DISCONTINUATION OF PROPHYLAXIS AGAINST *MYCOBACTERIUM AVIUM* COMPLEX DISEASE IN HIV-INFECTED PATIENTS WHO HAVE A RESPONSE TO ANTIRETROVIRAL THERAPY

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ABSTRACT

Background Several agents are effective in preventing *Mycobacterium avium* complex disease in patients with advanced human immunodeficiency virus (HIV) infection. However, there is uncertainty about whether prophylaxis should be continued in patients whose CD4+ cell counts have increased substantially with antiviral therapy.

Methods We conducted a multicenter, double-blind, randomized trial of treatment with azithromycin (1200 mg weekly) as compared with placebo in HIV-infected patients whose CD4+ cell counts had increased from less than 50 to more than 100 per cubic millimeter in response to antiretroviral therapy. The primary end point was *M. avium* complex disease or bacterial pneumonia.

Results A total of 520 patients entered the study; the median CD4+ cell count at entry was 230 per cubic millimeter. In 48 percent of the patients, the HIV RNA value was below the level of quantification. The median prior nadir CD4+ cell count was 23 per cubic millimeter, and 65 percent of the patients had had an acquired immunodeficiency syndrome–defining illness. During follow-up over a median period of 12 months, there were no episodes of confirmed *M. avium* complex disease in either group (95 percent confidence interval for the rate of disease in each group, 0 to 1.5 episodes per 100 person-years). Three patients in the azithromycin group (1.2 percent) and five in the placebo group (1.9 percent) had bacterial pneumonia (relative risk in the azithromycin group, 0.60; 95 percent confidence interval, 0.14 to 2.50; P=0.48). Neither the rate of progression of HIV disease nor the mortality rate differed significantly between the two groups. Adverse effects led to discontinuation of the study drug in 19 patients assigned to receive azithromycin (7.4 percent) and in 3 assigned to receive placebo (1.1 percent; relative risk, 6.6; P=0.002).

Conclusions Azithromycin prophylaxis can safely be withheld in HIV-infected patients whose CD4+ cell counts have increased to more than 100 cells per cubic millimeter in response to antiretroviral therapy. (N Engl J Med 2000;342:1085-92.)

THE identification of effective strategies to prevent opportunistic infections has been an important advance in the care of patients with human immunodeficiency virus (HIV) infection.[1] Primary prophylaxis is instituted on the basis of CD4+ cell thresholds for increased risks of specific opportunistic infections, including *Mycobacterium avium* complex disease, a serious and life-threatening complication of HIV disease.[2] Several agents, including azithromycin, clarithromycin, and rifabutin, provide protection against this condition,[3-6] and prophylaxis is recommended for all HIV-infected persons with CD4+ cell counts of less than 50 per cubic millimeter.[7] Azithromycin has been widely used for this purpose because it can be administered in a convenient weekly dose. Azithromycin prophylaxis also reduces the risk of *Pneumocystis carinii* pneumonia and bacterial infections.[3,4,8]

Since the studies of prophylaxis against *M. avium* complex disease were performed, more potent antiretroviral regimens have been introduced that suppress HIV replication and increase the CD4+ cell count.[9] Marked decreases in the incidence of major infectious complications, especially *P. carinii* pneumonia and *M. avium* complex disease, have been reported in patients treated with these regimens.[9,10] The question now is whether patients whose CD4+ cell counts have been below the threshold for the initiation of prophylaxis against opportunistic infection should continue to receive prophylaxis once their cell counts rise above the threshold. Because of concern about the function of CD4+ cells in patients receiving antiretroviral therapy, the 1997 guidelines for the prevention of opportunistic infections recommended continued prophylaxis despite an increase in the CD4+ cell count.[7]

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We performed a study to determine whether patients whose CD4+ cell counts had increased substantially in response to antiretroviral therapy should receive prophylaxis against *M. avium* complex disease and bacterial pneumonia.

METHODS

Study Population

HIV-infected patients 13 years of age or older were eligible for the study if they had had a CD4+ cell count of less than 50 per cubic millimeter (at any time in the past), followed by a count of more than 100 cells per cubic millimeter on two consecutive occasions in response to antiretroviral therapy. Patients with a history of intolerance of azithromycin, prior or current disseminated *M. avium* complex disease, or a condition requiring treatment with agents that have activity against *M. avium* complex were excluded.

The study was approved by the institutional review board at each participating center, and written informed consent was obtained from all patients.

Study Design

The study was a randomized, double-blind clinical trial comparing the efficacy of azithromycin (Zithromax, Pfizer), given at a dose of 1200 mg once weekly, with that of a matched placebo. Patients were randomly assigned to the study groups in a 1:1 ratio, with stratification according to the clinical center and according to whether the patients had received prophylaxis for *M. avium* complex disease at any time before enrollment. Patients whose CD4+ cell counts fell below 50 per cubic millimeter after enrollment were offered open-label azithromycin.

The sample size (850 patients) and the duration of follow-up (27 months) were chosen to provide the study with 80 percent power to detect a 40 percent difference in the primary end point between the study groups (22.0 percent vs. 13.2 percent). We also assumed that the death rate would be 34 percent at 27 months and that 4 percent of the patients would be lost to follow-up.

End Points and Follow-up

The primary end point of the study was the development of either confirmed *M. avium* complex disease or confirmed or probable bacterial pneumonia. One of two criteria had to be met for a diagnosis of confirmed *M. avium* complex disease: a positive culture of a blood specimen or a specimen from another normally sterile site or a positive culture of a specimen from a nonsterile site with clinical evidence of dissemination. One of three criteria had to be met for a diagnosis of confirmed bacterial pneumonia: histologic evidence of bacterial pneumonia, a positive quantitative culture of a protected-brush specimen for a likely pathogen, or clinical and radiographic abnormalities consistent with the diagnosis. The third criterion had to be accompanied by at least one of two additional types of evidence: a positive culture or Gram's stain for a likely pathogen in a blood specimen, a specimen from another normally sterile site, a bronchoalveolar-lavage specimen, or a lung aspirate or the predominance of such a pathogen in an adequate specimen of sputum, or serologic evidence of recent infection with legionella, *Mycoplasma pneumoniae,* or *Chlamydia pneumoniae.* Probable bacterial pneumonia was defined as clinical and radiographic evidence (as described above), the absence of another diagnosis, and a response to antibiotic therapy.

The secondary end points were death, the development of *P. carinii* pneumonia, grade IV adverse events (i.e., severe and potentially life-threatening events, as graded on a five-point scale developed by the Division of AIDS of the National Institute of Allergy and Infectious Diseases), and toxic effects requiring permanent discontinuation of azithromycin or placebo. A clinical-events committee, which was unaware of the treatment assignments, reviewed all cases of *M. avium* complex disease and bacterial pneumonia that were not confirmed.

Follow-up visits were scheduled for every four months. At each visit, a clinical evaluation was performed to determine whether any primary or secondary end points had occurred, and the CD4+ cell count and HIV-1 RNA level were measured (by either a polymerase-chain-reaction [PCR] assay or a branched-chain DNA assay).

Statistical Analysis

The investigators were unaware of the interim results, which were reviewed by an independent data and safety monitoring board. On July 28, 1999, the board recommended closure of the study because of the low rates of *M. avium* complex disease and bacterial pneumonia.

The study groups were compared with use of the chi-square test or Fisher's exact test for categorical data and with use of Student's t-test for continuous data. Time-to-event analyses were performed with proportional-hazards regression. All analyses were performed on an intention-to-treat basis, and all reported P values are two-sided. Exact 95 percent confidence intervals for incidence rates were calculated on the basis of the Poisson distribution.

RESULTS

Characteristics of the Patients

Between October 1997 and July 1999, 520 patients at 15 centers were enrolled in the study; 258 patients were randomly assigned to azithromycin, and 262 to placebo. The median prior nadir CD4+ cell count was 23 per cubic millimeter. The median CD4+ cell count at base line was 230 per cubic millimeter. The median count was higher in the placebo group than in the azithromycin group (243 vs. 226 per cubic millimeter, $P=0.02$). The two groups were otherwise similar with regard to base-line characteristics (Table 1). At enrollment, 50 percent of the patients in whom HIV RNA was measured by PCR had less than 400 copies per milliliter, and 37 percent of those in whom HIV RNA was measured by a branched-chain DNA assay had less than 500 copies per milliliter. Sixty-five percent of the patients had received a clinical diagnosis of the acquired immunodeficiency syndrome (AIDS); 41 percent had a history of *P. carinii* pneumonia; and 14 percent had a history of bacterial pneumonia. At enrollment, 93 percent of the participants were receiving prophylaxis against *P. carinii* pneumonia; 69.4 percent of the patients in the azithromycin group and 68.7 percent of those in the placebo group were receiving trimethoprim–sulfamethoxazole ($P=0.87$). Sixty-nine percent of the patients had received prophylaxis against *M. avium* complex disease. Of the 242 patients (47 percent) who were receiving prophylaxis against *M. avium* complex disease at base line, 210 were receiving azithromycin, 26 clarithromycin, and 5 rifabutin. Similar proportions of patients in the two groups had undergone pneumococcal vaccination (64.3 percent in the azithromycin group and 69.9 percent in the placebo group, $P=0.18$).

All the study participants were receiving antiretroviral therapy at enrollment, with 94 percent receiving regimens that included a protease inhibitor. At 12 months, 98 percent of the patients were receiving

TABLE 1. BASE-LINE CHARACTERISTICS OF THE PATIENTS.*

CHARACTERISTIC	AZITHROMYCIN (N=258)	PLACEBO (N=262)
Race or ethnic group (%)		
Hispanic	12.0	15.3
Black	38.0	36.6
White	47.7	46.6
Other	2.3	1.5
Prior intravenous drug use (%)	17.5	17.2
Prior AIDS diagnosis (%)	67.4	62.6
Female sex (%)	11.2	13.4
Age (yr)	41.7±7.4	41.9±8.5
Prior prophylaxis against *M. avium* complex infection (%)		
Prescribed ≤30 days before randomization	45.7	47.3
Prescribed >30 days before randomization	23.6	21.0
No prior use	30.6	31.7
CD4+ cell count		
Nadir (cells/mm³)		
Median	22.0	25.0
Mean	23.1±14.6	24.4±14.4
At base line (cells/mm³)		
Median	225.5	243.0
Mean	248.8±106.9	273.7±131.3
Distribution at base line (%)		
100–199 cells/mm³	38.8	31.3
200–299 cells/mm³	33.3	35.5
300–399 cells/mm³	15.1	19.1
≥400 cells/mm³	12.8	14.1
HIV RNA undetectable (%)†	47.1	48.5

*Plus–minus values are means ±SD.

†The lower limit of detection was 400 copies per milliliter with the PCR assay and 500 copies per milliliter with the branched-chain DNA assay.

antiretroviral therapy, with 92 percent receiving regimens that included a protease inhibitor. The antiretroviral regimens did not differ significantly between the two study groups.

Duration of Follow-up and Study Treatment

At the time that the treatment assignments were revealed, the median duration of follow-up was 12.7 months (range, 0.5 to 21.2) in the azithromycin group and 12.0 months (range, 0.1 to 21.4) in the placebo group. Seven patients (1.3 percent) were lost to follow-up (four in the azithromycin group and three in the placebo group).

Eight of the 258 patients in the azithromycin group (3.1 percent) and 4 of the 262 patients in the placebo group (1.5 percent) received open-label azithromycin during follow-up. Fifty-one patients in the azithromycin group (19.8 percent) and 32 patients in the placebo group (12.2 percent) discontinued the assigned treatment but were not eligible for open-label azithromycin (relative risk in the azithromycin group as compared with the placebo group, 1.67; P=0.02).

Primary End Point

Confirmed or probable bacterial pneumonia developed in three patients in the azithromycin group (1.2 percent) and in five patients in the placebo group (1.9 percent; relative risk in the azithromycin group, 0.60; 95 percent confidence interval, 0.14 to 2.50; P=0.48) (Table 2). There were no cases of confirmed *M. avium* complex disease. Bacterial pneumonia was confirmed in two of the three patients in the azithromycin group and in three of the five patients in the placebo group. The 95 percent confidence interval for the rate of bacterial pneumonia was 0.2 to 3.5 episodes per 100 person-years in the azithromycin group and 0.6 to 4.7 episodes per 100 person-years in the placebo group. The 95 percent confidence interval for the rate of *M. avium* complex disease in each group was 0 to 1.5 episodes per 100 person-years.

Deaths and AIDS-Defining Events

In each group, five patients (1.9 percent) died. Three patients died from liver failure, three from cardiovascular disease, two from cancer, one from an overdose of methadone, and one from wasting. In addition, the progression of HIV disease (including death) was reported in 14 patients assigned to receive azithromycin (5.4 percent) and in 13 patients assigned to receive placebo (5.0 percent) (Table 2). None of the patients had cytomegalovirus disease, cryptococcosis, histoplasmosis, Kaposi's sarcoma, or progressive multifocal leukoencephalopathy. There were six cases of *P. carinii* pneumonia, four of esophageal candidiasis, and one each of tuberculosis, toxoplasmosis, AIDS-related dementia, and lymphoma. There were 47 cases of bacterial infections, which were distributed similarly in the two groups. The rates of events that could have been associated with azithromycin treatment (i.e., *P. carinii* pneumonia, toxoplasmosis, sinusitis, and bacteremia) were low and did not differ significantly between the two groups (Table 2).

Adverse Events and Discontinuation of Study Drugs

Grade IV adverse events occurred in 27 patients in the azithromycin group (10.5 percent) and in 36 patients in the placebo group (13.7 percent; relative risk in the azithromycin group, 0.73; P=0.22). Toxic effects required discontinuation of the assigned treatment in 19 patients in the azithromycin group (7.4 percent) and in 3 patients in the placebo group (1.1 percent; relative risk, 6.64; P=0.002) (Table 3). Most toxic effects requiring discontinuation of the study drug were grade II. In 11.6 percent of the patients assigned to receive azithromycin and in 5.3 percent of those assigned to receive placebo, the study drug was discontinued at the patient's request (relative risk, 2.30; P=0.01). The blinded study drug was discontinued because of a switch to open-label azithromycin (in patients with CD4+ cell counts that dropped below 50 per cubic millimeter) in 3.1 per-

TABLE 2. FIRST OCCURRENCE OF CLINICAL EVENTS.*

EVENT	AZITHROMYCIN		PLACEBO		RELATIVE RISK (95% CI)	P VALUE
	NO. OF PATIENTS	EVENTS/100 PERSON-YEARS	NO. OF PATIENTS	EVENTS/100 PERSON-YEARS		
Disseminated *M. avium* complex infection (confirmed)	0	0	0	0	—	—
Bacterial pneumonia (confirmed or probable)	3	1.2	5	2.0	0.60 (0.14–2.50)	0.48
Death	5	2.0	5	2.0	1.00 (0.29–3.46)	1.00
Progression of HIV disease (including death)	14	5.7	13	5.3	1.06 (0.50–2.25)	0.88
P. carinii pneumonia	3	1.0	3	1.0	0.97 (0.20–4.82)	0.97
Toxoplasmosis	0	0	1	0.3	—	1.00
Sinusitis	16	5.4	20	6.9	0.78 (0.41–1.51)	0.47
Bacteremia	2	0.7	0	0	—	0.25

*The relative risk of an event and the associated confidence interval (CI) and P value were derived from a Cox proportional-hazards regression model. The relative risks shown are for the azithromycin group as compared with the placebo group. For comparisons involving no events in one group, the P values were calculated with Fisher's exact test.

TABLE 3. GRADE IV ADVERSE EVENTS AND DISCONTINUATION OF THE STUDY DRUG.*

EVENT	AZITHROMYCIN		PLACEBO		RELATIVE RISK (95% CI)	P VALUE
	NO. OF PATIENTS	EVENTS/100 PERSON-YEARS	NO. OF PATIENTS	EVENTS/100 PERSON-YEARS		
Grade IV adverse event	27	11.5	36	15.7	0.73 (0.44–1.20)	0.22
Discontinuation of study drug	59	24.7	36	14.4	1.78 (1.18–2.70)	0.01
Reason for discontinuation†						
Toxicity	19	8.0	3	1.2	6.64 (1.97–22.46)	0.002
Grade I	3	1.3	1	0.4	3.17 (0.33–30.43)	0.32
Grade II	13	5.4	2	0.8	3.16 (1.54–30.31)	0.01
Grade III	1	0.4	0	0	—	0.50
Grade IV	1	0.4	0	0	—	0.50
Grade V	1	0.4	0	0	—	0.50
Death	4	1.7	3	1.2	1.39 (0.31–6.20)	0.67
Patient's request	30	12.6	14	5.6	2.30 (1.22–4.34)	0.01
Switch to open-label azithromycin	8	3.3	4	1.6	2.28 (0.68–7.57)	0.18
Other	16	6.7	15	6.0	1.18 (0.58–2.38)	0.65

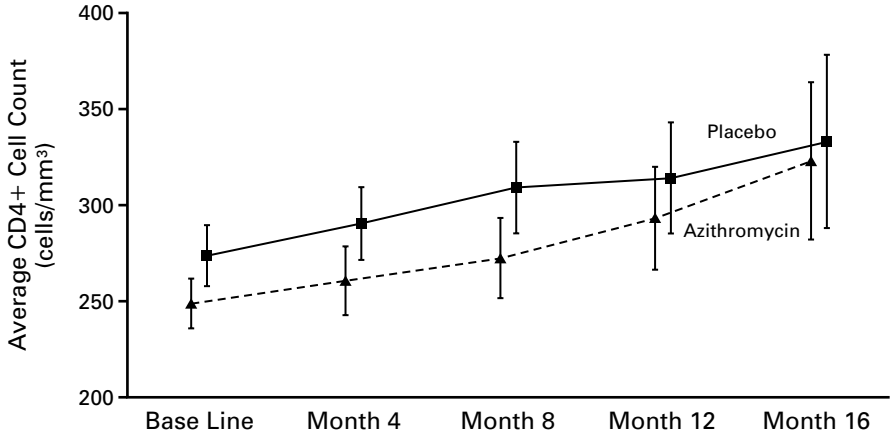
*The relative risk of an event and the associated confidence interval (CI) and P value were derived from a Cox proportional-hazards regression model. The relative risks shown are for the azithromycin group as compared with the placebo group. For comparisons involving no events in one group, the P values were calculated with Fisher's exact test.

†Reasons for discontinuation were not mutually exclusive.

cent of the azithromycin group and in 1.5 percent of the placebo group, because of death in 1.6 percent of the azithromycin group and in 1.1 percent of the placebo group, and for other reasons in 6.2 percent of the azithromycin group and in 5.7 percent of the placebo group (Table 3). In some cases, there was more than one reason for discontinuation.

CD4+ Cell Counts and HIV RNA Levels

In both study groups, the average CD4+ cell count rose during follow-up (Fig. 1). At 12 months, the average increase from base line in the CD4+ cell count was 37.6 per cubic millimeter in the azithromycin group and 40.7 per cubic millimeter in the placebo group. During follow-up, 12 patients in the azithro-



No. of Patients					
Azithromycin	258	209	179	134	76
Placebo	262	215	166	129	77

Figure 1. Average CD4+ Cell Count at Base Line and during Follow-up in 520 HIV-Infected Patients Assigned to Receive Azithromycin or Placebo. The bars represent 95 percent confidence intervals.

mycin group (4.7 percent) and 10 patients in the placebo group (3.8 percent) had a CD4+ cell count of less than 50 per cubic millimeter on at least one occasion.

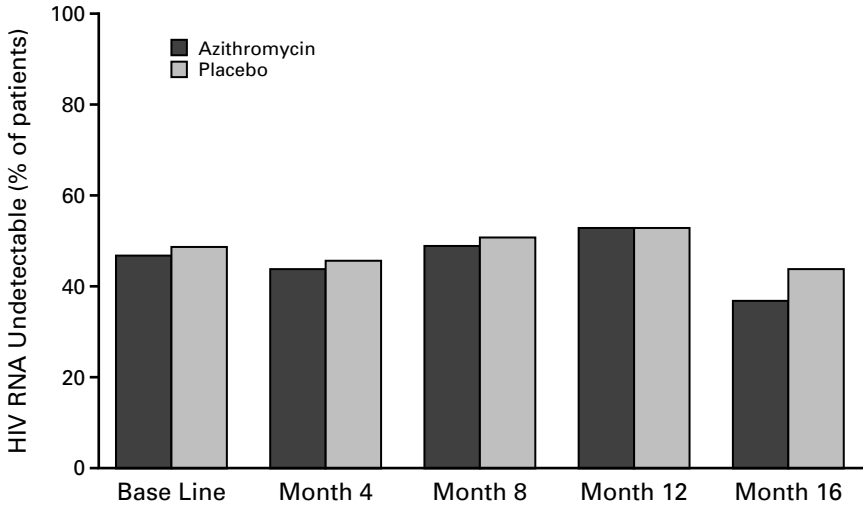
The HIV RNA values declined slightly in both groups. Figure 2 shows the proportions of patients with values that were below the limit of detection at base line and at months 4, 8, 12, and 16. Of the 216 patients in whom HIV RNA was measured by a PCR assay at 12 months, 53 percent of those assigned to receive azithromycin and 55 percent of those assigned to receive placebo had an HIV RNA level of less than 400 copies per milliliter. There were no significant differences in HIV RNA levels between the two groups.

DISCUSSION

The results of our randomized, placebo-controlled trial show that it is safe to withhold azithromycin prophylaxis in HIV-infected patients whose CD4+ cell counts have risen to more than 100 per cubic millimeter in response to antiretroviral therapy. Even though our patients had advanced AIDS, there were no cases of confirmed *M. avium* complex disease during approximately 500 patient-years of follow-up, and the rates of bacterial pneumonia were low in both the placebo group and the azithromycin group.

The dramatic effect of improved immune function on the rates of *M. avium* complex disease and bacterial pneumonia in our study can be recognized by comparing the rates of these two disorders before effective antiretroviral therapy was available. In that era, the rate of *M. avium* complex disease in patients with a CD4+ cell count of 20 to 30 per cubic millimeter (a value similar to the nadir count in the patients in our study) was 20 to 30 percent per year.[11,12] Even with the use of clarithromycin or azithromycin as prophylaxis, the annual risk of *M. avium* complex disease in patients with a base-line CD4+ cell count of less than 100 per cubic millimeter was 7 to 8 percent per year.[3-5] Similarly, rates of bacterial pneumonia were much higher before the introduction of effective antiretroviral therapy. For example, in one prospective study, the rate of bacterial pneumonia was 10.8 episodes per 100 person-years among patients with a base-line CD4+ cell count of less than 200 per cubic millimeter and 2.8 episodes per 100 person-years among those with a base-line count of more than 500 per cubic millimeter.[13] Both groups in our study had lower rates of bacterial pneumonia, even though they had a median nadir CD4+ cell count of only 23 per cubic millimeter and a median base-line count of 230 per cubic millimeter.

Our finding that it is safe to withhold azithromycin prophylaxis in patients with a CD4+ cell count of more than 100 per cubic millimeter in response to antiretroviral therapy parallels the results of recent studies of the safety of withdrawing prophylaxis against *P. carinii* pneumonia in patients whose CD4+ cell counts have increased to more than 200 per cubic millimeter. Two observational studies,[14,15] two nonrandomized prospective studies,[16,17] and the preliminary results of one randomized trial[18] all indicate that the withdrawal of primary prophylaxis against *P. carinii* pneumonia is safe in patients with a sufficient increase in the CD4+ cell count in response to an-



No. of Patients					
Azithromycin	258	210	176	135	73
Placebo	262	217	168	129	77

Figure 2. Proportions of Patients in the Azithromycin and Placebo Groups Who Had Undetectable Levels of HIV RNA.

The limit of detection was 400 copies per milliliter with the PCR assay and 500 copies per milliliter with the branched-chain DNA assay.

tiretroviral therapy. The recently updated guidelines recommend the discontinuation of prophylaxis against *M. avium* complex and *P. carinii* pneumonia under these circumstances, although in the case of *M. avium* complex disease, the recommendation until now was based only on observational studies.[19]

The rates of other opportunistic conditions were also low in our study. The rate of *P. carinii* pneumonia was 1.0 episode per 100 person-years, as compared with 3.5 episodes per 100 person-years in the largest trial of trimethoprim–sulfamethoxazole,[20] the most effective prophylactic agent.[21] The rate of cytomegalovirus disease in our study was 0 episodes per 100 person-years, as compared with 14 episodes per 100 person-years among similarly immunocompromised patients who received ganciclovir prophylaxis in the era before potent antiretroviral therapy was available.[22,23] Although some investigators have postulated that progressive HIV infection causes irreversible damage to the immune system,[24] the low rates of all opportunistic illnesses in our study demonstrate that effective immunity can be restored with antiretroviral therapy, even in patients with nadir CD4+ cell counts below 50 per cubic millimeter.

Despite the relative simplicity of azithromycin prophylaxis, there are a number of reasons to defer antimicrobial prophylaxis if the rate of the target opportunistic infection is low. Rates of antibiotic resistance among common bacterial pathogens, such as *Streptococcus pneumoniae*, have increased dramatically in the past 10 years,[25,26] and prior exposure to antibiotics is a strong risk factor for infection with antibiotic-resistant bacteria.[27] Patients with advanced AIDS have high rates of colonization and infection with antibiotic-resistant *S. pneumoniae*,[28,29] probably in part because of the use of prophylaxis against *M. avium* complex disease and *P. carinii* pneumonia.[30] In one study involving patients with HIV infection, both weekly treatment with azithromycin and daily treatment with clarithromycin were associated with the isolation of macrolide-resistant respiratory flora in all the study participants.[31]

In addition, polypharmacy carries the risk of drug interactions and may reduce adherence to treatment regimens.[32] Finally, the risk of drug intolerance is a reason for withholding prophylaxis. In our study, side effects led to the discontinuation of the study drug in 7 percent of the patients assigned to receive azithromycin but in only 1 percent of those assigned to receive placebo.

Our study has several limitations. The patients had a marked increase in the CD4+ cell count, from a median previous nadir of 23 per cubic millimeter to a median of 230 per cubic millimeter at the time of enrollment. Furthermore, the CD4+ cell count continued to increase over the course of the study. It is unclear whether the results of this study apply to patients with less dramatic increases in the CD4+ cell

count or to patients in whom the CD4+ cell count drops after an initial increase in response to antiretroviral therapy. In addition, our study cannot answer the question of whether the recommended threshold CD4+ cell count of less than 50 per cubic millimeter should be used as a criterion for restarting prophylaxis in this population. Until this question is answered, prophylaxis against *M. avium* complex disease is recommended for all patients with a CD4+ cell count of less than 50 per cubic millimeter, as specified by the current guidelines.[19]

In summary, our study shows that prophylaxis against disseminated *M. avium* complex disease can be safely withheld in patients with CD4+ cell counts that have increased from less than 50 to more than 100 per cubic millimeter in response to antiretroviral therapy, because the risk of disseminated *M. avium* complex disease in this population is low. In addition, our study shows that azithromycin prophylaxis does not significantly affect the rates of bacterial pneumonia, progression of HIV disease, or death in such patients. These findings contribute to the efforts to simplify treatment regimens and improve adherence to them, decrease the risk of antimicrobial resistance, and avoid adverse events associated with additional medications.

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APPENDIX

The following centers and investigators participated in the study: AIDS Research Alliance, Chicago — M. Diaz-Linares, R. Luskin-Hawk, C. Peterson; AIDS Research Consortium of Atlanta, Atlanta — P. Couey, M. Thompson, B. Weaver; Community Consortium of San Francisco, San Francisco — S. Crawford, H. Lampiris, R. Scott; Denver Community Programs for Clinical Research on AIDS, Denver — B. Barber, D. Cohn, R. Fernandez; Harlem AIDS Treatment Group, New York — C. Guity, S. Barnaby, L. Fuentes; Henry Ford Hospital, Detroit — B. Braxton, B. Campbell, L. Faber; Louisiana Community AIDS Program, New Orleans — C.L. Besch, D. Mushatt, J. Osterberger; North Jersey Community Research Initiative, Newark, N.J. — P. Andrew, N. Regevik, R. Roland; Partners in Research New Mexico, Albuquerque — C. Angel, K. Hammer, J. Magill; Philadelphia FIGHT, Philadelphia — P. Cooper, B. Gallagher, P. Loynd; Richmond AIDS Consortium, Richmond, Va. — M. Britton, P. Dodson, M. Howe; Research and Education Group, Portland, Oreg. — D. Antoniskis, S. Peterson, S. Pierson; Southern New Jersey Clinical Trials, Camden — K. Casey, D. Condoluci, J. Muratore; Washington Regional AIDS Program, Washington, D.C. — B. Rashbaum, K. Shade, S. Zubairi; and Wayne State University, Detroit — R. MacArthur, P. Reitenga, M. Yoder.

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