

## Lack of Association between Azithromycin and Death from Cardiovascular Causes

**TO THE EDITOR:** Azithromycin (at a single dose of 1 g) is one of two therapies recommended by the Centers for Disease Control and Prevention (CDC) for the treatment of chlamydia, and it is part of the regimen recommended by the CDC for the treatment of gonorrhea.<sup>1</sup> Recently, Ray and colleagues<sup>2</sup> reported an increased risk of death from cardiovascular causes associated with a 5-day course of azithromycin. This finding was not confirmed in a subsequent Danish study.<sup>3</sup> Data are lacking on the use of azithromycin and the risk of death from cardiovascular causes among patients with sexually transmitted diseases (STDs).

We studied data from the Oregon Public Health Division on cases of chlamydia and gonorrhea in patients who received treatment between 1996 and 2012 and data from Public Health–Seattle and King County on cases of these infections in patients who received treatment between 1993 and 2010. We matched case-report data to death-record data (using Registry Plus Link Plus software<sup>4</sup>) to determine how many of these patients died within 10 days after treatment.

Cases of gonorrhea, chlamydia, or both in 269,179 patients were reported during the study period; complete treatment information was available for 260,048 of these patients (97%). Among the patients for whom data were available, 162,385 (62%) received azithromycin; among the 97,663 who did not receive azithromycin, the majority (77%) received a tetracycline. The mean age of the patients was 24 years, 65% were fe-

male, and 84% had chlamydia. We identified no deaths from cardiovascular causes among patients treated with azithromycin or another drug (Table 1). Five deaths that were not from cardiovascular causes were classified as being due to suicide (2 patients), homicide (1 patient), drug overdose (1 patient), and rectal cancer (1 patient).

Our findings are consistent with those of the study by Svanström et al.<sup>3</sup> that examined the association between azithromycin and the risk of death from cardiovascular causes among Danish adults between 18 to 64 years of age who had a low baseline risk of cardiovascular disease, but they differ from the findings in the study by Ray and colleagues, which included a substantially older population (patients who were 30 to 74 years of age) than patients who are typically treated for an STD (patients between the ages of 15 and 25 years).<sup>2</sup> Of note, Ray observed only one death in 144,165 persons in the lowest four deciles of risk scores for cardiovascular disease (Ray W: personal communication). At that low level of risk (seven deaths per 1 million 5-day courses), we would expect only one death from cardiovascular causes associated with azithromycin use in our study population, and our study would have to involve more than 1 million persons to define the upper limit of the 95% confidence interval as being less than seven deaths per 1 million doses.

Our findings should be reassuring to health care providers who prescribe azithromycin to treat gonorrhea and chlamydia, and they support the conclusion of the CDC that research related

**Table 1. Cumulative Incidence of Death among 260,048 Patients with Chlamydia, Gonorrhea, or Both, According to Prescribed Treatment (Oregon, 1996–2012, and King County, Washington, 1993–2010).\***

Deaths	Azithromycin (N=162,385)	Other Drug (N=97,663)	Relative Risk (95% CI) <sup>†</sup>
Cardiovascular cause			
No. of deaths	0	0	Not determined
No. of deaths per 1 million doses (95% CI)	0 (0–18.5)	0 (0–30.7)	
Other cause			
No. of deaths	3	2	0.90 (0.15–5.40)
No. of deaths per 1 million doses (95% CI)	18.5 (3.8–54.0)	20.5 (2.5–74.0)	

\* CI denotes confidence interval.

<sup>†</sup> The group of patients who received other treatment was the reference group.

to possible cardiac toxicity associated with azithromycin should not lead to a change in current treatment guidelines for STDs.<sup>5</sup>

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Disclosure forms provided by the authors are available with the full text of this letter at NEJM.org.

1. Sexually transmitted diseases treatment guidelines, 2010. *MMWR Recomm Rep* 2010;59(RR-12):1-110. [Erratum, *MMWR Recomm Rep* 2011;60(1):18.]
2. Ray WA, Murray KT, Hall K, Arbogast PG, Stein CM. Azithromycin and the risk of cardiovascular death. *N Engl J Med* 2012;366:1881-90.
3. Svanström H, Pasternak B, Hviid A. Use of azithromycin and death from cardiovascular causes. *N Engl J Med* 2013;368:1704-12.
4. Registry Plus, a suite of publicly available software programs for collecting and processing cancer registry data. Atlanta: Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, 2010.
5. Recent press coverage linking azithromycin to increased risk of sudden death. Atlanta: Centers for Disease Control and Prevention, 2012 (<http://www.cdc.gov/std/treatment/azithromycin.htm>).

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#### CORRECTION

Case 8-2014: A 29-Year-Old Man with Headache, Vomiting, and Diplopia (March 13, 2014;370:1049-59). In the Pathological Discussion (page 1055), the second sentence should have begun, "The diagnostic procedure on the second admission was a left frontal craniotomy . . .," rather than ". . . a right frontal craniotomy . . ." The article is correct at NEJM.org.

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