SUPPLEMENTARY MATERIAL

Using data on survival with idiopathic pulmonary fibrosis to estimate survival with other types of progressive fibrosis interstitial lung disease: a Bayesian framework

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Bayesian analysis: additional methodological information

Example OpenBUGS code (nintedanib gamma model)

```
model
{
 # Priors
beta1 ~ dunif(0.0, 1000)
shape ~ dgamma(72.70688, 55.28968)

 # Likelihood
for(a in 1 : m) {
mu[a] <- inprod(x[a], beta1)
t.obs[a] ~ dgamma(shape,mu[a])I(t.cen[a],)
}
}
END
#INITS
list(shape=2, beta1=0.001)
END
list(shape=5, beta1=0.010)
END
list(shape=1, beta1=0.005)
END
```

Weibull shape parameters:

Placebo: dgamma(32.74437, 15.12299)

Nintedanib: dgamma(117.3925, 94.57444)

Logistic shape parameters (on log-transformed dataset):

Placebo: dnorm(6.977042, 5.053302)

Nintedanib: dnorm(7.769123, 8.058745)

Gamma shape parameters:

Placebo: dgamma(21.32053, 8.690048)

Nintedanib: dgamma(72.70688, 55.28968)

Generation of the informative priors

The estimates of the mean (μ) and standard deviation (SD) of the shape parameter produced by the frequentist analysis of the matched IPF data were used to inform the gamma (α,β) distribution of the informative prior for the Bayesian analysis of the gamma and Weibull survival models using the following equations:

$$\alpha = \mu\beta$$

$$\beta = \frac{\mu}{SD^2}$$

For the log-logistic model, the logistic distribution was fitted to the log-transformed survival data. An informative normal prior distribution was used to inform the location parameter of the logistic distribution, using the estimates of the mean (μ) and standard deviation (SD) of the shape parameter produced by the frequentist analysis of the matched IPF data. A noninformative prior was used for the scale parameter in all analyses.

Iterations, burn-in and thinning factor Convergence was assessed and a sufficient burn-in selected.

Autocorrelation was also evaluated and a thinning factor applied when required.

Supplementary Table 1. Model specifications in OpenBUGS

Distribution	Treatment	Number of iterations	Burn-in length	Thinning factor (if applied)
Gamma	Nintedanib	200,000	40,000	NA
	Placebo	200,000	40,000	NA
Log-logistic*	Nintedanib	100,000	20,000	NA
	Placebo	100,000	20,000	NA
Weibull	Nintedanib	400,000	100,000	10
	Placebo	400,000	100,000	20

*A logistic distribution was used on log-transformed data. NA, not applicable.

Supplementary Table 2. Patients' baseline characteristics before and after propensity score matching

Baseline characteristic	PF-ILD	Unmatched IPF	Matched IPF	% bias	% bias reduction
Nintedanib					
Age (continuous)	65.3	66.4	65.2	0.4	97
Gender (% female)	46.0	21.6	47.2	-2.6	95.1
Race (% Asian)	25.5	33.8	26.1	-1.4	92.4
Percent predicted DLco	44.4	47.3	44.3	0.4	98.2
Percent predicted FVC	68.6	79.3	70.4	-10.6*	83.4
Smoking (% ex-smokers)	50.6	68.3	49.0	3.3	91
Smoking (% current smokers)	0.9	3.6	1.2	-2.1	88.2
Placebo					
Age (continuous)	66.4	66.6	66.4	-0.7	73.2
Gender (% female)	46.0	22.0	46.5	-0.9	98.2
Race (% Asian)	24.4	32.0	25.4	-2.2	87.1
Percent predicted DLco	47.9	46.9	46.7	8.6*	-24.9
Percent predicted FVC	69.2	79.8	70.2	-6.4*	90.1
Smoking (% ex-smokers)	48.8	65.1	49.1	-0.6	98.3
Smoking (% current smokers)	2.4	5.0	2.5	-0.2	98.2

*Absolute % bias greater than 5%. DLco, diffusing capacity for carbon monoxide; FVC, forced vital capacity; IPF, idiopathic pulmonary fibrosis; PF-ILD, progressive fibrosing interstitial lung disease

Supplementary Table 3. AIC and BIC values for matched IPF survival models used to generate analysis prior

Distribution	Nintedanib		Placebo	
	AIC	BIC	AIC	BIC
Weibull	1468.961	1476.535	567.0736	574.6227
Exponential	1471.934	1475.721	580.1805	583.9613
Generalised gamma	1470.677	1482.037	569.1665	580.4714
Log-logistic	1469.346	1476.920	567.0456	574.5948
Log-normal	1470.437	1478.010	568.6821	576.2312
Gompertz	1470.285	1477.859	568.4749	576.0240
Gamma	1468.814	1476.388	567.2287	574.7778

Note: For nintedanib, the exponential distribution gave the lowest BIC value. However, this distribution gave unrealistic long-term survival estimates for the placebo cohort. Because of this, combined with the recommendation that the same survival model should be used for all treatments when comparing across treatments,[1] the exponential distribution was not considered further.

Grey shading denotes the three lowest AIC and BIC values for each treatment cohort. AIC, Akaike information criteria; BIC, Bayesian information criteria; IPF, idiopathic pulmonary fibrosis.

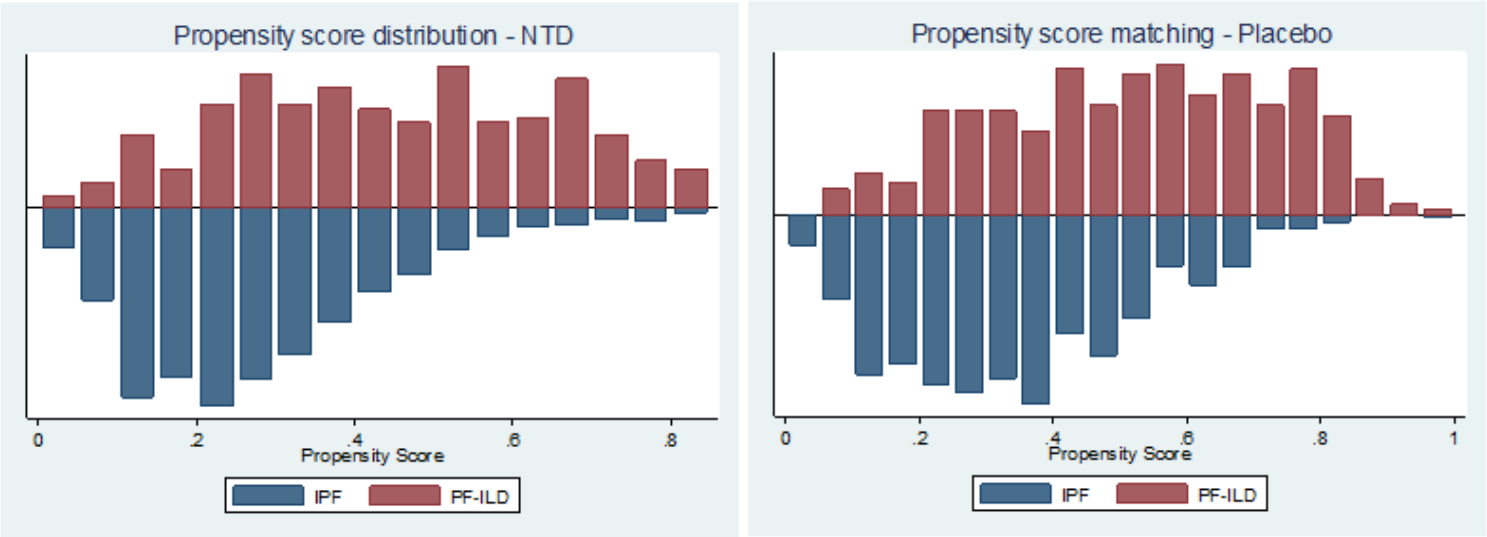
1. Latimer N. NICE DSU Technical Support Document 14: Survival analysis for economic evaluations alongside clinical trials – extrapolation with patient-level data. 2011. Available at: http://www.nicedsu.org.uk [accessed January 2021

Supplementary Table 4. Results of the Bayesian survival analysis

Distribution	Treatment	Parameter	Correlation	Mean	SD	MC error	2.5%	Median	97.5%
Gamma	Nintedanib	Shape	0.8667	1.404	0.137	0.001155	1.149	1.4	1.685
		Rate		4.653E-4	1.167E-4	1.11E-6	2.641E-4	4.566E-4	7.197E-4
	Placebo	Shape	0.9509	2.493	0.3407	0.004001	1.874	2.476	3.207
		Rate		0.001596	3.848E-4	4.673E-6	9.273E-4	0.001567	0.002429
Log-logistic*	Nintedanib	Location	-0.8306	7.759	0.2048	0.004255	7.395	7.747	8.186
		Scale		1.564	0.2145	0.003942	1.187	1.551	2.02
	Placebo	Location	-0.815	7.225	0.1284	0.002574	7.0	7.216	7.506
		Scale		2.244	0.2913	0.005058	1.715	2.23	2.851
Weibull	Nintedanib (no thinning)	Shape	-0.8646	1.308	0.1038	0.001781	1.109	1.306	1.517
		Lambda		3.4E-5	2.511E-5	4.038E-7	6.844E-6	2.733E-5	1.006E-4
	Nintedanib (with thinning)	Shape	NR	1.308	0.1038	0.002038	1.109	1.306	1.517
		Lambda		3.401E-5	2.514E-5	4.566E-7	6.859E-6	2.732E-5	1.008E-4
	Placebo (no thinning)	Shape	-0.5771	2.128	0.2256	0.005011	1.705	2.122	2.59
		Lambda		4.777E-7	1.059E-6	2.024E-8	9.169E-9	1.863E-7	2.732E-6
	Placebo (with thinning)	Shape	NR	2.128	0.2256	0.007905	1.706	2.123	2.591
		Lambda		4.779E-7	1.061E-6	2.645E-8	9.18E-9	1.857E-7	2.738E-6

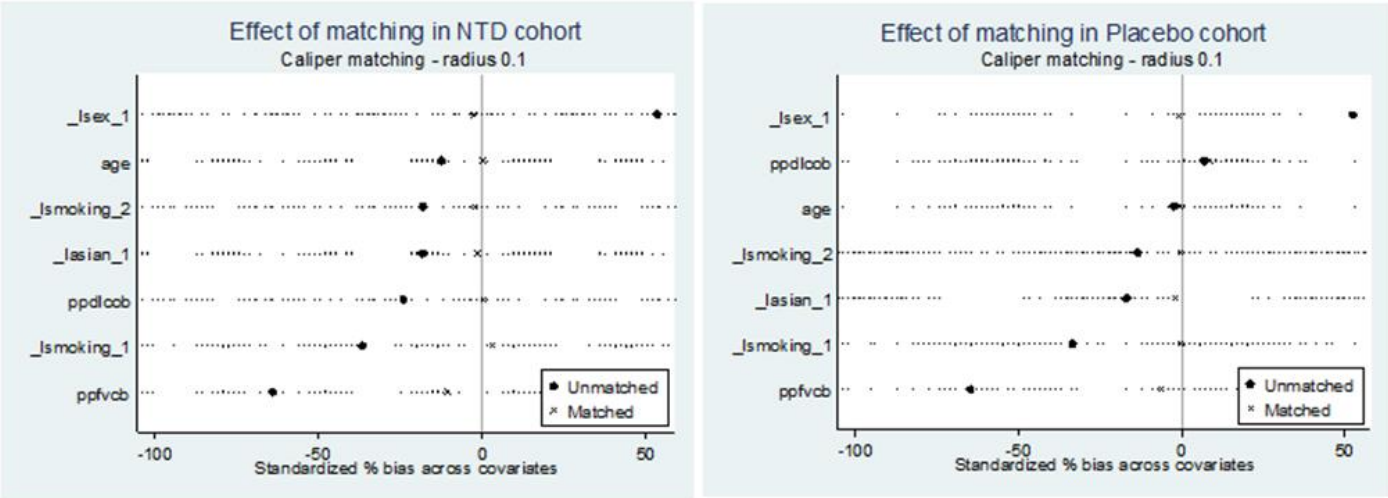
*A logistic distribution was used on log-transformed data. NA, not applicable

Supplementary Figure 1. Propensity score distribution of the IPF and PF-ILD datasets after matching for Nintedanib (left) and placebo (right)



IPF, idiopathic pulmonary fibrosis; PF-ILD, progressive fibrosing interstitial lung disease; NTD, nintedanib

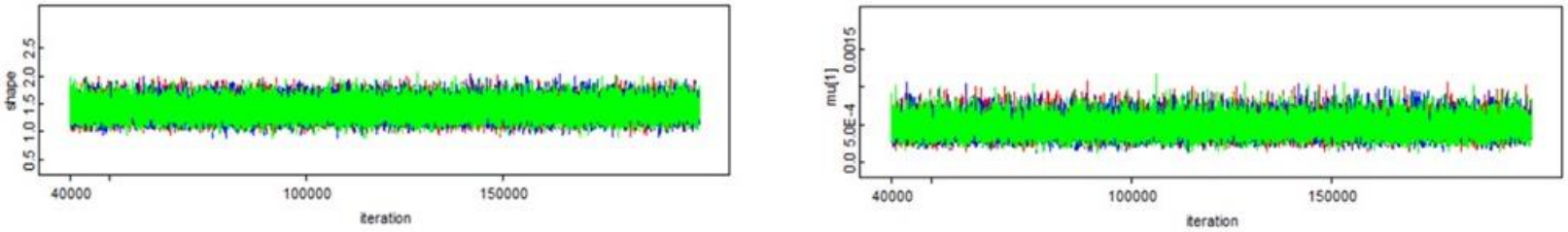
Supplementary Figure 2. Standardised percentage bias across covariates after matching for nintedanib (left) and placebo (right)



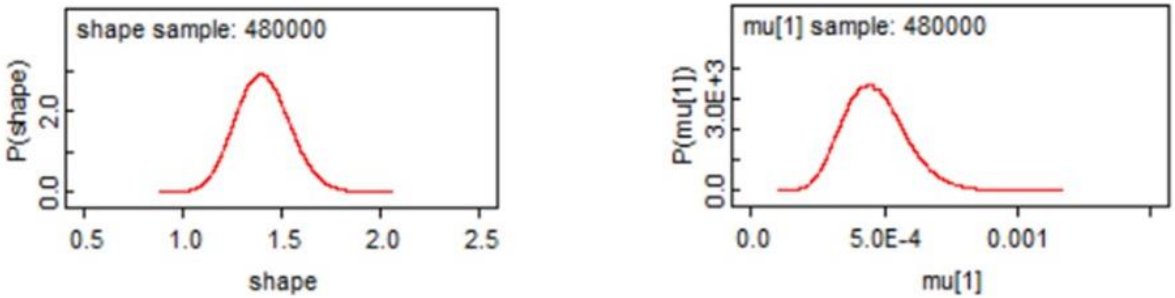
NTD, nintedanib

Supplementary Figure 3. Diagnostic plots for nintedanib gamma distribution: (A) chain history, (B) kernel density, (C) autocorrelation. Left-hand panels show plots for shape; right-hand panels show plots for rate

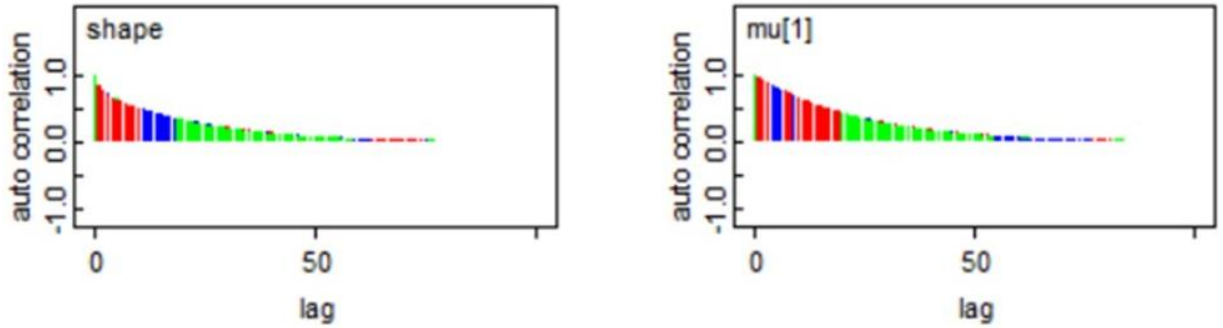
A



B

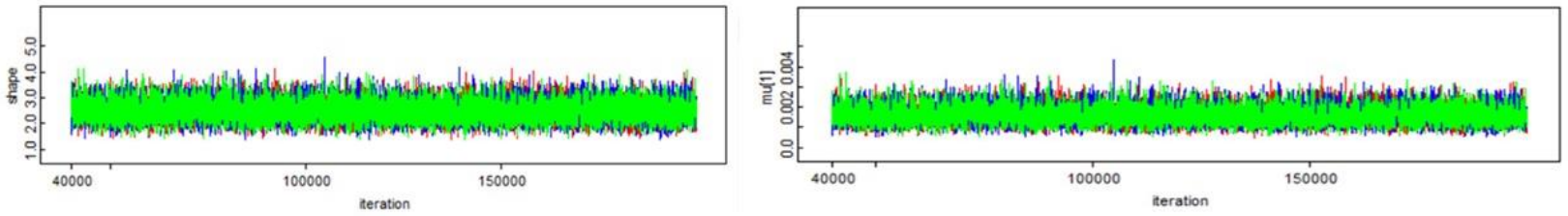


C



Supplementary Figure 4. Diagnostic plots for placebo gamma distribution: (A) chain history, (B) kernel density, (C) autocorrelation. Left-hand panels show plots for shape; right-hand panels show plots for rate

A



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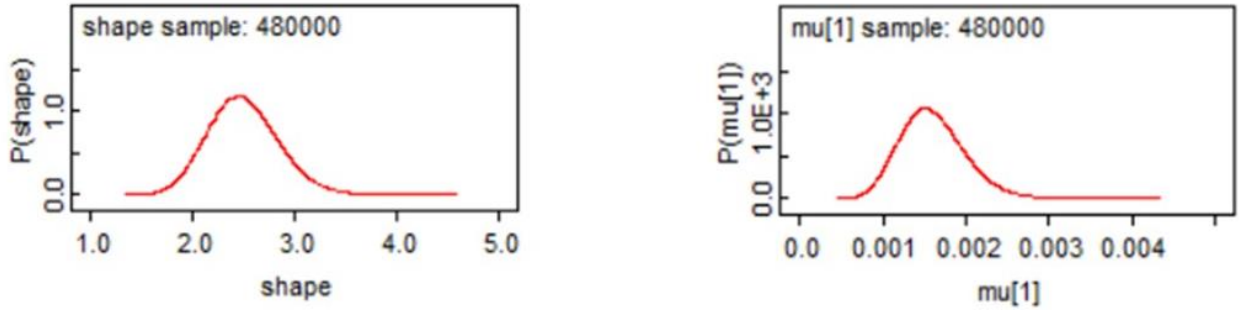

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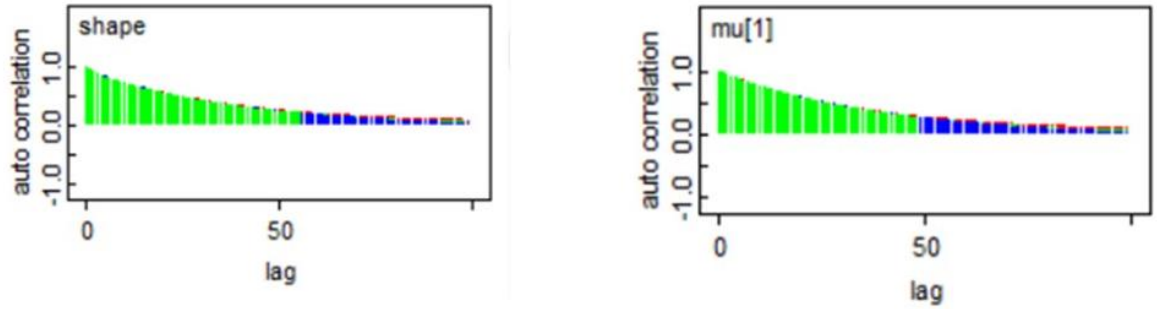
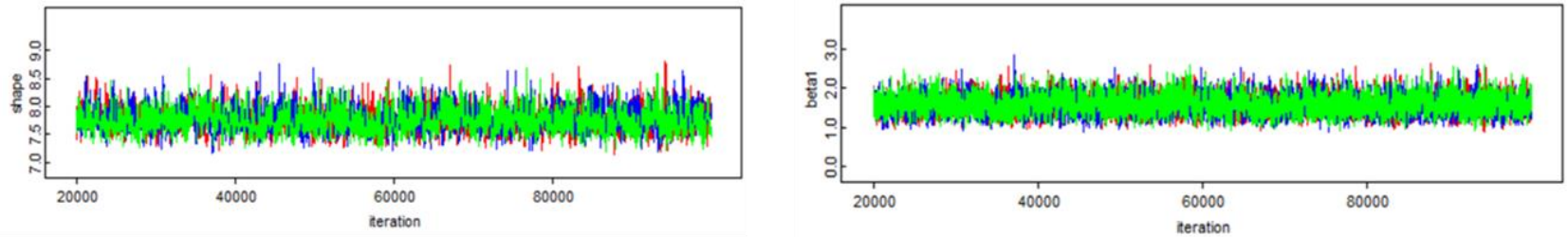


Supplementary Figure 5. Diagnostic plots for nintedanib log-logistic distribution: (A) chain history, (B) kernel density, (C) autocorrelation. Left-hand panels show plots for location; right-hand panels show plots for scale

A



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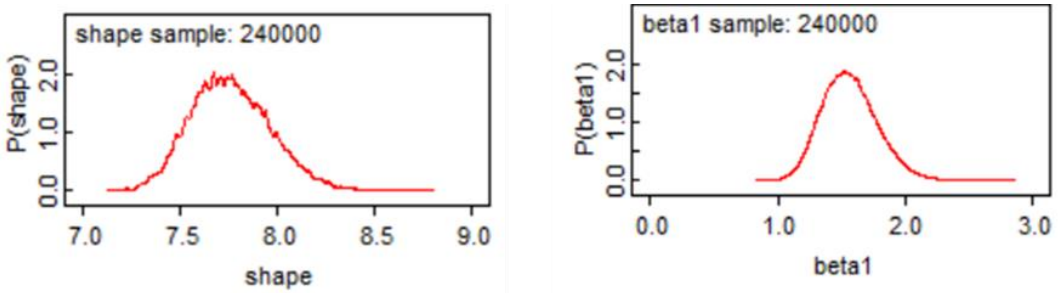

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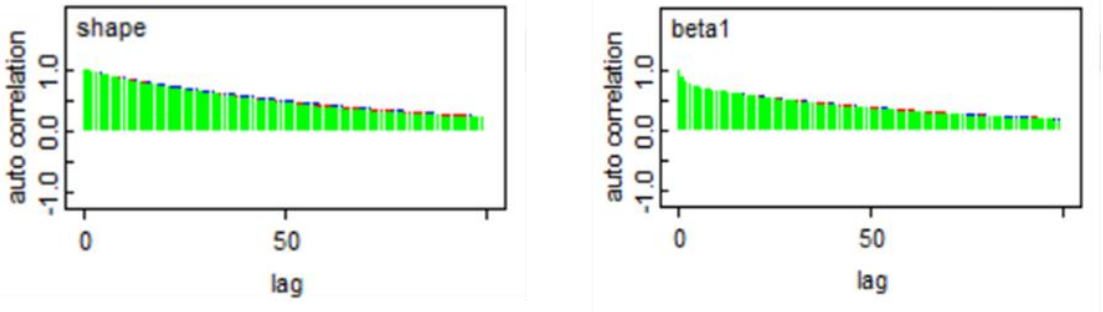
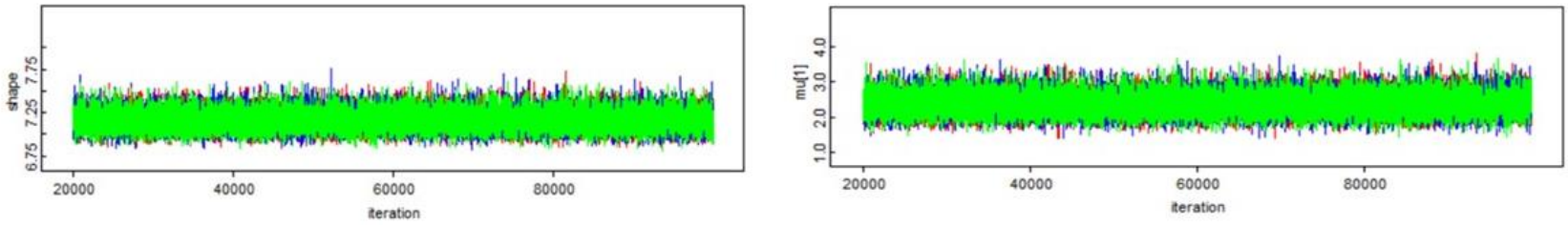
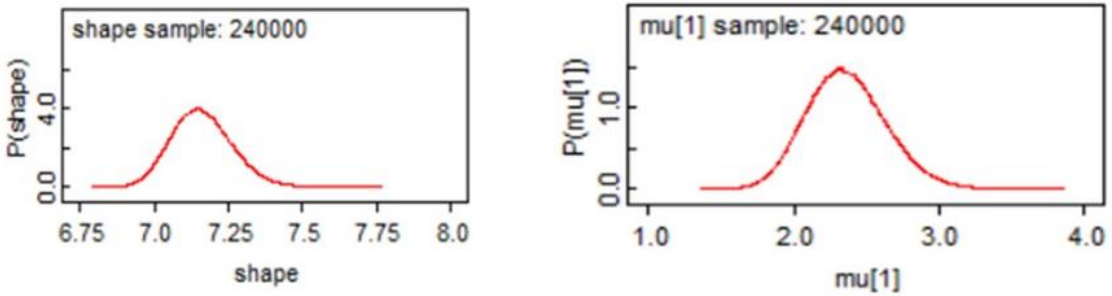


Supplementary Figure 6. Diagnostic plots for placebo log-logistic distribution: (A) chain history, (B) kernel density, (C) autocorrelation. Left-hand panels show plots for location; right-hand panels show plots for scale

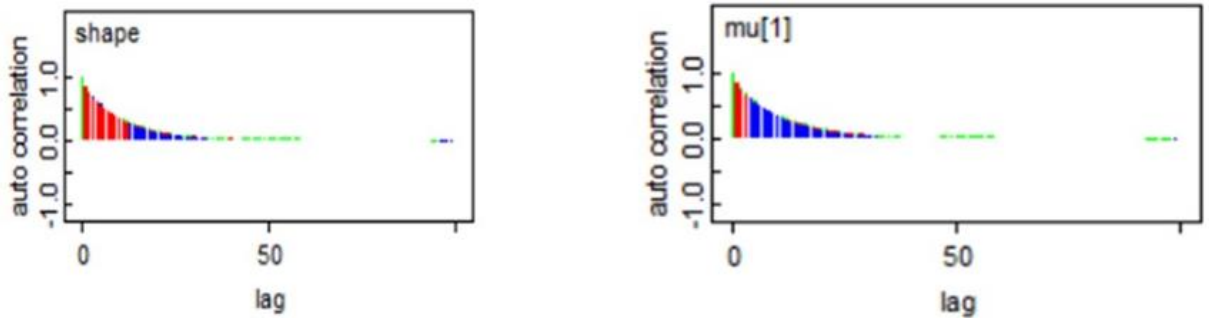
A



B

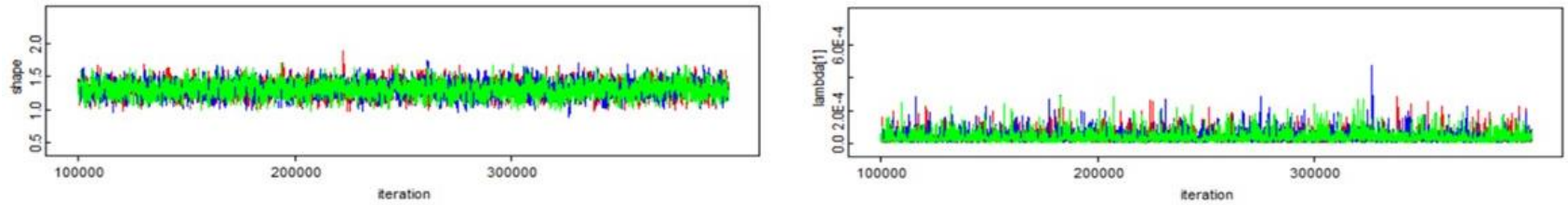


C



Supplementary Figure 7. Diagnostic plots for nintedanib Weibull distribution: (A) chain history, (B) kernel density, (C) autocorrelation. Left-hand panels show plots for shape; right-hand panels show plots for lambda

A



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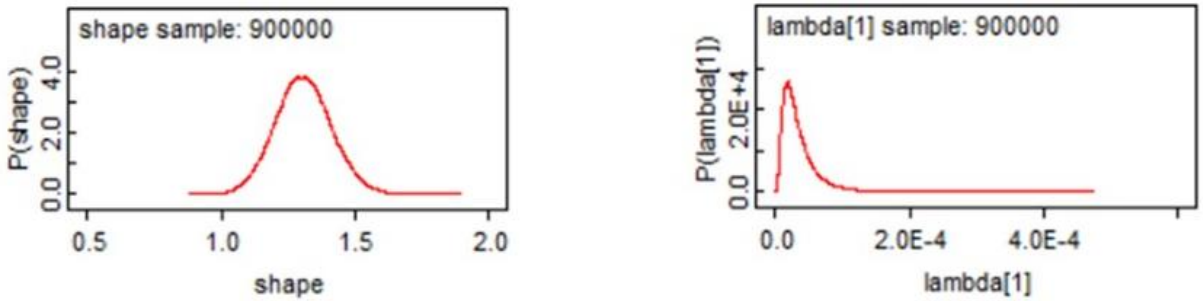

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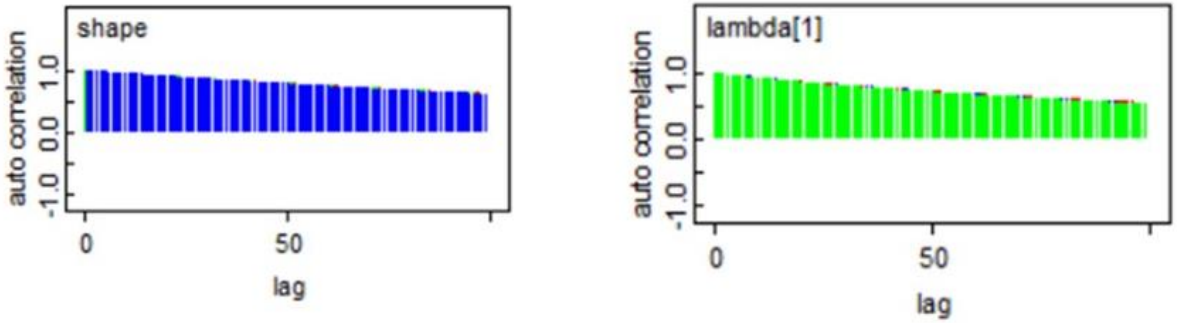
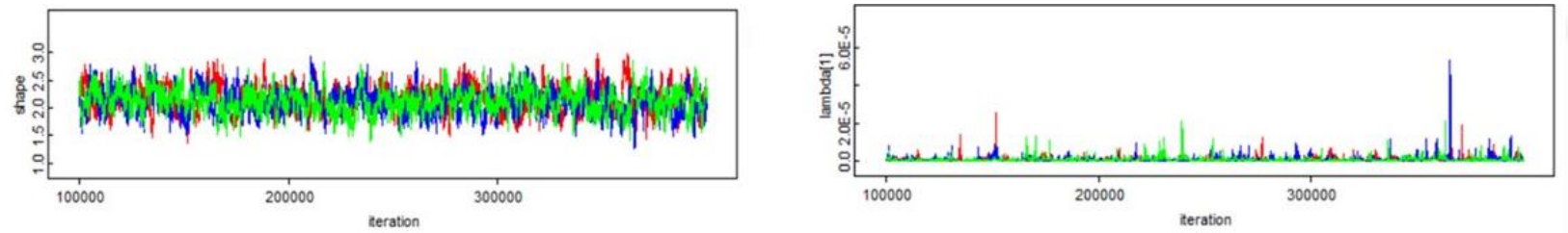


Results without thinning are shown.

Supplementary Figure 8. Diagnostic plots for placebo Weibull distribution: (A) chain history, (B) kernel density, (C) autocorrelation. Left-hand panels show plots for shape; right-hand panels show plots for lambda

A



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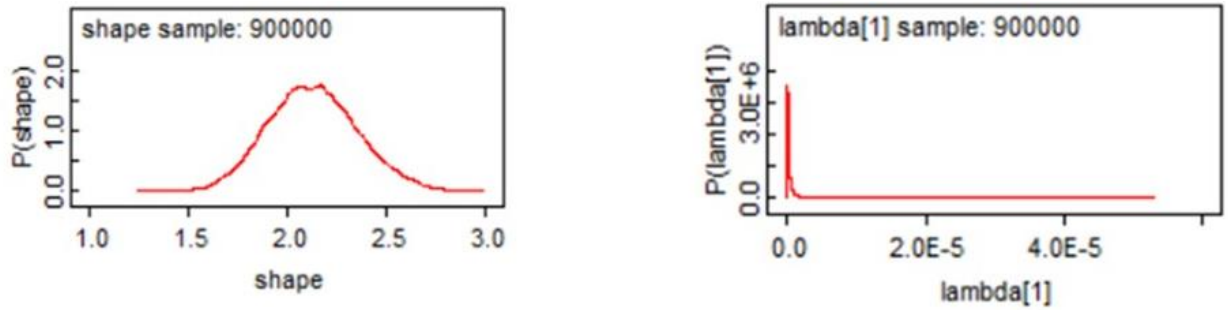

C

Results without thinning are shown. Note that if the thinning factor did not impact parameter estimates, the estimates without the thinning factor were used.