Cover Page for SAP

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NN7415-4311

Statistical Analysis Plan
Week 56 cut-off

Redacted protocol
Includes redaction of personal identifiable information only.

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[redacted], [redacted] Statistician
Biostatistics, Biopharm 1

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Version history

This Statistical Analysis Plan (SAP) describes the data evaluation planned for the 56 weeks cut-off as mentioned in the NN7415-4311 trial protocol version 7.0 (dated 18-Jun-2021).

SAP Version	Approval Date	Change	Rationale
1	18-Dec-2019	Not Applicable	Original version
2	27-Jul-2022	Updated Description for Defined Analysis Data Set "On-treatment" in section 4	Second bullet of the "On-treatment" analysis data set in section 4, was not updated when updating SAP from primary analysis cut-off to 56 weeks cut-off. Wording in second bullet has now been changed from "The last direct subject-site contact, at or prior to the *primary analysis* cut-off" to "The last direct subject-site contact, at or prior to the *56 weeks* cut-off".

1 Introduction

This SAP describes descriptive analyses for the endpoints/assessments related to bleeding episodes, safety and PK/PD for the evaluation made at the 56-week cut-off of trial NN7415-4311. The 56-week cut-off is defined as when all patients in arms 2, 3 and 4 have completed visit 13a (or permanently discontinued treatment). For a description of the analyses planned for the main part of the trial please refer to the SAP for the primary analysis cut-off.

All confirmatory conclusions for this trial are based on the analyses done at the primary analysis cut-off. No further confirmatory conclusions can be made based on the descriptive analyses described in this SAP.

Additional details on the derivation and calculation based on the measurements collected in this trial will be described in the analysis data reviewer's guide (ADRG). In addition, specifications of tables, figures and listings (TFL) are described in the mock TLFs.

Note, in this document 'bleeds' refer to 'bleeding episodes'.

1.1 Objectives and endpoints

No specific objectives are defined to specifically relate to the 56 weeks cut off. For the objectives related to PACO, please refer to the protocol.

All the details of the endpoints, assessments and timeframes for the week 56 cut-off are explained in the appendix 2.

1.2 Trial design

The following is a brief sum up of the most important parts of the trial design. For further details refer to the trial protocol version 7.

- This is a prospective, multicentre, open label clinical trial with four arms with the aims to evaluate the effect and safety of daily concizumab prophylaxis administered s.c. in subjects with HAwI and HBwI. The four arms of the trial consist of:
    - Arms 1 and 2 consist of subjects previously treated on demand who are randomised to
        - Arm 1: On-demand administration
        - Arm 2: Concizumab PPX treatment
    - Arms 3 and 4 are allocated to receive concizumab PPX treatment and consist of subjects who are
        - Arm 3: Transferred from trial 4310
        - Arm 4: Previously treated on PPX or on demand
- In the second quarter of 2020, the protocol was amended (protocol version 3.0) to incorporate measures to mitigate the risk of thromboembolic events. These measures include the handling of factor treatment for BTB and changes to the dosing regimen. As a result of these changes and the pause in the treatment while the protocol was to be amended, all statistical analyses were reconsidered and adjusted accordingly.
- The primary analysis is made when all subjects in arm 1 have completed visit 9/9a (or withdrawn) and all subjects in arm 2 have completed visit 10a (or withdrawn).
- After the main part of the trial, all patients have offered to continue in the extension part of the trial and receive treatment with concizumab for up to an additional 128 weeks (arms 2−4) or 136 weeks (arm 1)
- After 56 weeks of treatment in arms 2, 3 and 4, an additional evaluation will be made assessing bleed-related endpoints and safety for concizumab. This SAP describes in more detail the descriptive analyses that are relevant for this cut-off.
- After the last patient has been randomised, any patient that due to the COVID-19 pandemic is prevented from restarting the new dosing regimen will no longer be used to determine the primary analysis cut-off and the 56-week cut-off.

2 Statistical hypotheses

For the analyses related to the week 56 cut-off no statistical hypotheses are tested.

Multiplicity Adjustment

No adjustment for multiplicity is needed since no statistical hypotheses are tested.

3 Sample size determination

The sample size considerations are described in detail in section 10.1 of the protocol version 7.

4 Analysis sets

For the purposes of analysis, the following analysis sets are defined for the week 56 cut-off.

Subject Analysis Set	Description
Full Analysis Set (FAS)	All subjects randomised to concizumab PPX or on-demand treatment or allocated to arms 3 or 4. Subjects from arms 1 and 2 will contribute to the evaluation 'as randomised'.
Safety Analysis Set (SAS)	All subjects exposed to concizumab PPX or randomised to on-demand treatment. All subjects will contribute to the evaluation 'as treated'.

Defined Analysis Data Sets	Description
On-treatment	The time period where subjects are considered to be affected by on-demand treatment or concizumab treatment. For safety endpoints/assessments relating to events (number of thromboembolic events, number of hypersensitivity type reactions, number of injection site reactions, number of patients with antibodies to concizumab, number of adverse events) the 'on-treatment' analysis data set is defined as follows. For subjects in **arm 1 during on-demand treatment**, the period begins on the date of randomisation (as registered in IWRS) and ends at the first occurrence of: 1. Time of permanently ending on-demand administration and initiation of any PPX regimen 2. The last direct subject-site contact, at or prior to the 56 weeks cut-off 3. Withdrawal date for subjects who withdraw informed consent 4. The last subject-investigator/site contact as defined by investigator for subjects who are completely lost to follow up 5. Date of death for subjects For subjects in **arm 1 during concizumab PPX treatment**, the period begins at the time of initiation of concizumab PPX treatment and ends at the first occurrence of: 6. Date of last dose of concizumab + 7 weeks 7. Items 2., 3., 4. or 5. above For subjects in **arms 2-4 that start on the new concizumab dosing regimen and who have not been exposed to the initial dosing regimen**, the period begins at the time of start of the new concizumab PPX regimen.

	For subjects in **arms 2-4 that are only exposed to the initial concizumab dosing regimen**, the period begins at the time of start of the initial concizumab PPX regimen. For subjects in **arms 2-4 that start on the new concizumab dosing regimen and who have been exposed to the initial dosing regimen**, the period consists of two periods with a pause in between. The first period begins at the time of start of the initial concizumab PPX regimen and ends 7 weeks after the treatment was paused while the second period begins at the time of start of the new concizumab PPX regimen. For all cases of arms 2-4 above the periods end at the first occurrence of: • Items 2., 3., 4., 5. or 6. above
On-treatment without data on initial regimen	The time period where subjects are considered to be affected by on-demand treatment or treatment with the new concizumab dosing regimen. The analysis data set is defined similarly as the 'on-treatment' analysis data set with the exception: • Observation time during the initial concizumab PPX regimen is excluded
On-treatment without ancillary therapy[a] excl. data on initial regimen for subjects exposed to both regimens	The time period where subjects are treated by either the new concizumab dosing regimen or the initial concizumab dosing regimen (only included if not exposed to the new concizumab dosing regimen) or are treated by on-demand treatment and additionally have not used factor-containing products not related to treatment of a bleed during any of the cases. The analysis data set is defined similarly as the 'on-treatment' analysis data set with the exception: • Periods where factor containing products not related to treatment of a bleed have been used are excluded • For subjects in arms 2-4 that start on the new concizumab dosing regimen and who have been exposed to the initial dosing regimen, the data on the initial concizumab PPX regimen are excluded

[a] Ancillary therapy is defined as use of factor-containing products not related to treatment of a bleed.

5 Statistical analyses

5.1 General considerations

This SAP will address the details of the descriptive statistics implemented on all arms (1, 2, 3 and 4) at the 56-week cut-off of trial NN7415-4311. The 56-week cut-off is defined as when all patients in arms 2, 3 and 4 have completed visit 13a (or permanently discontinued treatment). After the last patient has been randomised, any patient that due to the COVID-19 pandemic is prevented from restarting the new dosing regimen will no longer be used to determine the 56-week cut-off.

Unless specified otherwise, the endpoints/assessments will be presented using the analysis sets as displayed in Table 1.

Table 1 Analysis sets used for analyses and/or presentations of endpoints/assessments

Endpoint/assessment categories[a]	Subject Analysis Set	Analysis Data Sets
Bleeding episodes	FAS	On-treatment without ancillary therapy excl. data on initial regimen for subjects exposed to both regimens
PK, PD and safety not relating to events	SAS	On-treatment without data on initial regimen
Safety relating to events[b]	SAS	On-treatment and On-treatment without data on initial regimen

[a]Which endpoints/assessments that belong under each category can be found in section 9 of the protocol version 7.
[b]This specifically refers to: number of thromboembolic events, number of hypersensitivity type reactions, number of injection site reactions, number of patients with antibodies to concizumab, and number of adverse events.

For arms 2-4 the target joints registered at baseline will be used for the assessment done at week 56. For arm 1 the target joint evaluation done at visit V9a will be used for assessment at week 56.

Continuous endpoints/assessments will be presented using descriptive statistics which will include min, max, mean, SD, median, and quartiles. For PK endpoints/assessments, the descriptive statistics will also include geometric mean and geometric CV. Event data (including AEs) will be summarised including number of subjects with an event/episode, percentage of subjects with an event/episode, number of events/episodes and rate of events/episodes. Categorical assessments will be summarised by number and percent of subjects in each category. Presentations of results will be by arm and visit (when applicable) and when relevant arm 1 will be split into two parts with on-demand treatment and concizumab treatment.

Baseline for the assessments done at week 56 is defined as the latest non-missing measurement recorded before the time of the first administration of concizumab with the new dosing regimen (arms 2-4 and arm 1 after receiving concizumab) or recorded before randomisation to the on-demand administration (arm 1). If this measurement is missing for arms 2-4 or a subject from arms 2-4 chooses not to restart on concizumab, then the baseline obtained prior to the initial dosing regimen will be used (if available). If the V9a measurement is missing for arm 1 concizumab part,

the latest measurement recorded prior to V9a will be used as a concizumab baseline for arm 1 subjects.

As described in the protocol, if a patient withdraws from trial prior to visit 9/9a/10a (last treatment visit in the main part of the trial), the investigator should ask the patient if he is willing, as soon as possible, to have assessment performed according to visit 9/9a/10a. If the patient withdraws from trial after visit 9a/10a, he should have assessment performed according to visit 26a (last treatment visit in the extension part of the trial). Any values obtained because of this are in scope for being reallocated to a (planned) scheduled visit. Only the value(s) that fulfil the below reallocation rules can be used in summaries and the analyses. The value(s) will be reallocated to a (planned) scheduled visit if the following apply:

- The visit falls within an extended visit window of +/- 7 days of the (planned) scheduled visit.
- The same parameter was planned for assessment but was not assessed at the scheduled visit.
- The scheduled visit is neither a screening visit (visit 1/1a), a randomisation visit (visit 2/2a) or a V9/V9a (only relevant if the patient withdraws from the trial after V9a/10a).

In terms of bleed related endpoints, the bleed rate is defined as the number of bleeds over the respective observation periods. Multiple bleeding locations at the same time point will be counted as one bleeding episode. As a general rule, a treated bleed is defined as any bleed where the use of a factor-containing product is reported between the start and stop time of a bleed. Further, the endpoints will not include re-bleeds. A re-bleed is defined as a bleeding episode (worsening of bleeding site conditions e.g. swelling, pain) starting within 72 hours after stopping treatment of a previous treated bleeding episode (or re-bleed) at the same anatomical location. Note that there can be more than one re-bleed related to the same bleed. If a bleeding episode occurs in the same location more than 72 hours after stopping treatment of a previous bleeding episode (or re-bleed) in the same location, the bleed is defined as a new bleeding episode.

Pharmacokinetic concentration values below lower limit of quantification (LLOQ) is handled as described below:

Timing of values below LLOQ	Imputation	Use of imputed values
Values below LLOQ obtained before time of the first administration with the initial dosing regimen and with the new dosing regimen	Set to 0 (zero)	Plots and derivation of AUC
All other values below LLOQ	Set to LLOQ/2	Plots and derivation of AUC

5.2 Subject disposition

See mock TFLs.

5.3 Primary endpoint analysis

Refer to SAP for PACO.

5.4 Secondary endpoint analysis

Refer to SAP for PACO.

5.5 Exploratory efficacy endpoints analysis

5.5.1 Bleed-related assessments

The assessments related to bleeding episodes are defined in section 6.2.

The definition of bleeding rate, treated bleeds and re-bleeds are defined in the section 5.1 of this document and in section 10.3 of protocol version 7. The definition of a target joint is given in the protocol section 9.1.4.

ABR will be calculated at an individual basis as

$$ABR = \left(\frac{\text{Number of treated spontanous or traumatic bleeds}}{\text{Number of days in the analysis data set}}\right) x\ 365.25$$

The continuous/categorical assessments will be presented using descriptive statistics as described in section 5.1. The descriptive statistics for the bleed related assessments up until week 56 will be presented by treatment arms and 'Total concizumab'. Furthermore, it will be presented by haemophilia types (HAwI, HBwI).

The evaluation of bleeding episodes at target joints up until 56 weeks will be done between treatment arms and as 'Total concizumab'.

These descriptive statistics tables will enumerate results for treated bleeds, zero treated bleeds, cause of bleeds (Spontaneous, Traumatic, Surgical), anatomical location of bleeds (Target joints, Joints, Muscular, Skin, Gastrointestinal, Mouth-gums-nose, Urinary system, Central nervous system, Other), classification of bleeds (Mild/moderate, Severe) and location of severe bleeds (Target joints, Joints, Muscular, Skin, Gastrointestinal, Mouth-gums-nose, Urinary system, Central nervous system, Other). The analysis data set use for these descriptive statistics are mentioned in section 5.1 of this document.

5.5.2 Pharmacokinetic and pharmacodynamic assessments

The assessments related to PK and PD are defined in section 6.2.

Concizumab concentrations collected during the trial will be used to derive the pharmacokinetic endpoints and assessments based on non-compartmental methods.

All PK and PD endpoints and assessments are continuous and will be presented using the descriptive statistics and analysis sets as described under section 5.1.

5.6 Exploratory safety analyses

5.6.1 Extent of exposure

A summary showing subjects that escalate, deescalate, or remain on the 0.20 mg/kg/day dose will be presented by arm.

The length of the periods constituting the analysis data sets and the number of doses taken will be presented descriptively. The output will differentiate between before the pause, after the pause and in total.

5.6.2 Adverse events

All exploratory safety endpoints are defined in section 6.2.

All adverse events will be coded using the current version of MedDRA. Hypersensitivity reactions, medication errors and injection site reactions are categorised in the CRF as AEs requiring additional data collection. Additional information on these events will be collected using separate forms. Further, a MedDRA search will also be used to define these events. Thromboembolic events are defined and categorised as AESIs.

Adverse events will be evaluated using descriptive statistics based on the analysis data sets as described in section 5.1. These descriptive statistics tables will also be presented by treatment arms and 'Total concizumab'.

Furthermore, for the on-treatment analysis data set the outputs on adverse events will also include information on

- System organ class
- Severity (mild/moderate/severe), seriousness (serious/non-serious) and relation to treatment (possibly/probably/unlikely)
- Adverse events leading to drug discontinuation
- Most frequent adverse events (occurring in more or equal to 5% of subjects)
- Deaths
- Medication errors

The outputs may differentiate between the initial part of the trial and the part after the restart of the trial if deemed relevant.

5.6.3 Additional safety assessments

Assessments in relation to planned safety laboratory measurement, body measurements, vital signs and physical examinations are defined in section 6.2. The assessments will be presented using descriptive statistics as described in section 5.1. Number of patients with a positive antibody test will be presented as described in section 5.1 and furthermore a list of all positive antibodies recorded during the trial will be presented.

5.7 Subgroup analyses

Descriptive statistics by subgroups are specified for haemophilia types (HAwI or HBwI) above in each of the sections concerning the specific assessments, such as bleed related endpoints.

5.8 Interim analyses

No formal interim analyses are planned.

Several evaluations are to be made during the conduct of the trial:

- at the primary analysis cut-off
- after 56 weeks
- at the end of the extension part

After the initial evaluation at the primary analysis cut-off no further confirmatory conclusions can be made.

5.8.1 Data monitoring committee

A Data Monitoring Committee (DMC) is established to review and evaluate accumulating data from the trial in order to protect the safety of the subjects.

The DMC members are not having direct contact with any Novo Nordisk staff involved with the trial except for Novo Nordisk global safety. Details in relation to DMC can be seen in Appendix 4 of the protocol version 7.

6 Supporting documentation

6.1 Appendix 1: List of abbreviations

ABR	Annual Bleeding Rate
ADRG	Analysis Data Reviewer's Guide
AE	Adverse event
AESI	Adverse event of special interest
AUC	Area under the curve
DMC	Data monitoring committee
FAS	Full analysis set
HAwI	Haemophilia A with inhibitors
HBwI	Haemophilia B with inhibitors
IWRS	interactive web response system
LLoQ	Lower limit of quantification
MedDRA	Medical dictionary for regulatory activities
PACO	Primary analysis cut-off
PD	Pharmacodynamic
PK	Pharmacokinetic
PPX	Prophylaxis
SAP	Statistical Analysis Plan
SAS	Safety analysis set
TFL	tables, figures and listings
TFPI	Tissue factor pathway inhibitor

6.2 Appendix 2: Definition of exploratory efficacy/safety endpoints and assessments

Type	Title	Time frame	Unit	Details	Section
Assessment	Number of treated spontaneous and traumatic bleeding episodes	On demand (arm 1) • From randomisation (week 0) up until start of concizumab treatment (at least 24 weeks) Concizumab (arm 1) • From start of the new concizumab dosing regimen up until week 56 cut-off Concizumab (arms 2-4) • From start of the new concizumab dosing regimen (week 0) up until week 56 cut-off	Count	Week 56 cut-off is when all patients from arm 2-4 have completed visit 13a assessments or permanently discontinued treatment. Concizumab (arm 1) data available up until week 56 cut-off will be presented.	5.5.1
Assessment	Number of treated spontaneous bleeding episodes	On demand (arm 1) • From randomisation (week 0) up until start of concizumab treatment (at least 24 weeks) Concizumab (arm 1) • From start of the new concizumab dosing regimen up until week 56 cut-off	Count	Week 56 cut-off is when all patients from arm 2-4 have completed visit 13a assessments or permanently discontinued treatment. Concizumab (arm 1) data available up until week 56 cut-off will be presented.	5.5.1

		Concizumab (arms 2-4) • From start of the new concizumab dosing regimen (week 0) up until week 56 cut-off			
Assessment	Number of treated spontaneous and traumatic joint bleeds	On demand (arm 1) • From randomisation (week 0) up until start of concizumab treatment (at least 24 weeks) Concizumab (arm 1) • From start of the new concizumab dosing regimen up until week 56 cut-off Concizumab (arms 2-4) • From start of the new concizumab dosing regimen (week 0) up until week 56 cut-off	Count	Week 56 cut-off is when all patients from arm 2-4 have completed visit 13a assessments or permanently discontinued treatment. Concizumab (arm 1) data available up until week 56 cut-off will be presented.	5.5.1
Assessment	Number of treated spontaneous and traumatic target joint bleeds	On demand (arm 1) • From randomisation (week 0) up until start of concizumab treatment (at least 24 weeks) Concizumab (arm 1)	Count	Week 56 cut-off is when all patients from arm 2-4 have completed visit 13a assessments or permanently discontinued treatment. Concizumab (arm 1) data available up until week 56 cut-off will be presented.	5.5.1

		• From start of the new concizumab dosing regimen up until week 56 cut-off Concizumab (arms 2-4) • From start of the new concizumab dosing regimen (week 0) up until week 56 cut-off			
Assessment	The number of all spontaneous and traumatic bleeds (treated and untreated)	On demand (arm 1) • From randomisation (week 0) up until start of concizumab treatment (at least 24 weeks) Concizumab (arm 1) • From start of the new concizumab dosing regimen up until week 56 cut-off Concizumab (arms 2-4) • From start of the new concizumab dosing regimen (week 0) up until week 56 cut-off	Count	Week 56 cut-off is when all patients from arm 2-4 have completed visit 13a assessments or permanently discontinued treatment. Concizumab (arm 1) data available up until week 56 cut-off will be presented.	5.5.1
Assessment	Pre-dose concizumab plasma concentration	Concizumab (arms 2-4) • From start of the new concizumab dosing	ng/mL	Summary of pre-dose assessments from start of the new concizumab dosing regimen (week 0) up until week 56.	5.5.2

		regimen (week 0) up until week 56 cut-off			
Assessment	Thrombin peak	At visits where thrombin generation assessments are planned to be measured in the trial up to 56 weeks	nmol/L	Summary of these assessments up until week 56. From start of the new concizumab dosing regimen (week 0) up until week 56.	5.5.2
Assessment	Free TFPI concentration	At visits where free TFPI assessments are planned to be measured in the trial up to 56 weeks	ng/mL		5.5.2
Assessment	Endogenous thrombin potential (ETP)	At visits where thrombin generation assessments are planned to be measured in the trial up to 56 weeks	nmol/L*min		5.5.2
Assessment	Endogenous thrombin Potential ratio	At visits where thrombin generation assessments are planned to be measured in the trial up to 56 weeks	Ratio		5.5.2
Assessment	Velocity index	At visits where thrombin generation assessments are planned to be measured in the trial up to 56 weeks	nmol/L*min		5.5.2
Assessment	Thrombin lag time	At visits where thrombin generation assessments are planned to be measured in the trial up to 56 weeks	min		5.5.2

Assessment	Time to thrombin peak	At visits where thrombin generation assessments are planned to be measured in the trial up to 56 weeks	min		5.5.2
Assessment	Number of adverse events	On demand (arm 1) • From randomisation to on demand treatment up until start of concizumab treatment Concizumab (arm 1) • From start of the new concizumab dosing regimen up until week 56 cut-off Concizumab (arms 2-4) • Before the pause: From start of concizumab treatment (week 0) up until 7 weeks after the treatment pause as well as • After the pause: From start of the new concizumab treatment (week 0) up until week 56 cut-off	Count	Week 56 cut-off is when all patients from arm 2-4 have completed visit 13a assessments or permanently discontinued treatment. Concizumab (arm 1) data available up until week 56 cut-off will be presented.	5.6.2
Assessment	Number of thromboembolic events		Count		5.6.2
Assessment	Number of hypersensitivity type reactions		Count		5.6.2
Assessment	Number of injection site reactions		Count		5.6.2

Assessment	Number of patients with antibodies to concizumab	Concizumab (arms 2-4) • From start of the new concizumab dosing regimen (week 0) up until week 56 cut-off	Count	Week 56 cut-off is when all patients from arm 2-4 have completed visit 13a assessments or permanently discontinued treatment.	5.6.3
Assessment	Change in <safety laboratory parameter>	On demand (arm 1) • From randomisation (week 0) up until start of concizumab treatment (at least 24 weeks) Concizumab (arm 1) • From start of the new concizumab dosing regimen up until week 56 cut-off Concizumab (arms 2-4) • From start of the new concizumab dosing regimen (week 0) up until week 56 cut-off From start of treatment (week 0) to every visit where the <safety laboratory parameter> is planned to be measured up until V13a (week 56)	Multiple units	<safety laboratory parameter> refers to each safety laboratory parameter for haematology, biochemistry and coagulation parameters as listed in table 18 of the protocol version 7. Week 56 cut-off is when all patients from arm 2-4 have completed visit 13a assessments or permanently discontinued treatment. Concizumab (arm 1) data available up until week 56 cut-off will be presented.	5.6.3

Assessment	Change in body weight	On demand (arm 1) • From randomisation (week 0) up until start of concizumab treatment (at least 24 weeks) Concizumab (arm 1) • From start of the new concizumab dosing regimen up until week 56 cut-off Concizumab (arms 2-4) • From start of the new concizumab dosing regimen (week 0) up until week 56 cut-off From start of treatment (week 0) to every visit where body weight is planned to be measured up until V13a (week 56)	kg	Week 56 cut-off is when all patients from arm 2-4 have completed visit 13a assessments or permanently discontinued treatment. Concizumab (arm 1) data available up until week 56 cut-off will be presented.	5.6.3
Assessment	Change in systolic blood pressure	On demand (arm 1) • From randomisation (week 0) up until start of concizumab treatment (at least 24 weeks) Concizumab (arm 1)	mmHg	Week 56 cut-off is when all patients from arm 2-4 have completed visit 13a assessments or permanently discontinued treatment. Concizumab (arm 1) data available up until week 56 cut-off will be presented.	5.6.3
Assessment	Change in diastolic blood pressure		mmHg		5.6.3
Assessment	Change in pulse rate		beats/min		5.6.3

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		• From start of the new concizumab dosing regimen up until week 56 cut-off Concizumab (arms 2-4) • From start of the new concizumab dosing regimen (week 0) up until week 56 cut-off From start of treatment (week 0) to every visit where the vital signs are planned to be measured up until V13a (week 56)			
Assessment	Change in physical examination	Concizumab (arm 1) • From start of the new concizumab dosing regimen up until week 56 cut-off Concizumab (arms 2-4) • From start of the new concizumab dosing regimen (week 0) up until week 56 cut-off From start of treatment (week 0) to every visit where physical examination is planned to	%	Week 56 cut-off is when all patients from arm 2-4 have completed visit 13a assessments or permanently discontinued treatment. Concizumab (arm 1) data available up until week 56 cut-off will be presented.	5.6.3

		be measured up until V13a (week 56)			