Effects of nintedanib on markers of epithelial damage in subjects with IPF: data from the INMARK® trial

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Introduction

- IPF is believed to occur in genetically susceptible individuals following repeated or persistent epithelial injury.[1]
- CA-125 and CA19-9 are markers of epithelial damage that have been associated with disease progression in patients with IPF.[2,3]
- Nintedanib is an approved treatment for IPF, which reduces the rate at which the disease progresses.[4]

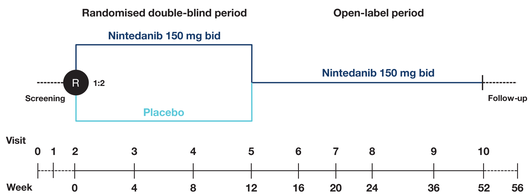
Aim

- To investigate the effects of nintedanib compared with placebo on CA-125 and CA19-9 in subjects with IPF using data from the INMARK trial.

Methods

Trial design[5]

- Subjects with IPF and FVC ≥80% predicted were randomised 1:2 to receive nintedanib or placebo for 12 weeks, followed by an open-label period during which all subjects received nintedanib for 40 weeks.



R, randomisation.

- Blood samples were taken at weeks 4, 8, 12, 16, 20, 24, 36, and 52.

Analyses

- We assessed:
  - the rate of change in CA-125 and CA19-9 from baseline to week 12 using random coefficient regression
  - changes in CA-125 and CA19-9 over 52 weeks using a mixed model for repeated measures.
- Data were $\log_{10}$ transformed before analysis.
- Analyses were performed in subjects who received ≥1 dose of trial drug and had analysable data for the biomarker.

Results

Subjects

Baseline characteristics of subjects in the INMARK trial

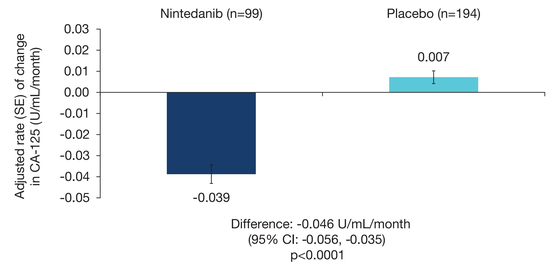
	Nintedanib (n=116)	Placebo (n=230)
Age, years, mean (SD)	70.5 (7.7)	70.2 (7.2)
Male, n (%)	93 (80.2)	169 (73.5)
Race, n (%)		
White	70 (60.3)	144 (62.6)
Asian	35 (30.2)	68 (29.6)
Missing*	11 (9.5)	18 (7.8)
Former/current smoker, n (%)	85 (73.3)	167 (72.6)
FVC, % predicted, mean (SD)	96.6 (15.2)	98.0 (12.6)
DLco, % predicted†, mean (SD)	60.9 (16.6)	65.5 (21.2)

*Data on race were not collected in France due to local regulation. †Corrected for haemoglobin.

Effect of nintedanib on changes in CA-125

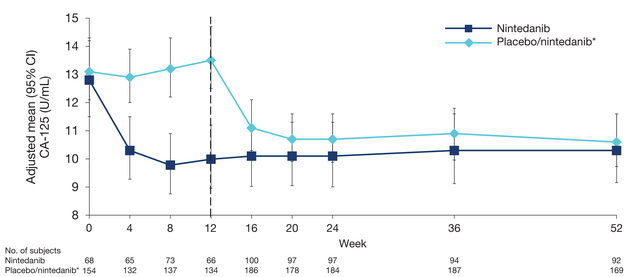
- The adjusted rate of change in CA-125 from baseline to week 12 was significantly different between the nintedanib and placebo groups (Figure 1).
- Adjusted mean CA-125 levels decreased with nintedanib vs placebo from week 4. After week 12, a decrease in CA-125 was observed in patients who switched from placebo to nintedanib, which was comparable to the initial decrease seen in the nintedanib group. From week 20, CA-125 levels were similar between the groups (Figure 2).

Figure 1. *Rate of change in CA-125 from baseline to week 12*



Based on $\log_{10}$ transformed values.

Figure 2. *CA-125 over 52 weeks*

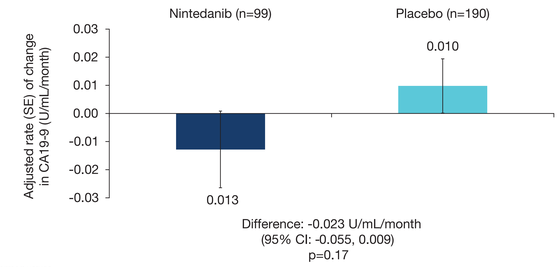


*Subjects received placebo (blinded) for 12 weeks followed by nintedanib (open-label) for 40 weeks.

Effect of nintedanib on changes in CA19-9

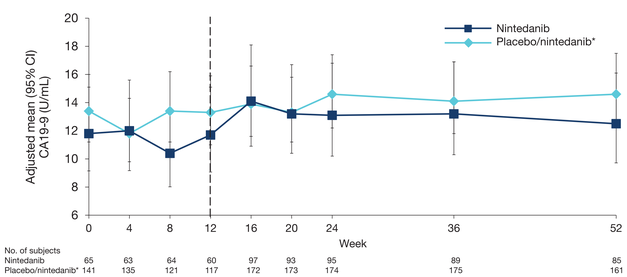
- There was no significant difference between the nintedanib and placebo groups in the adjusted rate of change in CA19-9 levels from baseline to week 12 (Figure 3).
- Adjusted mean CA19-9 levels were similar in both groups over 52 weeks (Figure 4).

Figure 3. *Rate of change in CA19-9 from baseline to week 12*



Based on $\log_{10}$ transformed values.

Figure 4. *CA19-9 over 52 weeks*



*Subjects received placebo (blinded) for 12 weeks followed by nintedanib (open-label) for 40 weeks.

Conclusions

- **These analyses of data from the INMARK trial suggest that a reduction in CA-125, a marker of epithelial injury, may be a biomarker of response to nintedanib in patients with IPF.**
- **Further studies are needed to validate CA-125 as a predictor of disease progression and a biomarker of response to nintedanib in patients with IPF.**

References

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