United Therapeutics
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United Therapeutics Corporation
Phase 3 *TETON-2* Results Webcast

SEPTEMBER 28, 2025

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INTRODUCTION

Today's Speakers

Dr. Leigh Peterson

Executive Vice President,
Product Development and
Xenotransplantation

Dr. Steve Nathan

Schar Chair, Advanced Lung Disease and Lung Transplant Program, Inova Fairfax Hospital & Chair of the *TETON* Steering Committee

Dr. Peter Smith

Senior Vice President,
Product Development and
Lead for the Global *TETON* Program

Dr. C.Q. Deng

Senior Vice President, Biostatistics, Statistical Programming & Data Management

Dr. Leigh Peterson

EVP, PRODUCT DEVELOPMENT AND XENOTRANSPLANTATION

TETON-2 RESULTS

TETON-2 Headline Conclusions

1

The study met its primary endpoint of change from baseline in absolute FVC at week 52

2

The study also met statistical significance for several key secondary efficacy endpoints, such as time to first clinical worsening, percent predicted FVC, KBILD and DLCO

3

Nebulized Tyvaso (inhaled treprostinil) was well tolerated, and the safety profile was consistent with previous inhaled treprostinil studies and known prostacyclin-related adverse events

The use of Tyvaso (inhaled treprostinil) for IPF is an investigational use and has not been approved by the FDA

Dr. Peter Smith

SVP, PRODUCT DEVELOPMENT AND LEAD FOR THE GLOBAL TETON PROGRAM

TETON DESIGN

TETON 2 Study Design[1]

PRIMARY ENDPOINT

Change in absolute FVC[2] from baseline to week 52

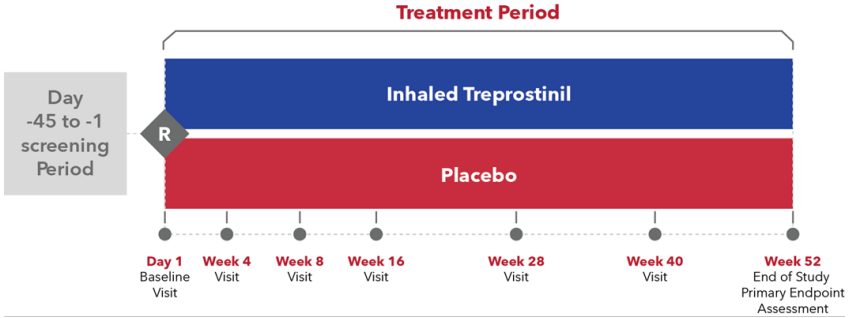
SECONDARY ENDPOINTS

Time to clinical worsening event[3]
Time to first acute exacerbation of IPF[4]
Overall survival at week 52
Percent predicted FVC at week 52
K-BILD[5] score at week 52
DLCO[6] at week 52

SAFETY ENDPOINTS

Adverse events & serious adverse events
Clinical laboratory parameters
Vital signs[7]

STUDY VISIT SCHEDULE



1. https://clinicaltrials.gov/study/NCT05255991. 2. FVC = forced vital capacity. 3. Time to clinical worsening is determined to be the first occurrence of any of the following: death (all causes); respiratory-related hospitalization; or ≥ 10% relative decline in % predicted FVC. 4. IPF = idiopathic pulmonary fibrosis. 5. K-BILD = the King's Brief Interstitial Lung Disease (KBILD) questionnaire, Patel AS, Siegert RJ, Brignall K, et al. The development and validation of the King's Brief Interstitial Lung Disease (K-BILD) health status questionnaire. Thorax. 2012;67(9):804-8106. DLCO = diffusing capacity of the lung for carbon monoxide. 7. Vital signs include saturation of peripheral capillary oxygenation (SpO2) and12-lead electrocardiograms (ECGs).

TETON DESIGN

TETON 2 Study Design[1]

SELECTED KEY INCLUSION CRITERIA

Age 40+

FVC[2] ≥ 45% predicted

If on pirfenidone or nintedanib:

stable dose for ≥ 30 days prior to baseline

Diagnosis of IPF[3,4]

HRCT[5] within the last 12 months[6]

SELECTED KEY EXCLUSION CRITERIA

Primary obstructive disease, FEV_1[7]/FVC < 0.70

>10 L/min of supplemental oxygen use at baseline

Use of PAH[8] agents 60 days prior to baseline[9]

IPF exacerbations or infections[10]

1. https://clinicaltrials.gov/study/NCT05255991. 2. FVC = forced vital capacity. 3. IPF = idiopathic pulmonary fibrosis. 4. diagnosis must be based on the 2018 ATS/ERS/JRS/ALAT Clinical Practice Guidelines, Raghu, G., et al. (2018). Diagnosis of idiopathic pulmonary fibrosis. An official ATS/ERS/JRS/ALAT clinical practice guideline. American Journal of Respiratory and Critical Care Medicine, 198 (5), e44–e68. https://doi.org/10.1164/rccm.201807-1255ST. 5. HRCT = high-resolution computed tomography. 6. HRCT must be consistent with usual interstitial pneumonia and confirmed by a central reader. 7. FEV_1 = forced expiratory volume in one second, a key metric from spirometry that measures how much air a person can forcefully exhale in the first second after taking a deep breath. 8. PAH = pulmonary arterial hypertension. 9. The subject must not receive any PAH-approved therapy, including prostacyclin therapy (epoprostenol, treprostinil, iloprost, or beraprost; except for acute vasoreactivity testing), IP receptor agonists (selexipag), endothelin receptor antagonists, phosphodiesterase type 5 inhibitors (PDE5-Is), or soluble guanylate cyclase stimulators within 60 days prior to baseline. 10. Any IPF exacerbation, active pulmonary infection, or upper respiratory infection ≤30 days prior to baseline.

TETON BASELINE

TETON-2 Baseline Characteristics Balanced Between Treatment Groups

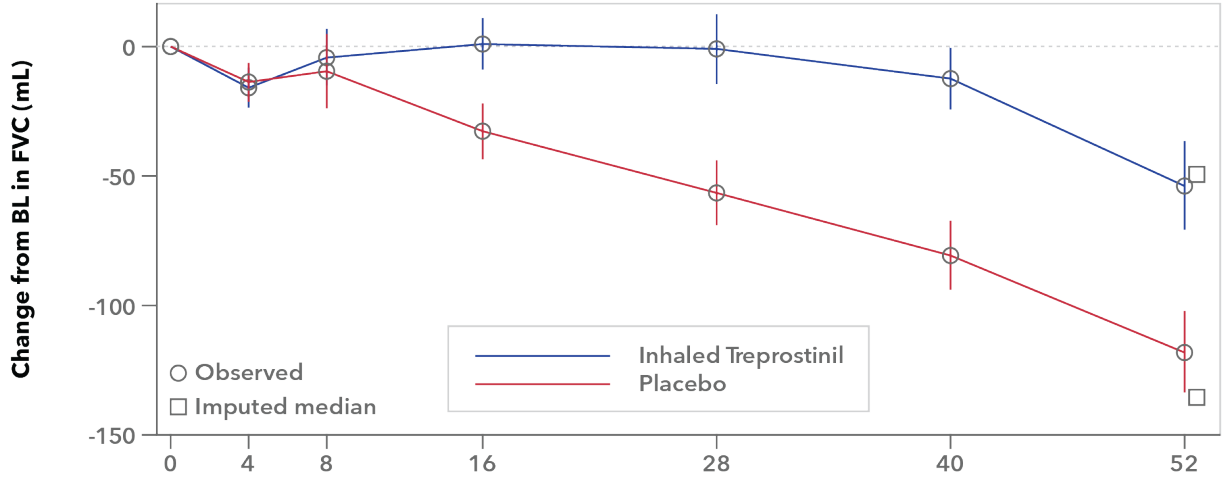
	Inhaled Treprostinil (n=298)	Placebo (n=295)
Age (yrs)	71.9	71.6
Male %	79.9%	80.3%
Female %	20.1%	19.7%
Years since diagnosis	4.0	3.7
FVC (mL), mean	2683.7	2708.3
FVC (% predicted), mean	76.4%	77.2%
DLCO (% predicted), mean	47.1	49.9
FEV1/FVC Ratio, mean	0.81	0.81
Supplemental O2 Usage, %	11.4%	14.6%
No Background Therapy, n (%)	73 (24.5%)	73 (24.7%)
Nintedanib, n (%)	105 (35.2%)	109 (36.9%)
Pirfenidone, n (%)	120 (40.3%)	113 (38.3%)

Dr. Steve Nathan

SCHAR CHAIR, ADVANCED LUNG DISEASE AND LUNG TRANSPLANT PROGRAM, INOVA FAIRFAX HOSIPITAL & CHAIR OF THE TETON STEERING COMMITTEE

TETON-2 RESULTS

Primary Endpoint
Change from Baseline in Absolute FVC at 52 Weeks



No. of Subjects							
Inhaled Treprostinil	298	271	253	235	232	212	203
Placebo	295	259	255	251	238	226	212

95.6 mL*
(95% CI, 52.2, 139.0)
P<0.0001

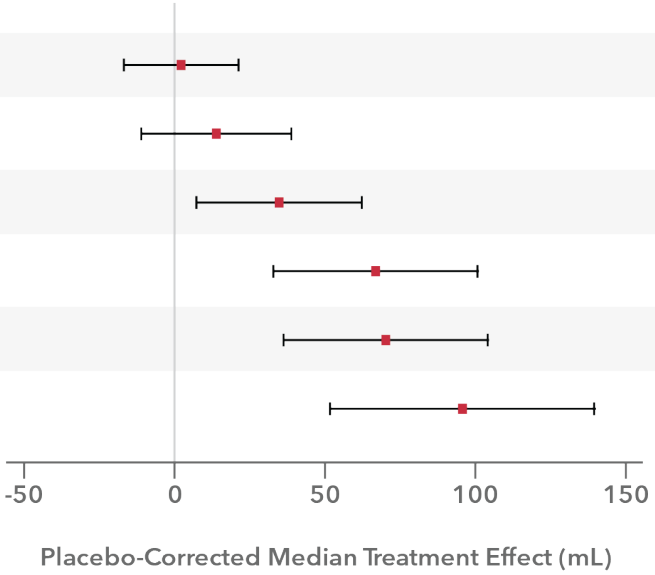
*(H-L estimate)

Hodges-Lehmann estimate and non-parametric aligned stratified rank Wilcoxon test

TETON-2 RESULTS

Primary Endpoint
TETON Forest Plot of FVC by Visit

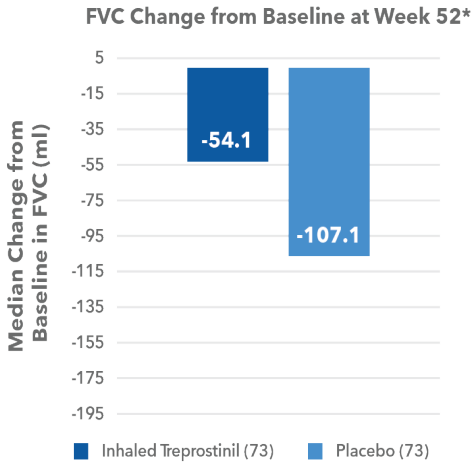
Study Visits	H-L Est.	95% CI
Week 4	1.9	(-17.3, 21.2)
Week 8	13.8	(-10.9, 38.5)
Week 16	34.5	(7.2, 61.8)
Week 28	66.5	(32.5, 100.4)
Week 40	70.2	(36.1, 104.3)
Week 52	95.6	(52.2, 139)



TETON-2 RESULTS

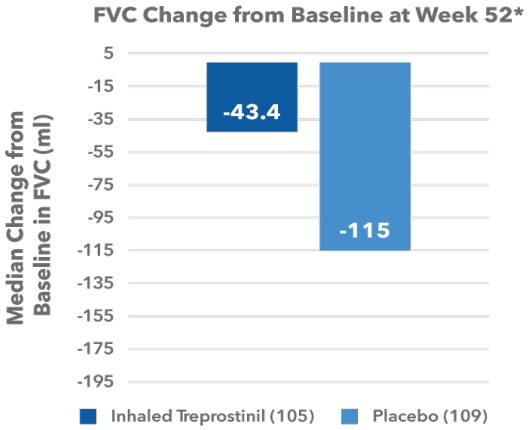
Change by Background Therapy

No Background Therapy



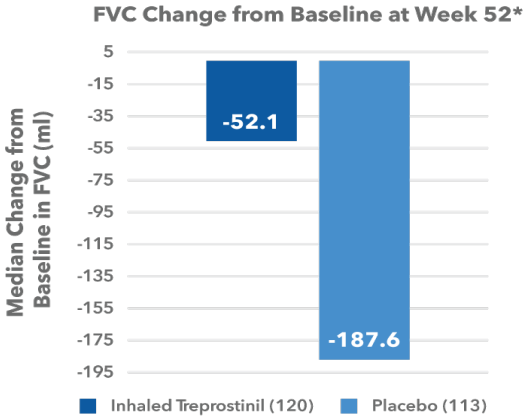
43.9 mL (H-L estimate)
(95% CI, -45.0, 132.8);
P=0.3329

Background Nintedanib



97.6 mL (H-L estimate)
(95% CI, 26.1, 169.2);
P=0.0075

Background Pirfenidone



127.9 mL (H-L estimate)
(95% CI, 58.8, 196.9);
P=0.0003

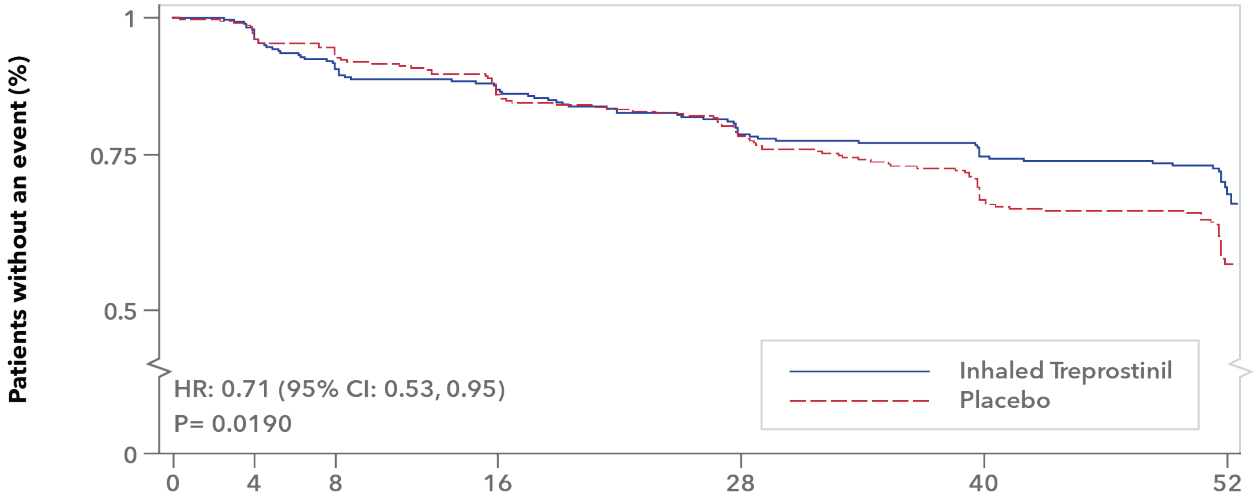
*Imputed Medians

TETON-2 RESULTS

Secondary Endpoints
Time to First Clinical Worsening Event

Inhaled treprostinil resulted in a **29%** reduction in risk of clinical worsening compared to placebo (cox-regression: P=0.0190)

81 (27.2%) inhaled treprostinil and **115 (39%)** placebo patients experienced clinical worsening (chi-square: P=0.0023)



No. at Risk							
Inhaled Treprostinil	298	286	261	242	215	198	135
Placebo	295	285	271	249	225	198	130

TETON-2 RESULTS

Secondary Endpoints
Summary of First Clinical Worsening Events

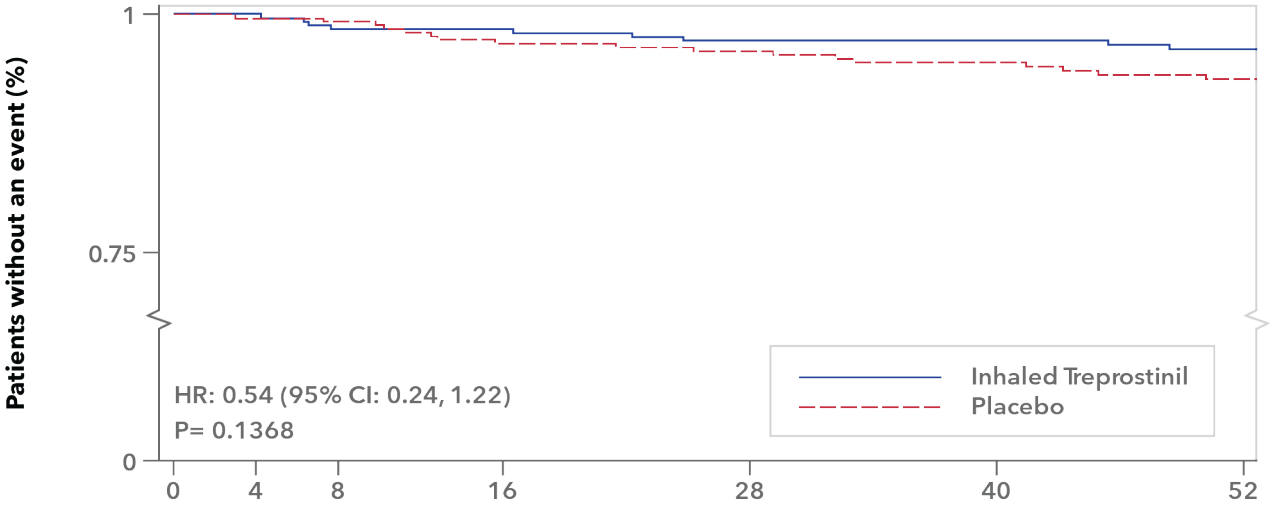
	Inhaled Treprostinil (n=298)	**Placebo** (n=295)	**P value**
Clinical Worsening Event	81 (27.2%)	115 (39.0%)	0.0023 (chi-square)
Death (all cause)	4 (1.3%)	3 (1.0%)	
Respiratory Hospitalization (adjudicated)	30 (10.1%)	38 (12.9%)	
≥10% Relative Decline in % Predicted FVC	47 (15.8%)	74 (25.1%)	
Hazard Ratio (95% CI)	0.71 (0.53, 0.95)		0.0190

TETON-2 RESULTS

Secondary Endpoints
Time to First Acute Exacerbation of IPF

Inhaled treprostinil resulted in a **46%** reduction in risk of first acute exacerbation of IPF (cox-regression: P=0.1368)

9 (3%) inhaled treprostinil and **17 (5.8%)** placebo patients experienced a first acute exacerbation of IPF (chi-square P=0.1029)



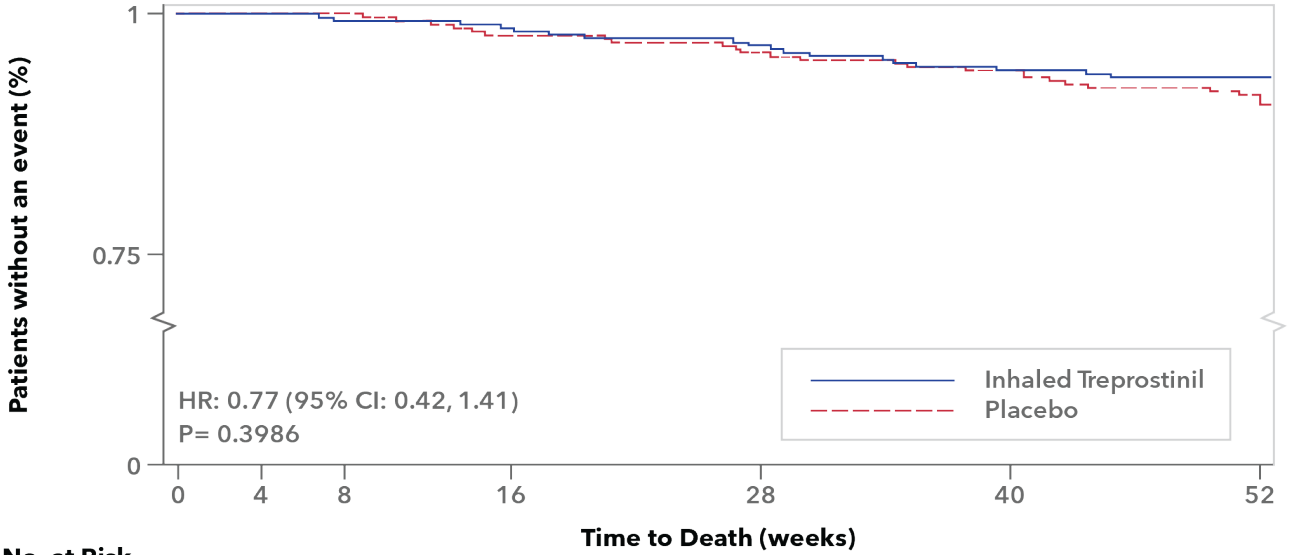
No. at Risk							
Inhaled Treprostinil	298	291	278	268	250	237	163
Placebo	295	289	284	269	259	247	170

TETON-2 RESULTS

Secondary Endpoints
Overall Survival at Week 52

Inhaled treprostinil resulted in a **23%** reduction in the risk of death (cox-regression: P=0.3986)

19 (6.4%) inhaled treprostinil and **24 (8.1%)** placebo patients died prior to week 52 (chi-square: P=0.4087)

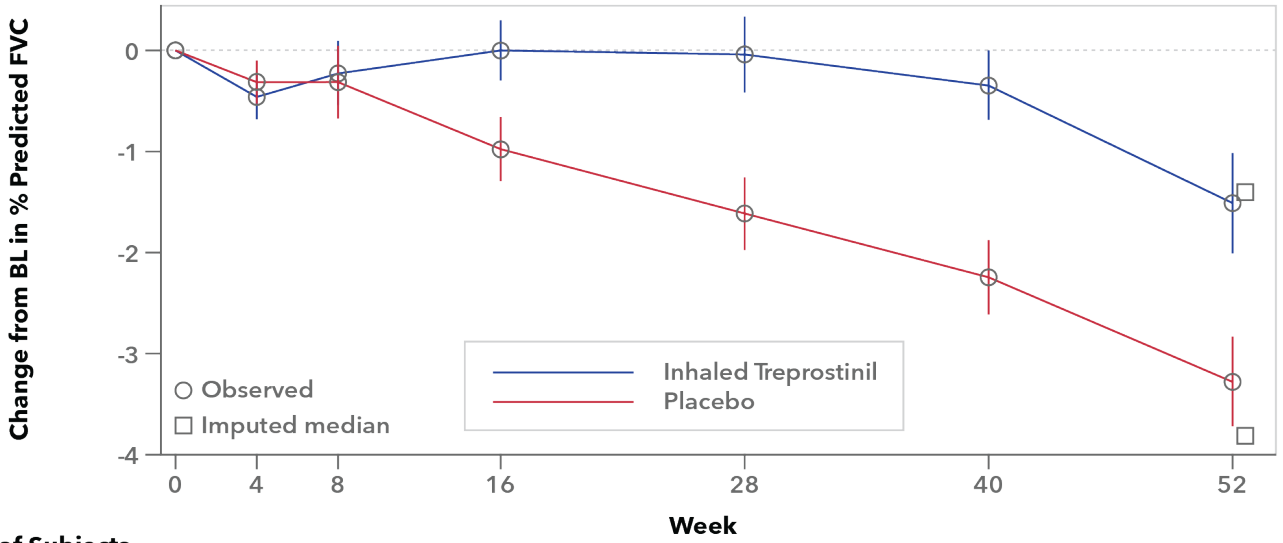


No. at Risk							
Inhaled Treprostinil	298	298	295	290	284	277	206
Placebo	295	294	294	288	283	278	200

TETON-2 RESULTS

Secondary Endpoints

Change from Baseline in % Predicted FVC at Week 52



No. of Subjects							
Inhaled Treprostinil	298	271	253	235	232	212	203
Placebo	295	259	255	251	238	226	212

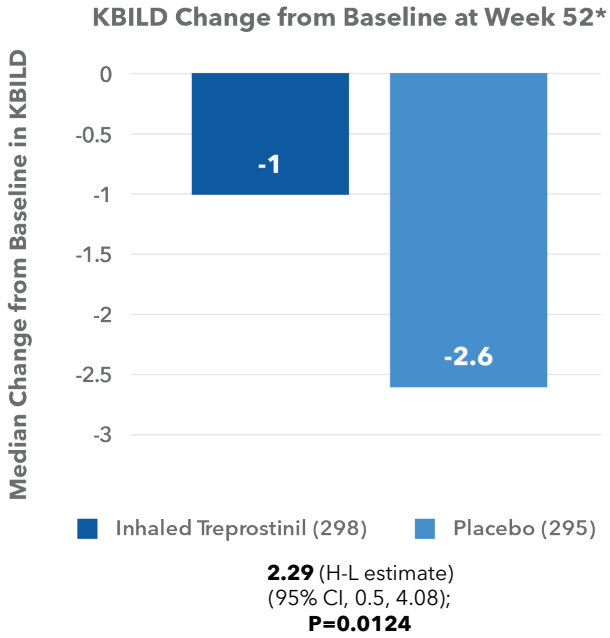
2.7%*
(95% CI, 1.5, 4.0)
P<0.0001

*(H-L estimate)

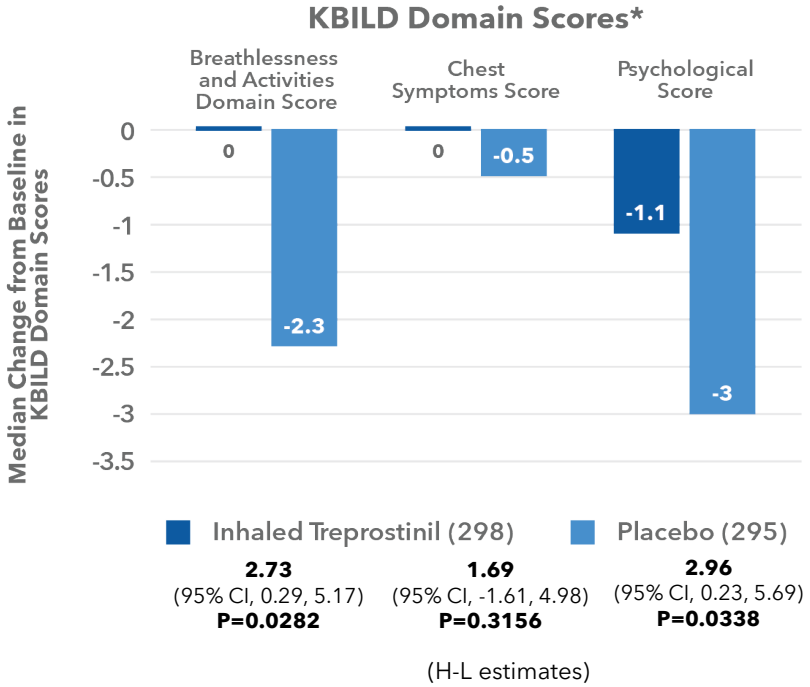
Hodges-Lehmann estimate and non-parametric aligned stratified rank Wilcoxon test

TETON-2 RESULTS

Secondary Endpoints
Change from Baseline in K-BILD Total and Domain Scores



2.29 (H-L estimate)
(95% CI, 0.5, 4.08);
P=0.0124



2.73
(95% CI, 0.29, 5.17)
P=0.0282

1.69
(95% CI, -1.61, 4.98)
P=0.3156

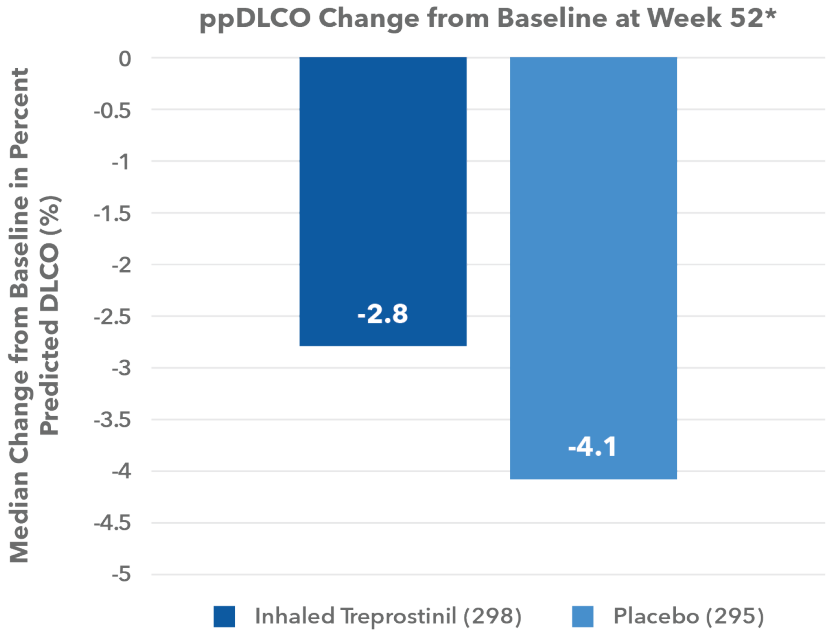
2.96
(95% CI, 0.23, 5.69)
P=0.0338

(H-L estimates)

**Imputed Medians*

TETON-2 RESULTS

Secondary Endpoints
Change from Baseline in % Predicted DLCO (ppDLCO)



1.91%
(95% CI, 0.07, 3.75);
P=0.0416

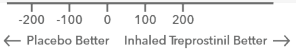
(H-L estimate)

**Imputed Median*

TETON-2 RESULTS

Forest Plot of Subgroup Analyses of FVC (mL) at Week 52

Subgroup	Inhaled Treprostinil # of Subjects	Placebo # of Subjects	Hodges-Lehmann location shift (95% CI)
Overall	298	295	95.6 (52.2, 139.0)
Background Therapy			
Nintedanib	105	109	97.6 (26.1, 169.2)
Pirfenidone	120	113	127.9 (58.8, 196.9)
No background therapy	73	73	43.9 (-45.0, 132.8)
Sex			
Male	238	237	107.1 (56.3, 157.9)
Female	60	58	53.7 (-25.7, 133.1)
Age Group			
<65 yrs	48	48	136.9 (26.4, 247.4)
65 - <80 yrs	209	215	86.8 (36.8, 136.7)
≥80 yrs	41	32	109.8 (-48.5, 268.0)
Time Since Diagnosis			
<median (3.31 yrs)	145	151	105.5 (40.3, 170.7)
≥median (3.31 yrs)	153	144	90 (32.5, 147.4)
Smoking History			
Smoker	207	218	107.9 (56.6, 159.2)
Never	91	77	70 (-10.6, 150.5)
Corticosteroid Use for IPF			
Yes	25	22	239 (40.7, 438.4)
No	273	273	85 (41.7, 128.2)



Subgroup	Inhaled Treprostinil # of Subjects	Placebo # of Subjects	Hodges-Lehmann location shift (95% CI)
Last Study Drug Dose			
<9 breaths/session	62	30	63.5 (-79.1, 206.1)
9-12 breaths/session	236	265	107.8 (63.0, 152.7)
Supplemental Oxygen Use			
Yes	34	43	84.4 (-62.2, 231.0)
No	264	252	94.8 (-48.6, 141.0)
Race			
White	262	235	85.5 (37.8, 133.3)
Not White	36	60	147.4 (46.1, 248.8)
Ethnicity			
Hispanic or Latino	85	74	52.8 (-37.8, 143.5)
Not Hispanic or Latino	202	203	113.6 (63.0, 164.2)
Not Reported/Unknown	11	18	29.7 (-224.1, 283.4)
Geographic Region			
South and Latin America	63	63	60.1 (-43.7, 164.0)
Asia-Pacific	63	73	141.8 (44.6, 239.1)
Europe and the Middle East	172	159	84.8 (29.1, 140.6)
BMI at Baseline			
<25 kg/m2	107	92	130.0 (47.9, 212.1)
25 to <30kg/m2	143	151	90.0 (30.0, 150.0)
≥30 kg/m2	48	52	59.9 (-38.2, 158.1)

TETON-2 RESULTS

Summary of Adverse Events

	Inhaled Treprostinil (n=298)	Placebo (n=295)
Total number of AEs	1558	1302
Number of subjects with at least one AE	273 **(91.6%)**	264 **(89.5%)**
Total number of SAEs	115	96
Number of subjects with at least one SAE	75 **(25.2%)**	68 **(23.1%)**
Total number of Drug-related AEs	618	286
Number of subjects with at least one study drug-related AE	193 **(64.8%)**	125 **(42.4%)**
Total number of Drug-related SAEs	13	7
Number of subjects with at least one study drug-related SAE	10 **(3.4%)**	6 **(2.0%)**
Number of subjects with at least one AE leading to death	10 **(3.4%)**	22 **(7.5%)**

TETON-2 RESULTS

Summary of Common Adverse Events

	Inhaled Treprostinil (n=298)	Placebo (n=295)
Cough	144 (48.3%)	71 (24.1%)
Headache	59 (19.8%)	35 (11.9%)
Diarrhea	41 (13.8%)	50 (16.9%)
Dyspnea	36 (12.1%)	31 (10.5%)
Bronchitis	30 (10.1%)	30 (10.2%)
Dizziness	29 (9.7%)	19 (6.4%)
Worsening idiopathic pulmonary fibrosis	28 (9.4%)	37 (12.5%)
Nasopharyngitis	25 (8.4%)	30 (10.2%)

TETON-2 RESULTS

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The study met its primary endpoint of change from baseline in absolute FVC at week 52

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The study also met statistical significance for several key secondary efficacy endpoints, such as time to first clinical worsening, percent predicted FVC, KBILD and DLCO

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Nebulized Tyvaso was well tolerated, and the safety profile was consistent with previous inhaled treprostinil studies and known prostacyclin-related adverse events

Dr. Leigh Peterson

EVP, PRODUCT DEVELOPMENT AND XENOTRANSPLANTATION

Q&A

Dr. Leigh Peterson
EVP, Product Development and Xenotransplantation

Dr. Steve Nathan
Schar Chair, Advanced Lung Disease and Lung Transplant Program, Inova Fairfax Hospital & Chair of the TETON Steering Committee

Dr. Peter Smith
SVP, Product Development and Lead for the Global TETON Program

Dr. C.Q. Deng
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Investor Relations