Estimating long-term survival in progressive fibrosing interstitial lung disease (PF-ILD) other than IPF using matched IPF data

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BACKGROUND

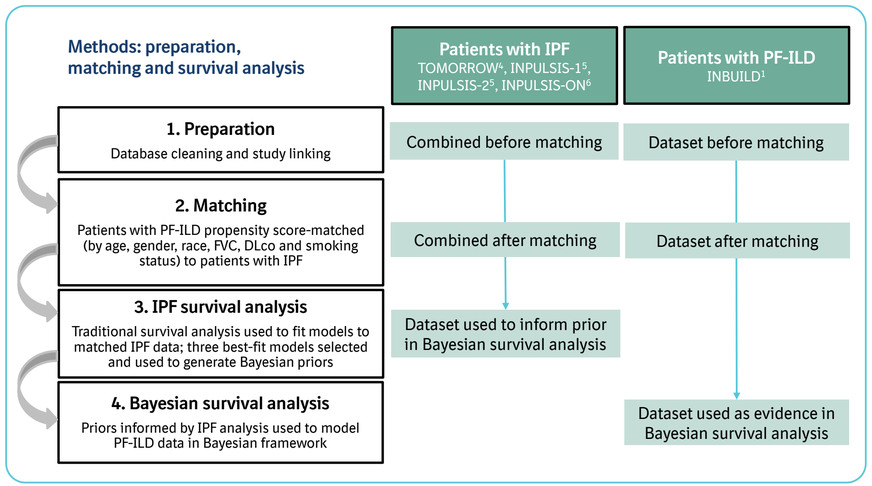
- There is a lack of survival data from clinical trials and real-world evidence in ILD with a progressive fibrosing phenotype other than IPF (non-IPF PF-ILD).
- The Phase III INBUILD trial showed that nintedanib slows disease progression in non-IPF PF-ILD. [1]
- Since IPF has a similar disease course to PF-ILD, data from long-term IPF studies may be suitable for informing estimates of PF-ILD survival.[2,3]

AIM

- To develop models of long-term survival in patients with PF-ILD in the INBUILD trial using propensity score-matched long-term IPF data.

METHODS

- Propensity score matching was used to weight and match patients with IPF from four nintedanib trials (TOMORROW[4], INPULSIS 1[5] and 2[5], and the long-term extension INPULSIS-ON[6] trial) to patients with PF-ILD in the INBUILD trial.
- Seven traditional survival models were fitted to the matched, weighted IPF data and the three best-fitting models, according to standard statistical tests, were used to generate informative priors for the shape parameter of the Bayesian model.
- These three distributions were then fitted to the PF-ILD data and extrapolated over the long-term.



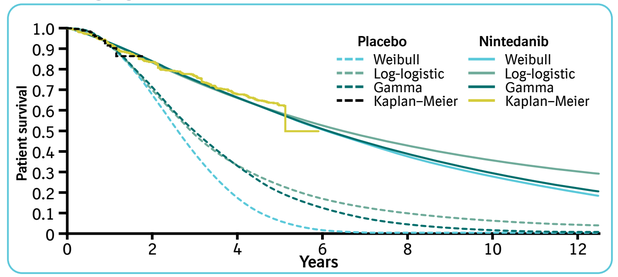
Bayesian analyses informed by IPF trial data can be used to extrapolate survival estimates in patients with non-IPF PF-ILD

CONCLUSION

- Using Bayesian analyses informed by IPF trial data provides robust 5-year survival estimates for patients with non-IPF PF-ILD treated with nintedanib or placebo.
- Our results are consistent with clinical experience and real-world evidence from patients with IPF.[7–9]
- These estimates can be used to inform future decision-making in the absence of long-term PF-ILD data.

RESULTS

Gamma, log-logistic and Weibull survival models were the best fit for the matched IPF data



Survival estimates for matched IPF data

	Median OS (years)	
	Nintedanib	Placebo
Gamma	6.13	2.93
Log-logistic	6.48	3.00
Weibull	6.06	2.60

OS estimates for PF-ILD from the Bayesian survival models

Distribution	Median OS (years)		5-year survival (%)	
	Nintedanib	Placebo	Nintedanib	Placebo
Gamma	6.50	3.76	60	32
Log-logistic	6.34	3.73	59	34
Weibull	6.45	3.42	60	21

Nintedanib
Median OS and 5-year survival estimates were consistent across the three models

Placebo
The Weibull model gave a lower estimate of 5-year survival than the other models

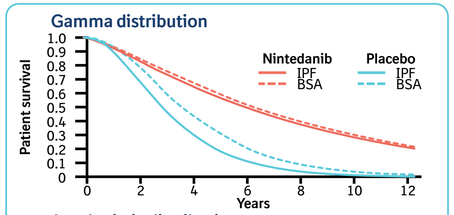
Traditional survival analysis results (frequentist approach using INBUILD data alone)

Median OS (years)					
Distribution	Nintedanib	Placebo	**Distribution**	Nintedanib	Placebo
Exponential	11.91	8.46	**Log-logistic**	8.46	3.70
GenGamma	5.75	3.12	**Log-normal**	16.67	5.17
Gompertz	3.94	2.63	**Weibull**	6.90	3.37

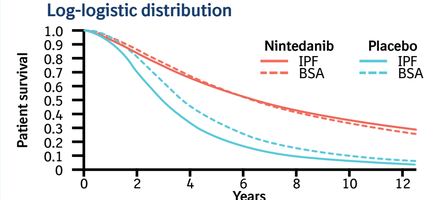
- Compared with survival estimates based on INBUILD data only, the Bayesian estimates of median OS in PF-ILD provided less variation and uncertainty.

Bayesian survival analysis using:

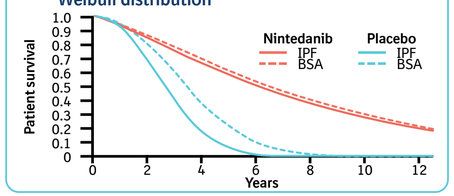
Gamma distribution



Log-logistic distribution



Weibull distribution



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Abbreviations

BSA, Bayesian survival analysis;
DL_{CO}, diffusing capacity of the lung for carbon monoxide; FVC, forced vital capacity;
ILD, interstitial lung disease;
IPF, idiopathic pulmonary fibrosis; OS, overall survival;
PF-ILD, progressive fibrosing ILD.

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