Pulmonary Therapy

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Modelling Forced Vital Capacity in Idiopathic Pulmonary Fibrosis: Optimising Trial Design

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Poster PA1733

Forced vital capacity (FVC) decline in idiopathic pulmonary fibrosis (IPF) – modelling the myth

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Disclosures

Marlies Wijsenbeek reports no personal fees; the Erasmus MC received an advisory board fee from Galapagos, speaker and advisory board fees from Boehringer Ingelheim and Hoffmann-La Roche, and grants from Boehringer Ingelheim, Hoffmann-La Roche, The Netherlands Organisation for Health Research and Development (ZoNMW), the Dutch Lung Foundation, the Dutch Pulmonary Fibrosis Patients Association, and the Erasmus MC Thorax Foundation.

Rationale and objective

- FVC is the only registrational endpoint in IPF clinical trials
- As most new treatments will be administered **on top of standard of care (SOC; pirfenidone or nintedanib)**, estimating treatment response will become more challenging

- The objective of this study was to use data simulations to **quantify the variability associated with FVC decline over time** to model effects of an investigational drug for IPF when given on top of SOC in a clinical trial setting, and to **model the impact of a range of clinical trial scenarios**

FVC, forced vital capacity; IPF, idiopathic pulmonary fibrosis; SOC, standard of care

Methods

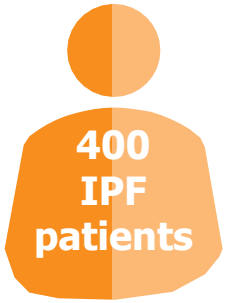
Publicly available **summary data** from FDA review of **nintedanib**

Source data

Daily **home spirometry** data from 50 patients with IPF

FVC data simulation*

50% assumed to be taking SOC at study start and **50%** not



Base simulation setting

(illustrative example of a clinical trial)

1:1

Investigational drug

Measurements at: Weeks 0, 2, 4, 8, 12, 18, 26, 34, 42 and 52

Placebo

Assumed treatment difference in FVC change from baseline: 90 mL

Data analysis

ANCOVA | LMM | MMRM

Simulated trial scenarios

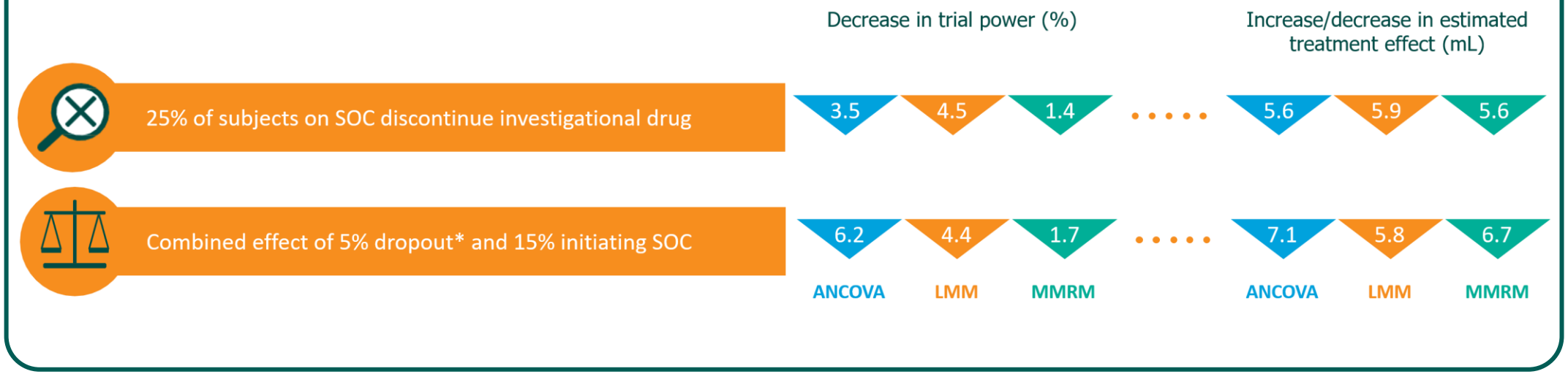
*Based on assumptions for the correlation structure (CAR[1]), mean and variance; ANCOVA, analysis of covariance model; CAR(1), continuous-time autoregressive model of order 1; IPF, idiopathic pulmonary fibrosis; LMM, linear mixed model; MMRM, mixed model repeated measures; FVC, forced vital capacity; SOC, standard of care

Results

The analysis method used impacts the results obtained

	ANCOVA	LMM	MMRM
Power %	90.3	86.7	97.3
SEM	27.4	29.1	27.5

Simulated trial scenarios



Based on 10,000 simulations per setting. Power is calculated as the percentage of simulated trials in which a significant treatment difference is found (5% significance level).*Dropout due to unobserved FVC decline; ANCOVA, analysis of covariance model; FVC, forced vital capacity; LMM, linear mixed model; MMRM, mixed model repeated measures; SEM, standard error of the mean; SOC, standard of care

Conclusions

A full paper has been published simultaneously in *Advances in Therapy*

- Modeling allows us to **quantify variability** associated with **FVC decline** in a number of clinical trial scenarios
- This permits robust power calculations to **optimize clinical trial design**

- This helps healthcare professionals **better understand the pattern of FVC decline** seen in clinical practice, ultimately **benefitting patients**

For further information please see Poster PA1733 and symposium “Management approaches in idiopathic pulmonary fibrosis: can we do better for patients?” 17:15–19:15 in RETIRO

FVC, forced vital capacity

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Compliance with Ethics Guidelines. This article is based on previously conducted studies and does not contain any studies with human participants or animals performed by any of the authors.

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