Single Arm Study of ALXN1210 in Complement Inhibitor Treatment-naïve Adult and Adolescent Patients with Atypical Hemolytic Uremic Syndrome (aHUS)

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Alexion Pharmaceuticals, Inc.

STATISTICAL ANALYSIS PLAN

PROTOCOL NUMBER: ALXN1210-aHUS-311

SINGLE ARM STUDY OF ALXN1210 IN COMPLEMENT INHIBITOR TREATMENT-NAÏVE ADULT AND ADOLESCENT PATIENTS WITH ATYPICAL HEMOLYTIC UREMIC SYNDROME (aHUS)

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1. APPROVAL SIGNATURES

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23 May 2018

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1. APPROVAL SIGNATURES

{PPD, Director, Biostatistics}	Date dd Mmm yyyy
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PPD {PPD, Director, Global Medical Sciences}	23-May-2018 Date dd Mmm yyyy

2. TABLE OF CONTENTS, LIST OF TABLES, AND LIST OF FIGURES

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3. LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS

The following abbreviations and acronyms are used in this Statistical Analysis plan (SAP).

Table 1: Abbreviations and Acronyms

Abbreviation or acronym	Explanation
ADA	Antidrug antibodies
ADAMTS13	A disintegrin and metalloproteinase with a thrombospondin type 1 motif, member 13
ADL	Activities of daily living
AEs	Adverse events
aHUS	Atypical hemolytic uremic syndrome
BP	Blood pressure
C5	Complement component 5
CDF	Cumulative distribution function
CI	Confidence interval
CKD	Chronic kidney disease
CSR	Clinical Study Report
CTCAE	Common Terminology Criteria for Adverse Events
ECG	Electrocardiogram
eCRF	Electronic Case Report Form
eGFR	Estimated Glomerular Filtration Rate
EQ-5D-3L	EuroQol 5 dimensions 3 level
FACIT	Functional assessment of chronic illness therapy
FAS	Full Analysis Set
IV	Intravenous
LDH	Lactate dehydrogenase
LLT	Lowest level term
LOCF	Last Observation Carried Forward
MedDRA	Medical Dictionary for Regulatory Activities
mITT	Modified intent to treat
MMRM	Mixed model for repeated measures
PD	Pharmacodynamic
PE/PI	Plasma exchange/plasma infusion
PK	Pharmacokinetic
PT	Preferred Term (MedDRA)
PTAEs	PreTreatment Adverse Events
QoL	Quality of life
q8w	Once every 8 weeks
SAEs	Serious adverse events
SAS®	Statistical Analysis Software®
SAP	Statistical Analysis Plan
SD	Standard deviation
SOC	System Organ Class (MedDRA)
SOP	Standard operating procedure
TEAEs	Treatment-Emergent Adverse Events
TMA	Thrombotic microangiopathy

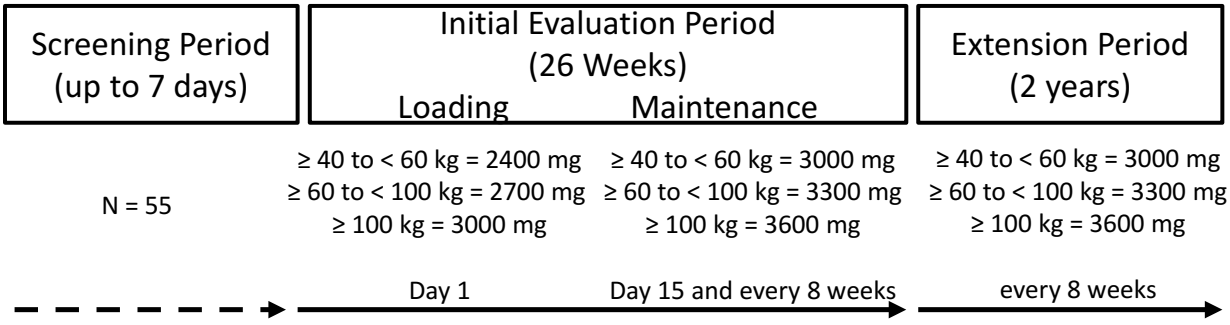
4. DESCRIPTION OF THE PROTOCOL

ALXN1210-aHUS-311 is a Phase 3, single arm, multicenter study to evaluate the safety and efficacy of ALXN1210 administered by intravenous (IV) infusion to adolescent (12 to < 18 years of age) and adult (≥ 18 years of age) patients with atypical hemolytic uremic syndrome (aHUS). All patients must be naïve to complement inhibitor treatment; at least 6 and up to 10 adolescent (12 to < 18 years of age at Screening) patients and at least 10 and up to 25 patients with prior kidney transplants will be included.

The study consists of an up to 7 day Screening Period, a 26-week Initial Evaluation Period, and an Extension Period of up to 2 years. Dosages are based on the patient's last recorded study visit body weight. Patients will receive a loading dose of ALXN1210 IV (2400 mg for patients weighing ≥ 40 to < 60 kg, 2700 mg for patients weighing ≥ 60 to < 100 kg, 3000 mg for patients weighing ≥ 100 kg) on Day 1, followed by maintenance doses of ALXN1210 IV (3000 mg for patients weighing ≥ 40 to < 60 kg, 3300 mg for patients weighing ≥ 60 to < 100 kg, 3600 mg for patients weighing ≥ 100 kg) on Day 15 and once every 8 weeks (q8w) thereafter for a total of 26 weeks of treatment. After the Initial Evaluation Period, patients will enter an Extension Period and receive ALXN1210 until the product is registered or approved (in accordance with country specific regulations) or for up to 2 years, whichever occurs first. The end of trial is defined as the last patient's last visit.

Figure 1: Study Design Schematic for Clinical Protocol ALXN1210-aHUS-311 illustrates the study design.

Figure 1: Study Design Schematic for Clinical Protocol ALXN1210-aHUS-311



The primary objective of the study is to assess the efficacy of ALXN1210 in patients with aHUS to inhibit complement-mediated thrombotic microangiopathy (TMA) as characterized by thrombocytopenia, hemolysis, and renal impairment, as determined by Complete TMA Response following treatment.

Secondary objectives of the study include the following:

1. To characterize the safety and tolerability of ALXN1210 in this patient population
2. To evaluate the efficacy of ALXN1210 by the following additional measures:

a. Dialysis requirement status
b. Time to Complete TMA Response
c. Complete TMA Response status over time
d. Observed value and change from baseline in estimated glomerular filtration rate (eGFR)
e. Chronic kidney disease (CKD) stage, as evaluated by eGFR at select target days and classified as improved, stable (no change), or worsened compared to baseline
f. Observed value and change from baseline in hematologic parameters (platelets, lactate dehydrogenase (LDH), hemoglobin)
g. Increase in hemoglobin of ≥ 20 g/L from baseline, observed at two separate assessments obtained at least 4 weeks (28 days) apart, and any measurement in between
h. Change from baseline in quality of life (QoL), as measured by EuroQol 5 dimensions 3 level (EQ-5D-3L; all patients), Functional Assessment of Chronic Illness Therapy (FACIT) Fatigue version 4 (patients ≥ 18 years of age), and Pediatric FACIT Fatigue (patients < 18 years of age) questionnaires

3. To characterize the pharmacokinetic (PK)/pharmacodynamics (PD) of ALXN1210 by the following measures:
   a. Changes in serum ALXN1210 concentration over time
   b. Changes in free complement component 5 (C5) concentrations over time
4. To evaluate the long term safety and efficacy of ALXN1210

For additional details, refer to the protocol.

4.1. Changes from Analyses Specified in the Protocol

None

4.2. Changes from Analyses Specified in the Previous Version of the SAP

The original SAP (dated 30 January 2017) was amended 3 times. A summary of the changes is presented below.

4.2.1. SAP version 2 (dated 24 March 2017)

- In Section 9.4.7, applied changes to the list of preferred terms to search for adverse events related to meningococcal infection. The following preferred terms were removed: Neisseria infection, Septic arthritis neisserial, and Neisseria test positive.
- In Section 5.2.1, added footnotes to Table 2.
- In Section 6.2, deleted the requirement for satisfaction of exclusion criteria 1 and 2 for inclusion in the per protocol set. This was a redundant condition because these criteria need to be satisfied to be included in the full analysis set.
- In Section 7.1.2, fixed an omission error by adding exclusion criterion 2 to the 5th item on the list for consistency.

- In Section 7.1.2, removed the specification for production of a table presenting the number and percentage of patients meeting or not meeting inclusion/exclusion criteria. A listing is deemed sufficient.
- In Section 7.2.1.1, removed the statement "If a Day 1 pretreatment assessment is missing, the Screening assessment will be used as the baseline assessment" which is superfluous given that the baseline value is based on the average of the Screening and Day 1 assessments.
- In Section 7.2.2.8, the description for a new table was added. The number and proportion of patients with a 3 point improvement from baseline in the FACIT Fatigue score will be summarized over time by presenting the number and proportion of patients along with a 2-sided 95% CI for each postbaseline time point.

4.2.2. SAP version 3 (dated 15 September 2017)

- In Section 5.2.3, added text explaining that evaluation of Inclusion Criteria 2a and 2b may be based on local laboratory results within 28 days prior to the start of the Screening Period or laboratory results obtained during the Screening Period from a local or central laboratory.
- In Section 6.1, adjusted the first bullet in the list of criteria to be met for inclusion in the full analysis set to reflect the change in Protocol Amendment 3, dated 19 July 2017.
- In Section 6.2, added inclusion criterion 2 and exclusion criterion 7 to the list of criteria to be satisfied for inclusion in the per protocol set.
- In Section 7.1.2, item 5 was adjusted to reflect that violation of inclusion criterion 2c should result in study discontinuation to reflect the change in Protocol Amendment 3, dated 19 July 2017. Item 6 was deleted as there is no randomization and enrollment quotas will be verified.
- In Section 7.2.1.2, added a subgroup for patients that met all laboratory criteria for TMA as determined by the central laboratory at Day 1.

4.2.3. Current SAP (version 4)

- In Section 5.2.3, added text specifying that local laboratory results may be used for analysis when no central laboratory results are available. Text was also added to this section to address in vitro erythrocyte lysis referred to as table top hemolysis (TTH) caused by sample mishandling.
- In Section 7.2.2.3 an example indicating patients to be included in a summary of response by visit was deleted as it was incorrectly implying that certain patients would be excluded from some time points.
- In Section 9.4.10, added text indicating that the exclusion from analysis of hemoglobin and platelets results when concurrent with blood transfusion is only

applicable to postbaseline assessments. Because pre-treatment assessments, even if concurrent with blood transfusion, need to meet the inclusion criteria.

4.3. Planned Analyses

An interim analysis is planned for this study at the end of the 26-week Initial Evaluation Period after all patients have completed or withdrawn from the 26-week Initial Evaluation Period. This analysis will allow for evaluation of the primary endpoint and will be the basis for the initial clinical study report (CSR).

The final analysis which will summarize long-term efficacy, safety, and PK parameters will be performed at the end of the 2-year Extension Period.

The present document serves to describe both of these planned analyses.

5. DEFINITIONS

5.1. Efficacy

5.1.1. Primary Endpoint(s)

The primary efficacy endpoint of the study is Complete TMA Response during the 26 week Initial Evaluation Period. The criteria for Complete TMA Response are the following:

1. Normalization of platelet count (defined as platelet count ≥ 150,000 per microliter)
2. Normalization of LDH (defined as LDH ≤ upper limit of normal)
3. ≥ 25% improvement in serum creatinine from baseline

Patients must meet all Complete TMA Response criteria at 2 separate assessments obtained at least 4 weeks (28 days) apart, and any measurement in between.

5.1.2. Secondary Endpoints

The secondary efficacy endpoints of the study are the following:

1. Dialysis requirement status
2. Time to Complete TMA Response
3. Complete TMA Response status over time
4. Observed value and change from baseline in eGFR
5. CKD stage, as evaluated by eGFR at select target days and classified as improved, stable (no change), or worsened compared to baseline
6. Observed value and change from baseline in hematologic parameters (platelets, LDH, hemoglobin)
7. Increase in hemoglobin of ≥ 20 g/L from baseline, observed at 2 separate assessments obtained at least 4 weeks (28 days) apart, and any measurement in between
8. Change from baseline in QoL, as measured by EQ-5D-3L (all patients), FACIT Fatigue version 4 (patients ≥ 18 years of age), and Pediatric FACIT Fatigue (patients < 18 years of age) questionnaires

5.1.3. Exploratory Endpoints

Patients will report signs or symptoms of aHUS and resource utilization using the Patient-reported aHUS Symptoms Questionnaire and the Resource Utilization Patient Questionnaire, respectively.

The Investigator will evaluate extra-renal signs or symptoms of aHUS using a composite of clinical laboratory measurements, vital signs, and an organ system review.

5.1.4. Other Efficacy Endpoints

Not applicable

5.2. Safety

The safety and tolerability of ALXN1210 will be evaluated by physical examinations, vital signs, electrocardiograms (ECGs), laboratory assessments, and incidence of adverse events (AEs) and serious adverse events (SAEs). The proportion of patients who develop antidrug antibodies (ADA) will also be assessed.

5.2.1. Adverse Events

Treatment-emergent AEs (TEAEs) are defined as any event not present prior to exposure to Investigational Product or any event already present that worsens in either intensity of frequency following exposure to Investigational Product. An AE will be considered a TEAE if the start date and time is on or after the start date and time of the first study drug infusion. All other AEs are considered PreTreatment Adverse Events (PTAEs).

The severity of AEs will be graded using Common Terminology Criteria for Adverse Events (CTCAE) version 4.03 or higher. A grading (severity) scale is provided for each AE term. Each LLT will be coded to a MedDRA preferred term.

Grade refers to the severity of the AE. The CTCAE assigns a grade of 1 through 5, with unique clinical descriptions of severity for each AE (Table 2).

Table 2: Adverse Event Severity Grading Scale

Grade	Description
Grade 1	Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated
Grade 2	Moderate; minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental activities of daily living (ADL)[a]
Grade 3	Severe or medically significant, but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care ADL[b]
Grade 4	Life-threatening consequences; urgent intervention indicated.
Grade 5	Death related to AE.

Abbreviations: ADL = activities of daily living; AE = adverse event

[a] Instrumental ADL refers to preparing meals, shopping for groceries or clothes, using the telephone, managing money, etc.

[b] Self-care ADL refers to bathing, dressing and undressing, feeding self, using the toilet, taking medications, and not bedridden.

An Investigator must provide a causality assessment (Unrelated, Unlikely, Possible, Probable, or Definite) for all AEs (both serious and nonserious) based upon the Investigator's medical judgment and the observed symptoms associated with the event (Table 3).

Table 3: Causality Assessment Descriptions

Assessment	Description
Not Related/Unrelated	Suggests that there is no causal association between the investigational product and the reported event.

Assessment	Description
Unlikely Related	Suggests that the clinical picture is highly consistent with a cause other than the investigational product but attribution cannot be made with absolute certainty and a relationship between the investigational product and AE cannot be excluded with complete confidence.
Possibly Related	Suggests that treatment with the investigational product may have caused or contributed to the AE (ie, the event follows a reasonable temporal sequence from the time of drug administration and/or follows a known response pattern to the investigational product, but could also have been produced by other factors).
Probably Related	Suggests that a reasonable temporal sequence of the event with the investigational product administration exists and the likely causal association of the event with the investigational product. This will be based upon the known pharmacological action of the investigational product, known or previously reported adverse reactions to the investigational product or class of drugs, or judgment based on the Investigator's clinical experience.
Definitely Related	Temporal relationship to the investigational product, other conditions (concurrent illness, concurrent medication reaction, or progression/expression of disease state) do not appear to explain event, corresponds with the known pharmaceutical profile, improvement on discontinuation, reappearance on rechallenge.

For more details see Section 11.7 of the protocol, and Section 9.4 of this SAP.

5.2.2. Vital Signs

Vital sign measurements will be taken after the patient has been resting for at least 5 minutes, and will include systolic and diastolic blood pressure (BP) (millimeters of mercury [mmHg]), pulse oximetry, heart rate (beats/minute), respiratory rate (breaths/minute), and oral or tympanic temperature (degrees Celsius [°C] or degrees Fahrenheit [°F]).

5.2.3. Laboratory Assessments

Laboratory assessments are defined in section 11.4 of the protocol. Laboratory values will be graded according to the National Cancer Institute CTCAE version 4.03 or higher. Parameters which are not present in the CTCAE document will not be graded.

Samples collected at Screening may be tested at either a local or central laboratory. If local laboratory tests are used for LDH, platelet count, hemoglobin, and serum creatinine, duplicate samples will be collected for central laboratory testing to ensure baseline and postbaseline measurements for analyses are resulted from the central laboratory. In the event of duplicate samples from local and central laboratories (for any time point), central laboratory results will be used for analysis. Local laboratory results will only be used for analysis if no central laboratory results are available. Although local laboratory results may be used to expedite assessment of eligibility, the final determination of these Inclusion Criteria will be based on the central laboratory results. However, evaluation of Inclusion Criteria 2a and 2b may be based on local laboratory results within 28 days prior to the start of the Screening Period or laboratory results obtained during the Screening Period from a local or central laboratory.

It has been observed in other studies that up to 1% of central laboratory chemistry samples undergo in vitro erythrocyte lysis referred to as table top hemolysis (TTH) caused by sample mishandling. Due to the artefactual increase in LDH in samples affected by TTH, the potassium, ALT, AST, magnesium, phosphorous, and LDH values in samples affected by TTH will not be used in the analysis of any efficacy or safety endpoints. TTH samples from the central lab will be defined as having serum potassium ≥ 6 mmol/L and LDH ≥ 2x ULN, and will be excluded from analyses as described above.

5.2.4. Physical Examinations

A physical examination will include the following assessments: general appearance; skin; head, ear, eye, nose, and throat; neck; lymph nodes; chest; heart; abdominal cavity; limb; central nervous system; and musculoskeletal system. An abbreviated physical examination consists of a body system relevant examination based upon Investigator judgment and patient symptoms.

5.2.5. Electrocardiograms

For each patient, single 12-lead digital ECGs will be collected according to the Schedule of Assessments. Patients must be supine for approximately 5 to 10 minutes before ECG collection and remain supine but awake during ECG collection.

The Investigator or designee will be responsible for reviewing the ECG to assess whether the ECG is within normal limits and to determine the clinical significance of the results. These assessments will be indicated on the CRF. For any clinically significant abnormal ECG results, the Investigator must contact the Medical Monitor to discuss the patient's continued eligibility to participate in this protocol.

5.2.6. Immunogenicity

Blood samples will be collected to test for presence and titer of ADAs to ALXN1210 in serum prior to study drug administration as indicated in the Schedule of Assessments.

5.2.7. Other Safety Events of Special Interest

Meningococcal infections will be considered as AEs of special interest.

6. DATA SETS ANALYZED (STUDY POPULATIONS)

6.1. Full Analysis Set

The full analysis set (FAS) will be used for the primary analysis of efficacy. The FAS will be based on a modified intent to treat (mITT) approach where patients that were enrolled and treated based on verification of inclusion and exclusion criteria through local laboratory results and the assumption that all inclusion and exclusion criteria were satisfied will be excluded from the FAS if it is later shown that certain inclusion and exclusion criteria were in fact not satisfied once all Screening laboratory results are available. Based on the above, the FAS will include all patients who receive at least 1 dose of ALXN1210, have at least 1 postbaseline efficacy assessment, and meet all of the following criteria:

- Patients who satisfy Inclusion Criterion number 2c
- Patients who satisfy Exclusion Criterion number 1
- Patients who satisfy Exclusion Criterion number 2

See protocol sections 8.1 and 8.2 for the full list and description of the inclusion and exclusion criteria.

6.2. Per Protocol Set

The per protocol set (PPS) will consist of FAS patients who meet all of the following criteria:

- Received 100% of the planned number of infusions during the 26 week Initial Evaluation Period
- Did not take any prohibited medications or undergo any prohibited procedures (see protocol section 9.7)
- Satisfied inclusion criteria 2 and 8, and exclusion criteria 3, 7, 10, 11, 12, 13, 15, 16, 17, 18, 21, 22 and 26

6.3. Safety Set

Safety analyses will be performed on the Safety Set defined as all patients who receive at least 1 dose of study drug.

6.4. Other Sets

Not applicable.

7. STATISTICAL ANALYSIS

All analyses will be performed using Statistical Analysis Software® (SAS®) release, version 9.4 or higher (SAS Institute Inc., Cary, NC, USA) or other validated statistical software. Continuous variables will be summarized using descriptive statistics, including number of observations, mean, standard deviation (SD), median, minimum, and maximum values. Categorical variables will be summarized by frequency counts and percentage.

7.1. Study Patients

7.1.1. Disposition of Patients

All patients will be included in the summaries of patient disposition, which will describe the frequency and percentage of patients enrolled and treated and who completed or withdrew from the study, along with reason for withdrawal from the study. The number and percentage of patients who are treated, discontinue treatment (along with reason for treatment discontinuation), complete or withdraw from the Initial Evaluation Period (along with reason for withdrawal), enter the Extension Period, and complete or withdraw from the Extension Period (along with reason for withdrawal) will be tabulated.

7.1.2. Protocol Deviations

Important protocol deviations will be determined per the standard operating procedure (SOP) "Identification, Handling, and Documentation of Protocol Deviations" (SOP-G-CL-0044). The number and percent of patients with specific protocol deviations will be summarized for all enrolled patients by major and minor deviations.

To ensure completeness of the list of important protocol deviations, the following will be identified programmatically from the database:

1. Patients from whom informed consent was not obtained
2. Patients who violated any inclusion/exclusion criteria
3. Patients who took prohibited medications or underwent any prohibited procedure
4. Patients who received less than 100% of the protocol specified number of doses of study drug during the Initial Evaluation Period
5. Patients found not to satisfy one or more of the following inclusion/exclusion criteria (Inclusion Criterion number 2c or Exclusion Criteria numbers 1 and 2) whom are not discontinued from the study.

A by-patient listing of inclusion/exclusion criteria, as well as protocol deviations will be presented, separately.

7.1.3. Demographics, Disease Characteristics, and History

Patient demographic and baseline characteristics, including medical history and transplant history, will be summarized for the FAS and Safety Set.

7.1.3.1. Demographics

The following demographic variables will be summarized:

- Gender
- Race
- Age (years) at first Infusion
- Weight at first Infusion
- Height at first Infusion

A by-patient listing of demographics will be generated.

7.1.3.2. Disease Characteristics

The following disease characteristics will be summarized:

- Age at first aHUS symptoms
- Pretreatment extra-renal signs or symptoms of aHUS
- A disintegrin and metalloproteinase with a thrombospondin type 1 motif, member 13 (ADAMTS-13) activity

A table summarizing pretreatment extra-renal signs or symptoms of aHUS will also be presented.

A by-patient listing of disease characteristics will be generated.

7.1.3.3. Medical History and Baseline Physical Examination

Medical history will be summarized by number and percentage of patients within each Body System. Patients will be counted only once at the Body System level.

A separate table summarizing history of emergency room visits and hospitalizations due to aHUS, a table summarizing kidney transplant history, as well as a table presenting baseline physical examination results will also be generated.

By-patient listings of these data will be generated.

7.1.4. Prior and Concomitant Medications / Nonpharmacologic Procedures

Prior and concomitant medications (including vitamins and herbal preparations) will be coded using the World Health Organization Drug Dictionary (WHO-DRUG), while prior and concomitant nonpharmacologic therapies and procedures (any therapeutic intervention, such as surgery/biopsy or physical therapy) will be coded using MedDRA.

Prior medications or procedures are defined as any non-study medications or procedures that were started, and were stopped, prior to the date of first infusion. Concomitant medications or procedures are defined as any non-study medications or procedures that were taken or occurred while the patient also received study medication. Prior and concomitant summaries will be presented separately.

Medications will be summarized by Anatomic-Therapeutic-Chemical (ATC) level 4 class and preferred drug name using frequency counts and percentages of patients for the Safety Set. Procedures will be summarized similarly, but by MedDRA Class and preferred term.

A table summarizing pretreatment plasma exchanges and plasma infusion as well as kidney dialysis will be generated. A similar table will summarize concomitant kidney dialysis.

In the event a patient receives a prohibited medication or undergoes a prohibited procedure, this will be reported as a protocol deviation as described in Section 7.1.2.

By-patient listings of these data will be provided separately.

7.2. Efficacy Analyses

The FAS is the primary analysis set for all efficacy analyses. The primary analysis and selected secondary efficacy analyses will be repeated on the PPS as sensitivity analyses.

7.2.1. Primary Analysis

The primary efficacy endpoint is Complete TMA Response during the 26-week Initial Evaluation Period. The primary analysis will consist in estimating the proportion of complete TMA responders among ALXN1210 treated patients. This will be performed by calculating the point estimate and a 2-sided 95% confidence interval (CI) for the proportion of complete TMA responders in ALXN1210 treated patients, where the numerator will be the number of patients achieving complete TMA response during the 26-week Initial Evaluation Period and the denominator will be the number of patients in the FAS. The CI will be based on the asymptotic Gaussian approximation method with a continuity correction.

The criteria for Complete TMA response are presented in Section 5.1.1 . Patients must meet all Complete TMA Response criteria at 2 separate assessments obtained at least 4 weeks (28 days) apart, and any measurement in between. To be considered a responder during the 26-week Initial Evaluation Period, the latest time point a patient can first meet the response criteria is 28 days before the Day 183 assessment.

Formal statistical comparison analyses are not planned for this estimation study. Results from ALXN1210 treated patients will be evaluated in the context of results observed in patients treated with eculizumab in prospective eculizumab studies.

7.2.1.1. Handling of Dropouts or Missing Data

For evaluation of Complete TMA Response during the 26-week Initial Evaluation Period (primary endpoint), patients missing an efficacy assessment that is part of the definition of Complete TMA Response while still on-study, will have their last observation carried forward (LOCF). For patients who will have discontinued from the study prior to Week 26, their data up to the time of discontinuation will be used to assess Complete TMA Response. A confirmatory result cannot be from an assessment that was carried forward from the initial assessment when all Complete TMA Response criteria were met.

For laboratory data, in the event of duplicate samples from local and central laboratories (for any time point), central laboratory results will be used for analysis.

7.2.1.2. Subgroup Analysis

The primary efficacy analysis will be repeated separately by the following subgroups:

- gender (male, female)
- race
- ethnicity
- geographic region (by country)
- age at enrollment categories (12-17, 18 years of age and up)
- kidney transplant history (yes, no)
- immunogenicity status (ever positive, always negative)
- dialysis within 5 days prior to treatment initiation (yes, no)
- met all laboratory criteria for TMA as determined by the central laboratory at Day 1

Given that the number of patients in these subgroups may be limited, the CIs will be based on exact confidence limits using the Clopper-Pearson method. For the same reason, some subgroup categories may be combined.

7.2.1.3. Multicenter Studies

The number of patients at each center is expected to be very small. Therefore, there will be no summarization of efficacy analyses by site.

7.2.1.4. Hypothesis Testing and Significance Level

This is an estimation study and no formal statistical tests are planned. The primary efficacy endpoint will be analyzed using an asymptotic 95% 2-sided confidence interval for the proportion of complete TMA responders.

7.2.1.5. Sensitivity Analyses

The primary and selected secondary efficacy endpoints will be analyzed based on the on the PPS to determine if the results are materially different from the analysis based on the FAS.

7.2.2. Secondary Analyses

Secondary Analyses will be performed on the FAS. Separate by-patient listings will be created for all secondary efficacy analysis parameters.

Continuous variables will be summarized using descriptive statistics, including number of observations and mean, standard deviation, median, minimum, and maximum values. Categorical variables will be summarized by frequency counts and percentage of patients.

7.2.2.1. Dialysis Requirement Status

An analysis will present the number and proportion of patients that are requiring dialysis over time. A 2-sided 95% CI for the proportion will be provided. The CI will be based on exact confidence limits using the Clopper-Pearson method. The summary will be produced for patients requiring dialysis within 5 days prior to ALXN1210 treatment initiation, not requiring dialysis within 5 days prior to ALXN1210 treatment initiation, and overall. A patient will be considered as not requiring dialysis at a specific postbaseline time point if they have been dialysis free for at least 5 days prior to that time point. A by-patient figure showing dialysis status or events over time will be presented.

7.2.2.2. Time to Complete TMA Response

For the secondary efficacy endpoint of time to Complete TMA Response, Kaplan Meier cumulative distribution curves will be generated along with 2-sided 95% CIs. The corresponding summary table will present the cumulative distribution function (CDF) estimate, the number of patients at risk, the number of patients responding, and the number of patients censored at each postbaseline time point. The table will also present first quartile, median, and third quartile, along with corresponding 2-sided 95% CI, of time to complete response.

Complete TMA response is defined in Section 5.1.1 . Patients must meet all Complete TMA Response criteria at two separate assessments obtained at least 4 weeks (28 days) apart, and any measurement in between. The time of the event of a confirmed complete TMA response will be considered as the first time point at which all the criteria for complete TMA response were met.

Patients that did not have a response will be censored at the date of last visit or study discontinuation at the time when the analysis is performed.

7.2.2.3. Complete TMA Response Status Over Time and Alternative Definitions

Complete TMA Response will also be summarized over time by presenting the number and proportion of responders along with a 2-sided 95% CI for each postbaseline time point. This summary will be accompanied by a similar presentation for the components of complete TMA response: proportion of patients with platelet count normalization, proportion of patients with LDH normalization, proportion of patients with hematologic normalization (platelet count and LDH), proportion of patients with $\geq$ 25% improvement in serum creatinine from baseline. The CIs will be based on the asymptotic Gaussian approximation method with a continuity correction. These tabular summaries will be accompanied by a bar chart graphical figure displaying for each time point a bar for Complete TMA Response and each component in its definition, where the bar will represent the proportion of patients meeting that specific criterion.

A patient will be included in the analysis for a specific postbaseline time point if it was possible for the result at that time point to be confirmed or to serve as a confirmatory result.

A set of summaries similar to the ones described above will be produced without any requirement for a confirmatory result. This summary will be strictly based on a patient meeting the criterion at a specific time point.

A slightly modified version of complete TMA response will also be evaluated. The modification will only affect patients considered to be on dialysis at baseline (ie. patients requiring dialysis within 5 days prior to ALXN1210 treatment initiation). For these patients, the criterion requiring

an improvement from baseline of 25% or more in serum creatinine, will be replaced by a postbaseline change in dialysis status (from requiring dialysis at baseline to no longer requiring dialysis) that is maintained for at least 4 weeks. A set of summaries similar to the ones described above will be produced based on this alternative definition.

The tabular summary of complete TMA response over time will also be performed on the PPS.

7.2.2.4. eGFR Value and Change from Baseline

Kidney function evaluated by eGFR will be summarized at baseline and each postbaseline time point using descriptive statistics for continuous variables for the observed value as well as the change from baseline. A value for eGFR will be imputed for patients requiring dialysis for acute kidney injury (see Section 9.4.9 for details). This summary will be repeated by the kidney transplant status at enrollment, and on the PPS

A mixed model for repeated measures (MMRM) will be used to improve the precision of estimation of changes in eGFR over time. The model will include the fixed, categorical effect of visit and fixed, continuous effect of the baseline value as covariates. An unstructured covariance structure will be used to model the within patient errors. If this analysis fails to converge, the following structures will be tested and the final covariance structure will be determined by selecting the one with the lowest Akaike's information criterion (AIC): first-order autoregressive, compound symmetry, and Toeplitz. The Kenward-Roger approximation will be used to estimate denominator degrees of freedom. The estimation of change from baseline on defined weeks alongside with 95% confidence intervals will be provided.

Figures presenting the observed values and the model based values over time will be provided.

7.2.2.5. CKD Stage

CKD stage will be summarized over time by presenting the number and proportion of patients that improved (excluding those with Stage 1 at baseline as they cannot improve), worsened (excluding those with Stage 5 at baseline as they cannot worsen), and stayed the same compared to CKD stage at baseline. Stage 5 will be considered the worst category, while stage 1 will be considered the best category (see Section 9.4.11 for details). A 2-sided 95% CI for each proportion will be provided. The CIs will be based on exact confidence limits using the Clopper-Pearson method. This summary will be repeated by the kidney transplant status at enrollment.

7.2.2.6. Hematologic Parameters

Hematologic parameters (platelets, LDH, hemoglobin) will be summarized at baseline and each postbaseline time point using descriptive statistics for continuous variables for the observed value as well as the change from baseline. This summary will be repeated on the PPS. As suggested in Section 7.2.2.4, a mixed model for repeated measures (MMRM) will be used to improve the precision of estimation of changes over time.

Figures presenting the observed values and the model based values over time for these hematologic parameters will be provided.

7.2.2.7. Hemoglobin Response

The number and proportion of patients with an increase from baseline in hemoglobin ≥ 20g/L, observed at 2 separate assessments obtained at least 4 weeks (28 days) apart, and any measurement in between will be summarized over time by presenting the number and proportion of responders along with a 2-sided 95% CI for each postbaseline time point.

A patient will be included in the analysis for a specific postbaseline time point if it was possible for the result at that time point to be confirmed (ie, the patient has to be in the study for a subsequent confirmatory assessment at least 28 days later). For example, a patient on-study at the Day 71 assessment and at the Day 99 assessment would be included in the Day 71 summary. However, a patient on-study at the Day 71 assessment that did not remain on-study until the Day 99 assessment or later would not be included in the Day 71 summary.

A set of summaries similar to the ones described above will be created without any requirement for a confirmatory result. This summary will be strictly based on a patient meeting the criterion at a specific time point.

7.2.2.8. Quality of Life

Quality of life will be evaluated using EQ-5D-3L (all patients), FACIT Fatigue version 4 Questionnaire (patients ≥ 18 years of age), Pediatric FACIT Fatigue Questionnaire (patients < 18 years of age). These measures will be summarized at baseline and each postbaseline time point using descriptive statistics for continuous variables for the observed value as well as the change from baseline. The FACIT Fatigue results will be presented separately and combined for adults and pediatric patients. As suggested in Section 7.2.2.4, a mixed model for repeated measures (MMRM) will be used to improve the precision of estimation of changes over time.

The number and proportion of patients with a 3 point improvement from baseline in the FACIT Fatigue score will be summarized over time by presenting the number and proportion of patients along with a 2-sided 95% CI for each postbaseline time point.

Figures presenting the observed values and the model based values over time for these quality of life assessments will be provided.

7.2.3. Exploratory Analyses

Resource Utilization Questionnaire (all patients) data will be summarized at each postbaseline assessment using discrete data summary statistics.

Patient-reported aHUS Symptoms Questionnaire (all patients) data will be summarized at each postbaseline assessment by presenting the number and proportion of patients with a specific symptom present. Extra-Renal Sings and Symptoms of aHUS data will be presented similarly.

These data will also be presented in detailed by-patient listings.

7.2.4. Other Efficacy Analyses

Not applicable.

7.2.5. Pharmacokinetic and Pharmacodynamic Analyses

All Pharmacokinetic and Pharmacodynamic analyses will be summarized prospectively in a separate analysis plan.

7.3. Safety Analyses

All safety analyses will be conducted on the Safety Set. All safety data will be provided in patient listings. AEs will be coded in MedDRA version 18 or higher and presented by MedDRA system organ class (SOC) and preferred term. All safety analyses will be presented by age category (12-17, 18 years of age and up) except for immunogenicity and physical examination summaries. No formal hypothesis testing is planned.

7.3.1. Study Duration, Treatment Compliance, and Exposure

Two summary tables of the extent of exposure to ALXN1210 will be presented. The duration on treatment (in weeks), the number of infusions, and the total dose (in mg) through the first 26 weeks (ie, Initial Evaluation Period) will be summarized using descriptive statistics. In addition, a similar table will be produced for exposure throughout the entire study.

7.3.2. Adverse Events (AEs)

The following definitions will be used for AEs:

- Pretreatment adverse events: Any AE that starts after providing informed consent, but before the first infusion of study drug
- Treatment-emergent adverse event: Any AE that starts during or after the first infusion of study drug.
- Treatment-emergent SAE: A treatment-emergent AE (TEAE) that is serious.

PreTreatment Adverse Events will be summarized in listings and Treatment-Emergent Adverse Events will be tabulated and presented as described below.

7.3.2.1. Overall Summary of Adverse Events

An overall summary of AEs and SAEs will be presented. The number of events (n), and number and percentage of patients with events (n, %) will be shown for the following event subcategories:

Table 4: Adverse Events (AEs) and Serious AEs

Relationship	Severity: Toxicity Grade
Related AEs (Possibly, Probably, or Definitely Related)	Grade 1
Not Related AEs (Not Related or Unlikely Related)	Grade 2
	Grade 3
	Grade 4
	Grade 5

Fatal TEAEs, TEAEs resulting in study treatment discontinuation, TEAEs resulting in withdrawal from the study, and TEAEs that start during study drug administration will also be included in this overall summary. These statistics will be prepared separately for all AEs and SAEs.

Detailed listings of all AEs, SAEs, and related AEs, will be presented. These listings will include severity and relationship to treatment, as well as action taken regarding study treatment, other action taken, and AE outcome.

7.3.2.2. AEs and SAEs by System Organ Class (SOC) and Preferred Term (PT)

The number of TEAEs, and the number and percentage of patients with events will be presented by SOC and PT. Patients will be counted once in each SOC and PT. Percentages will be based on the total number of treated patients (safety set). SOCs will be listed in descending order of frequency of occurrence. SAEs will be summarized similarly.

7.3.2.3. AEs and SAEs by SOC, PT, and Relationship

The number of TEAEs, and the number and percentage of patients with events will be presented by SOC and PT as described above by relationship (related, not related). If a patient has more than one occurrence of an AE, the strongest relationship to study treatment will be used in the relationship to treatment summary table. SAEs will be summarized similarly.

7.3.2.4. AEs and SAEs by SOC, PT, and Severity

The number of TEAEs, and the number and percentage of patients with events will be presented by SOC and PT as described above by severity (using toxicity grade). If a patient has more than one occurrence of an AE, the most severe occurrence of the AE will be used in the severity summary table. SAEs will be summarized similarly.

7.3.2.5. Deaths, Other SAEs, and Other Significant Adverse Events

Individual listings will be presented for AEs leading to study treatment discontinuation, AEs leading to withdrawal from the study, AEs starting during study drug administration, and fatal AEs.

In addition, a summary table and a listing of AEs related to meningococcal infections will be provided. See Section 9.4.7 for a list of AE preferred terms that will be considered for these summaries of meningococcal infections.

7.3.3. Other Safety

7.3.3.1. Analyses for Laboratory Tests

Observed values and changes from baseline in clinical chemistry, hematology, and urinalysis results will be summarized descriptively at baseline, and at each postbaseline time point. For laboratory results that can be classified as normal, low, or high based on normal range values, shifts from baseline in classification will be summarized for all study visits.

All data will be presented in listings, and a specific listing of abnormal results will be provided. For analysis purposes, laboratory results based upon standardized units will be used.

7.3.3.2. Vital Signs

Observed values as well as changes from baseline in body weight and vital signs (blood pressure, heart rate, respiratory rate, pulse oxymetry, and temperature) at each time assessment will be summarized descriptively. A listing of vital signs data will be presented by patient, vital sign, and visit.

7.3.3.3. Other Safety Parameters of Special Interest

7.3.3.3.1. Electrocardiograms

By-patient data listings of ECG parameters will be provided. Electrocardiograms will be evaluated and summarized as normal, abnormal not clinically significant, or abnormal clinically significant. A shift from baseline to worst on-study ECG table will be presented for ECG results. Observed values and change from baseline in ECG intervals (PR, RR, QT, and QTc) will be summarized descriptively at baseline and each postbaseline time point. QT interval will be corrected for heart rate using Friderica's formula (QTcF).

7.3.3.3.2. Immunogenicity

The number and percentage of patients with positive titers for ADAs to ALXN1210 and different titer categories will be summarized over time. The proportion of patients ever positive and the proportion of patients always negative will also be summarized.

7.3.3.3.3. Physical Exam

Physical Exam parameters collected include General Appearance, Skin, HEENT (head, ears, eyes, nose and throat), Neck, Lymph Nodes, Chest, Heart, Abdominal Cavity, Limbs, Musculoskeletal, and Central Nervous System. Each parameter is assessed by the Investigator as Normal, Abnormal, or Not Examined. A listing of Physical Exam results will be presented by patient, Physical Exam parameter, and visit.

8. REFERENCES

KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney International Supplements. 2013; 3:19-62.

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Garrett M. Fitzmaurice, Nan M. Laird, and James H. Ware (2004) Applied Longitudinal Analysis. John Wiley & Sons, Inc., p. 326-328.

Clopper, C.; Pearson, E.S. (1934). "The use of confidence or fiducial limits illustrated in the case of the binomial". *Biometrika* **26**: 404–413.

9. APPENDICES

9.1. Protocol Schedule of Events

See protocol section 7.3.

9.2. Changes from Analyses Specified in the Previous Version of the SAP

Not applicable.

9.3. Sample Size, Power, and Randomization

Approximately 55 patients will be enrolled in this study in order to yield at least 50 evaluable patients by Day 183. This sample size is deemed appropriate to provide complete safety information and the necessary precision level for the planned estimation. Assuming a proportion of Complete TMA response of 65%, 50 patients would yield a 95% confidence interval for the proportion of response with a half-width of approximately 15%.

The sample size was increased to 55 patients to account for a potential 10% drop-out rate, thus yielding a total planned sample size of 55 patients.

9.4. Technical Specifications for Derived Variables

9.4.1. Age

Table 5: Age and Reference Date

AGE	REFERENCE DATE
• Age at Enrollment	• Date of Informed Consent Form Signing
• Age at First Symptoms	• Date of First Symptoms
• Age at First Infusion	• Date of First Infusion

9.4.2. Definition of Baseline Values

For the analysis, the baseline value is defined as the average of the values from the assessments performed prior to the first study drug infusion (these can include results from Screening and the Day 1 visit).

When a patient is on dialysis at baseline, then the first valid creatinine value to be used as the baseline value will be the first assessment ≥ 6 days post-dialysis. If a patient is on dialysis during the entire 26 week Initial Evaluation Period, then the baseline creatinine will not be calculated.

9.4.3. Change from Baseline

Change from baseline will be calculated as the baseline value subtracted from the value at a particular time point. If one of the values is missing and there are no pre-specified missing value imputation rules (see Section 7.2.1.1), then a change from baseline will not be calculated.

9.4.4. Analysis Visits

Summaries over postbaseline time points or analyses at specific postbaseline time points will be performed based on the list of visits described in the schedule of assessment of the protocol. For all assessments, the number of days from baseline will be calculated using the following formula: (date of assessment) - (date of first study treatment) + 1. This number of days will be used to assign analysis visit. This may not always correspond to the electronic case report form (eCRF) visit.

The analysis visit assignment for a specific assessment will be based on visit windows around each scheduled visit for that specific assessment. The windows for each scheduled visit will go from the midpoint (in days) between the current visit and the previous scheduled visit to the midpoint between the current visit and the subsequent scheduled visit. If the interval separating 2 scheduled visits is an even number of days, that middle day will be included in the later visit window and excluded from the prior visit window. For example, for an assessment with a scheduled visit Day 127, and a prior scheduled visit Day of 113 and subsequent scheduled visit Day of 141, the window will start at 120 days from baseline and will go to 133 days from baseline.

9.4.5. Analysis Value

The values being considered for analysis at a specific postbaseline time point will be based on the analysis visit assigned to that value. If there is more than one non-missing value for a specific assessment with the same analysis visit, the value used for analysis will be the one for which the calculated number of days from baseline is closest to the scheduled visit day. If two values have the same analysis visit and are the same distance away from the scheduled visit day, the earlier of the 2 values will be used for analysis.

9.4.6. Adverse Events

The analysis of Adverse Events is described in detail in Section 7.3.2.

Treatment-emergent AEs (TEAEs) are events with start dates and start times on or after the date and time of the first study drug dose. If the start date of an AE is partially or completely missing and the end (stop) date and time of the AE does not indicate that it occurred prior to first dose, then the determination of treatment-emergent status will be based on the following:

- If the start year is after the year of the first study drug dose, then the AE is treatment-emergent; else,

- If the start year is the same as the year of the first study drug dose and
    - the start month is missing, then the AE is treatment emergent; else if
    - the start month is present and is the same or after the month of the first study drug dose, then the AE is treatment-emergent; else,
- If the start date is completely missing, then the AE is treatment-emergent.

All other AEs are considered PreTreatment Adverse Events (PTAEs).

Related AEs are defined as possible, probable or definitely related. Unrelated AEs are defined as unlikely or not related.

9.4.7. Adverse Events Related to Meningococcal Infection

To find meningococcal events, the adverse event dataset will be searched for the following MedDRA Preferred Terms: Meningitis meningococcal, Meningococcal bacteraemia, Meningococcal infection, Meningococcal sepsis, Meningococcal carditis, Encephalitis meningococcal, Endocarditis meningococcal, Myocarditis meningococcal, Optic neuritis meningococcal, and Pericarditis meningococcal. In addition, a medical review will be done to ensure that no relevant events were missed.

9.4.8. Concomitant Medications/Therapies

The analysis of concomitant medications and therapies is described in detail in Section 7.1.4.

Concomitant medications or therapies are defined as any non-study medications or therapies that were taken or given while the patient also received study medication. A medication or therapy will be considered concomitant if the start date is on or after the date of the first study drug infusion, or if the start date is before the first infusion date and the end (stop) date is after the first infusion date. If the start date of a medication/therapy is partially or completely missing and the end (stop) date of the medication/therapy does not indicate that it eneded prior to first infusion, then the determination of the concomitant status will be based on the following:

- If the start year is after the year of the first study drug infusion, then the medication/therapy is concomitant; else,
- If the start year is the same as the year of the first study drug infusion and
    - the start month is missing, then the medication/therapy is concomitant; else if
    - the start month is present and is the same or after the month of the first study drug infusion, then the medication/therapy is concomitant; else,
- If the start date is completely missing, then the medication/therapy is concomitant.

All other medications/therapies are considered Prior Medications/Therapies.

9.4.9. Serum Creatinine and eGFR

Serum creatinine measurements are not reliable with concurrent dialysis. Therefore, all serum creatinine values obtained while a patient is on dialysis will be excluded from all analyses. Estimated Glomerular Filtration Rate (eGFR) will be imputed with a value of 10 (in mL/min/1.73 m^2) while a patient is on dialysis. A patient will be considered on dialysis from the first day of dialysis through 5 days after the end of dialysis.

9.4.10. Platelets and Hemoglobin

Platelet and hemoglobin measurements are not reliable with concurrent blood transfusions. Therefore, platelet values obtained from the day of a blood transfusion of platelets through 3 days after the transfusion will be excluded from all analyses. Hemoglobin values obtained from the day of a blood transfusion of either whole blood or packed red blood cells through 7 days after the transfusion will be excluded from all analyses. This rule will only be applied to postbaseline assessments of platelets and hemoglobin.

9.4.11. Assignment of CKD Stage

Chronic kidney disease (CKD) stage will be classified based on the National Kidney Foundation Chronic Kidney Disease Stage as follows:

Table 6: Stages of Chronic Kidney Disease

Stage	Description	eGFR (mL/min/1.73 m^2)
1	Normal or High	≥90
2	Mildly Decreased	60-89
3a	Mildly to Moderately Decreased	45-59
3b	Moderately to Severely Decreased	30-45
4	Severely Decreased	15-29
5	Kidney failure	< 15 (or dialysis)

Note: In the absence of evidence of kidney damage, neither stage 1 nor 2 fulfill the criteria for CKD
Source: KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. 2013. 3: 19-62.

9.5. Questionnaires and Patient Reported Outcomes

9.5.1. EQ-5D-3L

Health Questionnaire

English version for the USA

By placing a checkmark in one box in each group below, please indicate which statements best describe your own health state today.

Mobility

I have no problems in walking about	❑
I have some problems in walking about	❑
I am confined to bed	❑

Self-Care

I have no problems with self-care	❑
I have some problems washing or dressing myself	❑
I am unable to wash or dress myself	❑

Usual Activities *(e.g. work, study, housework, family or leisure activities)*

I have no problems with performing my usual activities	❑
I have some problems with performing my usual activities	❑
I am unable to perform my usual activities	❑

Pain / Discomfort

I have no pain or discomfort	❑
I have moderate pain or discomfort	❑
I have extreme pain or discomfort	❑

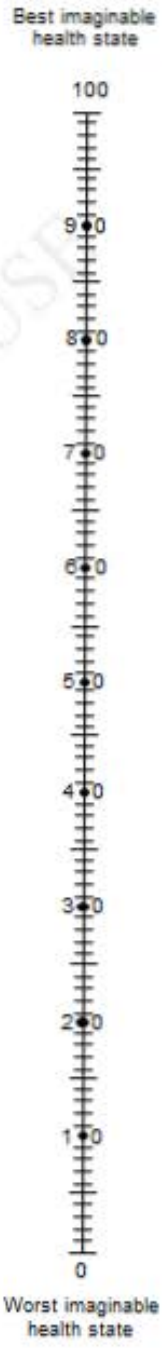
Anxiety / Depression

I am not anxious or depressed	❑
I am moderately anxious or depressed	❑
I am extremely anxious or depressed	❑

To help people say how good or bad a health state is, we have drawn a scale (rather like a thermometer) on which the best state you can imagine is marked 100 and the worst state you can imagine is marked 0.

We would like you to indicate on this scale how good or bad your own health is today, in your opinion. Please do this by drawing a line from the box below to whichever point on the scale indicates how good or bad your health state is today.

Your own health state today



3

9.5.2. FACIT-Fatigue

FACIT Fatigue Scale (Version 4)

ALXN1210-aHUS-311

Subject ID ☐☐☐☐-☐☐☐☐

Date Completed ☐☐-☐☐☐-☐☐☐☐
D D M M M Y Y Y Y

Below is a list of statements that other people with your illness have said are important. **Please circle or mark one number per line to indicate your response as it applies to the past 7 days.**

		Not at all	A little bit	Some-what	Quite a bit	Very much
[illegible]	I feel fatigued	0	1	2	3	4
[illegible]	I feel weak all over	0	1	2	3	4
An1	I feel listless ("washed out")	0	1	2	3	4
An2	I feel tired	0	1	2	3	4
An3	I have trouble starting things because I am tired	0	1	2	3	4
An4	I have trouble finishing things because I am tired	0	1	2	3	4
An5	I have energy	0	1	2	3	4
An7	I am able to do my usual activities	0	1	2	3	4
An8	I need to sleep during the day	0	1	2	3	4
An12	I am too tired to eat	0	1	2	3	4
An14	I need help doing my usual activities	0	1	2	3	4
An15	I am frustrated by being too tired to do the things I want to do	0	1	2	3	4
An16	I have to limit my social activity because I am tired	0	1	2	3	4

English (United States)
Copyright 1997, 2007

16 November 2007
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9.5.3. Pediatric FACIT-Fatigue

Pediatric (Paediatric) Functional Assessment of Chronic Illness Therapy – Fatigue

ALXN1210-aHUS-311

Subject ID ☐☐☐☐-☐☐☐☐

Date Completed ☐☐-☐☐☐-☐☐☐☐
D D M M M Y Y Y Y

Below is a list of statements that other people with your illness have said are important. **Please circle or mark one number per line to indicate your response as it applies to the past 7 days.**

		None of the time	A little bit of the time	Some of the time	Most of the time	All of the time
PF1	I feel tired	0	1	2	3	4
PF2	I have energy (or strength)	0	1	2	3	4
PF3	I could do my usual things at home	0	1	2	3	4
PF4	I had trouble starting things because I was too tired	0	1	2	3	4
PF5	I had trouble finishing things because I was too tired	0	1	2	3	4
PF6	I needed to sleep during the day	0	1	2	3	4
PF7	I got upset by being too tired to do things I wanted to do	0	1	2	3	4
PF8	Being tired made it hard for me to play or go out with my friends as much as I'd like	0	1	2	3	4
PF9	I needed help doing my usual things at home	0	1	2	3	4
PF10	I feel weak	0	1	2	3	4
PF11	I was too tired to eat	0	1	2	3	4
PF12	Being tired made me sad	0	1	2	3	4
PF13	Being tired made me mad (angry)	0	1	2	3	4

English (Universal)
Copyright 1987, 1997, 2006

22 June 2010
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9.5.4. Resource Utilization Patient Questionnaire

Patient Questionnaire

RESOURCE UTILIZATION

1. Have you visited your health care provider for management of complications related to your aHUS within the past month?
   - ☐ No
   - ☐ Yes, specify number of health care provider visits in the past month: _____

2. Have you gone to an Emergency Room primarily for treatment of complications related to your aHUS in the past month?
   - ☐ No
   - ☐ Yes, specify number of emergency room visits in the past month: _____

3. Have you been admitted to the Hospital primarily for treatment of complications related to your aHUS in the past month?
   - ☐ No
   - ☐ Yes, specify number of hospital admissions in the past month: _____

4. Have you missed work or school as a result of complications or symptoms related to your aHUS within the past month?
   - ☐ No
   - ☐ Yes, specify number of work days missed in the past month: _____

GENERAL HEALTH

5. In general would you say your health is:
   ☐ Excellent ☐ Very good ☐ Good ☐ Fair ☐ Poor

WORK STATUS

6. What is your current work status?
   - ☐ Work full time at a paid job
   - ☐ Work part time at a paid job (less than 30 hours per week)
   - ☐ Not in paid work force due to aHUS
   - ☐ Not working full time due to aHUS
   - ☐ Not working for pay for reasons unrelated to aHUS
   - ☐ Student
   - ☐ Retired
   - ☐ Other, specify: _____

9.5.5. Patient-Reported AHUS Symptoms Questionnaire

PATIENT-REPORTED aHUS SYMPTOMS

Date Completed: ____ / ____ / ____
dd mm yyyy

During the past week did you have any of the following symptoms?	Symptoms present?	If YES, how often did you have it?				If YES, how severe was it usually?				If YES, how much did it distress or bother you?				
		Rarely	Occasionally	Frequently	Almost constantly	Slight	Moderate	Severe	Very Severe	Not at all	A little bit	Somewhat	Quite a bit	Very much
Yellow discoloration of eyes and/or skin (jaundice)	□ No □ Yes	O	O	O	O	O	O	O	O	O	O	O	O	O
Chest pain	□ No □ Yes	O	O	O	O	O	O	O	O	O	O	O	O	O
Shortness of breath	□ No □ Yes	O	O	O	O	O	O	O	O	O	O	O	O	O
Headache	□ No □ Yes	O	O	O	O	O	O	O	O	O	O	O	O	O
Confusion	□ No □ Yes	O	O	O	O	O	O	O	O	O	O	O	O	O
Irritability	□ No □ Yes	O	O	O	O	O	O	O	O	O	O	O	O	O
Anxiety	□ No □ Yes	O	O	O	O	O	O	O	O	O	O	O	O	O
Weakness	□ No □ Yes	O	O	O	O	O	O	O	O	O	O	O	O	O
Fatigue	□ No □ Yes	O	O	O	O	O	O	O	O	O	O	O	O	O
Easy bruising/abdominal bleeding	□ No □ Yes	O	O	O	O	O	O	O	O	O	O	O	O	O
Abdominal pain	□ No □ Yes	O	O	O	O	O	O	O	O	O	O	O	O	O
Nausea/vomiting	□ No □ Yes	O	O	O	O	O	O	O	O	O	O	O	O	O
Diarrhea	□ No □ Yes	O	O	O	O	O	O	O	O	O	O	O	O	O
Swelling	□ No □ Yes	O	O	O	O	O	O	O	O	O	O	O	O	O
Other, specify:	□ No □ Yes	O	O	O	O	O	O	O	O	O	O	O	O	O
Other, specify:	□ No □ Yes	O	O	O	O	O	O	O	O	O	O	O	O	O
Other, specify:	□ No □ Yes	O	O	O	O	O	O	O	O	O	O	O	O	O
Other, specify:	□ No □ Yes	O	O	O	O	O	O	O	O	O	O	O	O	O
Other, specify:	□ No □ Yes	O	O	O	O	O	O	O	O	O	O	O	O	O
Other, specify:	□ No □ Yes	O	O	O	O	O	O	O	O	O	O	O	O	O