

Abstracts

New drugs for TB

New drugs, but also shorter, better-tolerated regimens are needed to tackle the high global burden of tuberculosis complicated by drug resistance and retroviral disease. This study, published in *The Lancet*, investigated new multiple-agent combinations over the first 14 days of treatment to assess their suitability for future development.

In this prospective, randomised, early bactericidal activity (EBA) study, treatment-naive, drug-susceptible patients with uncomplicated pulmonary tuberculosis were admitted to hospitals in Cape Town, South Africa, between 7 October 2010 and 19 August 2011. Patients were randomised centrally by computer-generated randomisation sequence to receive bedaquiline, bedaquiline-pyrazinamide, PA-824-pyrazinamide, bedaquiline-PA-824, PA-824-moxifloxacin-pyrazinamide, or unmasked standard antituberculosis treatment as positive control. The primary outcome was the 14-day EBA assessed in a central laboratory from the daily fall in colony-forming units (CFU) of *M. tuberculosis* per milliliter of sputum in daily overnight sputum collections. Clinical staff were partially masked but laboratory personnel were fully masked.

The mean 14-day EBA of PA-824-moxifloxacin-pyrazinamide ($n=13$; 0.233 [SD 0.128]) was significantly higher than that of bedaquiline (14; 0.061 [0.068]), bedaquiline-pyrazinamide (15; 0.131 [0.102]), bedaquiline-PA-824 (14; 0.114 [0.050]), but not PA-824-pyrazinamide (14; 0.154 [0.040]), and comparable with that of standard treatment (10; 0.140 [0.094]). Treatments were well tolerated and appeared safe. One patient on PA-824-moxifloxacin-pyrazinamide was withdrawn because of corrected QT interval changes exceeding criteria pre-specified in the protocol.

PA-824-moxifloxacin-pyrazinamide is potentially suitable for treating drug-sensitive and multidrug-resistant tuberculosis. Multi-agent EBA studies can contribute to reducing the time needed to develop new antituberculosis regimens.

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Walking speed and hypertension in older adults

Walking speed is emerging as an important measure of frailty in older adults. It's easy to measure, reproducible and associated with survival. Walking speed might also help identify older adults who need treatment for high blood pressure, according to an observational study from the USA. In a nationally representative cohort of 2 340 adults aged ≥ 65 years, systolic blood pressure of ≥ 140 mmHg predicted mortality in faster walkers (hazard ratio 1.35 (95% CI 1.03 - 1.77)) but not in slower walkers (hazard ratio 1.12 (0.87 - 1.45)). High blood pressure seemed protective in the small subset of adults who failed to complete the short walking test.

Doctors disagree about how to manage blood pressure in older adults, says a linked comment (doi:10.1001/archinternmed.2012.2642). Many are reluctant to accept that high blood pressure isn't always a bad sign. It may be a bad sign for those lucky enough to be well and physically fit (the kind of adults recruited to trials of antihypertensive drugs). But the direct association between blood pressure and



mortality breaks down, or even reverses, in older adults who are unable to walk 1.8 miles/hour for 20 feet (0.8 m/s for 6 m), which is the defining threshold used in this study.

The new data reinforce walking speed as a useful measure of frailty, says the comment, and remind us that there is no such thing as an average older person when it comes to blood pressure. Guidelines for treatment based on age alone will miss the mark and risk over-treating frail adults who may need