ity (as adjudicated by an independent clinical-events committee) was a prespecified secondary outcome. It should be noted (contrary to the interpretation by Andreotti et al.) that the incidence of cardiovascular death was similar in the two groups (21.9% in the PCI group and 24.9% in the medical-therapy group), with a hazard ratio of 0.88 (95% confidence interval, 0.65 to 1.20).

In response to Alfonso et al.: we provided the Canadian Cardiovascular Society angina classifications for the trial patients in Table S13 in the Supplementary Appendix. Angina levels were similar in the two groups at 6 months, 12 months, and 24 months. Although ischemia testing was not mandated in the protocol, some trial patients underwent stress perfusion cardiac MRI assessment at baseline. We are currently reviewing those data to provide insights into the relationship between ischemia and clinical outcomes in ischemic cardiomyopathy.

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Since publication of their article, the authors report no further potential conflict of interest.

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Regimens for Drug-Resistant Tuberculosis

TO THE EDITOR: Conradie et al. (Sept. 1 issue)[1] report impressive results of the ZeNix trial of a bedaquiline–pretomanid–linezolid regimen for drug-resistant tuberculosis, with doses of linezolid that were lower than the 1200-mg dose that has been associated with adverse events. In this trial performed in South Africa, the country of Georgia, Moldova, and Russia, 9 of the 181 participants (5.0%) had bedaquiline resistance (minimum inhibitory concentration, 2 to 4 μg per milliliter) at baseline. Despite reported 99.8% adherence to the trial regimen, 6 of 9 participants (67%) with bedaquiline-resistant tuberculosis at baseline had a favorable outcome, as compared with 153 of 169 participants (91%) with bedaquiline-susceptible tuberculosis. It is notable that 5 of the 6 participants with bedaquiline resistance at baseline who had favorable outcomes had received linezolid at a dose of 1200 mg, which was not the dose ultimately recommended. In operational settings, which are characterized by lower medication adherence and greater socioeconomic and medical complexity than that in the trial, bedaquiline resistance may be associated with a greater risk of unfavorable outcomes.[2]

In this trial, there were nine treatment failures (four microbiologic failures and five cases of clinical retreatment). Can the authors report how many of these outcomes were associated with resistance that developed during treatment? Were bedaquiline resistance–associated genomic variants (either at baseline or during treatment) identified by means of sequencing?

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TO THE EDITOR: Even before publication of their article, the results of the trial reported by Conradie et al. prompted the World Health Organization to recommend a short-course, 6-month regimen as the preferred treatment for multidrug-resistant or rifampin-resistant tuberculosis — a regimen that is not longer than that for patients affected by drug-susceptible tuberculosis.[1] This is a breakthrough. With 17 new compounds in clinical development, a wealth of possibilities exists to improve the care and treatment outcomes of patients with multidrug-resistant or rifampin-resistant tuberculosis.[2] However, there is a substantial shortage of capacity for drug-susceptibility testing with new medicines, and the use of standard treatment regimens for all patients creates a risk of selection of drug-resistant strains of *Mycobacterium tuberculosis*.[3] Rapid scale-up of drug-susceptibility testing of *M. tuberculosis* isolates is now urgently needed. In addition, knowledge about mutations that confer drug resistance is needed before new medicines are marketed, so that this information can be included in the latest generations of genotyping tests to predict drug resistance and to provide effective, tailor-made treatment regimens for every patient.[4]

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No potential conflict of interest relevant to this letter was reported.

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THE AUTHORS REPLY: In response to Perumal and colleagues: we would like to clarify that baseline bedaquiline-susceptibility data were available for 143 participants; therefore, 9 of 143 participants (6.3%) had confirmed bedaquiline resistance at baseline. Any analysis of the effect of baseline resistance on treatment outcomes should be based on the assessable population, so the percentage of participants with a favorable outcome among those with confirmed bedaquiline-susceptible tuberculosis was 87.9% (116 of 132 participants). We should always be cautious when attempting to draw conclusions from subgroup analyses, particularly those involving small numbers and imbalanced distributions, which was the case in this trial. Although Perumal and colleagues suggest that the participants with bedaquiline-resistant tuberculosis who received 600 mg of linezolid fared worse than those who received 1200 mg of linezolid, only 1 of the 9 participants with bedaquiline resistance at baseline received the 600-mg dose of linezolid. Finally, in the primary efficacy analysis, there were five cases of microbiologic treatment failure and four cases of clinical failure (retreatment during the follow-up period). We are completing a detailed analysis of *M. tuberculosis* phenotypic resistance to bedaquiline, pretomanid, and linezolid, as well as an analysis of underlying genetic factors in four TB Alliance trials of pretomanid, including the ZeNix trial.[1]

We concur with Lange and colleagues that rapid scale-up of susceptibility testing for all tuberculosis drugs is urgently needed. To this end, we have made available detailed protocols, pretomanid powder, and control *M. tuberculosis* strains to any tuberculosis laboratory expressing interest in pretomanid-susceptibility testing,[2] and we are contributing to the World Health Organization catalogue of *M. tuberculosis* complex mutations associated with drug resistance.[3]

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Spontaneous Intracerebral Hemorrhage

TO THE EDITOR: The review by Sheth (Oct. 27 issue)[1] on spontaneous intracerebral hemorrhage describes possible secondary prevention strategies for patients in whom oral anticoagulation is indicated for atrial fibrillation, but there is no mention of percutaneous occlusion of the left atrial appendage. When the focus is only on patients with spontaneous intracerebral hemorrhage and atrial fibrillation, the main concern about starting or reintroducing oral anticoagulation is the recurrence of intracerebral hemorrhage. Indeed, as stated by Sheth, patients with a history of spontaneous intracerebral hemorrhage are at high risk for recurrence, and with recurrence, the risk of death is high. Left atrial appendage occlusion may offer an alternative approach to reducing cardioembolic risk in patients with atrial fibrillation,[2] and this procedure has emerged as a reasonable option for patients with atrial fibrillation and previous intracerebral hemorrhage.[3,4] Accordingly, recent guidelines state that left atrial appendage occlusion should be considered for patients with previous intracerebral hemorrhage in whom oral anticoagulation is contraindicated by a multidisciplinary team.[5]

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TO THE EDITOR: In his review article on spontaneous intracerebral hemorrhage, Sheth states that "Cerebellar hemorrhage commonly causes obstruction of the fourth ventricle that leads to hydrocephalus, which requires placement of an external ventricular drain." Although the efficacy of, as well as the indication and appropriate timing for, surgical evacuation of hematoma with respect to improving functional outcomes in patients with cerebellar hematoma remains uncertain, the most recent guideline from the American Heart Association–American Stroke Association[1] states that "For patients with cerebellar ICH [intracerebral hemorrhage] and clinical hydrocephalus, EVD [external ventricular drainage] alone is, in theory, potentially harmful, especially if the basal cisterns are compressed. EVD alone may be insufficient when intracranial hypertension impedes blood supply to the brainstem." This caveat is certainly worth mentioning.

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