

A new way of improving tuberculosis treatment rejected

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Pulmonology department of Fann Hospital in Dakar, Senegal. Credit: IRD / J-J Lemasson

Tuberculosis kills 1.5 million people across the world every year. The existing treatment is effective but long. Many patients abandon it before completion, increasing the risk of a relapse and favouring the emergence of drug resistance in the bacillus responsible. Cutting down the duration of treatment is the priority for researchers. A team from IRD and a



number of other international institutions has just published the results of a 10-year long clinical trial carried out in five African countries and involving a shorter regimen, in the *New England Journal of Medicine*. However, this regimen has proven to be less effective than the standard treatment. Scientists are now pursuing their research into alternative medicinal therapies, drawing on the vast network of skills developed during this clinical trial, the first of its kind for over thirty years.

The current treatment for tuberculosis is effective in 95% of cases. However, this effectiveness is called into question by a high treatment drop-out rate, especially in the most underprivileged zones, often the most affected by the disease. Shortening and simplifying the treatment is therefore a priority. As such, researchers from IRD and a number of other international institutions tested a new treatment regimen in five sub-Saharan African countries, over ten years. They have just published their results in the *New England Journal of Medicine*.

Well-tolerated but less effective treatment

In 2003, IRD and its staff launched a vast clinical trial in Senegal, Benin, Guinea, South Africa and Kenya, to test a new combination of molecules including an antibiotic from the fluoroquinolone family - gatifoxacin. Treatment was administered for four months, instead of the six months required with the current standard combination therapy.

However, after tens years' worth of tests, the results turned out to be inconclusive. While the treatment including gatifoxacin was well-tolerated by the 1,350 patients included in the study, it was less effective than the standard regime: the success rate of the treatment is equivalent to that obtained with the standard six-month treatment, but the relapse rate over the following months turned out to be twice as high. As a result, the tested combination cannot provide an alternative to the current standard treatment.



Overcoming the risk of relapse and drug resistance

Shortening the length of treatment remains one of the preferred ways of combating the disease. The standard regimen currently recommended by the WHO combines several antibiotic drugs, administered over six to eight months. It is long, complex and is toxic to a certain degree, which explains why many patients fail to comply with the protocol. More than 10% of them drop out of treatment before the end, and mazny others do not comply with the frequency of administration. This compliance issue increases the risk of a relapse and favours the emergence of resistant strains of the responsible bacillus, Koch's bacillus. This resistance, along with the AIDS epidemic (with which 30% of new tuberculosis cases are associated in sub-Saharan Africa), contributes to the spread of the disease in the world.

The scientists thus need to continue with research into new combinations among the range of anti-<u>tuberculosis</u> antibiotics, to find an effective, well-tolerated <u>treatment</u> administered over a shorter period. They can now draw on the vast network of infrastructures and skills deployed during this clinical trial, the first of its kind in over thirty years, since the previous research dates from the 1980s.

More information: Merle C., Fielding K., Bah-Sow O., Gninafon M., Lo M., Mthiyane T., Odhiambo J., Amukoye E., Bah B., Kassa F., N'Diaye A., Rustomjee R., de Jong B., Horton J., Perronne C., Sismanidis C., Lapujade O., Olliaro P., Lienhardt Christian. A Four-Month Gatifloxacin-Containing Regimen for Treating Tuberculosis, *New England Journal of Medicine*, 2014, 371:1588-1598. DOI: 10.1056/NEJMoa1315817

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