EFFICACY OF RUTI IMMUNOTHERAPY AGAINST ACTIVE TB IN A MOUSE MODEL
CHALLENGES THE KOCH PHENOMENON.
CONFLICT OF INTEREST

*Inventor of RUTI

*Co-founder of Archivel Farma, s.l.

*Former CSO and CMO of Archivel Farma, s.l. (2004-2013)

*Nowadays, Medical and Scientific Consultor of Archivel Farma, s.l.
A short history of Robert Koch’s fight against tuberculosis: Those who do not remember the past are condemned to repeat it

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RUTI: a therapeutic vaccine made with fragments of *Mycobacterium tuberculosis*

Archivel Farma S.L. is developing RUTI®, a polyantigenic inactivated liposomal vaccine that acts as an immunotherapeutic agent in tuberculosis (TB) and bladder cancer (BC). Further, it is currently developing RUTI® for the treatment of the coronavirus disease (COVID-19) for RUTI immunotherapeutics SL.

RUTI® (IMP) is composed of purified, pasteurized and liposomal cellular wall fragments of *M. tuberculosis* (FCMtb) grown under stress conditions homogenized in a liposomed solution. These fragments of Mtb cell wall express multiple antigens classically described as representative of replicating and non-replicating Mtb.

The mechanism of action of the RUTI® vaccine is to induce an efficient cellular immune response that removes Mtb at the beginning of chemotherapy treatment.
RUTI: a therapeutic vaccine made with fragments of *Mycobacterium tuberculosis*

**Drug Substance**

**Drug product**

Freeze-fracturing preparation of liposomal concentrate suspension (LCS) bulk of RUTI (electronic microscopy).
Figure. Temporal strategy for the use of RUTI, indicating the effects of short-course chemotherapy and the requirement for subsequent immunotherapy.

Cardona et al 2006
RUTI: Mechanism of action.

Andersen P 1997

Cardona PJ 2016
Understanding the evolution towards active TB; the C3HeB/FeJ mice. Marzo et al 2013
Understanding the evolution towards active TB; the C3HeB/FeJ mice. Marzo et al 2013
Expected impact of RUTI immunotherapy in the treatment of active TB

![Graph showing the impact of RUTI immunotherapy on the log bacillary load in months. The graph illustrates the decrease in log bacillary load over time, with different treatments indicated by color: green for replicating bacilli and red for non-replicating bacilli. The X-axis represents time in months, and the Y-axis represents log bacillary load in hundreds. The graph shows the effectiveness of RUTI immunotherapy, with a decrease in bacillary load after treatment.]

**Experimental design**

Sputum culture negative

H = isoniazid; R = rifampicin; E = ethambutol; Z = pyrazinamide
RUTI alone reduces CFU against active TB, and synergizes with HRZE reducing 1.5 log the CFU.
RUTI increases cellular immune surveillance

PPD

ESAT-6

HSP16.3

PsTS1

[5 weeks Mtb infection] - S0w

[RZHE 0-4d] - S1w

[RUTI 200 ug 0d + HRZE 0-4d] - S1w

[S0w] - S1w

[RZHE 0-4d] - S1w

[RUTI 200 ug + HRZE 0-4d] - S1w

[S0w] - S1w

[RZHE 0-4d]

[RUTI 200ug 0d + HRZE 0-4d] - S1w

[S0w] - S1w

[RUTI 200ug 0d + HRZE 0-4d] - S1w
Proposed mechanism of action: RUTI helps from the very beginning to survey “daughter granulomas” stopping its progression.
The new clinical trial CONSTAN testing of effectiveness of the RUTI® vaccine to shorten tuberculosis treatment times

Wednesday, 29 December 2021

The biotechnology company Archivel Farma has designed and set up a phase Ib clinical study called CONSTAN to explore whether administering the immunotherapy RUTI®, known as the RUTI® vaccine, along with the standard treatment for patients with pulmonary tuberculosis (TB) improves results. The principal investigator of the project is Dr Cristina Vilaplana, leader of the Experimental Tuberculosis Unit (UTE) at the Germans Trias i Pujol Research Institute (IGTP). The study has been approved by the Spanish Agency of Medicines and Medical Devices (AEMPS) and the First Patient In will be welcomed in January 2022.

The study led by Archivel Farma will take place with the collaborations of the Microbiology Service of the Germans Trias i Pujol Hospital. The recruitment of the 56 patients who will take part will be carried out through 8 different healthcare centres in Catalonia, including the Germans Trias i Pujol Hospital.
THANK YOU VERY MUCH FOR YOUR ATTENTION !!!!!