Steroid-Sparing and Pulmonary Stability Across XTMAB-16 Dose Regimens in Pulmonary Sarcoidosis: Cohort-Level Findings from XTMAB-16-201 Part A

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INTRODUCTION

- Pulmonary sarcoidosis often requires prolonged corticosteroid therapy despite cumulative toxicity and limited approved steroid-sparing options[1].
- In chronic disease, reducing corticosteroid exposure while maintaining pulmonary stability remains a central goal[2].
- **XTMAB-16 is an investigational anti-TNFα being evaluated for pulmonary sarcoidosis[3]**.
- XTMAB-16-201 Part A was a first-in-patient, dose-ranging study.

Objectives:

- To characterize cohort-level corticosteroid reduction, pulmonary stability, and background immunosuppressant exposure across XTMAB-16 regimens, and **to support selection of 4 mg/kg every 4 weeks for further development**.

METHODS

Methods

- Adults with chronic active pulmonary sarcoidosis receiving oral corticosteroids and second-line immunosuppressive therapy were randomized 3:1 to placebo or XTMAB-16 2mg/kg Q4 weeks (W), 4mg/kg Q4W, 2mg/kg Q2W, or 4mg/kg Q2W.
- Descriptive cohort-level analyses characterized regimen-level patterns in corticosteroid reduction, pulmonary function, concomitant immunosuppressant use, and previously-presented exposure and immunogenicity findings[4].

KEY RESULTS

Baseline Characteristics

39 Patients were randomized and 38 patients completed study; *1 participant withdrew consent

Average Antimetabolite Dose All Participants	Placebo N=11	2 mg/kg Q4W N=8	4 mg/kg Q4W N=7	2 mg/kg Q2W N=6	4 mg/kg Q2W N=7
Methotrexate (mg/week)	22.5	62.14	15.83	13.57	13.57
Azathioprine (mg/day)	100	150	400	150	125
Mycophenolate (mg/day)	1305	2000	0	2000	1000
Hydroxychloroquine (mg/day)	266.67	200	300	200	400

Among ADA-positive patients, second-line therapy most commonly included methotrexate at an average dose of ~16mg per administration, with additional regimens including hydroxychloroquine 200mg QD, azathioprine 50mg BID/TID, and mycophenolate 1000mg BID.

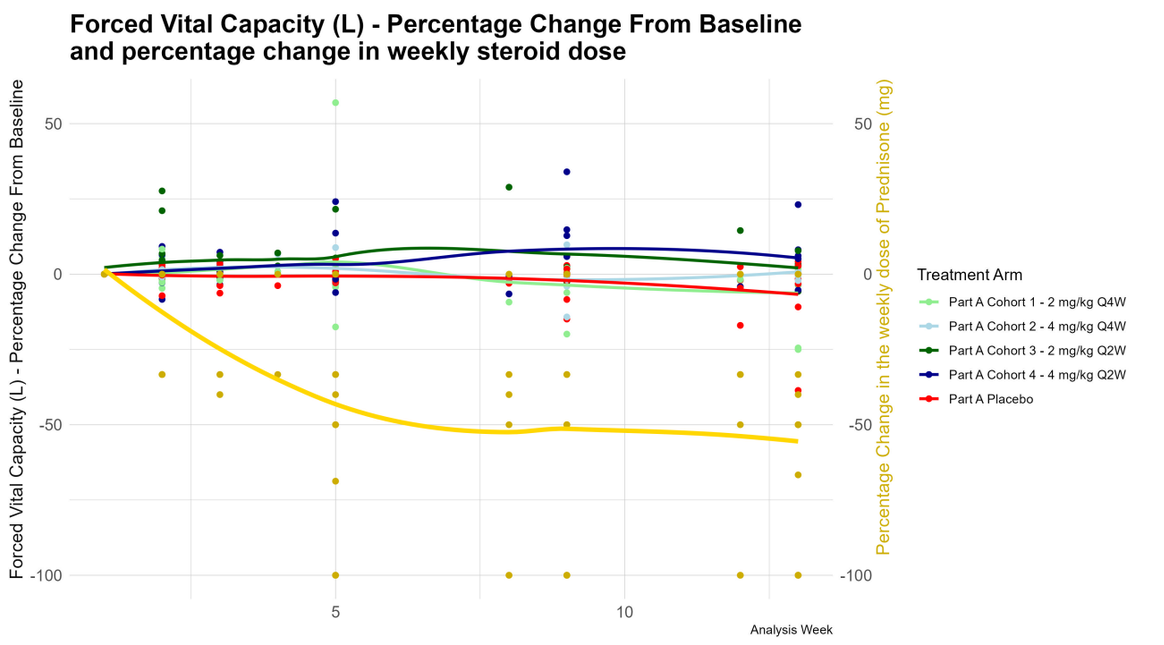
Pulmonary Function	Placebo N=11	2 mg/kg Q4W N=8	4 mg/kg Q4W N=7	2 mg/kg Q2W N=6	4 mg/kg Q2W N=7
Baseline mean FVC % predicted	97.4%	80%	87.7%	79.7%	86%

OCS Characteristics	Placebo N=11	2 mg/kg Q4W N=8	4 mg/kg Q4W N=7	2 mg/kg Q2W N=6	4 mg/kg Q2W N=7
Baseline mean OCS (mg/day)	8.7	9.4	10.4	8.0	10.4
Participants achieving complete OCS withdrawal at Wk 12	4/11 (36%)	2/8 (25%)	4/7 (57%)	0/6 (0%)	1/7 (14.3%)

OCS=Oral corticosteroid

Relationship Between Corticosteroid Taper and Pulmonary Function Stability at Week 12

Although corticosteroid withdrawal occurred in both placebo and active-treatment cohorts, pulmonary stability was more consistently maintained in XTMAB-16-treated participants, whereas placebo-treated participants demonstrated declines in FVC.



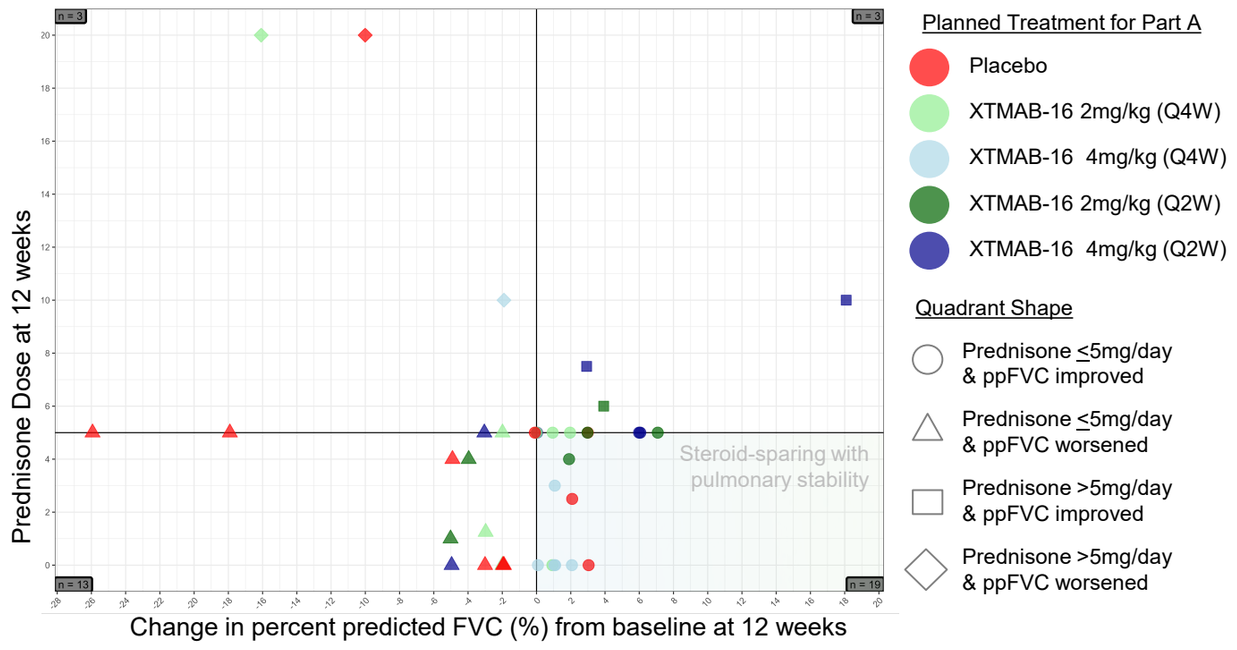


Figure 1. XTMAB-16-201 Part A Patient-level quadrant plot of change in percent predicted FVC (%) and prednisone dose at Week 12; *FVC=Forced Vital Capacity;*

Key Points

During corticosteroid withdrawal, XTMAB-16-treated participants more consistently maintained FVC stability, whereas placebo-treated participants showed FVC declines during tapering. Among evaluated dose regimens, **XTMAB-16 4 mg/kg Q4W demonstrated the most balanced descriptive profile** across corticosteroid reduction, pulmonary stability, exposure, and immunogenicity trends.

Conclusions

Cohort-level analyses supported selection of XTMAB-16 4 mg/kg Q4W for continued development. Because this early-phase study was not powered to demonstrate efficacy, the results should be interpreted as descriptive and hypothesis-generating. Overall, these findings support an integrated assessment of corticosteroid reduction, FVC stability, and treatment context when evaluating steroid-sparing therapies in pulmonary sarcoidosis.

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Future commercial use of XTMAB-16 is contingent upon positive clinical trial results and regulatory approval.