Appendix 1. Schedule of Assessments for Original Treatment Assignment

			Week[1]			Month								Post-Treatment Follow-up	
Time Point	**Screen-ing**	**Base-line[2]**	**1**	**2**	**3**	**1**	**2**	**4**	**6**	**9**	**12**	**15**	**18**	**Every 6 months after V12[3]**	**Common closing date**
Visit	**V–1[4]**	**V1**	**V2**	**V3**	**V4**	**V5**	**V6**	**V7**	**V8**	**V9**	**V10**	**V11**	**V12**	**$V_{6\text{-month interval}}$**	**V_{CCD}**
Day	**0**	**1**	**8**	**15**	**22**	**29**	**60**	**120**	**180**	**270**	**365**	**455**	**545**		
General Assessments															
Informed consent	X														
Inclusion and exclusion criteria	X	X													
Randomization		X													
SF-36 v.2™ Health Survey[5,6]	X	X				X	X	X	X	X	X	X	X	X	X
Demography	X														
Medical history (with vaccine)	X														
Skin tests (PPD, anergy panel)[7]	X														
Glucocorticoid log[8]	X	X	X	X	X	X	X	X	X	X	X	X	X		
Concomitant medications[9]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Adverse events		X	X	X	X	X	X	X	X	X	X	X	X	X	X
Safety officer adverse events[10]		X	X	X	X	X	X	X	X	X	X	X	X		
Vital signs[11]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Height	X														
Weight	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X

[1] For visit windows please refer to section 6.5.
[2] Assessments done within 14 days of baseline visit do not have to be repeated at the discretion of the investigator.
[3] Please record these visits on the Follow-up Visit CRFs and mark these visits sequentially as V13, V14, V15, etc. until V_{ccd}.
[4] The screening visit must be completed within 14 days of the baseline visit.
[5] Should be completed before the participant sees the physician, undergoes any tests or treatment, or receives any tests that day EXCEPTION: Screening Visit.
[6] Ideally should be performed at screening visit. May be performed at either screening visit or baseline visit but not both.
[7] Candida and tetanus booster formulation used. Note: skin test placement is required before starting the baseline infusion. Skin test readings are not required prior to infusion.) To be repeated for testing immunotolerance in a subset of participants after month 6 (see section 9)
[8] All glucocorticoids given as specified by the protocol for treatment of vasculitis should be recorded on the glucocorticoid logs. Glucocorticoids given for any other reason—i.e., for management of asthma or for management of a participant according to BMJ or CCC—should be recorded on the concomitant medications sheet.
[9] Within the last 30 days at the screening visit
[10] Not applicable after V12 or termination visit.
[11] During the infusion, every 15 minutes for 1 hour; then every 30 minutes; and then at least 1 hour after the completion of the infusion.

			Week[1]			Month								Post-Treatment Follow-up	
Time Point	**Screen-ing**	**Base-line[2]**	**1**	**2**	**3**	**1**	**2**	**4**	**6**	**9**	**12**	**15**	**18**	**Every 6 months after V12[3]**	**Common closing date**
Visit	**V–1[4]**	**V1**	**V2**	**V3**	**V4**	**V5**	**V6**	**V7**	**V8**	**V9**	**V10**	**V11**	**V12**	**$V_{6\text{-month interval}}$**	**V_{CCD}**
Day	**0**	**1**	**8**	**15**	**22**	**29**	**60**	**120**	**180**	**270**	**365**	**455**	**545**		
Safety officer assessment[12]		X	X	X	X	X	X	X	X	X	X	X	X		
Physical examination[13]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Chest x-ray or CT scan[14]	X					X		X	X	X	X	X	X		X
ECG[15]	X										X		X		X
BVAS/WG and flare history[16]	X					X	X	X	X	X	X	X	X	X	X
Physician Global Assessment Form[6]	X	X				X	X	X	X	X	X	X	X	X	X
Treatment questionnaire (MD)									X						
VDI		X							X		X		X	X	X
AVID		X							X		X		X	X	X
Hematology[17]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Chemistry[18]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
ANCA (clinical)[19]	X														
TPMT[20]	X														
Serum pregnancy test[21]	X														
UA with microscopy[22]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X

[12] Not applicable after V12 or termination visit.
[13] At baseline/V1 to Week 3/V4 if clinically indicated.
[14] CXR is required at either baseline or screening and months 1, 6, 9, 18 for all participants; and at months 2,4,12 and 15 for participants with abnormal CXR at any visit. CXRs obtained within 2 weeks of a study visit does not have to be repeated at the investigator's discretion. CT scans can be performed instead of CXRs at the investigator's discretion.

[15] After screening, an ECG must be done at V10, V12, and when the participant withdraws or terminates from the study.
[16] Flare history not required at screening and baseline.
[17] STAT on V2-V4. If a pre-infusion WBC <3,000/mm^3 is noticed, the infusion should be withheld; hematology includes WESR; does not need to be repeated at baseline if not clinically indicated
[18] Chemistry includes only BUN, creatinine, and C-reactive protein; it does not need to be repeated at baseline if not clinically indicated
[19] The clinical ANCA testing performed at the screening visit will be done locally and will determine the participant's eligibility.
[20] TPMT specimens will be drawn at screening, but results are not required for randomization. TPMT may determined by TPMT testing or a completed AZA course of at least 125 mg/day.
[21] Only for women of child-bearing potential
[22] Does not need to be repeated at baseline if not clinically indicated

			Week[1]			Month								Post-Treatment Follow-up	
Time Point	**Screen-ing**	**Base-line[2]**	**1**	**2**	**3**	**1**	**2**	**4**	**6**	**9**	**12**	**15**	**18**	**Every 6 months after V12[3]**	**Common closing date**
Visit	**V–1[4]**	**V1**	**V2**	**V3**	**V4**	**V5**	**V6**	**V7**	**V8**	**V9**	**V10**	**V11**	**V12**	**$V_{6\text{-month interval}}$**	**V_{CCD}**
Day	**0**	**1**	**8**	**15**	**22**	**29**	**60**	**120**	**180**	**270**	**365**	**455**	**545**		
Mechanistic Assays															
PBMC T-cell assay [23]	X					X	X	X	X		X		X	X	X
Whole-blood DNA HLA genotyping							X								
Whole-blood flow cytometry–panel staining [23]	X			X		X	X	X	X	X	X	X	X	X	X
Whole-blood gene expression profiling [23]	X			X		X	X	X	X	X	X		X	X	X
Serum-secreted cytokines [23]	X			X		X	X	X	X	X	X	X	X	X	X
Serum archive [23]	X			X		X	X	X	X	X	X	X	X	X	X
Plasma archive [23]	X			X		X	X	X	X	X	X	X	X	X	X
Serum HACA [23]	X							X	X	X			X	X	X
Serum ANCA [23,24]	X					X	X	X	X	X	X	X	X	X	X
Serum PK (rituximab levels)[25]	X			X		X	X	X	X	X			X	X	X
Medications															
Glucocorticoid IV[26]		X													
Glucocorticoid PO	X	X	X	X	X	X	X	X							
Rituximab/rituximab placebo[27]		X	X	X	X										
Oral study drug kits[28]		X	X	X	X	X	X	X	X	X	X	X			
Prophylactic medications	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X

[23] Also to be done at time of flare and switchover (discontinuation of CYC and start of AZA).
[24] For mechanistic assays. Not carried out locally
[25] See the manual of operation.
[26] A maximum of three 1-day glucocorticoid IV doses can be administered. Last glucocorticoid infusion must be given within 14 days before the first rituximab/placebo infusion. Infusion 1 and IV steroid can be administered on the same day. See section 6.1 for the roles of the investigator versus the role of the safety officer during the infusion.
[27] Participants will be premedicated with diphenhydramine (50 mg) and acetaminophen (650 mg) orally 1 hour (plus or minus 15 minutes) before each infusion. The infusion will be administered in a monitored setting, with access to resuscitative drugs, monitoring devices, and CPR equipment.
[28] CYC/CYC placebo during remission induction phase; AZA/AZA placebo during remission maintenance phase. Participants will be switched over from CYC/CYC placebo to AZA/AZA placebo between 3-6 months as per section 6.3.3.1.

Appendix 2. Schedule of Assessments for Crossover Participants

Participants can be crossed over to the alternate drug treatment any time between visit V5 (1 week after the last rituximab/rituximab placebo infusion) and visit V8 (month-6 study visit).Crossover participants will start over at baseline (V1A) and be followed according to the schedule below. All target visit dates for V9 to the common closing date for crossover participants will have the same visit window, but not the same dates that were calculated from V1. All remaining visits will be derived from the V1A visit. In order to get data as close to the time of flare as possible, samples for mechanistic studies should be collected at the visit when the participant is crossed over (this acts as V1A). Clinical samples are to be drawn before infusion either at time of flare or on the day of infusion. Mechanistic samples are not re-collected on day of infusion. Please also refer to the footnotes in Appendix 1.

		Week			Month								Post-treatment Follow-up	
Time Point	**Base-line**	**1**	**2**	**3**	**1**	**2**	**4**	**6**	**9**	**12**	**15**	**18**	**Every 6 months after V12**	**Common closing date**
Visit	**V1A[1]**	**V2A**	**V3A**	**V4A**	**V5A**	**V6A**	**V7A**	**V8A**	**V9**	**V10**	**V11**	**V12**	**$V_{6\text{-month interval}}$ [2]**	**V_{CCD}**
Day	**1**	**8**	**15**	**22**	**29**	**60**	**120**	**180**	**270**	**365**	**455**	**545**		
General Assessments														
SF-36 v.2™ Health Survey	X				X	X	X	X	X	X	X	X	X	X
Glucocorticoid log[3]	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Concomitant medications	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Adverse events	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Safety officer adverse events	X	X	X	X	X	X	X	X	X	X	X	X		
Vital signs	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Height	X													
Weight	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Safety officer assessment	X	X	X	X	X	X	X	X	X	X	X	X		
Physical examination	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Chest x-ray or CT scan[4]	X				X		X	X	X	X	X	X		X
ECG	X									X		X		X
BVAS/WG and flare history	X				X	X	X	X	X	X	X	X	X	X

[1] The participant will not need to undergo screening procedures or to observe the washout periods for prohibited medications.
[2] Please record these visits on the Follow-up Visit CRFs and mark these visits sequentially as V13, V14, V15, etc. until the V_{ccd}.
[3] All glucocorticoids given as specified by the protocol for treatment of vasculitis should be recorded on the glucocorticoid logs. Glucocorticoids given for any other reason—i.e., for management of asthma or for management of a participant according to BMJ or CCC—should be recorded on the concomitant medications sheet.
[4] Chest imaging results within 2 weeks of the first crossover visit (V1A) will be used for the BVAS/WG.

		Week			Month								Post-treatment Follow-up	
Time Point	**Base-line**	**1**	**2**	**3**	**1**	**2**	**4**	**6**	**9**	**12**	**15**	**18**	**Every 6 months after V12**	**Common closing date**
Visit	**V1A**[1]	**V2A**	**V3A**	**V4A**	**V5A**	**V6A**	**V7A**	**V8A**	**V9**	**V10**	**V11**	**V12**	$V_{6\text{-month interval}}$ [2]	V_{CCD}
Day	**1**	**8**	**15**	**22**	**29**	**60**	**120**	**180**	**270**	**365**	**455**	**545**		
Physician Global Assessment Form	X				X	X	X	X	X	X	X	X	X	X
Treatment questionnaire (MD)								X						
VDI	X							X		X		X	X	X
AVID	X							X		X		X	X	X
Hematology	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Chemistry	X	X	X	X	X	X	X	X	X	X	X	X	X	X
UA with microscopy	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Mechanistic Assays														
PBMC T-cell assay[5]	X				X	X	X	X		X		X	X	X
Whole-blood DNA HLA genotyping[6]						X								
Whole-blood flow cytometry[5]	X		X		X	X	X	X	X	X	X	X	X	X
Whole-blood gene expression profiling[5]	X		X		X	X	X	X	X	X		X	X	X
Serum-secreted cytokines[5]	X		X		X	X	X	X	X	X	X	X	X	X
Serum archive[5]	X		X		X	X	X	X	X	X	X	X	X	X
Plasma archive[5]	X		X		X	X	X	X	X	X	X	X	X	X
Serum HACA[5]	X						X	X	X			X	X	X
Serum ANCA[5]	X				X	X	X	X	X	X	X	X	X	X
Serum PK (Rituximab levels)	X		X		X	X	X	X	X			X	X	X
Medications														
Glucocorticoid IV	X													
Glucocorticoid PO	X	X	X	X	X	X	X							
Rituximab/rituximab placebo	X	X	X	X										
Oral study drug kits	X	X	X	X	X	X	X	X	X	X	X			

[5] Also to be done at time of flare and switchover (discontinuation of CYC and start of AZA).

[6] Only if this collection has not been made because (1) crossover has occurred before V6 during original treatment or (2) the blood draw has been missed for a reason other than nonconsent.

		Week			Month								Post-treatment Follow-up	
Time Point	**Base-line**	**1**	**2**	**3**	**1**	**2**	**4**	**6**	**9**	**12**	**15**	**18**	**Every 6 months after V12**	**Common closing date**
Visit	**V1A**[1]	**V2A**	**V3A**	**V4A**	**V5A**	**V6A**	**V7A**	**V8A**	**V9**	**V10**	**V11**	**V12**	$V_{6\text{-month interval}}$ [2]	V_{CCD}
Day	**1**	**8**	**15**	**22**	**29**	**60**	**120**	**180**	**270**	**365**	**455**	**545**		
Prophylactic medications	X	X	X	X	X	X	X	X	X	X	X	X	X	X

Appendix 3. Schedule of Assessments for Open-label Rituximab

Participants can receive open-label rituximab any time after visit V8 (month-6 study visit) and before visit V12 (month-18 study visit). Crossover participants can receive open-label rituximab any time after visit V8A (month-6 study visit) and before visit V12A (month-18 study visit). Once the decision to use open-label rituximab has been made, the participants will be followed according to the schedule below. All target visit dates for open-label rituximab participants will have the same visit window, but not the same dates that were calculated from V1. All visits after shifting to open-label rituximab will be derived from the V1B visit. In order to get data as close to the time of flare as possible, samples for mechanistic studies should be collected at the visit when the participant is put on open label (this acts as V1B). Clinical samples are drawn before infusion either at time of flare or on the day of infusion (V1B). Mechanistic samples are not re-collected on day of infusion. Please refer to footnotes in Appendix 1 for additional information regarding assessments.

		Week			Month					Post-treatment Follow-up	
Time point	**Base-line**	**1**	**2**	**3**	**1**	**2**	**4**	**6**	**12**	**Every 6 months after V12**	**Common closing date**
Visit	**V1B**[1]	**V2B**	**V3B**	**V4B**	**V5B**	**V6B**	**V7B**	**V8B**	**V10B**[2]	**$V_{6\text{-month interval}}$**[3]	**V_{CCD}**
Day	**1**	**8**	**15**	**22**	**29**	**60**	**120**	**180**	**365**		
General Assessments											
SF-36 v.2™ Health Survey	X				X	X	X	X	X	X	X
Glucocorticoid log[4]	X	X	X	X	X	X	X	X	X		
Concomitant medications	X	X	X	X	X	X	X	X	X	X	X
Adverse events	X	X	X	X	X	X	X	X	X	X	X
Vital signs	X	X	X	X	X	X	X	X	X	X	X
Height	X										
Weight	X	X	X	X	X	X	X	X	X	X	X
Physical examination	X	X	X	X	X	X	X	X	X	X	X
Chest x-ray or CT scan[5]	X				X		X				X
ECG	X										X
BVAS/WG and flare history	X				X	X	X	X	X	X	X
Physician Global Assessment Form	X				X	X	X	X	X	X	X
VDI	X							X	X	X	X
AVID	X							X	X	X	X
Hematology	X	X	X	X	X	X	X	X	X	X	X
Chemistry	X	X	X	X	X	X	X	X	X	X	X
UA with microscopy	X	X	X	X	X	X	X	X	X	X	X

[1] The participant will not need to undergo screening procedures or to observe the washout periods for prohibited medications.

[2] Month 12 after open-label rituximab is a clinical visit consisting of a mechanistic sample collection and the assessment of any adverse events related to the use of rituximab.

[3] Please record these visits on unscheduled visit CRFs and number these visits sequentially as 6 months after V10B, 12 months after V10B, etc. until the V_{CCD}.

[4] All glucocorticoids given as specified by the protocol for treatment of vasculitis should be recorded on the glucocorticoid logs. Glucocorticoids given for any other reason—i.e., for management of asthma or for management of a participant according to BMJ or CCC—should be recorded on the concomitant medications sheet.

[5] Chest imaging results within 2 weeks of the first open-label rituximab visit (V1B) will be used for the BVAS/WG.

		Week			Month					Post-treatment Follow-up	
Time point	**Base-line**	**1**	**2**	**3**	**1**	**2**	**4**	**6**	**12**	**Every 6 months after V12**	**Common closing date**
Visit	**V1B**[1]	**V2B**	**V3B**	**V4B**	**V5B**	**V6B**	**V7B**	**V8B**	**V10B**[2]	**$V_{6\text{-month interval}}$**[3]	**V_{CCD}**
Day	**1**	**8**	**15**	**22**	**29**	**60**	**120**	**180**	**365**		
Mechanistic Assays											
PBMC T-cell assay[6]	X				X			X			
Whole blood flow cytometry[6]	X		X		X			X	X		
Whole blood gene expression profiling[6]	X		X		X			X			
Serum-secreted cytokines[6]	X		X		X			X			
Serum archive[6]	X		X		X			X			
Plasma archive[6]	X		X		X			X			
Serum ANCA[6]	X		X		X			X			
Medications											
Glucocorticoid IV	X										
Glucocorticoid PO	X	X	X	X	X	X	X				
Rituximab[7]	X	X	X	X							
Prophylactic medications	X	X	X	X	X	X	X	X	X	X	X

[6] Also to be done at time of flare.
[7] Since the participant is not taking oral study drug, the safety officer is no longer involved in the management of this participant (see section 6.1).

Appendix 4. Schedule of Assessments for BMJ

	BMJ Follow-up	
Time point	**Every 6 months after**	**Common closing date**
Visit	**$V_{6\text{-month interval}}$**[42]	**V_{CCD}**
General Assessments		
Inclusion and exclusion criteria		
SF-36 v.2™ Health Survey	X	X
Concomitant medications	X	X
Adverse events	X	X
Vital signs	X	X
Height		
Weight	X	X
Physical examination	X	X
Chest x-ray or CT scan		
ECG		
BVAS/WG and flare history	X	X
Physician Global Assessment Form	X	X
VDI	X	X
AVID	X	X
Hematology	X	X
Chemistry	X	X
UA with microscopy	X	X
Medications		
Glucocorticoid IV		
Glucocorticoid PO		
Prophylactic medications	X	X
Rituximab (for AAV)		

[42] Please record these visits on unscheduled visit CRFs and number these visits sequentially as 6 months after BMJ, 12 months after BMJ, etc. until the V_{CCD}.