SUMMARY OF CHNGES IN STUDY PROTOCOL

A PROSPECTIVE, MULTI-CENTER, PHASE II STUDY TO EVALUATE THE SAFETY AND EFFICACY OF ECULIZUMAB IN SUBJECTS WITH GUILLAIN–BARRÉ SYNDROME (JET-GBS - Japanese Eculizumab Trial for GBS)

Document	Date	Section number	Description of Change(s)
Original study protocol Version 1.0	1/Apr/2015		-
Version 1.1	20/Apr/2015	Title Page, and page headers	Update to reflect current protocol, edition as 1.1 version
		5.	Change for a misprint from Guillain-Barré Syndrome to Guillain-Barré syndrome
		7.6.3.1.	Addition of information that subject diaries are source documents
		7.6.9.	Addition of missing information: Nerve Conduction Study: Measure distal latency, CMAP amplitude (proximal, distal), CMAP duration (proximal, distal), motor nerve conduction velocity, and minimum F-wave latency of the median, ulnar, fibular, and tibial nerves. CMAP amplitudes will be measured from the baseline to the peak of negative deflection (negative-peak amplitude). The CMAP duration will be measured from the beginning of the initial deflection to its return to the baseline (negative-peak duration). In case of polyphasic action potential, the duration from the onset of the first negative phase to the return of the last negative phase to the baseline will be measured (total duration).

Version 1.2	8/June/2015	Title Page, and page headers	Update to reflect current protocol, edition as 1.2 version
		1. 6.2.	Addition of a secondary efficacy endpoint as 16.Proportion of patients who undergo re-administration of IVIg, and its rationale for setting. Addition of details on how to determine the functional grade as follows: *1: Investigators will determine the duration required for improvement by at least one grade on the Hughes functional grading scale according to clinical assessments and the subject's diary.
		7.6.1.	Addition of collecting information on an antecedent infection/onset of weakness of GBS as subject background information
		7.6.3.1.	Addition on details how to treat subjects' diaries: If the subject has difficulty completing the diary due to muscular weakness, a family member or another person aside from the evaluating physician may record the subject's self-evaluation in the diary.
		7.6.7.	Addition that a family member or study coordinator may record a subject's self-evaluation in the R-ODS questionnaire if the subject has difficulty in writing due to weakness: If the subject has difficulty completing the questionnaire due to muscular weakness, a family member or study coordinator aside from the evaluating physician may record the subject's self-evaluation in the questionnaire.
		8.1. Table 6 Footnotes for table 6	Deletion of ※9 on nerve conduction test at Day 0 and Day 1 Changes of time windows from 3 days to 7 days for clinical laboratory test at the last follow up visit, and from -1 day to -5 days for nerve conduction study at Day 1 visit.
		8.2.	Addition of a procedure at screening visit

			1. Confirm the study target (GBS) [Cranial nerve involvement, Sensory symptoms, and CSF examination (Concentration of protein, Cell count)].
		8.3.	Addition of in general to hospitalization period Subjects will be admitted into hospital care for 4 weeks in general and receive a total of 4 doses of the IP (Day 1, Day 8, Day 15, Day 22).
		8.3.1.	Addition of a missing procedure: 10. Measure anti-ganglioside activity
		10.4.1.	Deletion of “or Day 22” for re-administration of IVIg. Re-administration of IVIg (400 mg/kg over 5 days) should be considered after the start of IP administration and after Day 15 ~~or Day 22~~, only if the subject is monitored for progressive worsening of symptoms more than one grade on the Hughes functional grading scale compared to before the administration of the IP.
		Appendix 2 R-ODS	Revision of the explanatory description to make it more easily understood by patients Deletion of the option of “Not applicable” to avoid any confusion
Version 1.3	19/Feb/2016	Title Page, and page headers	Update to reflect current protocol, edition as 1.3version Addition of information of clinical trial registration: Clinical Trial Registration : UMIN Clinical Trials Registry (UMIN 000018171) Clinical Trials.gov (NCT02493725)
		1.	Updated information and minor changes in wording
		5.1.	Addition of detailed description of subtypes of GBS
		5.1.2. 6.1.2. Table 2 7.5. –7.7.	Improved revision made to English translation

		8.1. 10.4.–10.5	
		7.5.2.	Minor editorial change from chapter 7.5.2. to 7.5.2.1
		12.2.8.2.	Minor correction of a misprint Addition of follow-up report procedure as follows: Alexion contact information provided below within 24 hours of their becoming aware of them. If any changes are made on the follow-up report, the following information also will be sent to Alexion promptly : Alexion Pharmacovigilance
		12.2.8.4.	Addition of details on how to unblind the emergency key-code: Before unblinding the emergency key-code, the Investigator or Subinvestigator must record all the information known at the point in the electronic data capture (EDC) as much as possible.
		13.4. 20.1 22 23	Improved revisions made to English translation
Version 1.4	1/December/2017	Title Page, and page headers	Update to reflect current protocol, edition as 1.4 version
		5.2.1.	Addition of translation missing information Atypical hemolytic uremic syndrome (aHUS) is a rare disease that involves complement mediated thrombotic microangiopahty, leading to various aHUS symptoms such as kidney failure or possibilities of death. Therefore, it is crucial to maintain the terminal complement inhibition completely and continuously for the disease. The target trough serum concentration is 50μg/ml by the dosing regimen of 900mg (induction dose) and 1200mg (maintenance dose),

			which have been approved for efficacy and safety for aHUS.
		Throughout the protocol	Minor grammatical, formatting, spelling changes or improved revisions to English translation were made