Study To Evaluate The Efficacy Of Tofacitinib In Patients With SJS/TEN

ClinicalTrials.gov ID NCT06474078
Sponsor Chang Gung Memorial Hospital
Information provided by Chun Bing Chen, Chang Gung Memorial Hospital (Responsible Party)

Study Overview

Brief Summary
The goal of this study is to evaluate the effect of tofacitinib in patients with Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN). The primary outcome of the study is the time to complete re-epithelialization. The secondary outcomes are to determine mortality, length of hospitalization, adverse events, the time to beginning of epithelization, the time to halting of progression of SJS/TEN, ocular complications, and infections.

Detailed Description
Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) belong to life-threatening severe cutaneous adverse drug reactions. SJS/TEN is classified by the extent of the detachment over the total body-surface area: SJS (<10%), SJS-TEN overlap (10%-30%), and TEN (>30%). TEN has the highest mortality (30-35%); SJS and transitional forms correspond to the same syndrome, but with less extensive skin detachment and a lower mortality (5-15%). Currently, there is still no conclusive effective immunomodulator treatment for SJS/TEN. And, there is still a clinical unmet need for the treatment of SJS/TEN.

According to our past research reports, interleukin-15 (IL-15) plays an important role in SJS/TEN, which is related to disease severity and mortality. Janus kinase (JAK) inhibitors can inhibit the downstream JAK to inhibit the production and transmission of inflammatory cytokines, as a treatment for severe skin drug hypersensitivity reactions. Tofacitinib, a JAK1/3 inhibitor, is an intervention known to effectively treat several inflammatory diseases including rheumatoid arthritis, psoriatic arthritis, and ulcerative colitis. Notably, a recent study identified a potential therapeutic target with JAK-STAT pathway in a patient with recalcitrant and refractory drug rash with eosinophilia and systemic symptoms (DRESS). Based the current evidence, a targeting therapy to IL-15 by tofacitinib treatment are suggesting likely to be effective in treating SJS/TEN.

This is an "open label" study, all patients enrolled in the study will receive the active medication; meaning that there will not be a placebo or control group. The aims of this project are (1) to investigate the effect of tofacitinib treatment for SJS/TEN patients, including healing time, mortality rate, adverse events, beginning of re-epithelialization time, internal organ recovery time, and ocular complications, and (2) to investigate the molecular mechanism of SJS/TEN after tofacitinib treatment through collection of timed samples to include DNA, RNA, PBMCs, blister cells and supernatant and skin tissue.

The primary outcome of the study is the time to complete re-epithelialization as defined by complete absence of erosion on the skin. The secondary outcomes are to determine the time to beginning of epithelization (defined as the time to start re-epithelialization of the erosions on the skin and mucosa), the time to halting of progression of SJS/TEN (considered significant progression if there are any new blistering lesions or any new detached or detachable skin), mortality, length of hospitalization, ocular complications, infections, and adverse events. The investigators also determine the molecular and cellular mechanisms of SJS/TEN through collection of timed samples to include DNA, RNA, PBMCs, blister cells and supernatant and skin tissue.

Official Title

An Open-Label Pilot Study to Evaluate the Safety, Tolerability,
and Efficacy of Tofacitinib in Patients With Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN)

Intervention / Treatment

Drug: Tofacitinib

Other Study ID Numbers

IRB No. 202102411A3

Contacts and Locations

This section provides the contact details for those conducting the study, and information on where this study is being conducted.

Study Contact (Project Leader)
Name: Chun Bing Chen
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Study Contact Backup (Co-Investigator)

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Participation Criteria

Researchers look for people who fit a certain description, called eligibility criteria. Some examples of these criteria are a person's general health condition or prior treatments.

Eligibility Criteria

Description

Inclusion Criteria:

1. Willing to sign inform consent form
2. Subject has been diagnosed with Stevens-Johnson syndrome or toxic epidermal necrolysis by at least two dermatologists.
3. Male or female aged over 20 years old and under 90 years old.

Exclusion Criteria:

1. Subject or legally authorized representative is not willing to provide informed consent.
2. Women who are pregnant or breastfeeding
3. Subject has an active, untreated, or serious infectious disease that is ineffective in treatment, such as sepsis.
4. Subject suffers from severe life-threatening cardiac arrhythmia, such as ventricular tachycardia, have had myocardial infarction (myocardial infarction), severe hypertension that has not responded to treatment within the past week, or other cardiologist diagnosed severe cardiovascular disease
5. Subject has active viral hepatitis
6. Subject has active tuberculosis
7. Subject received live vaccination during the illness

Study Protocol

This section provides details of the study plan, including how the study is designed and what the study is measuring.

How is the study designed?

Design Details

Primary Purpose : Treatment

Allocation : N/A

Interventional Model : Single Group Assignment

Masking : None (Open Label)

Arms and Interventions

Participant Group/Arm	Intervention/Treatment
Experimental: Tofacitinib treatment 1. Meet the conditions of inclusion and exclusion, seek the consent of the patient 2. Fill out the case report form 3. Blood test and physiological assessment, and do serum granulysin concentration and peripheral blood mononuclear spherical granulysin expression analysis 4. Tofacitinib administration: The experimental group received tofacitinib 5mg-10mg, twice daily, for the first week; and maintained tofacitinib 5mg-10mg, daily, for the second week.	Drug: Tofacitinib • Dosage/Frequency: 5mg - 10mg, oral, twice daily • Other Names: ▫ XELJANZ

What is the study measuring?

Primary Outcome Measures

Outcome Measure	Measure Description	Time Frame
Time to complete re-epithelialization of SJS/TEN	Definition of complete re-epithelialization as the absence of erosions on the skin.	up to 4 weeks

Secondary Outcome Measures

Outcome Measure	Measure Description	Time Frame
Mortality	Number of participants with mortality at 30 days, 3 months and 1 year	up to 1 year
Length of hospitalization	Duration of hospital stay	up to 3 months
Adverse events	Adverse events related to the treatment with tofacitinib	up to 3 months

Study endpoint

The endpoint of this clinical trial was defined as the absence of serious or treatment-related adverse events within three weeks after the final tofacitinib dose. Most SJS/TEN patients were monitored for 3–4 weeks post-treatment, with the total observation period spanning 1–2 months. Patients without AEs during this window were considered to have completed the trial and met the safety endpoint.

Study duration

Start Date from 2022-08-01 to 2025-07-31

Statistical Analysis Plan

For evaluating the time taken to heal skin erosion, the Kaplan-Meier product-limit estimates method was performed.

Collaborators and Investigators

This is where you will find people and organizations involved with this study.

Sponsor

Chang Gung Memorial Hospital

Investigators

- Principal Investigator: Chun Bing Chen, Chang Gung Memorial Hospital