2. STUDY SYNOPSIS

Name of Sponsor/Company:	**Individual Study Table Referring to Part of the Dossier**	*For National Authority Use Only*
Name of Finished Product:	**Volume:**	
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TITLE OF STUDY:
A Phase II Multi-Centre, Extension Study to Investigate the Long Term Safety of ONO-2506PO in Patients Diagnosed with Amyotrophic Lateral Sclerosis (ALS)

INVESTIGATORS:
This was a multi-centre study. A total of 24 centres were planned, but only 6 centres recruited subjects before the sponsor's decision to stop the study following an interim analysis of the ONO-2506POE014 study, which indicated that ONO-2506PO was of no clear benefit to subjects with ALS. A full list of participating investigators and addresses is provided in Appendix 16.1.2.

STUDY CENTRES:
Two centres in Belgium and 4 centres in Germany.

PUBLICATIONS: None

STUDIED PERIOD: First subject recruited 13 June 2008 Last subject completed 24 October 2008	**DEVELOPMENT PHASE:** Phase II

OBJECTIVES:
The primary objective of this study was to evaluate the long term safety of ALS patients following dosing of ONO-2506PO, 1200 mg once daily (OD).

METHODOLOGY:
This multi-centre, Phase II extension study was planned to consist of 2 phases: a double-blind phase in which subjects had to continue to take double-blind study medication (1200 mg ONO-2506PO or placebo) that was allocated to them in the parent study (ONO-2506POE014) plus standard riluzole therapy (50 mg twice daily), until un-blinding of the study results; and an open label phase in which subjects who were allocated to ONO-2506PO in the ONO-2506POE014 study were to receive 1200 mg ONO-2506PO OD plus stable standard riluzole therapy for the duration of their participation in the study.

The study was stopped early in the double-blind phase since planned interim analysis of data from the ONO-2506POE14 study indicated that ONO-2506PO was of no clear benefit to subjects with ALS.

NUMBER OF SUBJECTS:
Planned: 400; Enrolled: 15; Analysed for Safety: 15.

INDICATION AND MAIN CRITERIA FOR INCLUSION:
Indication: ALS

Main criteria for inclusion: adult male and female subjects over the age of 18 years with diagnosis of ALS, who had completed 18 months treatment (1200 mg ONO-2506PO and standard riluzole therapy) in ONO-2506POE014 study and were willing to provide written informed consent, were included in this study. Subjects had to have the ability to swallow study medication without the requirement for nasogastric or percutaneous endoscopic gastrostomy (PEG) feeding as evidenced by a score of ≥3 on ALS functional rating scale (ALSFRS-R) question # c (swallowing).

INVESTIGATIONAL DRUG:
ONO-2506PO was supplied as 300 mg soft gel capsules for oral administration in bottles containing 56 capsules each. Subjects assigned to 1200 mg ONO-2506PO were asked to self administer a total of 4 capsules orally OD at approximately the same time each morning. The drug lot number for ONO-2506PO was X7X2.

REFERENCE THERAPY:
Placebo soft gel capsules identical to ONO-2506PO capsules were supplied to maintain the blind during the double-blind phase. During the double-blind phase, subjects assigned to placebo had to self administer a total of 4 capsules orally OD at approximately the same time each morning. The drug lot number for placebo was X7X1.

DURATION OF TREATMENT:
ONO-2506PO or matching placebo capsules were to be administered OD until un-blinding of ONO-2506POE014 study. Following un-blinding, subjects assigned to ONO-2506PO were intended to continue with open label treatment indefinitely until one of the following occurred: subject was unable to swallow; subject withdrew consent or was withdrawn due to an unacceptable adverse event (AE); diagnosis of ALS was determined to be incorrect and was revised to another condition; study was terminated by sponsor; or subject died.

CRITERIA FOR EVALUATION:
Safety:
AEs, survival, occurrence of tracheotomy and permanent assisted ventilation events assessment, and use of concomitant medications including interventional procedures and used study medications.

STATISTICAL METHODS:
No statistical analyses were performed.

RESULTS:
A total of 15 subjects were enrolled and treated. Seven subjects received ONO-2506PO and 8 subjects received placebo. In addition to approximately 18 months of dosing in the ONO-2506POE014 study, in this extension study subjects were dosed for between 22 and 94 days.

Safety:
There were no deaths, treatment-emergent serious adverse events (SAEs) or AEs, and discontinuations due to AEs reported during the study. Several AEs that were ongoing from the ONO-2506POE014 study were reported, including 2 non-treatment related SAEs of severe orthopnoea and decreased slow vital capacity (SVC).

CONCLUSIONS:
ONO-2506PO 1200 mg OD was well tolerated in this extension study. No deaths, new treatment-emergent SAEs or AEs, and discontinuations due to AEs were reported during this study. Two non-treatment related severe SAEs (orthopnoea and decreased SVC) that were ongoing from the ONO-2506POE014 study were reported. None of the subjects required tracheotomy or PAV during the study.

Since this extension study was terminated within 5 months of initiation, the primary objective of the study to further evaluate the long term safety of ONO-2506PO in ALS subjects could not be addressed.

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