Supplementary Material 14

Discussion

D.9 Discussion

Table S334: Trial Milestones

Milestone	Actual Date
Initial Ethics submission	14 Nov, 2014
Initial MHRA submission	14 Nov, 2014
Initial R & D submission	18 Nov, 2014
Ethics approval received	8 Dec, 2014
MHRA approval received	16 Dec, 2014
Central R & D approval received	30 Mar, 2015
First site open	14 Apr, 2015
First patient recruited	8 Sept, 2015
End of recruitment - last patient randomised	19 Jun, 2018

Table S335: A summary of approved protocol versions

Amendment
Version 1.0a, 18 March 2015
Section 7.6.1 – wording updated to prevent additional samples being taken.
Grammatical errors and line spacing errors corrected.
Version 2.0, 27 November 2015
Updated contact details throughout
Formatting, typographical errors and clarifications throughout
Updated and clarified Inclusion and Exclusion criteria
Screening period reduced to 6-8 weeks
Schedule of Events updated to include:
- ELF test included as a research sample
- Central ALP tests for Visits 3-11

Table S335: A summary of approved protocol versions *(continued)*

Protocol Version Number and Date	Amendment
	- ADA, PD and QoL not performed at Screening visit 1 & 2
	- MRI scansclarified
	Section 5.2 updated to include Screening Number details
	Section 6.2 updated to clarify and include Screening Number
	Section 7.3 Visit tests corrected and updated
	Section 7.5 & 7.6 updated to account for amendment changes
	Section 7.7 Clarified and 7.9 Updated regarding delay to infusion
	Section 7.11 Contraception and pregnancy section added
	Section 8.1 & 8.2 clarified
	Section 9.1 Details updated and CRF list updated
	References and Appendices updated
Version 3.0, 16 March 2016	
	Inclusion criteria for patients ALP value has been reduced from >2 x ULN to >1.5 x ULN
	Pre-medications updated (7.9 and where applicable) to include hydrocortisone at Visit 3-5

Table S335: A summary of approved protocol versions *(continued)*

Protocol Version Number and Date	Amendment
	Section 8.1.2 “Hypersensitivity, Infusion Reactions and Infusion Related Reactions” added
	Grammatical and continuity errors corrected
	Additional telephone number for Trial Office added throughout
Version 4.0, 27 March 2018	
	Contact telephone and fax details updated throughout protocol
	4.1 point 3 in the inclusion criteria has been clarified; validity of colonoscopy results have been altered from within 1 year to within the patient’s standard of care
	Inclusion criteria updated and clarified (minimum weight criteria added)
	Footers in Schedule of Events amended to match text in written protocol
	Grammatical errors and line spacing errors corrected
	Timing of interim analysis clarified - Information added regarding Acorda, Biotie’s parent company
	Section 3.3 Clarification of replaceable patients in stage 2 of the trial
	Section 7.13 Deleted sentence for clarity
	Section 12.2 Additional sentence added for completeness; and also a sentence amended for clarity

Table S335: A summary of approved protocol versions *(continued)*

Protocol Version Number and Date	Amendment
Version 5.0, 31 July 2018	
	Change of CI
	Change of Trial Coordinator
	Updated text regarding GDPR