Supplemental Online Content

Stevens KN, Creanor S, Jeffery A, et al; the PD STAT Study Group. Evaluation of simvastatin as a disease-modifying treatment for patients with Parkinson disease: a randomized clinical trial. *JAMA Neurol*. Published online October 31, 2022. doi:10.1001/jamaneurol.2022.3718

This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Summary Statistics of the Baseline Characteristics by Allocated Group of All Recruited Participants

Continuous covariates are reported by mean and standard deviation (SD), unless indicated and categorical covariates are reported by frequency and percentage.

	Placebo N = 118	Simvastatin N = 117	All N = 235
Age in years	65·0 (9·7)	65·9 (8·7)	65·4 (9·2)
Female	52 (44%)	45 (38%)	97 (41%)
Disease duration in years	10·0 (4·8)	9·6 (3·8)	9·8 (4·3)
Systolic Blood Pressure (mmHg)	129·7 (18·3)	126·7 (16·5)	128·2 (17·5)
BMI (kg/m^2)	26·9 (4·7)	26·2 (4·7)	26·6 (4·7)
MoCA	27·6 (2·5)	27·7 (2·2)	27·6 (2·4)
Ethnic Origin			
White	117 (99%)	116 (99%)	233 (99%)
Other	1 (1%)	1 (1%)	2 (1%)
Smoking Status			
Never-smoker	81 (69%)	77 (66%)	158 (67%)
Ex-smoker	33 (28%)	35 (30%)	68 (29%)
Light Smoker	4 (3%)	4 (3%)	8 (3%)
Moderate smoker	0 (0·0)	1 (1%)	1 (0·5%)
Relationship Status			
Single	7 (6%)	5 (4%)	12 (5%)
Married/civil partnership	97 (82%)	98 (84%)	195 (83)
Separated	3 (3%)	1 (1%)	4 (2%)
Divorced/partnership dissolved	6 (5%)	8 (7%)	14 (6%)
Widowed/surviving partner	4 (3%)	5 (4%)	9 (4%)
Living Status			
Live alone	10 (8%)	13 (11%)	23 (10%)
Spouse/partner	104 (88%)	101 (86%)	205 (87%)
Parent(s)	1 (1%)	··	1 (0·5)
Children under 18	10 (8%)	13 (11%)	23 (10%)
Children over 18	19 (16%)	15 (13%)	34 (14%)
Non-family	1 (1%)	1 (1%)	2 (1%)
QRisk			
N (%) ≥ 10%	57 (48·3)	53 (45·3)	110 (46·8)
Median (IQR)	9·6 (3·8 – 16·0)	8·6 (6 - 15·9)	9·2 (4·8 – 16·0)
Hoehn & Yahr			
1·0 to 2·0	80 (68%)	82 (70%)	162 (69%)
2·5 to 3·0	38 (32%)	35 (30%)	73 (31%)

eTable 2. Results of the COVID-19 Sensitivity Analyses of the Secondary Outcomes Mixed-Effects Linear Regression Models at 24 Months

The models were adjusted for sex, Hoehn and Yahr stratification variable and the participant's outcome measurement, age and PD duration at baseline as fixed effects and study centres as random effects.

Secondary Outcome	Fully Adjusted Mean Between-Group Difference (simvastatin minus placebo) (Two-sided 95% CI)
HDL (mmol/L)	0·000148 (-0·147 to 0·150)*
Total cholesterol (mmol/L)	-1·15 (-1·41 to -0·881)
Total cholesterol/HDL ratio	-0·691 (-0·905 to -0·476)
BTT - key presses in 30 seconds (OFF)	-1·25 (-4·39 to 1·89)
Mean 10MWT time (seconds) [OFF]	-0·658 (-1·57 to 0·256)*
10MWT completed at least one test [OFF]†	OR = 0·636 (0·192 to 2·10)
MDS-UPDRS part II [ON]	1·06 (-0·450 to 2·57)
MDS-UPDRS Total Score [ON]	0·413 (-4·18 to 5·00)
PDQ-39 Total Score	0·571 (-2·30 to 3·44)
NMSS Total Score	1·51 (-5·57 to 8·59)*
KPPS Total Score	0·592 (-2·41 to 3·60)*
LED	-19·0 (-87·0 to 48·9)
HbA1c (mmol/mol)	0·335 (-0·441 to 1·11)
Diabetes†	OR = 0·864 (0·0507 to 14·7)
ACE-III Total Score	0·4 (-01·0 to 1·9)*
MADRS Total Score	-0·1 (-1·2 to 1·1)

* Confidence interval calculated from bootstrapped standard error estimate

† Summary statistics reported as frequency and percentage allocated group difference reported as odds ratio (OR)

eTable 3. Frequency and Percentage of Serious Adverse Events (SAEs) by Reported Dose of Simvastatin at the Time of the SAE

	Simvastatin Dose at time of SAE	
N (%)	**0mg***	**80mg**
	(N = 37)	**(N = 37)**
Reason for SAE**		
Prolonged/required hospitalisation	34	33
Important medical event	7	10
Persistent/significant disability/incapacity	1	2
Event fatal	1	..
Life threatening	..	1
Outcome		
Recovered	21	25
Recovered with sequelae	13	12
Died	3	..
Related to trial treatment		
Possible	..	1
Unlikely	4	6
Not related	33	30
Organ Classification		
Surgical & medical procedures	12	14
Injury, poisoning & procedural complications	4	4
Gastrointestinal disorders	3	5
Infections & infestations	5	1
Nervous system disorders	2	3
Cardiac	3	2
Renal & urinary disorders	1	2
Neoplasms benign, malignant & unspecified	2	1
Respiratory, thoracic & mediastinal	2	..
Investigations	..	2
Hepatobiliary disorders	2	..
General & administration site conditions	1	1
Eye disorders	..	1
Endocrine	..	1

* Includes participants allocated to the placebo group and those who had discontinued simvastatin prior to the reported SAE
** SAE could be assigned more than one reason

eTable 4. Frequency and Percentage of Related Adverse Events (AEs) by Reported Dose of Simvastatin at the Time of the Related AE

N	Simvastatin dose at time of related AE		
	0mg*	40 mg	80mg
	(N = 171)	(N = 66)	(N = 84)
Related to trial treatment			
Definite	3	2	2
Probable	12	6	14
Possible	156	58	68
Organ Classification			
Musculoskeletal & connective tissue disorders	65	30	62
Gastrointestinal disorders	16	20	16
Nervous system disorders	30	8	..
General & administration site conditions	26	6	6
Skin & subcutaneous tissue disorders	10	..	..
Respiratory, thoracic & mediastinal	5	2	..
Investigations	6	..	..
Psychiatric disorders	4	..	..
Eye disorders	4	..	..
Cardiac	3	..	..
Vascular	2	..	..
Common Known Side Effect	**93**	**48**	**68**

* Includes participants allocated to the placebo group and those who had discontinued simvastatin 24 hrs or more prior to the reported related AE

eTable 5. Frequency and Percentage of Related Adverse Events (AEs) Identified as Common Adverse Effects of Simvastatin

N (%)	Simvastatin dose at time of related AEs identified as common side effect		
	0mg*	40 mg	80mg
	(N = 93)	(N = 48)	(N = 68)
Myalgia	62 (63%)	30 (63%)	54 (79%)
Headache	18 (18%)	··	··
Nausea	6 (6%)	8 (17%)	··
Gastrointestinal discomfort	2 (2%)	6 (13%)	2 (3%)
Constipation	··	··	8 (12%)
Diarrhoea	2 (2%)	··	4 (6%)
Sleep disorder	2 (2%)	2 (4%)	··
Flatulence	2 (2%)	2 (4%)	··
Asthenia	4 (4%)	··	··

eAppendix. Acknowledgement of Site Contributions

Derriford Hospital, Plymouth	**Addenbrooke's Hospital, Cambridge**
Jemma Inches	Simone Hargreaves
Donna Underwood	Danielle Johnson
Royal Cornwall Hospital, Truro	Lucy Worboys
Julie Frost	Paul Worth
Ali James	**Salford Royal Hospital**
Christine Schofield	Judith Brooke
Royal Devon and Exeter Hospital	Christopher Kobylecki
Rob James	Victoria Parker
Clare O'Reilly	**Fairfield General Hospital, Bury**
Ray Sheridan	Judith Brooke
Sarah Statton	Linda Johnson
Musgrove Park Hospital, Taunton	Rosane Joseph
Tamlyn Russell	Julie Melville
Alison Whitcher	Jason Raw
Yeovil District Hospital	**Royal Preston Hospital**
Alison Lewis	Janice Birt
Rani Sophia	Marianne Hare
Royal Bournemouth Hospital	Saifuddin Shaik
Khaled Amar	**Leeds General Infirmary**
Rochelle Hernandez	Jane Alty
Alison Pitcher	Jeremy Cosgrove
Royal United Hospital, Bath	**Clinical Ageing Research Unit, Newcastle upon Tyne**
Samantha Carvey	David Burn
Ruth Hamlin	Angela Green
Veronica Lyell	Ann McNichol
St Peters Hospital, Chertsey	Nicola Pavese
Louisa Aubry	Helen Pilkington
Gillian Carey	Maria Price
Jan Coebergh	Kathryn Walker
Charing Cross Hospital, London	**Kings College Hospital, London**
Idah Mojela	Ray Chaudhuri
Sophie Molloy	Aleksandra Podlewska
Royal Free Hospital, London	Prashanth Reddy
Yolanda Berceruelo Bergaz	Dhaval Trivedi
Bintou Camera	**Royal Hallamshire Hospital, Sheffield**
Philip Campbell	Oliver Bandmann
Huw Morris	**Norfolk and Norwich Hospital**
Tinashe Samakomva	Vaclav Dostal
Anette Schrag	Jodie Graham
Queen's Hospital, Romford	Godwin Mamutse
Sarah Fuller	Alex Miller-Fik
Anjum Misbahuddin	Alison Wiltshire
Laura Parker	Catherine Wright
Elisa Visentin	**Rotherham General Hospital**
John Radcliffe Hospital, Oxford	Ahmed Abdelhafiz
Stephanie Gallehawk	
Jacqueline Rudd	
Sudhir Singh	
Luton and Dunstable Hospital	
Julie Creven	
Yvonne Croucher	
Anette Schrag	
Susan Tluk	
Paul Watts	