BREAKING NEWS

A potential new oral drug for leishmaniasis has successfully been tested in healthy humans

A potential new oral drug (D121) for the treatment of cutaneous leishmaniasis (CL) has been successfully tested in Germany in healthy humans.

Current treatments for **Cutaneous leishmaniasis** (CL) are limited by effectiveness, tolerability, safety, administration and/or affordability. However, the **disease is endemic** in 98 countries with **around 700,000 to 1.2 million new people** per year suffering from a disease **hampering their quality of life and ability to work**, primarily in resource-poor regions. Due to globalization and climate change, this neglected disease is **gaining foothold in Europe** due to an increase in the range of the parasite's vector, the sandfly.

The drug candidate D121 is predicted to have a **broad anti-leishmania activity in preclinical experiments** and **can be administered orally**. The drug has been developed to be **affordable** and to be stable under the highest tropical climate zones. It was successfully investigated in a phase 1 clinical trial at the University of Tübingen, Germany, and is an **excellent drug candidate for further clinical studies**.

D121 holds great potential in reducing the social and economic burden of cutaneous leishmaniasis, thereby contributing to the **UN development goals**.

Cutaneous leishmaniasis

Leishmaniasis is a poverty-related, neglected infectious disease, that imposes a significant public health and socioeconomic burden in large parts of the world, particularly in resource-poor regions. Leishmaniasis manifests in three forms: **cutaneous, mucocutaneous and visceral. CL is the most common form**, causing localised skin lesions that can develop into ulcers, leading to severe mutilation and permanent disfiguring and stigmatising scars. **Visceral leishmaniasis** also known as kala azar and black fever, affects internal organs, causing chronic symptoms characterised by irregular bouts of fever, substantial weight loss, a distended spleen and liver and also anaemia. It is fatal, if untreated, in 95% of cases.

Climate change

Leishmaniasis might impact even more people due to climate change in already highly endemic regions worldwide but also the **US and Europe are no longer safe from leishmaniasis**.

Climatic factors such as temperatures, rainfall and changing weather patterns can influence the disease epidemiology. Rising temperatures have an impact on the parasite's vector reproduction, metabolism and survival, the pathogen replication and the vector and host distribution. Rainfall and changing precipitation have improved habitat suitability for vectors in previously temperate areas, allowing for autochthonous transmission of leishmaniasis in parts of southern Europe and the USA.

TT4CL

TARGETED TREATMENT FOR CUTANEOUS LEISHMANIASIS

Phase 1 Study Completed

D121 has been through the first essential step for drug development by **successfully completing a Phase 1 human study**. This investigation provides the basis for developing further studies to examine the potential of this orally administered treatment for cutaneous leishmaniasis, for which current treatments are difficult and of limited efficacy.

TT4CL: project addressing market failure for Neglected Infectious Diseases (NIDs)

TT4CL stands for "**targeted treatment for cutaneous leishmaniasis**". It is a **consortium project between academic and industrial partners throughout Europe**, granted under EU's research and innovation programme Horizon2020 (HaDEA grant agreement no. 815622).

NIDs often suffer from "market failure", characterized by high risk and low potential return on investment. This discourages the development and uptake of new treatments. Therefore, the ambition of this European Commission's call was to support new agents for prevention and/or treatment of neglected infectious diseases (NID).

In total, **four academic partners (from the UK and Germany)** worked together with 2 private companies (from Belgium and the Netherlands) as well as a 5th academic partner from a leishmania endemic region: the **Tehran University of Medical Sciences, Iran**. The TT4CL consortium received funding of **€3.75 million** from the EU H2020 programme. Together they made a **significant progress** in developing a new potential drug for cutaneous leishmaniasis. **The EU's targeted funding has enabled the advancement of a new drug candidate named D121 from preclinical to clinical development.**

For more information on leishmaniasis and D121, visit TT4CL's website
https://tt4cl-h2020.eu

Consortium Members of TT4CL

- St George's University Hospital, London (Coordinator, UK)
- Oblita Therapeutics (R&D company on D121, Belgium)
- Avivia (CRO for CMC, Netherlands)
- London School of Hygiene and Tropical Medicine (Preclinical, UK)
- University of York (Preclinical, UK)
- Eberhard Karl's Universität Tübingen (Clinical, Phase 1, Germany)
- Tehran University of Medical Sciences (Preclinical, Iran)

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