Effect of nintedanib in patients with progressive pulmonary fibrosis in subgroups with differing baseline characteristics

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Supplementary Material

Table S1. Baseline characteristics of subgroups by sex in the INBUILD trial.

	Male (n=356)	**Female (n=307)**
Age, years	66.7 (9.6)	64.7 (9.9)
BMI, kg/m^2	28.0 (4.5)	28.9 (6.0)
FVC % predicted	69.4 (16.4)	68.5 (14.7)
DLco % predicted	44.8 (12.7)	47.6 (14.5)

Data are mean (SD). *BMI,* body mass index, *DLco* diffusing capacity of the lung for carbon monoxide, *FVC* forced vital capacity.

Table S2. Baseline characteristics of subgroups by age in the INBUILD trial.

	Age <65 years (n=260)	**Age ≥65 years (n=403)**
Age, years	56.2 (7.1)	71.9 (5.3)
Male	123 (47.3)	233 (57.8)
BMI, kg/m^2	28.6 (5.7)	28.0 (5.0)
FVC % predicted	66.5 (14.5)	70.6 (16.1)
DLco % predicted	46.8 (13.5)	45.7 (13.7)

Data are mean (SD) or n (%) of patients. *BMI,* body mass index, *DLco* diffusing capacity of the lung for carbon monoxide, *FVC* forced vital capacity.

Table S3. Baseline characteristics of subgroups by race in the INBUILD trial.

	White (n=488)	**Asian (n=164)**	**Black (n=10)**
Age, years	65.9 (9.5)	65.6 (10.4)	61.6 (9.4)
Male	266 (54.5)	87 (53.0)	2 (20.0)
BMI, kg/m^2	29.4 (5.1)	24.5 (3.6)	31.1 (7.4)
FVC % predicted	68.7 (15.7)	69.4 (15.3)	77.5 (17.7)
DLco % predicted	46.8 (14.6)	44.2 (10.4)	46.6 (11.2)

Data are mean (SD) or n (%) of patients. *BMI,* body mass index, *DLco* diffusing capacity of the lung for carbon monoxide, *FVC* forced vital capacity.

Table S4. Baseline characteristics of subgroups by BMI in the INBUILD trial.

	BMI <25 kg/m^2 (n=188)	**BMI ≥25 to <30 kg/m^2 (n=242)**	**BMI ≥30 kg/m^2 (n=232)**
Age, years	65.7 (10.7)	66.6 (9.8)	64.9 (8.9)
Male	93 (49.5)	148 (61.2)	114 (49.1)
BMI, kg/m^2	22.5 (1.9)	27.4 (1.5)	33.9 (3.9)
FVC % predicted	69.8 (16.9)	69.2 (15.2)	68.1 (15.0)
DLco % predicted	44.0 (12.8)	45.9 (12.3)	48.1 (15.3)

Data are mean (SD) or n (%) of patients. *BMI,* body mass index, *DLco* diffusing capacity of the lung for carbon monoxide, *FVC* forced vital capacity.

Table S5. Baseline characteristics of subgroups by time since diagnosis of ILD in the INBUILD trial.

	≤1 year (n=134)	**>1 to ≤3 years (n=227)**	**>3 to ≤5 years (n=131)**	**>5 years (n=170)**
Age, years	65.6 (9.7)	66.2 (9.2)	65.4 (10.0)	65.6 (10.5)
Male	76 (56.7)	130 (57.3)	72 (55.0)	78 (45.9)
BMI, kg/m^2	28.6 (5.6)	28.3 (5.3)	28.3 (5.2)	28.0 (5.2)
FVC % predicted	69.5 (16.0)	68.8 (15.7)	69.3 (15.8)	68.7 (15.3)
DLco % predicted	47.4 (12.8)	46.6 (14.6)	46.6 (14.0)	44.0 (12.6)

Data are mean (SD) or n (%) of patients. *BMI,* body mass index, *DLco* diffusing capacity of the lung for carbon monoxide, *FVC* forced vital capacity, *ILD* interstitial lung disease.

Table S6. Baseline characteristics of subgroups by FVC % predicted in the INBUILD trial.

	FVC ≤50% predicted (n=75)	**FVC >50% to ≤70% predicted (n=314)**	**FVC >70% to ≤90% predicted (n=209)**	**FVC >90% predicted (n=65)**
Age, years	63.5 (9.9)	65.4 (9.7)	66.2 (9.7)	68.6 (9.3)
Male	44 (58.7)	161 (51.3)	109 (52.2)	42 (64.6)
BMI, kg/m^2	27.6 (5.2)	28.7 (5.6)	27.9 (5.2)	28.0 (4.1)
FVC % predicted	47.4 (1.8)	61.1 (5.6)	78.9 (5.4)	100.3 (9.8)
DLco % predicted	37.5 (6.9)	44.1 (13.9)	49.4 (12.8)	55.6 (12.9)

Data are mean (SD) or n (%) of patients. *BMI,* body mass index, *DLco* diffusing capacity of the lung for carbon monoxide, *FVC* forced vital capacity.

Table S7. Baseline characteristics in subgroups by DLco % predicted in the INBUILD trial.

	DLco ≤median (n=327)	**DLco >median (n=327)**
Age, years	66.6 (9.9)	65.0 (9.6)
Male	182 (55.7)	171 (52.3)
BMI, kg/m^2	27.8 (5.3)	28.8 (5.3)
FVC % predicted	63.5 (12.9)	74.3 (16.0)
DLco % predicted	35.9 (4.6)	56.3 (12.0)

Data are mean (SD) or n (%) of patients. Median DLco at baseline was 43.3% predicted. *BMI,* body mass index, *DLco* diffusing capacity of the lung for carbon monoxide, *FVC* forced vital capacity.

Table S8. Baseline characteristics of subgroups by CPI in the INBUILD trial.

	CPI ≤45 (n=202)	**CPI >45 (n=452)**
Age, years	64.7 (10.0)	66.3 (9.6)
Male	103 (51.0)	250 (55.3)
BMI, kg/m^2	28.7 (5.3)	28.1 (5.3)
FVC % predicted	81.0 (15.6)	63.5 (12.1)
DLco % predicted	61.5 (12.4)	39.2 (6.8)

Data are mean (SD) or n (%) of patients. *BMI,* body mass index, *CPI* composite physiologic index, *DLco* diffusing capacity of the lung for carbon monoxide, *FVC* forced vital capacity.

Table S9. Baseline characteristics of subgroups by GAP stage in the INBUILD trial.

	GAP stage I (n=294)	**GAP stage II or III (n=369)**
Age, years	60.6 (9.5)	69.8 (7.8)
Male	99 (33.7)	257 (69.6)
BMI, kg/m^2	28.8 (5.5)	27.9 (5.1)
FVC % predicted	74.5 (15.8)	64.6 (14.0)
DLco % predicted	53.6 (14.3)	40.3 (9.8)

Data are mean (SD) or n (%) of patients. *BMI,* body mass index, *DLco* diffusing capacity of the lung for carbon monoxide, *FVC* forced vital capacity.

Table S10. Baseline characteristics of subgroups by use of anti-acid therapy in the INBUILD trial.

	Taking anti-acid therapy (n=380)	**Not taking anti-acid therapy (n=283)**
Age, years	66.2 (9.5)	65.1 (10.1)
Male	212 (55.8)	144 (50.9)
BMI, kg/m^2	28.5 (5.5)	27.9 (4.9)
FVC % predicted	67.4 (14.7)	71.1 (16.6)
DLco % predicted	44.5 (13.1)	48.3 (14.0)

Data are mean (SD) or n (%) of patients. Anti-acid therapies were defined based on the WHO Drug Dictionary (version 19.MAR) (Anatomical Therapeutic Chemical codes for 'antacids' and 'drugs for peptic ulcer and gastro-oesophageal reflux disease [GORD]' and preferred name 'drugs for acid related disorders'). *BMI,* body mass index, *DLco* diffusing capacity of the lung for carbon monoxide, *FVC* forced vital capacity.

Table S11. Baseline characteristics of subgroups by use of DMARDs in the INBUILD trial.

	Taking DMARDs (n=91)	**Not taking DMARDs (n=572)**
Age, years	65.6 (10.7)	65.8 (9.6)
Male	52 (57.1)	304 (53.1)
BMI, kg/m^2	28.0 (4.8)	28.3 (5.4)
FVC % predicted	72.1 (16.1)	68.5 (15.5)
DLco % predicted	47.7 (14.2)	45.9 (13.5)

Data are mean (SD) or n (%) of patients. DMARDs were defined based on the WHO Drug Dictionary (version 19.MAR) standardised drug grouping excluding denosumab, plus baricitinib. *BMI,* body mass index, *DMARDs* disease-modifying anti-rheumatic drugs, *DLco* diffusing capacity of the lung for carbon monoxide, *FVC* forced vital capacity.

Table S12. Rate of decline in FVC (mL/year) over 52 weeks of the INBUILD trial in subgroups by baseline characteristics.

Baseline characteristic	Nintedanib		Placebo		Difference (95% CI)	Treatment-by-subgroup-by-time interaction
	n analysed	Rate (SE) of decline in FVC (mL/year) over 52 weeks	n analysed	Rate (SE) of decline in FVC (mL/year) over 52 weeks		
Sex						*p* = 0.06
Male	179	−88.9 (21.6)	177	−234.1 (21.6)	145.2 (88.5, 201.9)	
Female	153	−72.6 (23.2)	154	−136.8 (22.8)	64.2 (3.9, 124.6)	
Age						*p* = 0.51
<65 years	139	−58.9 (22.8)	121	−145.8 (24.3)	86.9 (21.5, 152.2)	
≥65 years	193	−97.5 (20.0)	210	−212.6 (18.7)	115.1 (61.4, 168.8)	
Race*						*p* = 0.77
White	242	−69.9 (17.8)	246	−180.5 (17.2)	110.6 (62.0, 159.2)	
Asian	84	−115.5 (29.6)	80	−208.5 (30.7)	93.0 (9.3, 176.7)	
Body mass index						*p* = 0.83
<25 kg/m^2	90	−123.4 (28.5)	98	−229.5 (27.5)	106.1 (28.3, 184.0)	

≥25 to <30 kg/m^2	130	−83.3 (24.2)	112	−176.9 (25.5)	93.7 (24.7, 162.6)	
≥30 kg/m^2	111	−46.9 (25.7)	121	−171.2 (24.0)	124.3 (55.4, 193.3)	
Time since diagnosis of ILD						*p* = 0.89
≤1 year	67	−62.2 (34.0)	67	−163.8 (33.7)	101.6 (7.5, 195.6)	
>1 to ≤3 years	115	−91.7 (25.6)	112	−179.5 (25.3)	87.8 (17.0, 158.5)	
>3 to ≤5 years	74	−89.0 (32.0)	57	−206.7 (35.9)	117.7 (23.2, 212.1)	
>5 years	75	−74.1 (32.1)	95	−203.5 (28.0)	129.4 (45.6, 213.1)	
FVC % predicted						*p* = 0.38
≤50	42	−178.2 (43.2)	33	−276.5 (51.1)	98.3 (−28.9, 225.5)	
>50 to ≤70	154	−95.3 (22.5)	160	−196.5 (21.5)	101.3 (41.7, 160.9)	
>70 to ≤90	104	−29.2 (27.0)	105	−127.8 (26.4)	98.6 (26.1, 171.1)	
>90	32	−51.7 (51.4)	33	−272.4 (48.6)	220.8 (92.7, 348.8)	
DLco % predicted[†]						*p* = 0.40
≤median (43.3)	177	−105.7 (21.1)	150	−198.1 (22.5)	92.4 (32.3, 152.5)	
>median (43.3)	149	−57.1 (22.3)	178	−185.6 (20.0)	128.4 (70.1, 186.8)	
CPI						*p* = 0.48
≤45	82	−12.9 (31.1)	120	−151.3 (24.6)	138.4 (62.7, 214.1)	

>45	244	−106.2 (17.7)	208	−212.0 (19.1)	105.9 (55.2, 156.5)	
GAP stage						*p* = 0.60
I	142	−43.6 (22.4)	152	−141.5 (21.2)	98.0 (37.6, 158.3)	
II or III	190	−110.7 (20.2)	179	−230.5 (20.5)	119.8 (63.4, 176.2)	
Taking anti-acid therapy‡						*p* = 0.66
Yes	200	−70.1 (19.5)	180	−184.0 (20.2)	113.9 (58.8, 169.0)	
No	132	−97.1 (23.9)	151	−192.3 (21.9)	95.2 (31.5, 158.9)	
DMARDs§						*p* = 0.44
Yes	43	−82.2 (44.2)	48	−230.6 (38.1)	148.4 (33.9, 262.9)	
No	289	−80.6 (16.0)	283	−180.1 (16.1)	99.5 (54.8, 144.2)	

CPI composite physiologic index, *DLco* diffusing capacity of the lung for carbon monoxide, *DMARDs* disease-modifying anti-rheumatic drugs*, FVC* forced vital capacity, *GAP* gender, age, lung physiology, *ILD* interstitial lung disease. *Data on Black patients are not shown as the number of patients in this subgroup (n=10) was too small for the data to be interpreted. †Corrected for haemoglobin. ‡Based on WHO Drug Dictionary (version 19.MAR) (Anatomical Therapeutic Chemical codes for 'antacids' and 'drugs for peptic ulcer and gastro-oesophageal reflux disease [GORD]' and preferred name 'drugs for acid related disorders'). §Based on WHO Drug Dictionary (version 19.MAR) standardised drug grouping excluding denosumab, plus baricitinib.