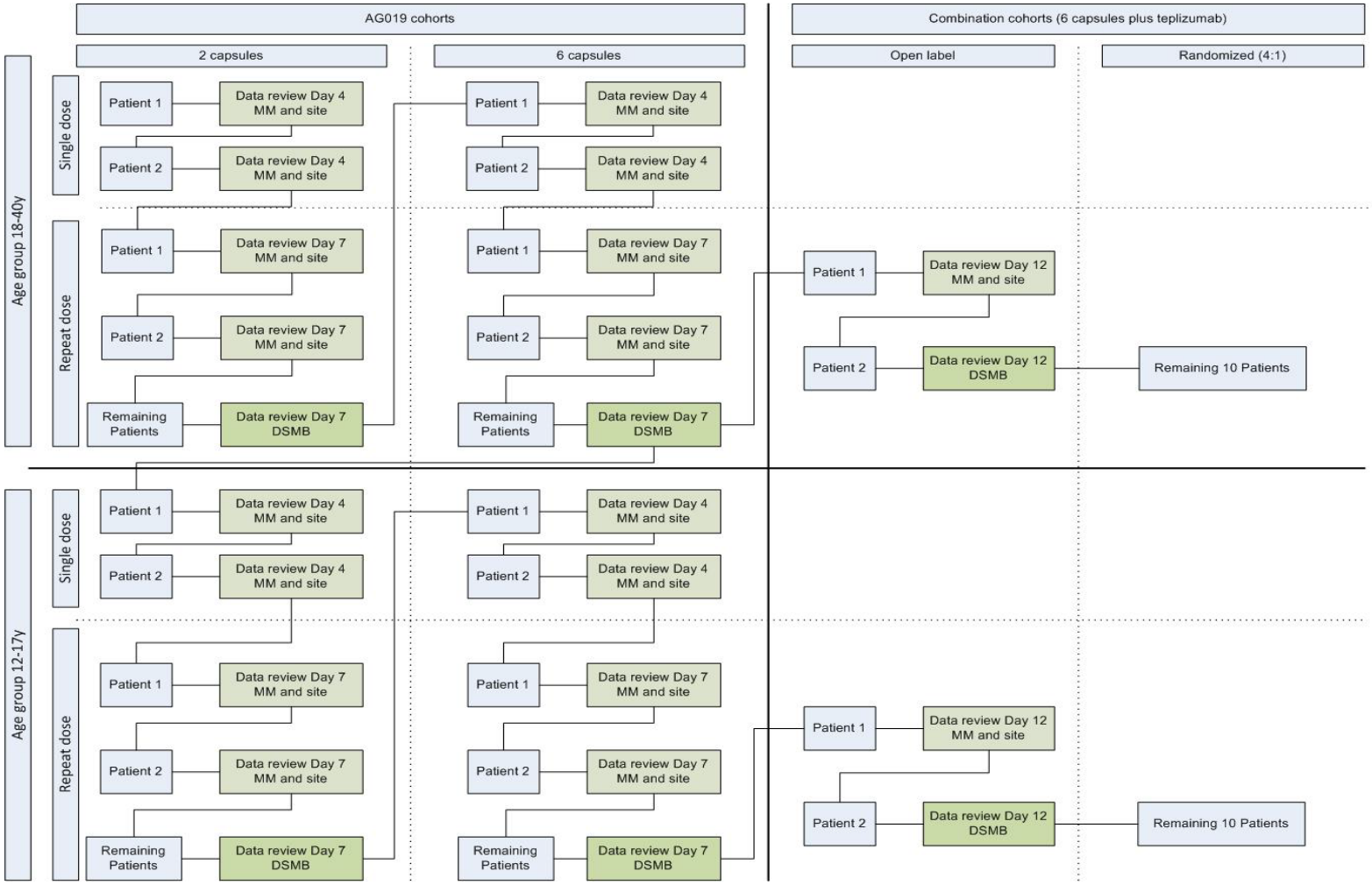
Figure 1. Overall enrollment plan



Abbreviations: DSMB; data safety monitoring board; MM, medical monitoring; y, years.

Table 1. Visit Schedule and Assessments – Single Dose Patients

Study Procedure	Screening	Treatment	Post treatment	Unscheduled
Visit	1	2	3	99[1]
Week	-4 to -1	1	1	N/A
Study Day	-29 to -1	1	4	N/A
Visit Window	N/A	0	0	N/A
GENERAL ASSESSMENTS				
Written informed consent	X			
Eligibility verification	X			
Register patient/visit through interactive response technology (IRT)	X[2]	X		X
Medical History / Demography	X			
Adverse Events	X	X	X	X
Concomitant medications	X	X	X	X
Physical Examination	X	X	X	X
Vital Signs[3]	X	X	X	X
Tuberculosis test	X			
12-lead electrocardiogram (ECG)	X		X[4]	X[4]
LABORATORY ASSESSMENTS – Local Laboratory				
Drugs of abuse test[5]	X			
Serum pregnancy test[6]	X			
Urine pregnancy test[6]		X	X	X
Hematology[7]	X		X	X
Chemistry[8]	X		X	X
Additional screening blood analysis[9]	X			
Autoantibodies[10]	X			
Viral Loads - Serology[11]	X			
STUDY DRUG ADMINISTRATION AND RELATED ASSESSMENTS				
Administer AG019		X		
Study drug accountability			X	

[1] If a patient returned for an unscheduled visit and it was determined that the patient had to withdraw, all End Of Study assessments were performed.

[2] Registration was done as soon as possible after confirmation of eligibility and completion of all screening assessments to allow for timely shipment of study drug.

[3] Vital signs included at least weight, blood pressure, respiratory rate, heart rate, temperature. Height was only measured at the visit 1.

[4] 12-lead ECG was only done if there was suspicion of cardiac problems.

[5] It was recommended that following drugs were assessed at a minimum: cannabis, cocaine, ecstasy, amphetamines.

[6] Only required for women of childbearing potential.

[7] Red blood cell (RBC) count, Hb, hematocrit (Hct), mean corpuscular volume (MCV), mean corpuscular Hb (MCH), mean corpuscular Hb concentration (MCHC), red blood cell distribution width (RDW), white blood cell count, differential count, platelet count

[8] Blood glucose, sodium, potassium, chloride, calcium, CO_2/bicarbonate, total protein, albumin, total bilirubin, alkaline phosphatase (ALP), aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactate dehydrogenase (LDH), C-reactive protein (CRP), INR.
[9] Following additional parameters were assessed at screening: uric acid, urea/blood urea nitrogen (BUN), creatinine, estimated glomerular filtration (eGFR), total cholesterol, triglycerides, high density lipoproteins (HDL), low density lipoproteins (LDL), very low density lipoproteins (VLDL) (optional), thyroid stimulating hormone (TSH). Assessments for which the result was within the normal lab ranges were not repeated at follow-up visits.
[10] If evidence of autoantibody positivity is found in the patient's medical file, this assessment does not have to be repeated at screening.
[11] Epstein-Barr virus (EBV), cytomegalovirus (CMV), human immunodeficiency virus (HIV), hepatitis C virus (HCV), hepatitis B virus (HBV).

Table 2. Visit Schedule and Assessments – Repeat Dose Patients in AG019 Monotherapy Cohorts and AG019/teplizumab Combination Cohorts

Study Procedure	Screening	Treatment									Post treatment									Unscheduled
Visit	1	2	3[1]	4[1]	5	6[1]	7[1]	8	9[1]	10[1]	11[1]	12[1]	13	14	15	16	17	18	19	99[2]
Week	-4 to -1	1	1	1	1	1	1	1	2	2	2	2	2	4	8	13	26	39	52	N/A
Study Day	-29 to -1	1	2	3	4	5	6	7	8	9	10	11	12	28	56	90	180	270	360	N/A
Visit Window[17]	N/A	0	0	0	0	0	0	0	0	0	0	0	0	±2	±2	±7	±7	±7	±7	N/A
GENERAL ASSESSMENTS																				
Written informed consent	X																			
Eligibility verification	X																			
Register / randomize patient through interactive response technology (IRT)	X[3]	X	X	X	X	X	X	X	X	X	X	X	X	X						X
Medical History / Demography	X																			
Tuberculosis test	X																			
Adverse Events	X	X	X	X	X	X	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	X	X	X	X	X	X
Physical Examination	X	X			X			X					X	X	X	X	X	X	X	X
Vital Signs[4]	X	X			X			X					X	X	X	X	X	X	X	X
12-lead electrocardiogram (ECG)	X														X		X[5]		X	X[5]
DISEASE SPECIFIC ASSESSMENTS																				
Insulin use	X	X			X			X					X	X	X	X	X	X	X	
hypoglycemic events	X	X			X			X					X	X	X	X	X	X	X	
Electronic patient reported outcomes (ePRO) training/review	X	X			X			X					X	X	X	X	X	X	X	
Continuous glucose monitoring (CGM) placement		X																		

Study Procedure	Screening	Treatment									Post treatment									Unscheduled
Visit	1	2	3[1]	4[1]	5	6[1]	7[1]	8	9[1]	10[1]	11[1]	12[1]	13	14	15	16	17	18	19	99[2]
Week	-4 to -1	1	1	1	1	1	1	1	2	2	2	2	2	4	8	13	26	39	52	N/A
Study Day	-29 to -1	1	2	3	4	5	6	7	8	9	10	11	12	28	56	90	180	270	360	N/A
Visit Window[17]	N/A	0	0	0	0	0	0	0	0	0	0	0	0	±2	±2	±7	±7	±7	±7	N/A
CGM readings					X			X					X	X	X	X	X	X	X	
LABORATORY ASSESSMENTS - Local Laboratory																				
Drugs of abuse test[6]	X																			
Serum pregnancy test[7]	X																			
Urine pregnancy test[7]		X			X			X					X	X	X	X	X	X	X	X
Hematology set & coagulation test (INR)[8, 10]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Full Chemistry set[9, 10]	X	X			X			X					X	X	X	X	X	X	X	X
Infusion Safety Chemistry set[10]			X	X		X	X		X	X	X	X								
Additional screening blood analysis[11]	X																			
Autoantibodies[12]	X																			
SARS-CoV-2 test – Polymerase chain reaction (PCR)	X	X[18]																		
Viral Loads – Serology[13]	X																			
Viral Loads – PCR[13]	X												X	X	X	X			X	X
LABORATORY ASSESSMENTS - Central Laboratory																				
HbA1c	X														X	X	X	X	X	
C-peptide (from 4h Mixed Meal Tolerance Test)	X															X	X		X	
Glucose (from 4h Mixed Meal Tolerance Test)	X															X	X		X	
Blood for PK	X												X		X	X				

Study Procedure	Screening	Treatment									Post treatment									Unscheduled
Visit	1	2	3[1]	4[1]	5	6[1]	7[1]	8	9[1]	10[1]	11[1]	12[1]	13	14	15	16	17	18	19	99[2]
Week	-4 to -1	1	1	1	1	1	1	1	2	2	2	2	2	4	8	13	26	39	52	N/A
Study Day	-29 to -1	1	2	3	4	5	6	7	8	9	10	11	12	28	56	90	180	270	360	N/A
Visit Window[17]	N/A	0	0	0	0	0	0	0	0	0	0	0	0	±2	±2	±7	±7	±7	±7	N/A
Feces for PK[14]	X														X					
MECHANISTIC ASSESSMENTS[15]																				
Serum	X	X											X		X	X	X	X	X	
Cellular Assays (Screening)	X																			
Cellular Assays (Follow-up)		X											X		X	X	X	X	X	
Gene Expression	X														X	X	X	X	X	
Bulk RNA	X														X	X	X	X	X	
DNA	X														X	X	X	X	X	
STUDY DRUG ADMINISTRATION AND RELATED ASSESSMENTS																				
teplizumab/placebo infusion[1, 16]		X	X	X	X	X	X	X	X	X	X	X	X							
AG019/placebo dispensing		X												X						
Study drug accountability					X			X					X	X	X					

[1] Only applicable for patients in the combination cohorts
[2] Registration was done as soon as possible after confirmation of eligibility and completion of all screening assessments to allow for timely shipment of study drug
[3] If a patient returned for an unscheduled visit and it was determined that the patient had to withdraw, all End Of Study assessments were performed.
[4] Vital signs included at least weight, blood pressure, respiratory rate, heart rate, temperature. Height was only measured at visit 1.
[5] 12-lead ECG was only done if there was suspicion of cardiac problems.
[6] It was recommended that following drugs were assessed at a minimum: cannabis, cocaine, ecstasy, amphetamines. The method of testing was left to the discretion of the investigator.
[7] Only required for women of childbearing potential.
[8] Complete Blood Count (CBC): RBC count, Hg, Hct, MCV, MCH, MCHC, RDW, white blood cell count, differential count, platelet count, INR.
[9] Blood glucose, sodium, potassium, chloride, calcium, CO_2/bicarbonate, total protein, albumin, total bilirubin, ALP, AST, ALT, LDH, CRP
[10] Total bilirubin, AST, ALT, and LDH were evaluated, in addition to the Full Hematology set and INR, before each (potential) teplizumab infusion to verify the need to withhold teplizumab infusion
[11] Following additional parameters were assessed at screening: uric acid, urea/BUN, creatinine, eGFR, total cholesterol, triglycerides, HDL, LDL, VLDL (optional), TSH. Assessments for which the result was within the normal lab ranges were not repeated at follow-up visits.

Study Procedure	Screening	Treatment									Post treatment									Unscheduled
Visit	1	2	3[1]	4[1]	5	6[1]	7[1]	8	9[1]	10[1]	11[1]	12[1]	13	14	15	16	17	18	19	99[2]
Week	-4 to -1	1	1	1	1	1	1	1	2	2	2	2	2	4	8	13	26	39	52	N/A
Study Day	-29 to -1	1	2	3	4	5	6	7	8	9	10	11	12	28	56	90	180	270	360	N/A
Visit Window[17]	N/A	0	0	0	0	0	0	0	0	0	0	0	0	±2	±2	±7	±7	±7	±7	N/A

[12] If evidence of autoantibody positivity was found in the patient's medical file, this assessment was not repeated at screening.
[13] EBV, CMV, HCV, HIV, HBV
[14] Feces samples were only collected from patients in AG019 cohorts 2 and 4 and the Combination cohorts. Feces were collected at screening, on the last day of treatment, and every 2 days thereafter for a total of 5 sampling points (Day 56, 58, 60, 62, 64). On collection days, one feces sample was collected in a separate container and labelled with date and time of sample collection. A pick-up was arranged after Day 64.
[15] Mechanistic assessments were only done for patients in AG019 cohorts 2 and 4 and the Combination cohorts.
[16] If teplizumab dosing was withheld, all evaluations outlined in Section 11.4.3.6. of the study protocol (see Appendix 16.1.1) were needed to be performed.
[17] Due to the COVID-19 pandemic, sites could be closed for patient follow-up visits or patients could not be willing to travel to the sites for assessments. For this reason, follow-up visits from Day 90 onwards could fall outside the foreseen visit window and investigators could record the actual date of collection of all data in the electronic data capture (EDC).
[18] To be completed no more than 3 days before the scheduled start of treatment.