EFZO-FIT™: A Phase 3 Study Of Efzofitimod, A Novel Immunomodulator For The Treatment Of Pulmonary Sarcoidosis

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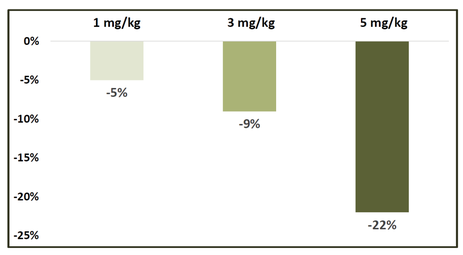
Introduction

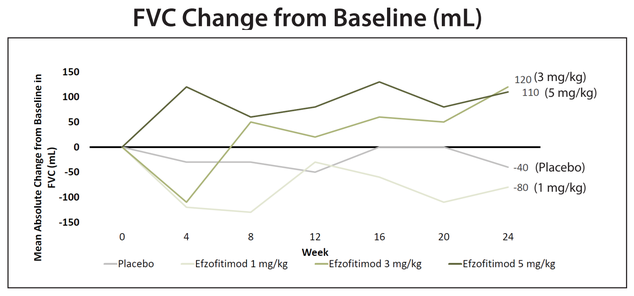
- **Efzofitimod - novel biologic immunomodulator[1]**
- **Phase 1b/2a Multiple Ascending Dose study - Methods**
  - Randomized, double-blind, placebo-controlled.
  - Three sequential dose cohorts; 2:1 randomization (efzofitimod to placebo) in each cohort.
  - Patient population (n=37) - chronic (duration > 6 months) sarcoidosis (biopsy proven), parenchymal lung involvement (CT, MRI), symptomatic (MRC dyspnea score at least 1), on stable (for ≥ 4 weeks) oral corticosteroids (OCS) (prednisone equivalent 10 to 25 mg/day).
  - Treatment period - 6 intravenous doses 4 weeks apart.
  - OCS taper to 5 mg/day by week 8 or to < 5mg/day after week 16.
  - Three families of endpoints – steroid taper, lung function and patient reported outcomes (PROs), not powered for efficacy.
- **Phase 1b/2a study results[2]**
  - Efzofitimod - safe and well tolerated.
  - Dose dependent improvement seen across all three families of endpoints.

Figure 1. Dose-dependent Reduction in Steroid Utilization.
Relative Reduction Compared to Placebo in OCS Dose



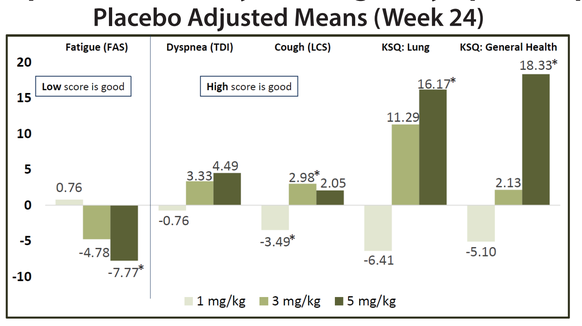
- Three patients on 5 mg/kg able to taper completely off OCS and maintain taper, compared to 0 in all other groups.

Figure 2. FVC Improved with Higher Efzofitimod Doses.
FVC Change from Baseline (mL)



- Dose dependent trends were consistent for all other pulmonary function tests performed (e.g. FVCpp, DLCO).

Figure 3. Dose-dependent Clinically Meaningful Symptom Improvements
Placebo Adjusted Means (Week 24)



*p<0.05

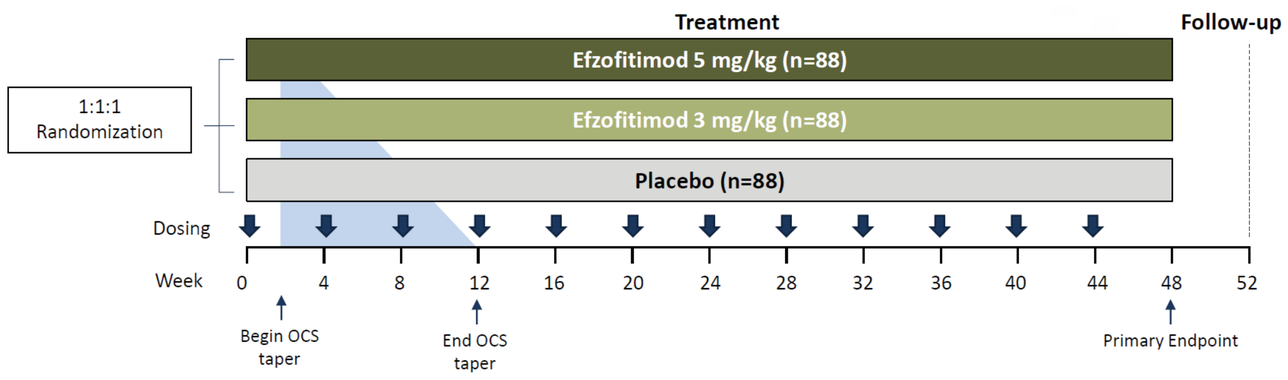
EFZO-FIT Study Study Design

The EFZO-FIT Study is a Phase 3, randomized, double-blind clinical research study investigating the efficacy and safety of intravenous efzofitimod versus placebo in patients with symptomatic pulmonary sarcoidosis.

Key Objectives:

To evaluate whether efzofitimod can reduce the dose of steroids in people with pulmonary sarcoidosis.

To evaluate whether efzofitimod will maintain symptom control and lung function when steroids are reduced.



Primary Endpoint
Steroid burden: change in daily steroid dose

Key Secondary Endpoints
Lung function: forced vital capacity
Symptom control: KSQ-Lung score

Actively Enrolling

Approximately 264 people will take part in the EFZO-FIT Study at up to 80 study centers around the world.

Additional Study Information

Study details and more information available on clinicaltrials.gov (NCT05415137).

Contact for Referrals

efzofit@atyrpharma.com

Study Population

Inclusion Criteria

Category	Criteria
Age; Weight	18 to 75 years; ≥ 40 kg and < 160 kg
Sarcoidosis	Documented by tissue biopsy (any organ)
Lung Involvement	On CT, MRI, or PET Scan
Symptomatic	MRC dyspnea at least 1 AND KSQ-Lung score < 70
Steroid Criteria (must meet all)	OCS for > 3 months OCS dose between ≥ 7.5 and ≤ 25 mg/day Stable dose for ≥ 4 weeks prior to Day 1 Willing to attempt OCS taper to 0 mg/day

Exclusion Criteria

Category	Criteria
Confounders in the evaluation of efficacy	Lofgren's syndrome Treatment with > 1 immunosupressive therapy Treatment within 4 months of Day 1 - TNF-α inhibitors or antifibrotics or interleukin inhibitors History of Addisonian symptoms that precluded previous steroid taper
Significant Fibrosis	CT fibrosis > 20%, FVC PP < 50%, or KSQ-Lung score < 30
Pulmonary co-morbidities	Bronchiectasis, cavitary sarcoidosis with mycetoma, Pulmonary Hypertension (requiring vasodilators)
Systemic sarcoidosis	Cardiac sarcoidosis, neuro-sarcoidosis, renal sarcoidosis
Other sarcoidosis	Clinically significant cutaneous and ocular sarcoidosis

Steroid Taper Guidelines

- PI is required to consider tapering the steroids from the day 15 assessment.
- The decision to taper is based on the Patients Global Assessment (PGA) and Investigator Assessment (IA)
- If both PGA and IA are stable or improved patient OCS will need to be tapered
- If either of them has worsened the patient will need to be rescued with OCS
- Taper should be attempted at least 3 times over the first 12 weeks; for patients who have not been tapered to 0 mg OCS at the end of 16 weeks - taper will be attempted another 3 times in the follow up period.

Safety - Adverse Events (AEs) of Special Interest

Immunogenicity	Development of anti drug or Jo-1 antibodies.
Infusion related reactions	Individual AEs (symptoms and signs) occurring within the first 24 hours from the start of infusion and are considered related or possibly related to study drug.
Carcinogenicity	AEs pertaining to newly occurring malignancies.

Conclusions

- Efzofitimod is a novel biologic immunomodulator.
- A Phase 1b/2a multiple ascending dose study evaluated efzofitimod in pulmonary sarcoidosis patients established proof of concept and guided the design of the Phase 3 EFZO-FIT study.
- EFZO-FIT is a multicenter, randomized, double-blind, placebo-controlled study comparing the efficacy and safety of intravenous efzofitimod 3 mg/kg and 5 mg/kg versus placebo after 48 weeks of treatment.
- EFZO-FIT will enroll symptomatic adults with histologically confirmed pulmonary sarcoidosis receiving stable treatment of OCS with or without immunosuppressant therapy.
- EFZO-FIT is actively enrolling globally for the study.

EFZO-FIT Website

References

1) Efzofitimod: A Novel Anti-Inflammatory Agent for Sarcoidosis. Baughman RP, Niranjan V, Walker G, Burkart C, Paz S, Chong YE, Siefker D, Sun E, Nangle L, Förster S, Muders MH, Farver CF, Lower EE, Shukla S, Culver DA. Sarcoidosis, Vasculitis and Diffuse Lung Diseases (2023).

2) Culver DA, Aryal S, Barney J, et al. Efzofitimod for the treatment of pulmonary sarcoidosis. CHEST. 2022 Nov 8; S0012-3692(22)04053-3. doi: 10.1016/j.chest.2022.10.037.

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