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# HIV patients should be included in early clinical trials of anti-TB drugs

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Tuberculosis is the number one cause of death in HIV-infected patients in Africa and a leading cause of death in this population worldwide, yet the majority of these patients are excluded from the early stages in the development of new, anti-tuberculosis drugs, according to findings presented today (29 September, 2015) at the European Respiratory Society's International Congress 2015.

Dr Florian von Groote-Bidlingmaier, director of Task Applied Science, which performs clinical trials in tuberculosis (TB) in Cape Town, South Africa, told the Congress that there was an urgent need to develop new drugs to treat TB and, in particular, drug-resistant TB. But one of the patient populations that was most in need of them, HIV patients, have been excluded from early phase clinical trials of these drugs. This resulted in slower development of new anti-tuberculosis drugs.

Dr von Groote-Bidlingmaier and his colleagues reviewed the records of 421 patients with multi-drug-resistant tuberculosis who had been referred to Brooklyn Chest Hospital in Cape Town for consideration for participation in clinical drug trials investigating a new anti-TB drug.

They found that 105 patients (24.9%) were disqualified as they had HIV with a low level of white blood cells (CD4+ cells) that fight infection or were on anti-retroviral therapy. Of the remaining eligible patients, 29 (6.9%) had died and 72 (17.1%) did not have multi-drug-resistant TB but resistance to rifampicin (an anti-TB drug) alone. Finally, of the 55 patients (13.1%) who did qualify for consideration for inclusion in the

trial, only 12 (2.9%) were eventually formally evaluated.

"HIV infection with a low CD4 count and anti-retroviral therapy were the number one reasons for non-consideration for inclusion in pivotal clinical trials of a novel anti-tuberculosis drug," he said.

"We need new anti-TB drugs and we need to develop them fast. Drug development is a lengthy and expensive process and should be accelerated as much as possible. It is very, very difficult to recruit suitable patients with multi-drug-resistant TB for trials of new drugs. Inclusion of HIV patients early on would increase the number of participants and the relevance of the results."

He said the lack of effective new anti-TB drugs, especially ones that could be used by HIV patients who take other potent drugs for their HIV infection, was a problem not just for South Africa but also for all countries with a high burden of TB and a high HIV infection rate.

"South Africa has one of the highest HIV rates in adults at just under 20% of the population, and HIV patients are more likely to contract TB, which is now the number one cause of death in HIV/AIDS patients. In South Africa, more than 60% of TB patients are HIV infected, and that rate is even higher in drug-resistant TB patients.

"HIV patients who have TB are an important group, who are a lot more complicated to treat and a lot more expensive for the health systems. Some TB drugs have drug interactions with anti-retroviral drugs, and so the compatibility of new TB drugs with concomitant anti-retroviral treatment should be investigated early in the clinical development, and HIV patients should be included in relevant clinical trials."

At present, HIV patients tend to be excluded from early phase clinical trials so that any confounding factors can be excluded in these "proof of

concept" studies investigating the tolerability and efficacy of new drugs. "This makes sense from the drug development point of view. However, since HIV patients make up more than half of the TB patients, at least in South Africa, investigation of interactions between TB drugs and anti-retroviral drugs should be a priority and done early on," he said.

He believes that early trials that look specifically at drug interactions may be the way forward. "If TB drugs cannot be used with anti-retrovirals, more than 60% of TB patients in South Africa and elsewhere will not be able to be treated with those drugs."

He concluded: "South Africa is one of the few countries where bedaquiline (one of the new TB drugs) is available without cost to the patient. This is a great success and a major breakthrough ten years after the first clinical trial with bedaquiline was done in Cape Town. Close collaboration between research groups and the government healthcare system is key to efficient drug development. The communities participating in these trials will benefit from that type of research directly."

**More information:** Abstract: HIV co-infection excludes many drug-resistant tuberculosis patients from clinical trials with novel antituberculosis drugs

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