used showed a ~70-80% decrease after 3 cycles of annual treatment. The safety and efficacy of albendazole, DEC and combinations of these drugs with ivermectin will now be studied in previously untreated villages.

Two studies have compared the efficacy of albendazole and its combinations with ivermectin or DEC against intestinal nematode infections. In a randomised placebo-controlled study in Haiti involving 853 children (mean age 7 years) of both sexes the anthelmintic efficacy and nutritional benefits of treatment with albendazole 400 mg alone, ivermectin 200-400 mcg/kg alone, a combination of albendazole / ivermectin, and placebo were compared[5]. The combination treatment reduced the prevalence of Trichuris infections significantly more than either drug alone. Only combination therapy resulted in nutritional benefits not found with either drug alone. The second study[9] of 176 children between the ages of 4 and 14 years of both sexes compared the efficacy of albendazole 400 mg alone, albendazole 400 mg with DEC 6 mg/kg, and albendazole 400 mg with ivermectin 200 mcg/kg against *Trichuris trichiura* infections. Fifty-five children with Trichuris infection showed a 'cure rate' of 79.3%, 3 weeks after treatment with albendazole / ivermectin combination which was significantly greater than that seen with the other two treatments. Thus, these two studies carried out concurrently in

Haiti and Sri Lanka have shown similarly enhanced efficacy against Trichuris infection with the albendazole / ivermectin combination treatment.

Three further studies in Ecuador, Gabon and the Philippines are underway to evaluate the comparative efficacy of single administrations of albendazole 400 mg, ivermectin 200 mcg/kg, DEC 6 mg/kg and their combinations against intestinal nematodes.

Safety of albendazole and albendazole combinations

Numbers of individuals assessed: During the past 20 years it is estimated that albendazole has been given for intestinal helminth infections to 200-300 million people (mostly children) living in filariasis-endemic areas. If only 1% of these had active filarial infections [more likely to be 10-30%], still at least several million co-infected children would already have been treated. Safety experience with the drug has been excellent, and no adverse reactions have ever been attributed to concurrent filarial infections.

In the present studies (funded by WHO, SB, USAID, CDC and DBL) 2 728 men, women and children have been treated (~25% being microfilaraemic) under conditions of both clinical and laboratory safety monitoring (668 with albendazole alone, 1 950 with albendazole-plus-ivermectin and 116 with albendazole-plus-DEC). Another 1 110 children with intestinal parasites received the same regimens and were clinically monitored for safety. By the end of 1998 the total number monitored for safety will be almost 4 000. Drug dosages generally were: albendazole 400mg, ivermectin 200 mcg/kg and DEC 6 mg/kg, given alone (albendazole) or in 2-drug combinations, but higher dosages and longer durations were used in ~100 patients (see Table).

Safety assessments: Clinically, single-dose albendazole, alone or co-administered, was extremely well tolerated. Systemic reactions of fever, headache and myalgia in microfilaraemic patients treated with albendazole were seen only when albendazole was co-administered with one of the microfilaricidal drugs DEC or ivermectin (as these reactions are caused by host responses to the dying microfilariae, and albendazole appears to be minimally or not microfilaricidal). Albendazole alone did not induce these systemic reactions and when co-administered did not increase their frequency or severity. Localized reactions (inflammatory nodules indicative of death of adult filarial worms) were seen occasionally after single-dose treatments and were generally well tolerated, but such reactions were frequent and severe in the 15 men treated with high-dose (800 mg) albendazole daily for 3 weeks. Blood chemistry, haematologic and renal indices were unaffected by albendazole (either alone or in combination), except for mild, self-limited liver transaminase elevations regularly seen in 10-20% of individuals treated with albendazole for any indication.

Efficacy of Albendazole in Lymphatic Filariasis

Numbers of individuals assessed: Completed studies have provided data for microfilaraemic patients treated with albendazole alone (n = 130), albendazole + ivermectin (n = 160) and albendazole + DEC (n = 45). Studies currently underway will add data from about 165, 1 070 and 211 patients to each of these three groups, respectively. Additionally, data from treated patients whose infections are defined by circulating-antigen positivity in the absence of microfilaraemia will shortly be available from ~100-400 individuals on each of these single-dose treatment regimens. Drug dosages were as described above; all received only 'single-dose' regimens except for the 15 receiving high-dose albendazole daily for 3 weeks (see Table).

Efficacy assessments: Albendazole was not demonstrably microfilaricidal when administered in single-dose regimens, though it does appear to reduce microfilaraemia by inhibiting adult worms from shedding additional microfilariae into the circulation. Therefore, assessment of anti-filarial effects of albendazole alone must be based on long-term 'suppression' of microfilaraemia (after the 'natural' clearance [death] of microfilariae over 6-12 months) and on decreasing levels of circulating antigen.

Albendazole in repeated high doses appears curative for *W. bancrofti* infections. As a single dose it demonstrated a killing or sterilizing effect on adult *W. bancrofti* (but not *B. malayi*) worms, that was either statistically significant or showed the same trend in all studies. When administered in combination with ivermectin or DEC it enhanced suppression of microfilaraemia (probably because of the activity against adult worms) for both *W. bancrofti* and *B. malayi* infections

Overall Conclusions

1. 'Single-dose' combinations of albendazole plus either ivermectin or DEC were found to be equally safely administered to patients with lymphatic filariasis (and other individuals living in endemic communities) as single doses of ivermectin or DEC alone.

2. 'Single-dose' 2-drug combinations of albendazole plus either ivermectin or DEC are superior in efficacy to single drug treatment for decreasing microfilaraemia in lymphatic filariasis.

3. Albendazole alone has a killing or sterilizing activity on lymphatic filarial adult worms.

4. There appears to be no reason why large-scale programmes to interrupt transmission of lymphatic filariasis should not be based on single-dose treatment regimens using albendazole plus either DEC or ivermectin.

5. Combination treatment for lymphatic filariasis creates programmatic opportunities for coordinated public health interventions.

Recommendations

1. The safety data accumulated during studies of albendazole in lymphatic filariasis should be collected, reviewed and prepared in a form suitable for publication/registration.

2. The numbers of patients treated with the albendazole-containing combinations in lymphatic filariasis should be expanded in further studies.

3. The first national programmes using these combinations to eliminate lymphatic filariasis should undertake active safety monitoring during the first 4 weeks after treatment to expand the safety evaluation data.

4. Pharmacokinetic data should be obtained on the albendazole-plus-ivermectin and albendazole-plus-DEC co-administration regimens.

5. Single-dose and multiple-dose regimens of albendazole should be studied to define the safest macrofilaricidal regimen for *curing* infections in individuals.

6. The effectiveness of albendazole-containing regimens in reversing the pathology induced by the filariae should be investigated.

7. Research should be undertaken to develop markers to identify potential 'resistance' of the filariae to all the anti-filarial drugs.

8. Efforts to coordinate the activities of lymphatic filariasis elimination programmes with other related public health activities should be enhanced.

9. Additional studies should be carried out, especially in Africa, on the comparative efficacy of ivermectin alone and its combination with albendazole against bancroftian filariasis in onchocerciasis and loiasis endemic areas.

10. The efficacy of albendazole combinations with ivermectin or DEC to interrupt transmission of lymphatic filariasis should be investigated in large-scale trials.

Combination of albendazole with ivermectin							
Investigator	**Country**	**Type of study**	**Species**	**Dose**	**No. of pts**	**Safety assessment**	**Remarks**
Ismail	Sri Lanka	Single dose	None (normal volunteers)	600 A / 400 I	5	+	Unpublished
Ismail	Sri Lanka	Single dose	*Wb*	600 A / 400 I	13	+	Published [4]
Addiss/Beach	Haiti	Single dose	*Wb* + Helm	400 A / 200 I	218 (24 mf+)	+	Published [5,8]
Ismail	Sri Lanka	Single dose	*Wb*	600 A / 400 I, 400 A / 200 I	16 + 16	+	Ongoing (x 21 months)
Ismail	Sri Lanka	Single dose	Trichuris		55	Clinical	In press [9]
Shenoy	India	Single dose	*Bm*	400 A / 200 I	16	+	Ms in preparation
Shenoy	India	Repeat single dose	*Bm*	400 A / 200 I	16	+	Ongoing (for 6 months)
Dunyo	Ghana	Single dose	*Wb*	400 A / 150 I	371 (75 mf+)	+	Ms in preparation
Dunyo	Ghana	Repeat single dose	*Wb*	400 A/ 150 I	1 184	Clinical	Ongoing (for 2 months)
Makunde	Tanzania	Single dose crossover	*Wb* + *Ov*	20	19	+	Ongoing (for 4 months)
Makunde	Tanzania	Single dose crossover	*Wb*	25	20	+	Ongoing (for 4 months)
Weerasooriya	Sri Lanka	Single dose	*Wb*	400 A / 200 I	50	Clinical	Ongoing (for 6 months)
Espinel	Ecuador	Single dose	Helm	400 A	200	Clinical	Ongoing (for 3 months)
Belizario	Philippines	Single dose	Helm	400 A / 200 I	200	Clinical	Ongoing (for 3 months)
Lenoble	Gabon	Single dose	Helm	400 A / 200 I	200	Clinical	Ongoing (for 5 months)
Kazura	PNG	Single dose	Wb	400 A / 200 I	75	Clinical	To start 12/98

Combination of albendazole with DEC							
Investigator	**Country**	**Type of study**	**Species**	**Dose**	**No. of pts**	**Safety assessment**	**Remarks**
Ismail	Sri Lanka	Single dose	Normal volunteers	600 A / 6 D	5	+	Unpublished
Ismail	Sri Lanka	Single dose	*Wb*	600 A / 6 D	13	+	Published [4]
Ismail	Sri Lanka	Single dose	*Wb*	600 A / 6 D	16	+	Ongoing (for 21 months)
Ismail	Sri Lanka	Single dose	Trichuris	400 A / 6 D	47	Clinical	In press [9]
Shenoy	India	Single dose	*Bm*	400 A / 6 D	16	+	Ms in preparation
Shenoy	India	Repeat single dose	*Bm*	400 A / 6 D	16	+	Ongoing (for 6 months)
Weerasooriya	Sri Lanka	Single dose	*Wb*	400 A / 6 D	50	Clinical	Ongoing (for 6 months)
Espinel	Ecuador	Single dose	Helm	400 A / 6 D	200	Clinical	Ongoing (for 3 months)
Belizario	Philippines	Single dose	Helm	400 A / 6 D	200	Clinical	Ongoing (for 3 months)
Beach	Haiti	Single dose	*Wb*	400 A / 6 D	400	+	To start 11/98
Kazura	PNG	Single dose	*Wb*	400 A / 6 D	75	Clinical	To start 12/98

Appendix 1

Informal Consultation on Albendazole Research Findings in Lymphatic Filariasis 13-14 October 1998, Room L 14, WHO, Geneva

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List of abbreviations

A	albendazole (in Table)
Alb	albendazole
B. malayi	*Brugia malayi*
Bm	*Brugia malayi*
CDC	Centers for Disease Control and Prevention
D	diethylcarbamazine (in Table)
d	day
DBL	Danish Bilharziasis Laboratory
DEC	diethylcarbamazine
I	Ivermectin (in Table)
Iver	Ivermectin
mcg	microgram
mg	milligram
SB	SmithKline Beecham
USAID	United States Agency for International Development
W. bancrofti	*Wuchereria bancrofti*
Wb	*Wuchereria bancrofti*
WHC	World Health Organization