

07:00-08:30, Wednesday, 26 July 2017
at the 9th IAS Conference on HIV Science (IAS 2017)
Room 242, Palais de Congrès
Paris, France



E D C T P

European & Developing Countries
Clinical Trials Partnership

IAS 2017 EDCTP Sponsored Symposium, in partnership with ANRS: Coinfections associated with high mortality in severely immunocompromised HIV patients

Concept Note

Background

The European & Developing Countries Clinical Trials Partnership (EDCTP) is a public–public partnership between countries in Europe and sub-Saharan Africa (SSA), and the European Union. This programme is focused on combating some of the greatest areas of unmet medical need in SSA where infectious diseases blight the lives of millions. EDCTP funds collaborative research to accelerate the development of new or improved drugs, vaccines, microbicides and diagnostics against HIV, tuberculosis and malaria as well as other poverty-related infectious diseases in SSA, with a focus on phase II and III clinical trials. The mission of ANRS (the National Agency for Research on AIDS and Viral Hepatitis) is to unite, coordinate, facilitate and finance public research on AIDS, its basic, clinical, vaccine or social sciences. This mission also extends to research in developing countries particularly affected by the disease. In 1999, in response to the scale of the viral hepatitis epidemic, the government extended the ANRS mission to clinical research on viral hepatitis in France and in developing countries.

According to WHO statistics (2015), lower respiratory infections are globally responsible for approximately 2.7 million deaths; tuberculosis (TB) for 1.8 million; HIV for 1.1 million; diarrhoeal diseases for 0.5 million (in children <5 years of age) and malaria for 438,000. Most of these deaths are in low-income countries, particularly in SSA where the burden of infectious diseases is highest. In addition, a high percentage people are affected by multiple pathogens. The emergence of the AIDS epidemic has fuelled the incidence of TB, especially in SSA, where the burden of HIV-associated TB is highest. Significant efforts and investments have been made in improving diagnostic, prognostic and treatment approaches for TB. However, not all HIV coinfections have received sufficient attention and, despite significant strides in HIV management, opportunistic infections (many of which are on the WHO list of neglected tropical diseases) are still a frequent cause of mortality in immunosuppressed HIV-positive individuals in SSA. Due in part to the highly immunocompromised status of these patients, these coinfections can result in unique diagnostic and treatment challenges. Major obstacles to effective management of these coinfections include overlapping toxicities, altered efficacy of treatments (e.g. drug-drug interactions), difficulties in medication adherence, and difficulties and/or delays in diagnosis. In some disease-specific cases, there is a paucity of available tools for the diagnosis and treatment of opportunistic infections, which causes further challenges.

This meeting will focus on coinfections causing high mortality in HIV-infected individuals and aims to highlight some recent advances in the areas of HIV/TB and HIV/cryptococcal coinfections, showcase recent EDCTP- and ANRS-funded projects and present EDCTP and ANRS funding strategy in this area.

Objectives

1. To share and widely disseminate research information with the global community on the activities supported by EDCTP and its Participating States (namely France, through a PSIA supported by ANRS: PSIA-2014-632) in the area of HIV coinfections

2. Highlight some recent advancements in the areas of HIV/TB and HIV/cryptococcal coinfections by showcasing recent EDCTP- and ANRS-funded projects
3. Generate discussion that can be used to inform the programme of the upcoming EDCTP stakeholder meeting on co-infections and co-morbidities.

Target Audience

Up to 250 people can be accommodated in the meeting room. Targeted audience includes researchers from public and private sector, clinicians, social scientists, other funders and public health experts.

Proposed format and content

The basic structure will be four main presentations on the themes of development of quantitative diagnostics, advances in efficacious, low toxicity treatments and implementation of treatment algorithms to reduce mortality, which will be followed by an extended cross-cutting discussion session lasting 30 minutes covering all topics and themes presented.

Presentations will be given on the following recently-funded EDCTP and ANRS projects, in the disease areas of HIV/cryptococcal and HIV/TB coinfections:

1. The **DREAMM project**, led by Dr Angela Loyse (St. George's University of London, UK, funded by EDCTP), which is a multi-centre study that aims to evaluate a semi-quantitative cryptococcal antigen lateral flow assay (CrAg LFA) developed by the Pasteur Institute, France. This test will identify at diagnosis HIV patients with cryptococcal meningitis with high CrAg titres. These patients may benefit from a more aggressive or prolonged antifungal therapy. CrAg LFA testing is embedded within an algorithm that strengthens health systems for patients with HIV-associated central nervous system (CNS) infections. It aims to reduce time to diagnostic tests such as a lumbar puncture, as well as the time to the patient starting effective treatments.
2. The **AMBITION project**, led by Dr Joseph Jarvis (London School of Hygiene & Tropical Medicine, UK, funded by EDCTP, MRC, DFID and Wellcome Trust), which is a multi-centre phase-III trial to determine whether short-course high-dose liposomal amphotericin (L-AmB, Ambisome) is as effective as 14-day amphotericin B-based therapy in averting all-cause mortality in HIV-associated cryptococcal meningitis. 850 patients will be recruited at six African partner-sites, making this the largest HIV-associated cryptococcal meningitis trial ever conducted. A novel short-course highly effective and safer L-AmB treatment regimen for cryptococcal meningitis would transform the management of late-stage HIV and will markedly improve outcomes in HIV programmes in Africa.
3. The **STATIS trial**, led by Professor Francois-Xavier Blanc (Centre Hospitalier Universitaire Nantes, France, funded by ANRS), evaluates a strategy of anti-TB treatment in severely immunosuppressed HIV patients. The trial investigates whether a systematic 6-month empirical TB treatment initiated two weeks before the introduction of antiretroviral treatment in HIV-infected adults with severe immunosuppression ($CD4 < 100/mm^3$) and no overt evidence of TB would reduce the risk of death and invasive bacterial infections. This strategy is compared to another strategy which involves extensive TB testing using point-of-care tests (Xpert MTB/RIF® and urine lipoarabinomannan LAM) and chest X-ray to identify and treat only patients with at least one positive test suggestive of TB.
4. The **TRIP (Translating Research Into Practice) study**, led by Dr Sayoki Godfrey Mfinanga (National Institute for Medical Research, Tanzania, funded by EDCTP), aims to determine the feasibility of scaling up the REMSTART intervention, which was previously reported to have reduced deaths by 28%, in routine health care and to inform and refine guidelines on HIV services for patients with advanced HIV. It will also determine the cost effectiveness of the TRIP intervention in reducing mortality in patients with advanced HIV in real health care settings when implemented on a large scale.