Poster Board # P536

EFZO-FIT™, the Largest Placebo-Controlled Trial in Sarcoidosis

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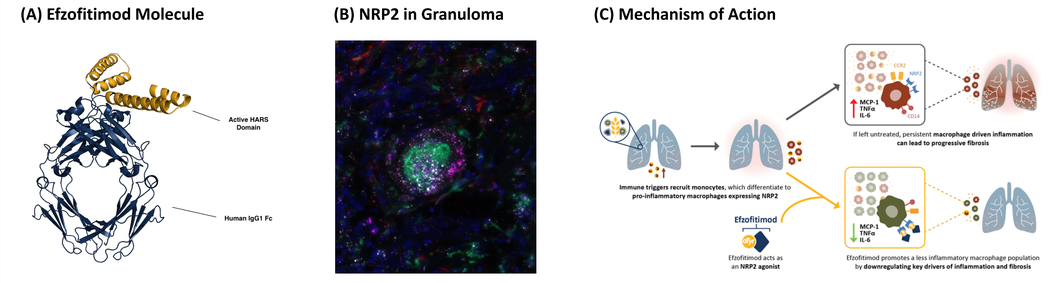
Introduction

Background: Sarcoidosis is a chronic inflammatory granulomatous disease. Oral corticosteroids (OCS) are potent anti-inflammatory agents, that are first line treatment for sarcoidosis. Chronic OCS use is associated with considerable side effects and steroid reduction is an important goal in managing sarcoidosis.

In an earlier Phase 1/2 study, efzofitimod showed favorable dose- and exposure-response results across multiple efficacy endpoints, including the ability to reduce steroids [1,2]. Efzofitimod is currently being evaluated in EFZO-FIT, the largest, interventional, placebo-controlled Phase 3 clinical trial. Enrollment was completed in July 2024; blinded follow-up continues for one year.

Figure 1. Efzofitimod is a first-in-class biologic immunomodulator for ILD

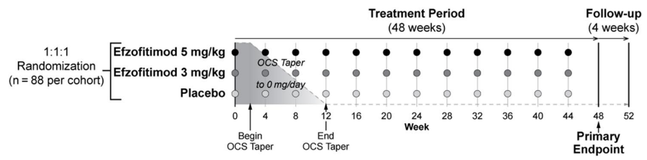


(A) Efzofitimod, a biologic immunomodulator, comprised of an active moiety derived from histidyl-tRNA synthetase (HARS), fused to the Fc region of human immunoglobulin G1 (IgG1). Efzofitimod's target receptor is neuropilin-2 (NRP2). **(B)** NRP2 RNA (white dots) is colocalized with macrophage markers CD68 (green) and CD163 (orange) in granulomas from pulmonary sarcoidosis patients. **(C)** Efzofitimod downregulates the expression of the inflammatory and profibrotic markers implicated in the pathology of inflammatory-fibrotic lung diseases: interleukin (IL)-6, TNF-α, IFN-γ, monocyte chemoattractant protein-1 (MCP-1), and IFN γ-induced protein 10 kDa (IP 10) [3,4].

Methods

- EFZO-FIT is a global, randomized, double-blind, placebo-controlled trial evaluating the efficacy and safety of efzofitimod in patients with pulmonary sarcoidosis (NCT05415137).
- Randomization was stratified based on the OCS dose at baseline (< 10 mg/day versus ≥ 10 mg/day [prednisone or equivalent]) and the presence or absence of concomitant immunosuppressants. Eligible patients were randomized 1:1:1 to efzofitimod 3.0 or 5.0 mg/kg, or placebo, dosed intravenously every 4 weeks for 12 doses (Figure 2).
- Steroid reduction is the primary efficacy parameter of EFZO-FIT. The primary endpoint is change from baseline in mean daily OCS dose at Week 48. Other key efficacy parameters are forced vital capacity and quality of life measures.
- The study was designed to include adults (≥ 18 years) with chronic (duration ≥ 6 months), symptomatic (modified medical research council [MRC] dyspnea score ≥1, King's sarcoidosis questionnaire [KSQ]-Lung Score ≤70), pulmonary sarcoidosis (biopsy proven) on OCS for 3 months (stable for 4 weeks) with a FVC percent predicted ≥50%. The starting dose for OCS was ≥ 7.5 and ≤ 25 mg/day (except Japan, ≥ 5 and ≤ 25 mg/day). Up to one concomitant immunosuppressant was allowed. Patients with active cardiac, neuro, or renal sarcoidosis requiring organ-specific therapy in the prior two years; or with cutaneous or ocular sarcoidosis, which the Investigator deemed at risk for exacerbation, necessitating OCS or other systemic therapy, were excluded.

Figure 2. Study Design



Results

The study enrolled 268 patients. Four were randomized but not dosed. The study population was consistent with moderate to severe chronic symptomatic pulmonary sarcoidosis (Table 1). Of the 264 patients, 101 (38.3%) were on concomitant immunosuppressants.

Unblinded reviews were conducted by an external independent Data Safety Monitoring Board (DSMB) (Figure 3). The last scheduled DSMB review of safety data occurred after all patients had been enrolled, with the last enrolled patient having completed 6 months. Following review of the unblinded data, the DSMB recommended – *"To continue trial unmodified until the next scheduled or triggered meeting (study does did not pose any undue risk to the patient that warrants additional safety measures)".*

Table 1. Baseline Demography (n=264)[1]

Demographics	
Age (years)	
Mean (SD)	53.8 (10.6)
Range	32-75
Gender (%)	
Female	114 (43.2)
Male	150 (56.8)
Weight (kg)	
Mean (SD)	85.5 (19.2)
Range	40.4-139
BMI (kg/m^2)	
Mean (SD)	29.1 (5.6)
Range	17.2-49.8
Race (%)	
White	169 (64)
Black or African American	42[2] (15.9)
Asian (Japanese)	36 (13.6)
Other[3]/Mixed/Unknown	17 (6.4)

Table 2. Disease Characteristics (n=264)[1]

Disease Characteristics	
Baseline OCS dose (prednisone equivalent, mg)	
Mean (SD)	10.55 (4.21)
Range	5–25
MRC dyspnea score (%)	
0	2 (0.7)[4]
1	132 (50)
2	100 (37.9)
3	28 (10.6)
4	2 (0.7)
Extrapulmonary sarcoidosis – at enrollment	
Lymph nodes	44
Cutaneous	16
Ophthalmic	11
Bone and joint	11
Hepatic	11
Cardiac	1
Neurological -peripheral	1
Other	10

[1] Data subject to change prior to database lock

[2] 36 from USA (31.9% of 113 USA patients)

[3] Includes Other + American Indian/Alaska native (2), Asian (2), Native Hawaiian/Other Pacific Islander (1)

[4] Patients met the eligibility criteria at screening

Figure 3. DSMB review - unblinded safety review

DSMB #1
48 patients
3 months safety data*

→ DSMB #2
96 patients
6 months safety data*

→ DSMB #3
192 patients
6 months safety data*

→ DSMB #4 (Final)
268 patients
6 months safety data*

* duration of safety data of last enrolled patient

Conclusions

EFZO-FIT is the largest, interventional, placebo-controlled clinical trial in patients with pulmonary sarcoidosis. The study population comprising patients with chronic symptomatic pulmonary sarcoidosis on long term steroids is appropriate for evaluating the primary end point of steroid reduction.

References

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