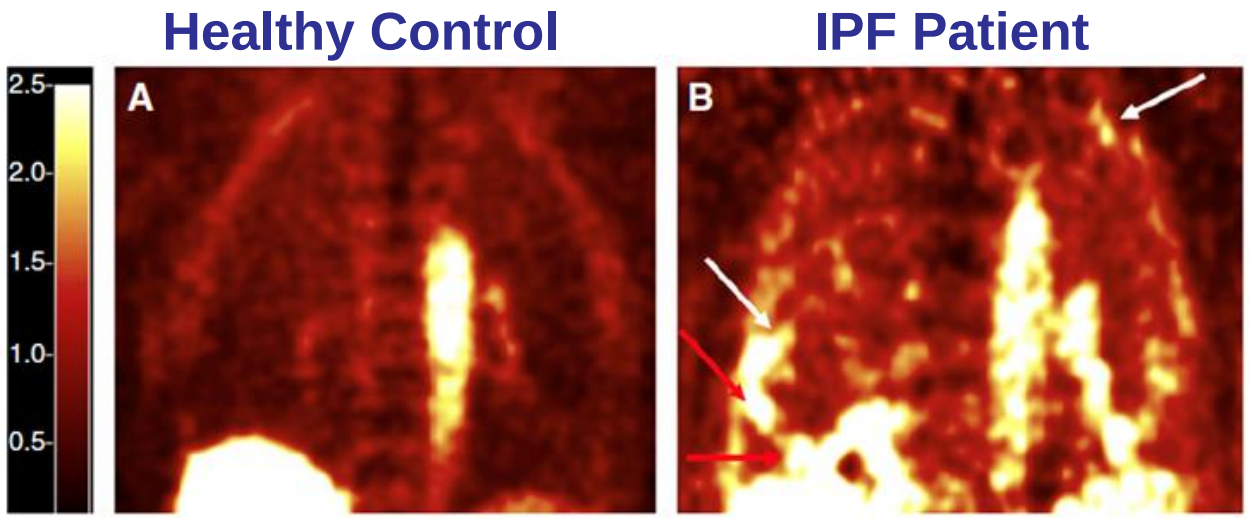
Phase 2a Collagen PET Study of Bexotegrast Topline Results

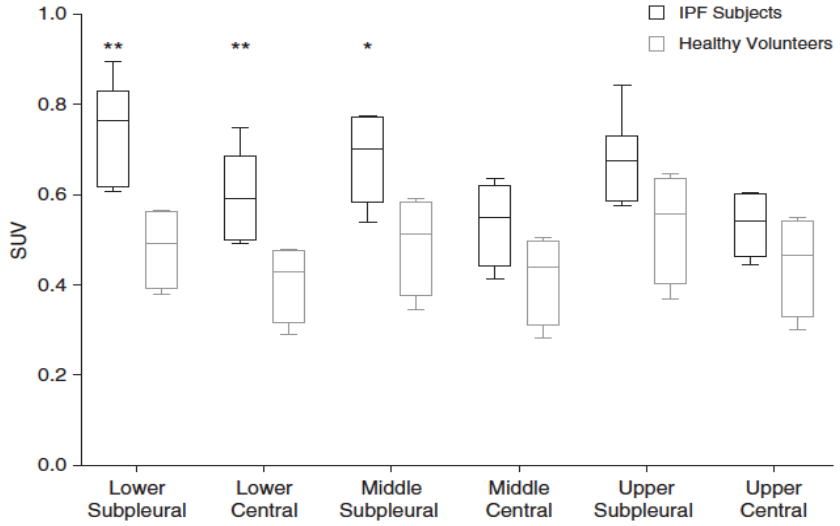
MAY 2024

Quantification of Collagen in the Lung using PET Imaging

- ^{68}Ga-CBP8 is a PET probe that binds type I collagen with high specificity[1]
- IPF patients have higher standardized uptake values (SUV) compared to healthy volunteers[2]
- The probe binds to both freshly synthesized and mature collagen
- ^{68}Ga-CBP8 previously detected treatment response to anti-fibrotic therapy in a mouse model of pulmonary fibrosis[1]



Note: Uptake in the heart and vasculature as well as in the liver is to be expected based on the probe's half-life and biodistribution



^{68}GA-CBP8: peptide-based collagen binding probe 8 tagged with Gallium-68 radioisotope
SUV: standardized uptake value; SUV measures the ratio of the uptake of a radiotracer in tissue
[1]Désogere et al, Sci Trans Med. 2017; [2]Montesi Am J Respir Crit Care Med 200:2 2019

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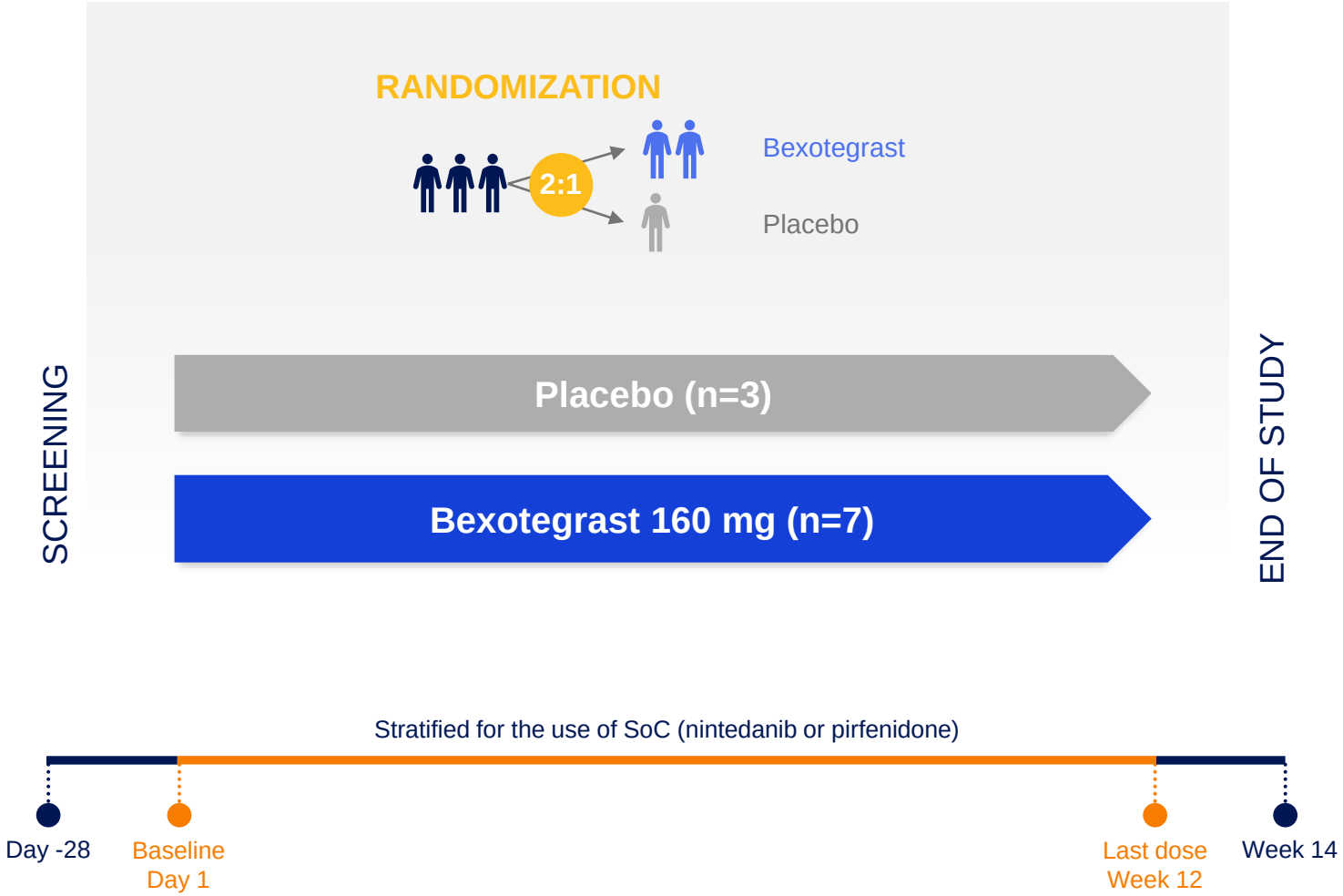
Design and Objectives

Quantification of Type 1 Collagen in the Lung using PET Imaging



PRIMARY AND SECONDARY ENDPOINTS

- Change in whole lung standardized uptake value (SUV) of ^{68}GA-CBP8 (type-1 collagen probe)
- Safety and tolerability

EXPLORATORY ENDPOINTS

- Changes in FVC and FVCpp
- Change in VAS for cough severity
- Changes in fibrosis biomarkers

INCLUSION CRITERIA

- Diagnosis of IPF (within 8 years)
- FVC percent predicted ≥ 45%
- DLCO ≥ 30%
- Estimated glomerular filtration rate ≥ 50mL/min

FVC: forced vital capacity, FVCpp: forced vital capacity percent predicted; SoC = Standard of care; VAS: visual analog scale
^{68}GA-CBP8: peptide-based collagen binding probe 8 tagged with Gallium-68 radioisotope

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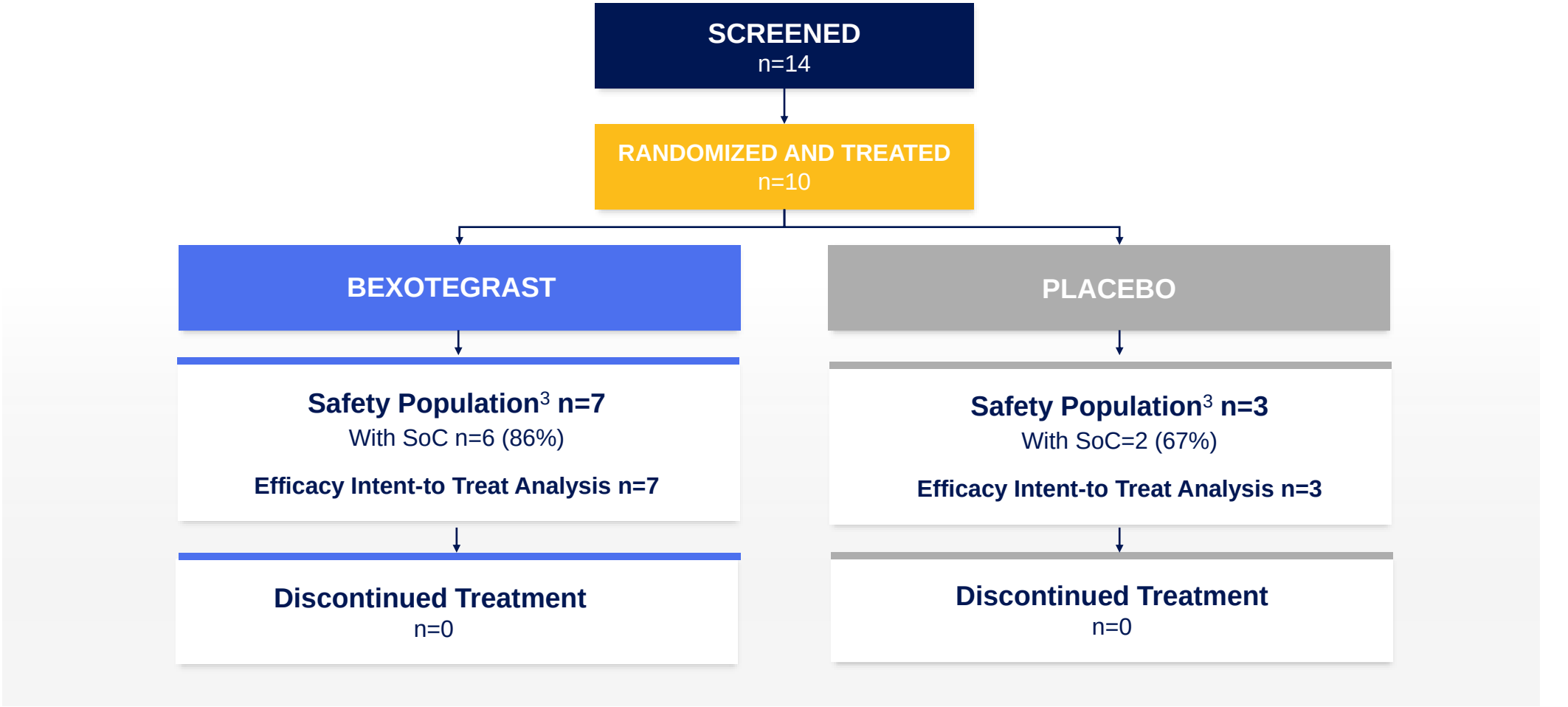
Participant Disposition



SoC = Standard of care

Baseline Demographics

Characteristic	Bexotegrast 160mg (n=7)	Placebo (n=3)
Male sex, n (%)	6 (85.7)	3 (100)
Age (yr), median (IQR)	70 (64 – 72)	74 (72 – 76)
Weight (kg), median (IQR)	81.2 (79.0 – 88.5)	78.0 (77.6 – 85.3)
BMI (kg/m^2), median (IQR)	25.7 (23.7 – 30.4)	26.4 (24.0 – 30.3)
Race, n (%)		
White	6 (85.7)	3 (100)
Black	0	0
Asian	1 (14.3)	0
Other / Not Reported / Unknown	0	0

IQR = Interquartile range (Q1, Q3); BMI = Body Mass Index

Baseline Disease Characteristics

Characteristic	Bexotegrast 160mg (n=7)	Placebo (n=3)
Time since diagnosis of IPF (mo), median (IQR)	50 (22 – 70)	9 (7 – 72)
Standard of Care Use, n (%)		
Nintedanib	5 (71.4)	1 (33.3)
Pirfenidone	1 (14.3)	1 (33.3)
Duration of Standard of Care at Randomization (mo), median (IQR)	34.5 (17 – 55)	40.0 (6 – 74)
FVC		
Absolute (mL), median (IQR)	2,750 (2,400 – 3,080)	2,250 (1,700 – 2,640)
Percent of predicted value (%), median (IQR)	66.0 (56.0 - 92.0)	58.0 (49.0 - 69.0)
Percent of predicted DLCO, corrected for the hemoglobin level (%), median (IQR)	49 (40.0 – 58.0)	43 (36.5 – 45.0)
GAP Stage, n (%)		
GAP Stage I	4 (57.1)	0
GAP Stage II	2 (28.6)	2 (66.7)
GAP Stage III	1 (14.3)	1 (33.3)

GAP Index score derived from Gender, Age, FVC, % Predicted and DLCO, % Predicted.
IQR = Interquartile range (Q1, Q3); DLCO= Diffusing Capacity for Carbon Monoxide; FVC = Forced Vital Capacity

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Key Findings

Bexotegrast cohort showed reduced PET ligand standardized uptake values (SUV) compared to placebo

- Reduction in SUV post-treatment indicates less total lung collagen, suggesting potential reversal of fibrosis
- Additional support of bexotegrast's antifibrotic mechanism of action

No new safety concerns identified over 12 weeks of treatment

- Most adverse events were mild with no study discontinuations observed
- No SAEs observed

Bexotegrast cohort showed improved lung function and decreased cough severity across all timepoints

- Positive FVC change compared to decline in placebo across all time points
- Decrease in cough severity observed at all time points compared to worsening seen on placebo

Biomarker results further support bexotegrast's antifibrotic mechanism

- Bexotegrast cohort showed reduced circulating PRO-C3 and Integrin Beta-6 levels at Weeks 4 and 12 compared to placebo

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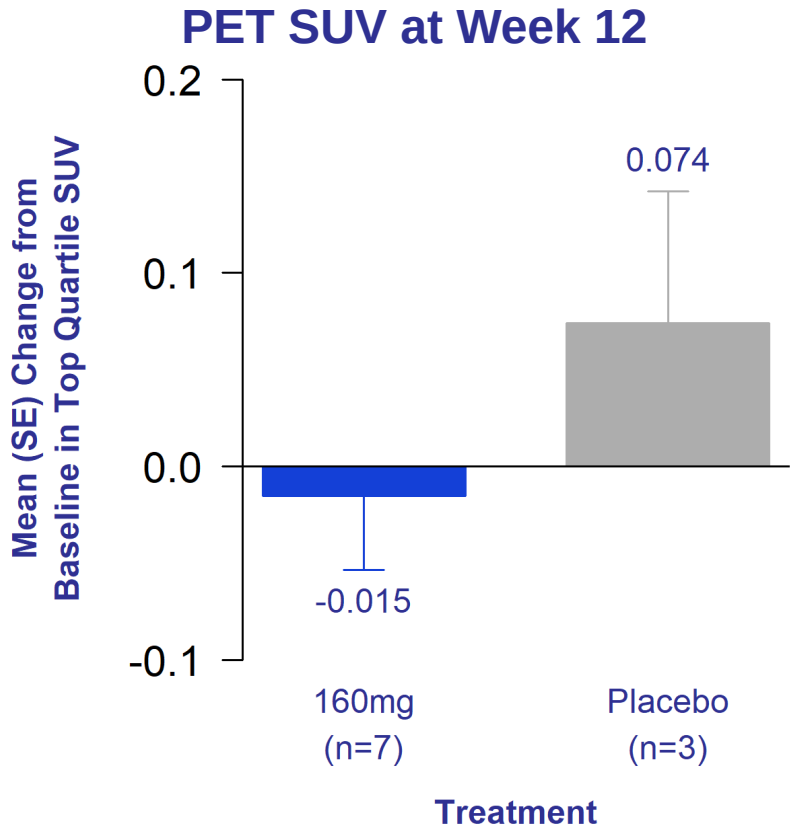
Safety Overview

- No serious adverse events (SAEs) occurred in the trial
- Most treatment emergent adverse events (TEAEs) were mild in nature
- No study discontinuations occurred
- Bexotegrast continues to demonstrate a favorable safety and tolerability profile in the IPF patient population

Bexotegrast Showed Reduced PET Tracer SUV Compared to Placebo

ITT Population



Reduction in post-treatment SUV indicates a reduction in total lung collagen

Reduced post-treatment total lung collagen suggests potential reversal of fibrosis

[2] Montessi AJRCCM 200:2 2019

SUV = Standardized Uptake Value; SE = Standard Error; ^{68}GA-CBP8: peptide-based collagen binding probe 8 tagged with Gallium-68 radioisotope
SUV measures the ratio of the uptake of a radiotracer in tissue; Top quartile SUV is the mean of SUVs within the top quartile for each lung section; Whole lung is the average of the left and right lungs

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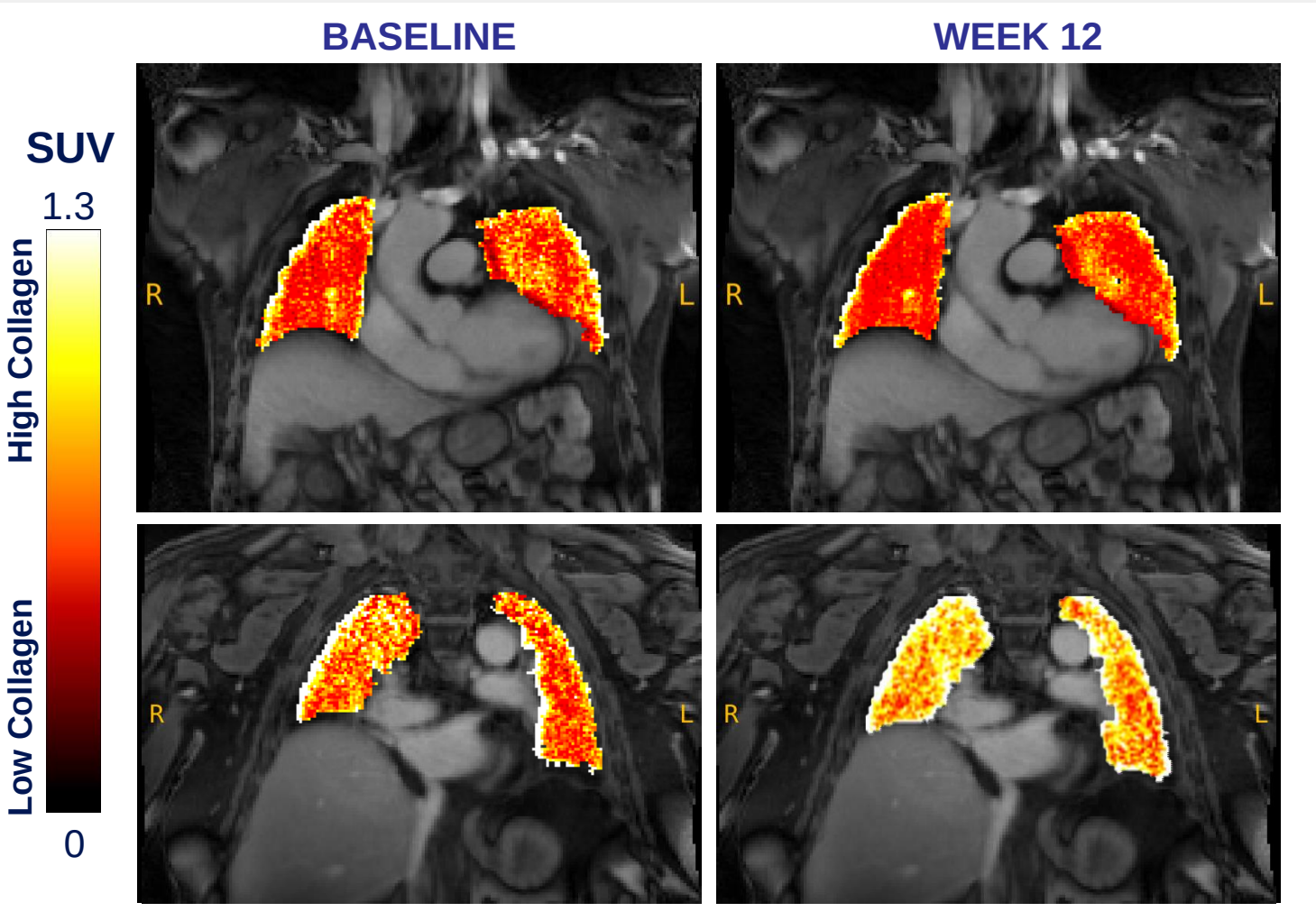
Clearly Visible Reduction of Total Lung Collagen



PARTICIPANT A

- Bexotegrast 160 mg for 12 weeks
- Decrease in SUV_{Q4}, -0.17 (-15.5%)
- Improvement in FVC, 130 mL

PARTICIPANT B

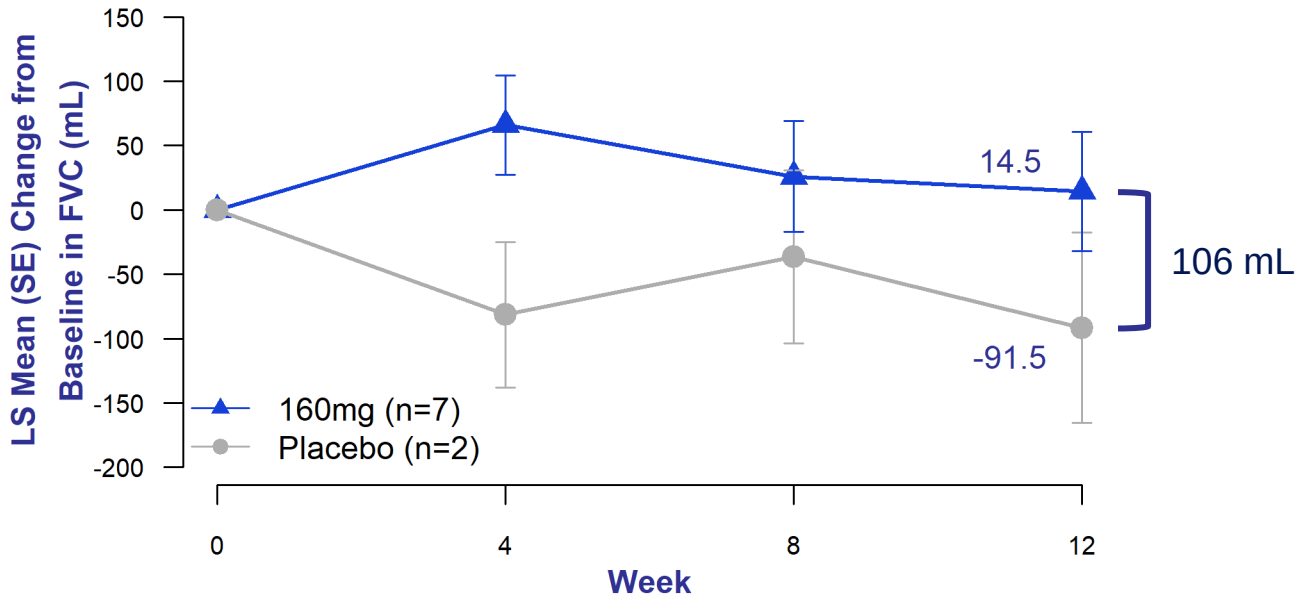
- Placebo for 12 weeks
- Increase in SUV_{Q4}, 0.21 (18.4%)
- Decline in FVC, -180 mL

SUV = Standardized Uptake Value; SUV_{Q4}: top quartile SUV; 68GA-CBP8: peptide-based collagen binding probe 8 tagged with Gallium-68 radioisotope
FVC: forced vital capacity; VAS; visual assessment scale for cough severity (0-100)
SUV measures the ratio of the uptake of a radiotracer in tissue and quantifies the amount of type I collagen detected

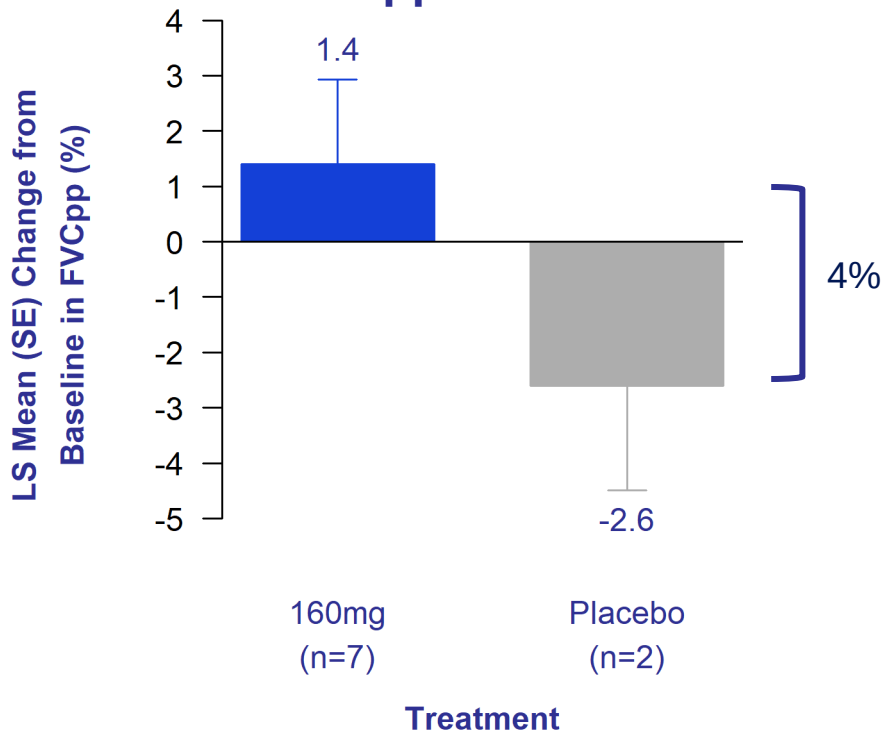
Bexotegrast Showed Improved Lung Function Compared to Placebo

ITT Population

FVC



FVCpp at Week 12



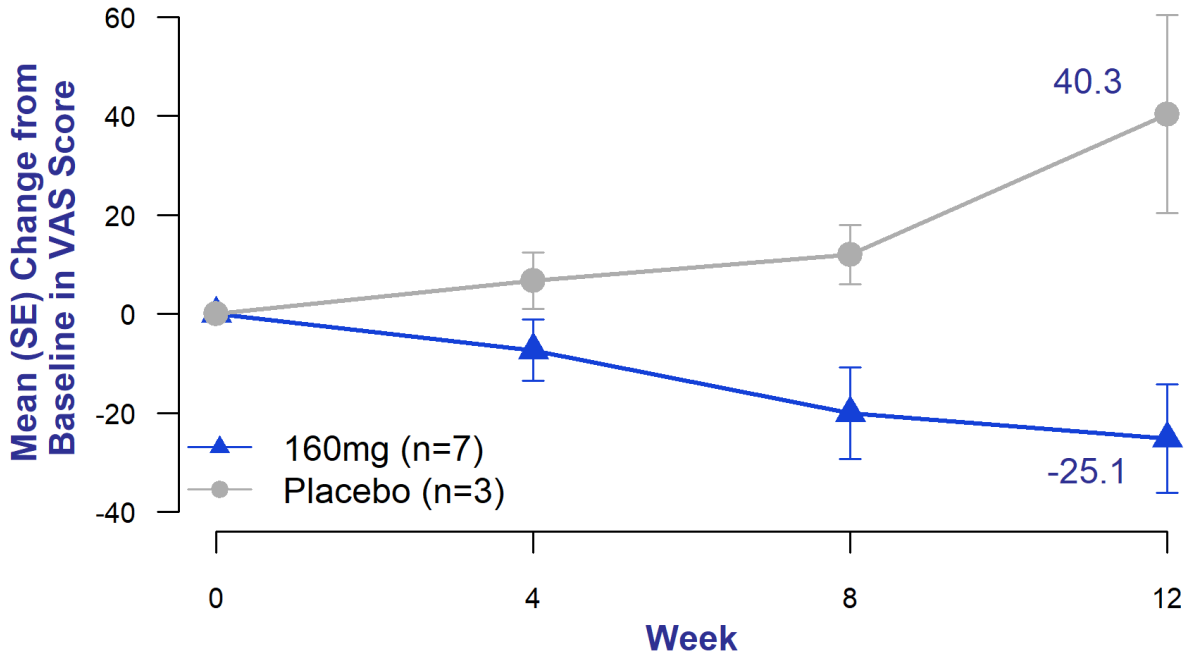
Bexotegrast cohort maintained a clear separation from placebo at all time points

Note: One placebo subject did not have FVC that meet quality standards per ATS guidelines at Weeks 4, 8 and 12
LS = Least Squares; SE = Standard Error; FVC = Forced Vital Capacity; FVCpp = Forced Vital Capacity Percent Predicted

Bexotegrast Showed Decreased Cough Severity Compared to Placebo

ITT Population

Cough Severity Over 12 Weeks of Treatment

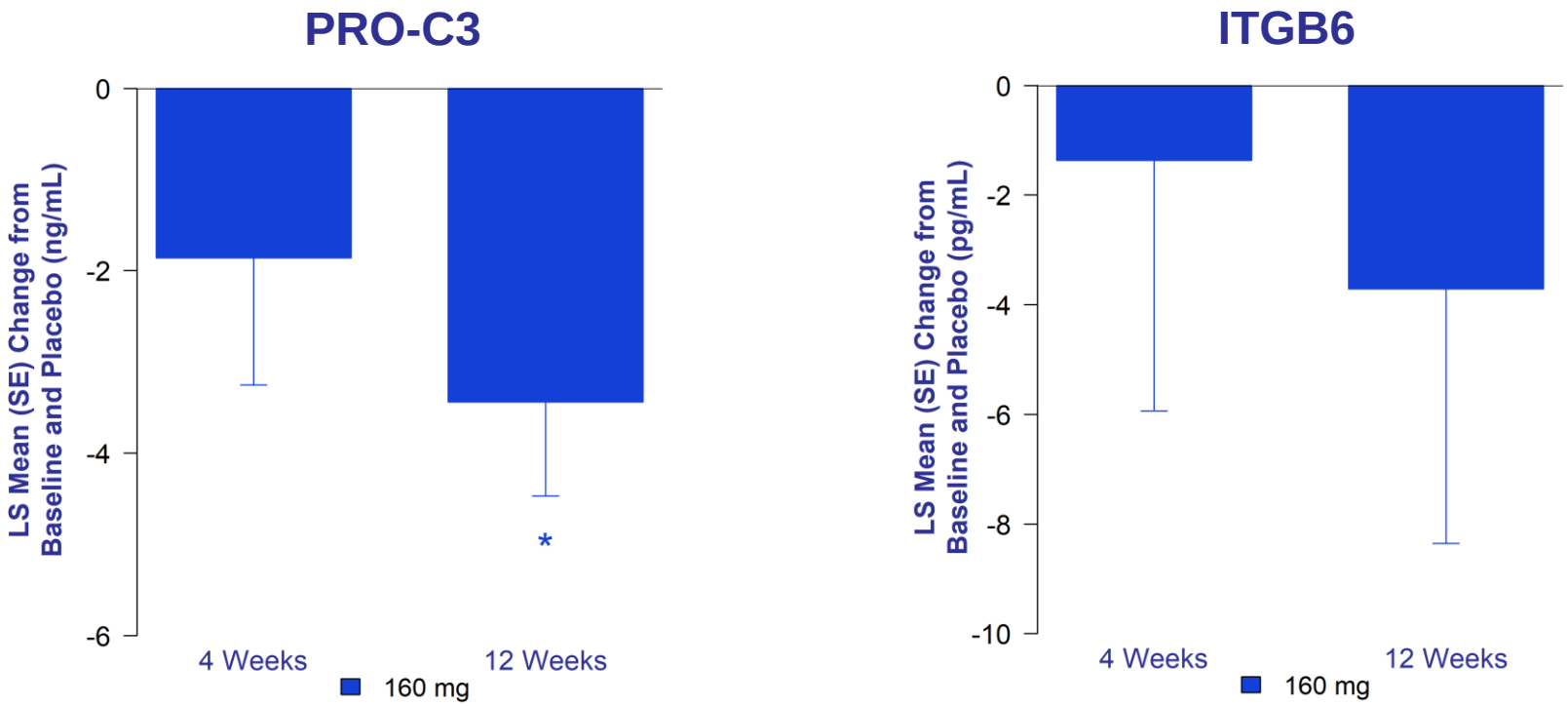


Bexotegrast cohort experienced decreased cough severity across all timepoints compared to increased severity on placebo

EOT: end of treatment; SE: standard error; VAS = Visual Analog Scale
Cough VAS measures patient reported cough severity over last 2 weeks on scale of 0-100 mm

Bexotegrast Showed Reduced Fibrosis Biomarkers Compared to Placebo

ITT Population



* $p < 0.05$ vs placebo

PRO-C3 has been shown to be elevated in patients with IPF and associated with progressive disease[3]

Elevated ITGB6 plasma levels have been shown to be associated with ILD progression[4]

[3]Respir Res. 2019 Jul 12;20(1):148. doi: 10.1186/s12931-019-1118-7; [4]Lancet Respir Med. 2022 Jun;10(6):593-602. doi: 10.1016/S2213-2600(21)00503-8. Epub 2022 Jan 18

ITGB6: Integrin Beta 6; LS = Least Squares; PRO-C3 = Type III Collagen Synthesis Neoepitope; SE = Standard Error

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Bexotegrast – Demonstrated Antifibrotic activity

- Bexotegrast continues to demonstrate antifibrotic activity as assessed using a novel PET tracer which measures total lung collagen, and with established serum biomarkers of fibrosis and ILD progression
- PET results build upon previous evidence of Bexotegrast's antifibrotic mechanism of action using quantitative lung imaging
- Bexotegrast cohort showed improvements in lung function and decreases in cough severity across all time points compared to placebo
- Bexotegrast continues to demonstrate a favorable safety and tolerability profile in the IPF patient population
- Bexotegrast 160 and 320 mg are currently being evaluated in a global Phase 2b/3 study

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