

## Prednisone reduces risk of TB-IRIS during antiretroviral treatment

Study published in the *New England Journal of Medicine* shows that corticosteroid treatment reduced risk of severe complication.

Analysis published today in the *New England Journal of Medicine* shows that a four-week course of moderate dose prednisone reduces the risk of TB-IRIS (tuberculosis-associated immune reconstitution inflammatory syndrome) by 30% in HIV-positive patients at high risk of developing the condition. This is the first trial to show that TB-IRIS can be prevented in these patients and represents an important contribution to the body of knowledge on management of HIV-TB co-infection.

“In patients with HIV, tuberculosis and very low CD4 counts, it is critical to start antiretrovirals within the first two weeks of treatment for tuberculosis, because this saves lives. But this also comes at the cost of a two-fold higher risk of developing a common inflammatory complication—TB-IRIS. Until now no management strategy existed for preventing this complication. The findings of our study provide clinicians with a strategy for reducing the risk of this complication.”—Prof. Graeme Meintjes, PredART Principal Investigator.

The PredART trial was conducted by the Wellcome Centre for Infectious Diseases Research in Africa (CIDRI-Africa), a research group based at the University of Cape Town (UCT), in collaboration with colleagues at the Institute of Tropical Medicine (ITM) (Antwerp, Belgium). PredART was conducted at the Site B HIV–TB clinic in Khayelitsha (Cape Town, Western Cape, South Africa) a state sector outpatient primary care clinic.

TB-IRIS is an immunopathological reaction characterized by severe inflammation occurring shortly after initiation of antiretroviral therapy (ART) for HIV in patients who are also receiving tuberculosis treatment. TB-IRIS is a serious risk in people with HIV-associated TB, resulting in hospitalisation of a quarter of people who develop it.

In the PredART trial, researchers investigated whether providing people at high risk of TB-IRIS with moderate-dose prednisone could prevent development of the condition. Prednisone is a corticosteroid medication that modulates the immune system and treats inflammation. The researchers enrolled HIV-positive patients who were initiating ART, who had started tuberculosis treatment within 30 days before enrolment, and who had a very low CD4 count (100 cells or fewer per microliter of blood).

A total of 240 patients were enrolled, 120 in each arm of the trial (prednisone or placebo). The researchers found that patients who received prednisone during the first four weeks of ART were less likely to develop TB-IRIS than those who received the placebo.

Tuberculosis-associated IRIS was diagnosed in 56 patients in the placebo group and in 39 patients in the prednisone group, a reduction of 30%. Moderate dose prednisone was also found to be well tolerated by patients and there was no evidence of an increased risk of severe infections or cancers with this treatment.



**EDCTP**

This project is part of the EDCTP programme supported by the European Union

Tuberculosis remains the leading global cause of death from infectious disease: an estimated 1.6 million people worldwide died of TB in 2017. In South Africa, approximately 322 000 South Africans (45 000 in the Western Cape) developed TB and 78 000 died of the disease last year (1,2).

### **About the PredART trial**

The PredART trial was a randomized, double-blind, placebo-controlled trial to assess whether prophylactic prednisone could safely reduce the incidence of TB-IRIS in patients at high risk. Patients received either prednisone or placebo.

The trial was sponsored by [UCT](http://www.uct.ac.za). The project is part of the [EDCTP1](http://www.edctp.org) programme supported by the European Union (grant number SP.2011.41304.074), and was also funded by the South African [Department of Science and Technology](http://www.dst.gov.za) (DST), the [Wellcome Trust](http://www.wellcome.ac.uk) (grant numbers 098316, 084323,104803, 203135), and the [ITM](http://www.itg.be).

The study protocol was approved by the University of Cape Town human research ethics committee, the Institute of Tropical Medicine institutional review board, and the Antwerp University Hospital ethics committee. An independent data and safety monitoring board performed two planned reviews of the trial.

UCT: [www.uct.ac.za](http://www.uct.ac.za); EDCTP: [www.edctp.org](http://www.edctp.org); DST: [www.dst.gov.za](http://www.dst.gov.za); Wellcome Trust: [www.wellcome.ac.uk](http://www.wellcome.ac.uk); ITM: [www.itg.be](http://www.itg.be)

### **About CIDRI-Africa**

The [Wellcome Centre for Infectious Diseases Research in Africa](http://www.cidri-africa.uct.ac.za) fosters investigator-led approaches via the overarching scientific objective of combatting infection, especially HIV-1 and tuberculosis, through clinical and laboratory research. Three interlinked platforms support clinical studies in the community, improve the depth of laboratory investigations for infected materials, and advance cutting-edge integration of high-dimensional, big data. CIDRI-Africa is supported by the Wellcome Trust.

CIDRI-Africa: [www.cidri-africa.uct.ac.za](http://www.cidri-africa.uct.ac.za)

### **Citation**

Meintjes G, Stek C, Blumenthal L, Thienemann F, Schutz C, Buyze J, et al. Prednisone for the prevention of paradoxical tuberculosis-associated IRIS. *N Engl J Med*. Massachusetts Medical Society; 2018 Nov 15;379(20):1915–25.

The full publication arising from the trial can be viewed at <https://www.nejm.org/doi/full/10.1056/NEJMoa1800762>

### **References**

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2. Western Cape Government. Help us fight TB [Internet]. 2018. Available from: <https://www.westerncape.gov.za/general-publication/help-us-fight-tb>