A Phase 2 Study of the Safety, Pharmacokinetics and Efficacy of Anabasum (JBT-101) in Cystic Fibrosis (CF)

James F. Chmiel, M.D., M.P.H., J. Stuart Elborn M.D., Scott Constantine M.S., Barbara White M.D., for the JBT101-CF-001 Investigators

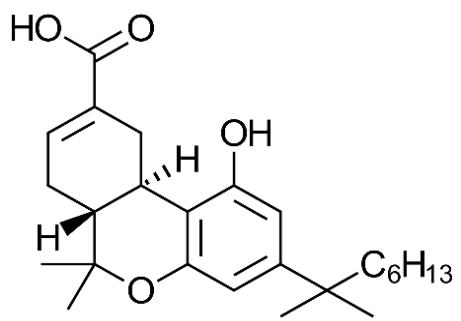
Disclosure of Presenter

- James F. Chmiel, MD, MPH has the following disclosures related to this presentation:
  - Cystic Fibrosis Foundation (Institution, Self)
  - Corbus Pharmaceuticals (Institution)

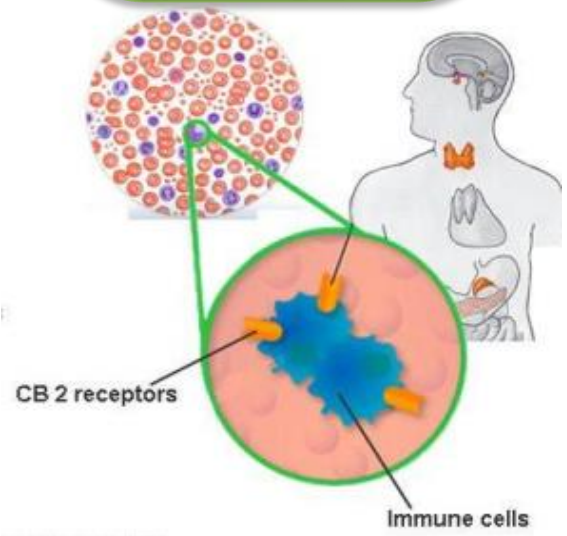
Background

- Cystic fibrosis is characterized by excessive and ineffective innate immune responses, often triggered by infection
- This “hyper-inflammation” contributes to pulmonary exacerbations and tissue destruction
- There is an unmet need for non-immunosuppressive medications to resolve inflammation in CF
- Anabasum or JBT-101 is an oral selective cannabinoid receptor type 2 agonist that activates the resolution phase of innate immune responses, reducing tissue inflammation without immunosuppression

Anabasum



CB2:
resolution receptors in immune system



JBT101-CF-001

A Phase 2 study was done to test safety and tolerability, pharmacokinetics, efficacy, and effects on biomarkers of anabasum in stable patients with CF with FEV1 ≥ 40% predicted

Primary Objective

- Evaluate safety and tolerability
  - Pulmonary exacerbations were an event of special interest

Secondary Objectives

- Evaluate plasma concentrations of anabasum
- Evaluate efficacy using FEV1, lung clearance index, and CFQ-R Respiratory Symptoms score

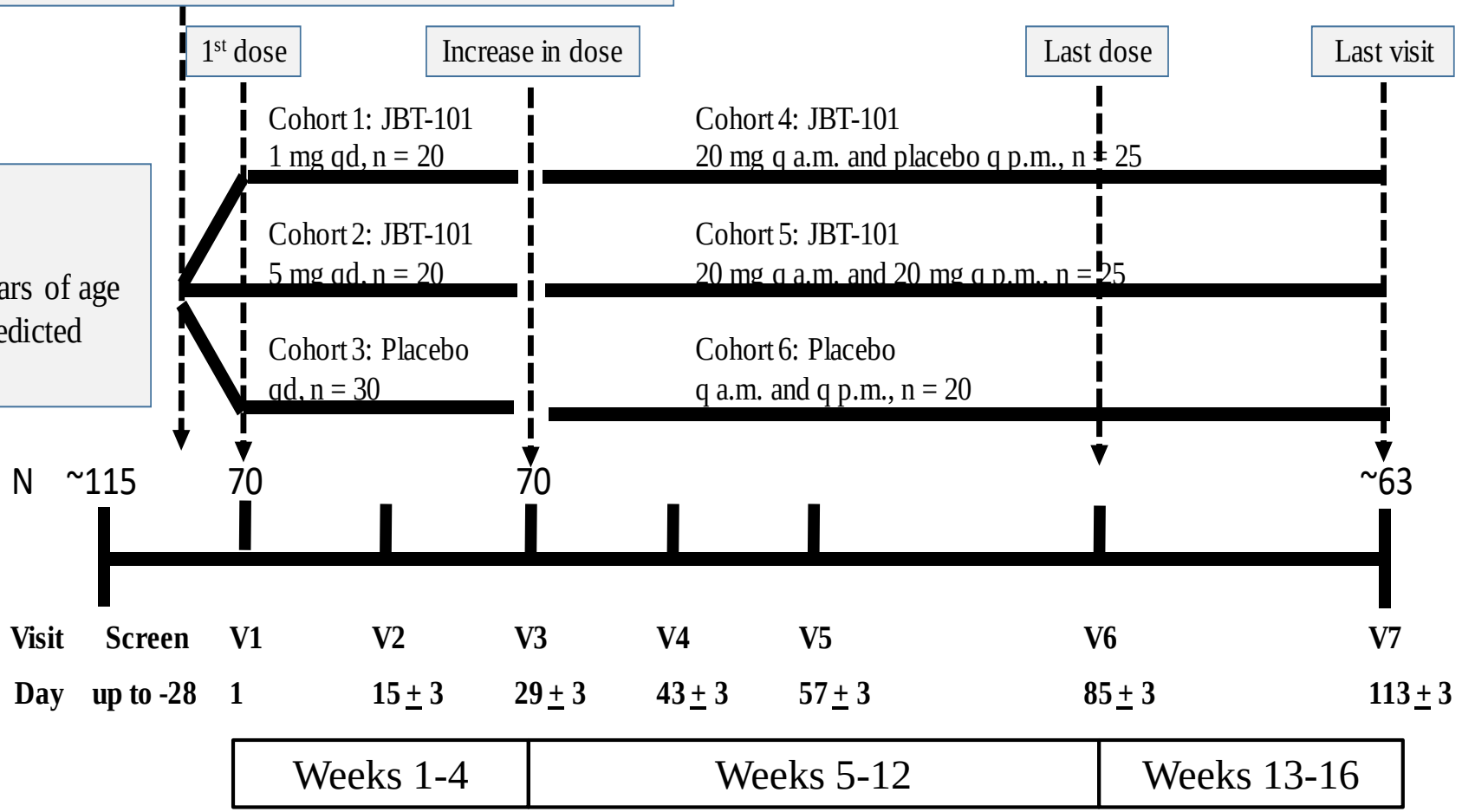
Exploratory Objective

- Evaluate sputum and blood biomarkers of disease activity and inflammation

JBT101-CF-001 Phase 2 Trial Design

Randomization prior to Visit 1
- All subjects randomized 2:2:3 to Cohorts 1, 2, and 3 for Days 1-28
- Cohorts 1 and 2 randomized 1:1 Cohorts 4 and 5 for Days 29-84
- Cohort 3 randomized 1:1:4 to Cohorts 4, 5 and 6 for Days 29-84

Inclusion criteria:
- Cystic fibrosis
- ≥ 18 and <65 years of age
- FEV1 ≥ 40% predicted
- Stable treatment



Baseline Disease Characteristics of Subjects

Characteristic	Weeks 1-4			Weeks 5-12		
	Anabasum 1 mg QD N = 26	Anabasum 5 mg QD N = 24	Placebo N = 35	Anabasum 20 mg QD N = 31	Anabasum 20 mg BID N = 30	Placebo N = 24
Male, %	65.4	50.0	48.6	51.6	50.0	62.5
Caucasian, %	96.2	100	94.3	96.8	96.7	95.8
Age, mean (range)	26.9 (19 -– 52)	28.8 (18 -– 62)	29.2 (18 – 59)	28.5 (18 – 62)	26.8 (19 – 46)	30.2 (18 – 59)
Exacerbations treated with IV antibiotics x 1 yr, N, mean (range)	0.73 (0 – 2)	0.75 (0 – 3)	0.63 (0 – 3)	0.87 (0 – 2)	0.67 (0 – 3)	0.50 (0 – 3)
FEV1 % predicted, mean (range)	65.6 (31.5 – 101.8)	63.1 (29.6 – 89.3)	65.3 (39.2 – 113.3)	64.2 (26.8 – 103.2)	64.0 (31.1 – 98.4)	64.9 (25.7 – 106.8)
CRQ-R Respiratory Symptom Score, mean (range)	65.8 (33.3 – 94.4)	69.9 (16.7 – 100)	71.6 (27.8 – 88.9)	74.4 (27.8 – 100)	66.9 (22.2 – 100)	76.6 (38.9 – 94.4)
Lumacaftor/ ivacaftor, n (%)	7 (26.9)	7 (29.2)	10 (28.6)	7 (22.6)	9 (30.0)	8 (33.3)
Ivacaftor, n (%)	3 (11.5)	0 (0.0)	4 (11.4)	1 (3.2)	5 (16.7)	1 (4.2)

Subjects with Treatment Emergent Adverse Events by Dose

Treatment-emergent Adverse Event (TEAE)	Subjects with TEAEs, n (%)					
	Weeks 1-4			Weeks 5-12		
	Anabasum 1 mg N = 26	Anabasum 5 mg N = 24	Placebo N = 35	Anabasum 20 mg N = 31	Anabasum 20 mg BID N = 30	Placebo N = 24
Any TEAE	14 (53.8)	13 (54.2)	15 (42.9)	21 (67.7)	19 (63.3)	14 (58.3)
Serious TEAEs	1 (3.8)	0	2 (5.7)	3 (9.7)	2 (6.7)	1 (4.2)
Serious TEAEs related to study drug	0	0	0	0	0	0
Severe TEAEs	0	0	1 (2.9)	0	2 (6.7)	1 (4.2)
Serious or severe TEAEs related to study drug	0	0	0	0	0	0
Any related TEAE	3 (11.5)	4 (16.7)	3 (8.6)	8 (25.8)	4 (13.3)	5 (20.8)
Related TEAEs leading to study discontinuation	1 (3.8)	0	1 (2.9)	0	1 (3.3)	0

Mild dry mouth was the only related TEAE that occurred in a higher proportion of anabasum-treated subjects (8/61, 13.1%) vs, placebo-treated subjects (0/0, 0.0%)

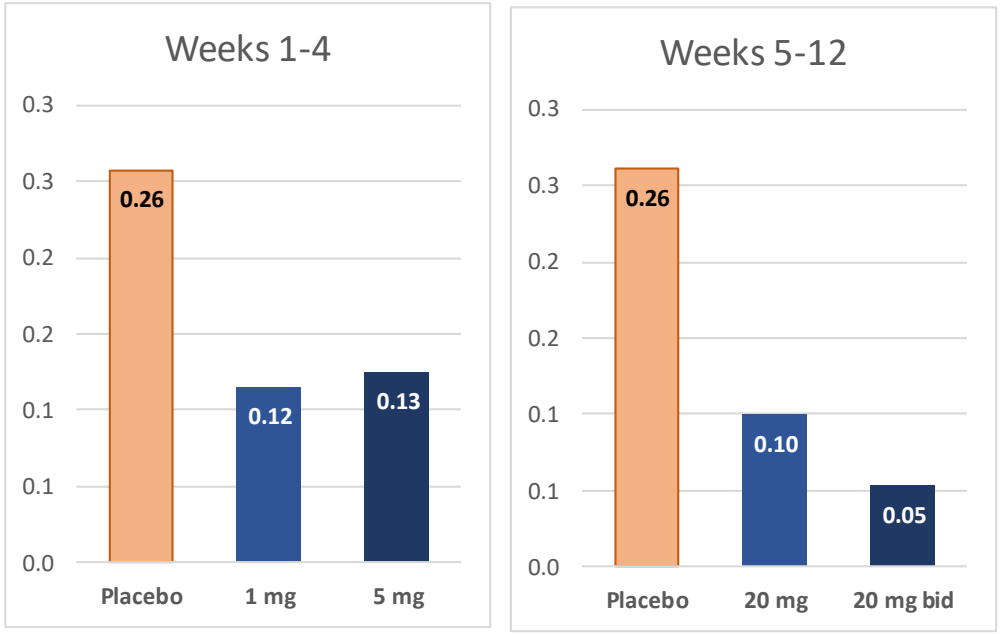
Pulmonary Exacerbations Requiring Treatment with Intravenous Antibiotics

- Pulmonary exacerbation was defined by treatment with new antibiotics for respiratory system or systemic symptoms
- Pulmonary exacerbations requiring treatment with intravenous (IV) antibiotics were captured as an event of special interest
- Assignment to cohort is by onset of symptoms that required antibiotic treatment

Subjects with pulmonary exacerbations post-entry requiring IV antibiotics

Cohort, N dosed in cohort	Subjects, n/N (%)	
	Weeks 1-4	Weeks 5-12
Placebo, N = 35	3 (8.6)	
Anabasum 1 mg, N = 26	1 (3.8)	
Anabasum 5 mg, N = 24	1 (4.2)	
Placebo, N = 23		4 (17.4)
Anabasum 20 mg, N = 30		2 (6.7)
Anabasum 20 mg BID, N = 28		1 (3.6)

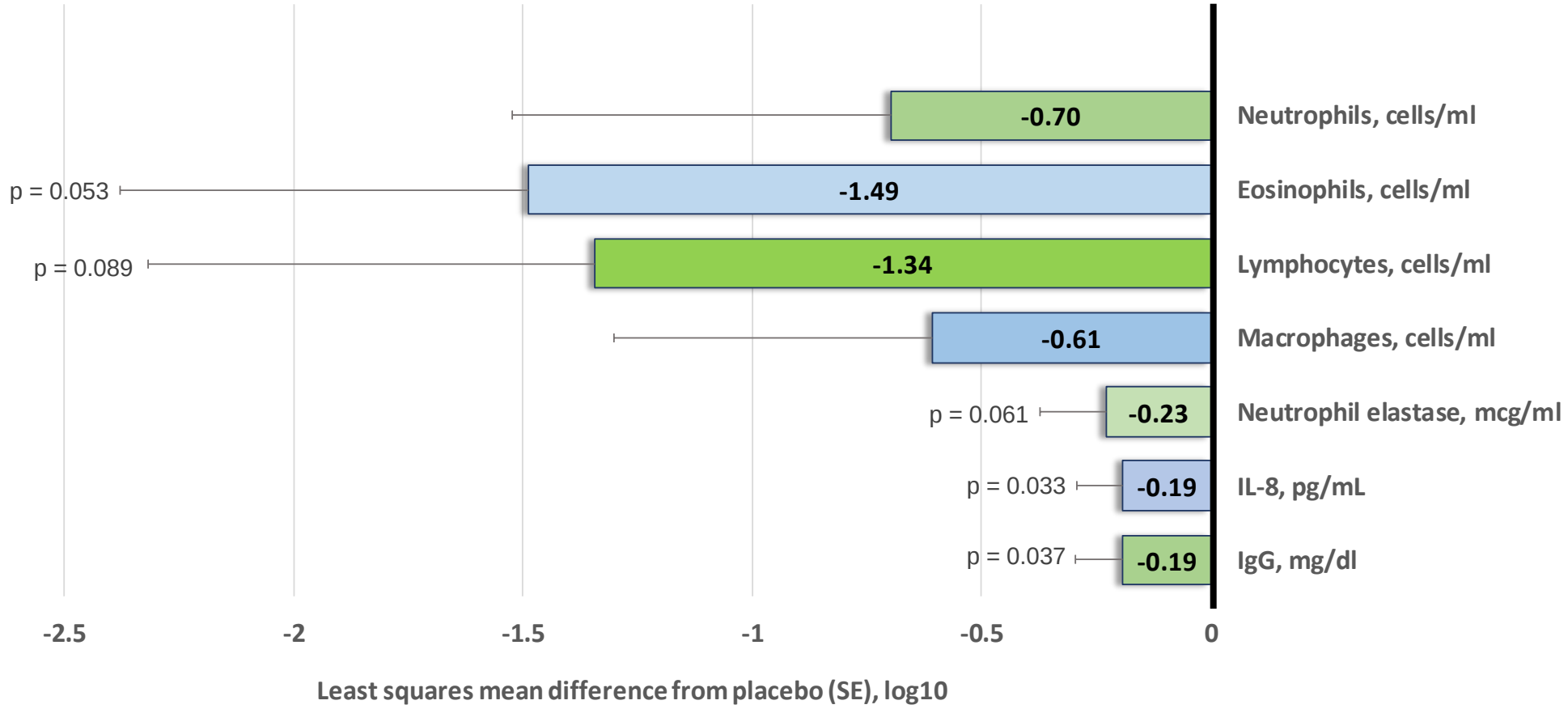
Rate of pulmonary exacerbations requiring IV antibiotics (events per subject per 12 weeks)



Anabasum treatment is associated with a reduction in rate of pulmonary exacerbations requiring IV antibiotics

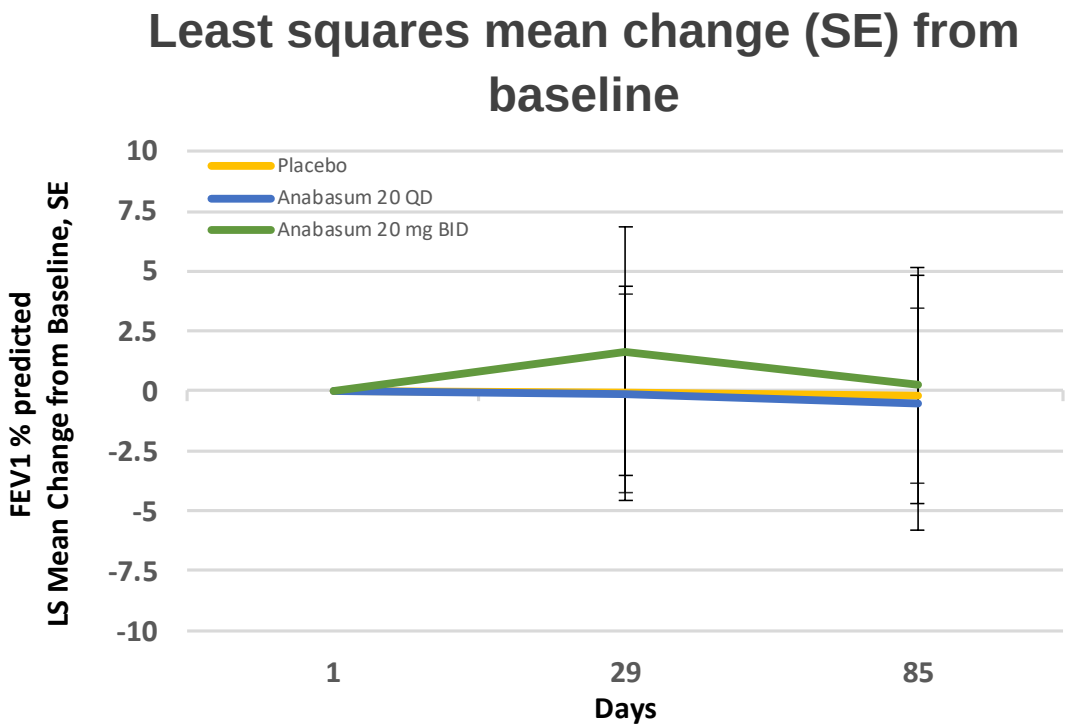
Biomarkers in Sputum

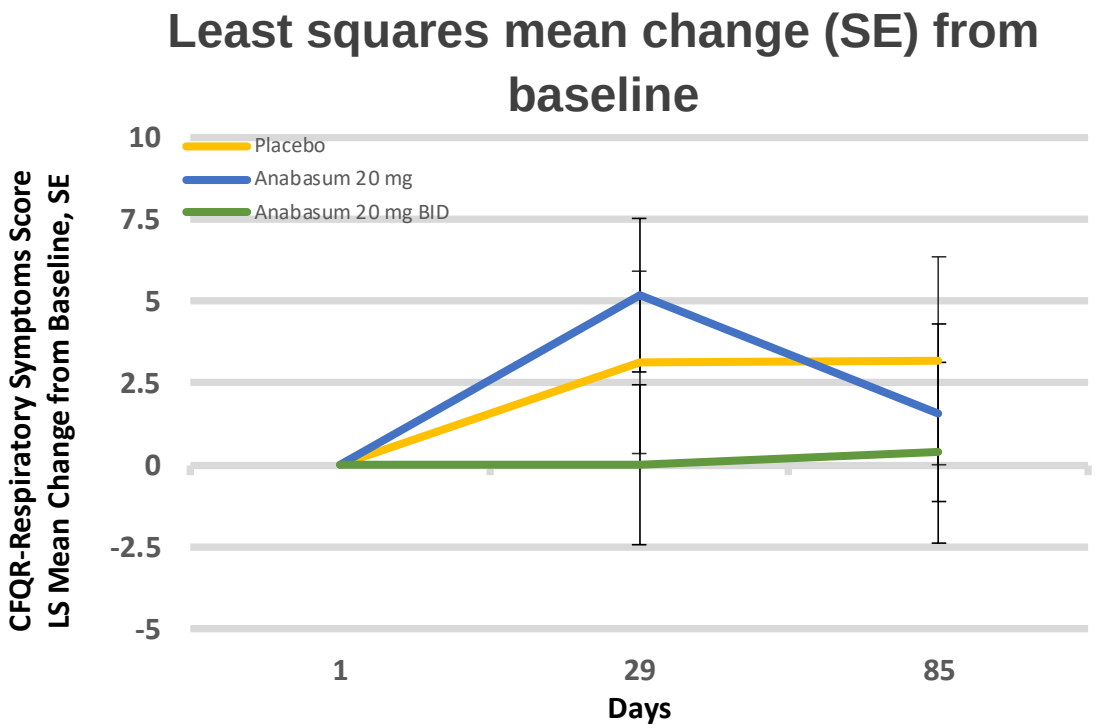
Change from baseline, least squares mean difference (SE) from placebo
Anabasum 20 mg BID compared to placebo (**log^{10}**)



CRP in blood also was reduced, least squares mean difference from placebo, $\log_{10}$ (SE) = -0.15 (0.13), p = 0.124

FEV1 Percent Predicted and CFQ-R Respiratory Symptoms Scores





FEV1 % predicted was stable throughout the study for anabasum and placebo-treated subjects

Summary and Conclusions

Summary

- Pharmacokinetics – plasma concentrations similar to those in healthy volunteers (not shown)
- Safety - no serious or severe TEAEs related to anabasum
- Tolerability - 2 study withdrawals for TEAEs related to anabasum versus 1 related to placebo
- Safety/efficacy - reduction in pulmonary exacerbations
- Biomarkers - reduction in inflammation cells and mediators in sputum

Conclusion

- These data support further clinical development of anabasum for treatment of CF and inform the design of the next clinical trial

Thank You!

- The participants who took part in our Phase 2 study
- The site study teams for their commitment to complete the study
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Investigators and Study Coordinators

Principal Investigator	Study Coordinator	Institution
James Chmiel	Cindy Schaefer Ellen Divoky	Case Western Reserve University
Damian Downey	Jolene Milligan	Queen's University Belfast
Tara Barto	Ellen Edwards Nicolene Schaap	Baylor College of Medicine
Terry Chin	Roxana Flores Cristina Nguyen	Long Beach Memorial
Carla Colombo	Simone Gambazza Arianna Bisogno	University of Milan
Henry Dorkin	Nicholas Fenton Robert Fowler	Harvard Medical School
Allen Dozor	Meighan Gallagher Armando Ramirez	New York Medical College
Olaf Eickmeier	Sandra Müller	Goethe-Universität Frankfurt am Main
Patrick Flume	Beth Costa Jill Spears	Medical University of South Carolina
Sabiha Hussain	Halina Malveaux	Robert Wood Johnson Medical School
Raksha Jain	Christopher Tran Ashley Keller	University of Texas Southwestern

Principal Investigator	Study Coordinator	Institution
Larry Johnson	Kathleen Hicks	University of Arkansas for Medical Sciences
Steven Lommatzsch	Marion Jones Caroline Jones	University of Colorado
Henryk Mazurek	Marzena Czapka Barbara Szlaga	Institute of Tuberculosis and Lung Diseases
Giovanna Pizzamiglio	Martina Contarini	University of Milan
Marta Rachel	Magdalena Rachel	University of Rzeszow
Ewa Sapiejka	Monika Wencel	Poznań University of Medical Sciences
Wojciech Skorupa	Katarzyna Lewandowska	National Institute of Tuberculosis and Lung Diseases
Sivagurunathan Sutharsan	Sarah Terjung Tanja Schmies Nadine Zmudzinski Stephanie Oelscher	Universitätsmedizin Essen Ruhrlandklinik
Janice Wang	Kathleen O'Connor Stacey Jackson	North Shore LIJ Health System
Lael Yonker	Hanna Pinsky Caitlin Doolittle	Harvard Medical School