Monocyte count and decline in forced vital capacity (FVC) in patients with IPF

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Introduction

- A higher monocyte count has been associated with disease progression and mortality in patients with idiopathic pulmonary fibrosis (IPF).[1-3]
- Nintedanib is an approved treatment for IPF that reduces the rate of decline in forced vital capacity (FVC).[4-5]

Aim

- Investigate the rate of decline in FVC in patients with IPF in subgroups by monocyte count at baseline.

Methods

- Data were pooled from patients who were randomised to receive nintedanib 150 mg bid or placebo in the TOMORROW trial[4] or the two INPULSIS trials.[5]
- In post-hoc analyses, we assessed the following over 52 weeks subgroups by monocyte count less than versus more than or equal to the mean level at baseline:
  - Rate of decline in FVC (mL/year)
  - Time to first investigator-reported acute exacerbation
  - Time to decline in FVC ≥5% predicted or death
  - Time to decline in FVC ≥10% predicted or death
  - Time to death
- Exploratory interaction p-values were calculated to assess potential heterogeneity in the treatment effect of nintedanib versus placebo across the subgroups. No adjustment for multiplicity was made.
- Adverse events are presented descriptively.

Results

- We analysed data from 1229 patients.

Monocyte count (K/μL)

Baseline characteristics in subgroups by monocyte count <0.51 and ≥0.51 K/μL

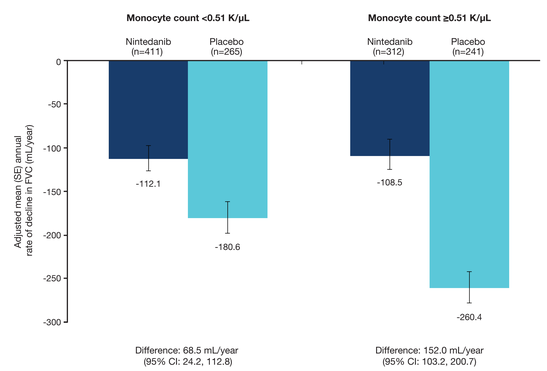
Monocyte count	Male (%)		Age (years)		Former or current smoker (%)	
	<0.51 K/μL	≥0.51 K/μL	<0.51 K/μL	≥0.51 K/μL	<0.51 K/μL	≥0.51 K/μL
	75.7	82.3	66.0	67.2	72.0	71.1
	2709	2742	80.9	78.1	47.7	46.6
	FVC (mL)		FVC % predicted		DLco % predicted	

Mean or % of patients.

Rate of decline in FVC (mL/year) over 52 weeks

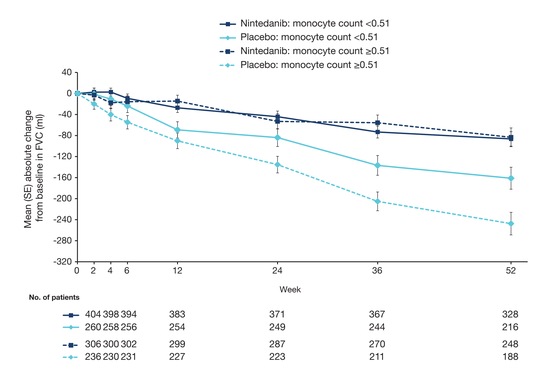
- In the placebo group, the rate of decline (mL/year) in FVC was numerically greater in patients with monocyte count ≥0.51 K/μL than <0.51 K/μL at baseline. In the nintedanib group, the rate of FVC decline was similar between these subgroups (Figures 1 and 2).
- Nintedanib reduced the rate of decline in FVC versus placebo in both subgroups, with a trend to a greater treatment effect in patients with monocyte count ≥0.51 K/μL compared to <0.51 K/μL at baseline.

Figure 1. *Rate of decline in FVC (mL/year) over 52 weeks in subgroups by monocyte count <0.51 and ≥0.51 K/μL at baseline*



Treatment-by-time-by-subgroup interaction p=0.013.

Figure 2. *Change from baseline in FVC (mL) in subgroups by monocyte count <0.51 and ≥0.51 K/μL at baseline*



Acute exacerbation, disease progression, and death

- In the placebo group, the proportions of patients with acute exacerbation; decline in FVC ≥5% predicted or death; decline in FVC ≥10% predicted or death; and death were numerically greater in patients with monocyte count ≥0.51 K/μL than <0.51 K/μL. In the nintedanib group, these proportions were similar between the subgroups (Table).
- There was a trend to a greater treatment effect of nintedanib on reducing the risk of a decline in FVC ≥10% predicted or death, and the risk of death, in patients with monocyte count ≥0.51 K/μL than <0.51 K/μL at baseline.

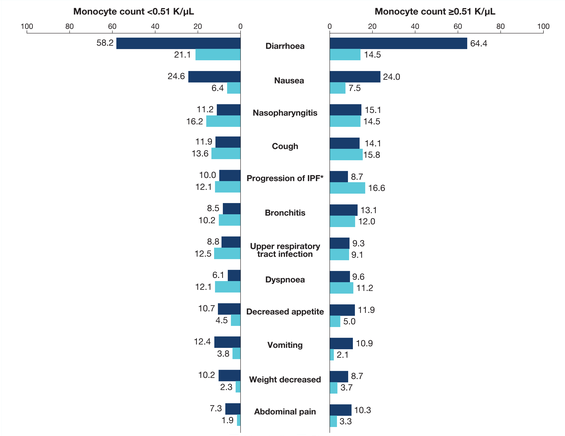
Table. *Time to first acute exacerbation, decline in FVC ≥5% predicted or death, decline in FVC ≥10% predicted or death, and death over 52 weeks in subgroups by monocyte count <0.51 and ≥0.51 K/μL at baseline*

	Monocyte count <0.51 K/μL		Monocyte count ≥0.51 K/μL	
	Nintedanib (n=411)	Placebo (n=265)	Nintedanib (n=312)	Placebo (n=241)
Acute exacerbation, n (%)	15 (3.6)	15 (5.7)	18 (5.8)	29 (12.0)
HR (95% CI)	0.63 (0.31, 1.29)		0.47 (0.26, 0.85)	
Treatment-by-subgroup interaction	p=0.53			
Absolute decline in FVC ≥5% predicted or death, n (%)	213 (51.8)	184 (69.4)	160 (51.3)	175 (72.6)
HR (95% CI)	0.64 (0.53, 0.79)		0.58 (0.47, 0.73)	
Treatment-by-subgroup interaction	p=0.50			
Absolute decline in FVC ≥10% predicted or death, n (%)	114 (27.7)	91 (34.3)	83 (26.6)	117 (48.5)
HR (95% CI)	0.79 (0.60, 1.04)		0.47 (0.35, 0.62)	
Treatment-by-subgroup interaction	p=0.01			
Death, n (%)	24 (5.8)	12 (4.5)	18 (5.8)	30 (12.4)
HR (95% CI)	1.29 (0.64, 2.59)		0.45 (0.25, 0.81)	
Treatment-by-subgroup interaction	p=0.03			

Adverse events

- The adverse event profile of nintedanib was generally consistent between the subgroups by monocyte count (Figure 3).

Figure 3. *Most frequent adverse events (reported irrespective of causality) in subgroups by monocyte count <0.51 and ≥0.51 K/μL at baseline*



Adverse events were coded using preferred terms in the Medical Dictionary for Regulatory Activities. Data are % of subjects with ≥1 such adverse event with onset after the first dose and up to 28 days (in INPULSIS trials) or 14 days (in TOMORROW trial) after the last dose of study drug. Adverse events reported in >10% of subjects in either of these subgroups are shown.
*Corresponded to preferred term 'IPF', which included disease worsening and acute exacerbations.

Conclusions

- **In patients with IPF, high monocyte count may be associated with faster disease progression.**
- **In post-hoc analyses of data from clinical trials, nintedanib slowed the rate of decline in FVC both in patients with monocyte count <0.51 and ≥0.51 K/μL at baseline.**
- **Further research is needed into the role of monocytes in the progression of IPF.**

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