RESOLVE-LUNG, a multinational Phase II, randomized, placebo-controlled trial of namilumab in chronic pulmonary sarcoidosis: Trial design and patient characteristics

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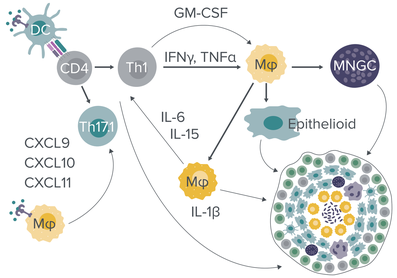
Introduction

- Pulmonary sarcoidosis is a chronic inflammatory disease characterized by granulomas forming in the lungs
- There are no approved drugs for pulmonary sarcoidosis; oral corticosteroids are the standard-of-care but are not always effective and are associated with significant long-term side effects
- This study evaluates the efficacy and safety of namilumab, a monoclonal antibody targeting granulocyte macrophage colony stimulating factor (GM-CSF) in patients with chronic pulmonary sarcoidosis
- In previous studies, namilumab was well-tolerated and showed anti-inflammatory activity in patients with COVID-19 pneumonia and rheumatoid arthritis[1,2]

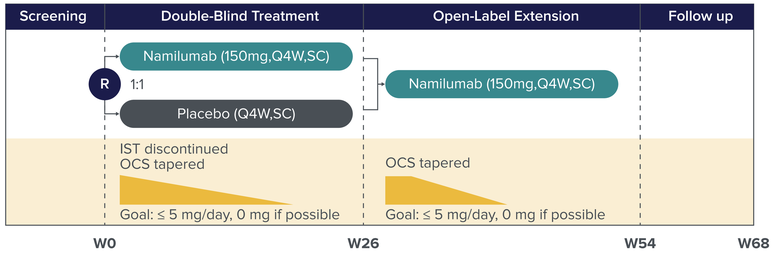
GM-CSF in sarcoidosis granuloma formation



- Granulocyte macrophage colony stimulating factor (GM-CSF) is a pro-inflammatory cytokine over-expressed in several inflammatory diseases, including sarcoidosis
- GM-CSF mediated pro-inflammatory signalling is thought to play a central role in recruitment of macrophages and monocytes to the lung and to trigger a granulomatous response, including the fusion of macrophages into multinucleated giant cells
- Namilumab potently inhibits GM-CSF, and therefore may suppress the inflammation associated with sarcoidosis

Study design

- Double-blind, randomized, placebo-controlled study to assess the efficacy and safety of namilumab in subjects with chronic active sarcoidosis who are not well controlled or do not tolerate OCS and/or immunosuppressive therapy
- Start of OCS taper and IST discontinuation at week 0 (Baseline) and OCS taper at week 30 as applicable



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- N=107 patients enrolled (October 2022–April 2024)

Primary endpoint:

- Proportion of patients with a rescue event* during the Double-Blind period

*As defined by worsening of sarcoidosis requiring treatment or failure to taper OCS or stop IST per protocol

Secondary endpoints include: change from baseline at week 26 in ppFVC, KSQ Lung score, Time to first rescue event, Proportion of patients successfully achieving OCS taper without rescue event, Safety and tolerability, (biomarkers exploratory)

Key inclusion criteria:

- Adults with ≥ 6-month history of pulmonary sarcoidosis
- HRCT showing parenchymal disease
- MRC > 1
- One or more of the following:
  - FDG-PET/CT scan with pulmonary parenchymal SUVmax ≥ 3
  - Worsening of pulmonary function parameters within the last 12 months
  - Failure to taper OCS and/or IST within the last 12 months
- On treatment with OCS (≤ 25 mg/day) and/or IST, or failed or did not tolerate treatment in past 2 years
- ppFVC ≥ 50% and ppDLco ≥ 40%

Key exclusion criteria:

- 20% fibrosis on HRCT scan
- Known extra-pulmonary sarcoidosis requiring treatment (cutaneous and ocular disease was allowed)
- History of heart disease such as cardiac sarcoidosis OR Significant ischemic heart disease
- Latent or active tuberculosis
- Significant laboratory abnormalities
- Use of any biologic immunomodulator agent (approved or investigational) within 6 months prior to Screening
- Other medical conditions that would affect the outcome of the trial

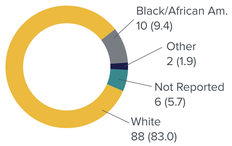
Patient characteristics

Patient demographics

Age, years Mean (SD): **53 (11)**

Gender n (%): Male 61 (58); Female 45 (42)

Ethnicity n (%):



1. Screening; 2. Baseline.
N=107 randomized and 106 treated

Clinical presentation	
Duration of disease, years, mean (SD)	8.0 (7.8)
BMI, mean (SD)[1]	28.5 (4.9)
MRC score, n (%)[1]	
2	71 (67)
3	31 (29)
4	4 (4)
KSQ-Lung score, mean (SD)[2]	54 (12)
FDG-PET SUVmax (g/mL), mean (SD); ≥ 3, n (%)[1]	8.0 (4.4); 98 (92)
FVC % predicted, mean (SD)[2]	86 (16)
FEV1/FVC ratio, mean (SD)[2]	0.70 (0.13)
DLCO % corrected for hemoglobin, mean (SD)[2]	76 (15)

Sarcoidosis treatment pre-randomization

All patients

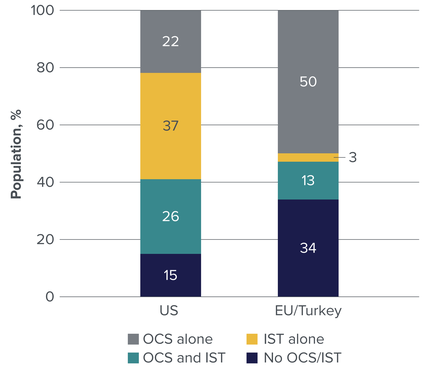
Group	%	Mean OCS dose mg/day
OCS alone	36	9.4
OCS and IST	20	6.5
IST alone	18	-
No OCS/IST	26	-

Mean dose OCS slightly lower when the patient is also on IST

Patients on IST

IST	%
Methotrexate	77.5
Hydroxychloroquine	22.5
Mycophenolate Mofetil	7.5
Azathioprine	7.5

15% of the patients on IST at Baseline were on two ISTs



- EU: higher proportion of patients on OCS alone and not on either OCS or IST
- US: higher proportion of patients on IST alone and IST + OCS

Summary

- Namilumab, by inhibiting GM-CSF, may treat granuloma formation and have an impact on clinical disease
- RESOLVE-LUNG is one of the largest Phase 2 trials in sarcoidosis to date, investigating the safety and efficacy of Namilumab in pulmonary sarcoidosis
- RESOLVE-LUNG features a novel sarcoidosis study design, including IST removal next to OCS taper, and rescue endpoint aiming to measure a relevant clinical outcome
- RESOLVE-LUNG successfully recruited 107 patients across 40 sites in 7 countries with active, symptomatic, disease not well controlled by standard of care
- Development of Namilumab aims to provide an improved treatment option for a patient population underserved by the current standard of care

References

1. Fisher *et al. Lancet Resp Med* 2022; **10:** 255–66.
2. Taylor *et al. Arthritis Res Ther* 2019; **21:** doi.org/10.1186/s13075-019-1879.

Acknowledgments

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The data presented is preliminary with a cut-off date; 30 June 2024.

Disclosure

B. Van Den Blink: receives consultation fees from Kinevant.

Abbreviations

BMI: body mass index; CD4: cluster of differentiation 4; CT: computed tomography; CXCL: CXC motif ligand; DC: dendritic cell; DLCO: diffusing capacity for carbon monoxide; FDG-PET: fluorodeoxyglugose-positron emission tomography; FEV: forced expiratory volume; FVC: forced vital capacity; GM-CSF: granulocyte macrophage colony stimulating factor; HRCT: high resolution computed tomography; IFNγ: interferon gamma; IL: interleukin; IST: immunosuppressive therapy; KSQ: Kings Sarcoidosis Questionnaire; MNGC: multinucleated giant cell; MRC: Medical Research Council; Mφ: macrophage; OCS: oral corticosteroid; ppDLco: percent predicted diffusing capacity of lung for carbon monoxide; ppFVC: percent predicted forced vital capacity; R: randomization; SC: subcutaneous; SD: standard deviation; SUV: Standard unit value; Th: T helper; TNFα: tumor necrosis factor alpha; W: week