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New oral drug candidate for African sleeping sickness

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A new oral-only treatment for sleeping sickness has entered Phase II/III clinical study in patients with late-stage sleeping sickness in the Democratic Republic of the Congo (DRC) and soon in Central African Republic (CAR). The study, initiated by the Drugs for Neglected Diseases initiative (DNDi) and its partners, will test the efficacy and safety of fexinidazole, with once-daily tablets for ten days.

Sleeping sickness – or human African trypanosomiasis – is fatal without treatment. Spread by the bite of a tsetse fly, the disease threatens the most remote areas of 36 sub-Saharan African countries and, while currently in a period of decline, is known to re-emerge to epidemic levels when surveillance efforts wane. Children below 15 years of age represent nearly a quarter of current patients and DRC alone accounts for the majority of reported cases throughout Africa.

Current treatments for stage 2 of the disease – or late stage, when the parasites cross the blood-brain barrier – are difficult to administer as they require infusions that are only possible within a hospital infrastructure, in addition to the heavy transport necessary to get them there. Patients living far from this type of structure often have to travel for days, even by foot, to access treatment centres.

'This is a major step in research and development for neglected tropical diseases. It shows that it is possible to bring a new chemical entity through the pipeline to offer an entirely new perspective on tackling a disease like sleeping sickness', comments Dr Bernard Pécoul, DNDi's

Executive Director. 'It is by connecting all of our partners in the endemic countries and around the world with the support of engaged donors – all with a common goal – that we can and will continue to search for adapted treatments for these diseases', he added.

Fexinidazole is the first success of the extensive compound mining efforts pursued by DNDi within the nitroimidazole project initiated in 2005 to explore new and old nitroimidazole drug leads. The objective is to progress fexinidazole through this pivotal Phase II/III study in order to register the drug as a new treatment for stage 2 sleeping sickness caused by the parasite Trypanosoma brucei (T.b.) gambiense, as well as for stage 1 sleeping sickness and sleeping sickness caused by T.b. rhodesiense.

If ultimately successful, fexinidazole would be the first oral treatment to be used for both stage 1 and stage 2 sleeping sickness, thereby replacing the complicated diagnosis and treatment paradigm, which includes systematic lumbar punctures of every diagnosed patient to determine the stage of the disease before deciding which treatment to administer.

'This new chemical entity gives us hope of a drastically simplified way to care for our patients', said Dr Wilfried Mutombo, National Human African Trypanosomiasis Control Programme , DRC, Investigator and Coordinator of the fexinidazole trial. 'In addition, the investments made into renovating the laboratories and hospital wards, training personnel, and introducing adapted technologies that allow us to report in real time on each patient, has elevated an entire group of dedicated professionals to international clinical research standards', he added.

The study was initiated and is conducted by DNDi in collaboration with the Swiss Tropical and Public Health Institute (Swiss TPH) and the Human African Trypanosomiasis national control programmes of the Democratic Republic of the Congo and Central African Republic, in

addition to collaboration with Médecins Sans Frontières (MSF). The French pharmaceutical company Sanofi and DNDi co-develop the drug: DNDi is responsible for preclinical, clinical, and pharmaceutical development, while Sanofi is responsible for the industrial development, registration, and production of the drug at its manufacturing sites.

Recruitment for the study will include 510 patients at five clinical sites in DRC and one site in Central African Republic.

More information: About the fexinidazole study

The efficacy and safety study is a pivotal, non-inferiority, open, multi-centric and randomized Phase II/III study. The treatment regimen for fexinidazole will consist of 1 dose of 1800mg (3 pills) once a day for the first 4 days and 1 dose of 1200mg (2 pills) once a day for the following 6 days (10 days in total). The reference treatment, NECT, which will be administered for 10 days as well, with 3 oral administrations per day of nifurtimox for 10 days in combination with 2 intra-venous infusions per day of elfornithine (2-hours long each) for 7 days. Two-thirds of patients will receive fexinidazole, and one-third will receive NECT. The study will measure the safety and efficacy of fexinidazole, with NECT as the active comparator. NECT is currently the first-line treatment for stage 2 of the disease, which notably has replaced since 2009 the toxic arsenic-based melarsoprol. The protocol for the fexinidazole study was reviewed by an international ethics working group convened by the Société Française et Francophone d'Ethique Médicale (SFFEM) with WHO support, before being approved by the national authorities and the MSF ethics committee.

Support for the study

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