Clinical Study Protocol Amendment	
Amendment Number	1
Drug Substance	D961H
Study Code	D961HC00006
Date	

A multicentre, randomised, double-blind, parallel-group, comparative study to compare the efficacy and safety of D961H 20 mg once daily oral administration with omeprazole 10 mg and D961H 10 mg once daily oral administration in maintenance treatment in patients with healed reflux esophagitis

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Sponsor:

AstraZeneca K.K.
1-88, 1-chome, Ohyodo-naka, Kita-ku, Osaka 531-0076, Japan

Centres affected by the Amendment:

All centres in the study

The protocol for the study (Version 1 dated 18 September 2007 including Appendices A-D and Supplement A, Administrative change 1 dated 28 November 2007 and Administrative change 2 dated 25 February 2008) is to be amended as follows:

Amendment 1

Section of protocol affected:

Page 16, "3.1 Overall study design and flow chart"

Table 1 Study Plan

Previous text:

Table 1 Study plan

	Screening		**Study Treatment**					
		Randomisation						
Visit	**1[1)]**	**2**	**3** **Week 4**	**4** **Week 8**	**5** **Week 12**	**6** **Week 16**	**7** **Week 20**	**8 (or at discontinuation)** **Week 24**
Days after Visit 2	**-7 to 0**	**0**	**28**	**56**	**84**	**112**	**140**	**168**
Time window (days)	**-**	**-**	**±4**	**±4**	**±4**	**±4**	**±4**	**±4**
Informed consent [2)]	X							
Inclusion/exclusion criteria	X	X[11)]						
Demographic data	X							
Medical/surgical history	X							
Underlying diseases	X	X						
Physical examination	X	X	X	X	X	X	X	X
Vital signs	X		X	X	X	X	X	X
Clinical laboratory tests [3)]	X		X		X			X
Pregnancy test (urine) [4)]	X							
Hp test (IgG antibody)	X[8)]							
Genetic test for CYP2C19	X[8)]							

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Days after Visit 2	**-7 to 0**	**0**	**28**	**56**	**84**	**112**	**140**	**168**
Time window (days)	**-**	**-**	**±4**	**±4**	**±4**	**±4**	**±4**	**±4**
GERD symptoms assessed by the investigator [5)]		X	X	X	X	X	X	X
EGD [6)]		X[9), 10)]	X[12)]		X[12)]			X
Randomisation		X						
Dispense investigational products		X	X	X	X	X	X	
Review/Collect returned investigational products			X	X	X	X	X	X
Check concomitant medications	←							→
AEs [7)]	←							→

1) In the case of subjects whose RE is healed by the initial treatment in the preceding study (D961HC00002) and enrolled in this study, the data at the end of preceding study (D961HC00002) (the data obtained at the latest visit after Visit 3 [Visit 1, if RE healed at Week 4] of the preceding study [D961HC00002] for the laboratory test values) are used as the Visit 1 data (excluding the pregnancy test. Refer to footnotes 3, 4 and 10 also.).
2) The signed informed consent for this study should be within 3 weeks (21 days) prior to Visit 2 (randomisation) of this study regardless of the background of healed RE (by initial treatment in the preceding study [D961HC00002] or by general treatment).
3) A central laboratory is used for laboratory tests in all the subjects. In the case of subjects whose RE has prospects (or was confirmed) to be healed by general treatment and enrolled in this study, if the results of test conducted within 2 weeks prior to randomisation at the laboratory test department of each participating medical institution are available at Visit 1, the eligibility may be checked using these test values even if obtained before informed consent. However, the baseline laboratory test values should be determined within 1 week before randomisation at the central laboratory.

4) Conducted in pre-menopausal females with a child-bearing potential. For the purpose of checking the eligibility (see Section 3.3.3), the pregnancy test is essential regardless of the background of healed RE (by the initial treatment in the preceding study [D961HC00002] or by general treatment).
5) The subject fills in the overall severity of GERD symptoms in the medical interview form (Appendix D). The investigator(s) checks the medical interview form and evaluates each symptom according to the severity classification.
6) Conducted in fasting condition.
7) As to serious adverse events (SAEs) and AEs resulting in discontinuation, all those that occur after informed consent are recorded in the electronic case report form (eCRF). As to the AEs other than serious or resulting in discontinuation, those that occur from the start of investigational product administration to the day of the last scheduled visit or withdrawal are stated in eCRF.
8) In the case of subjects whose RE has prospects (or was confirmed) to be healed by general treatment and enrolled in this study, the test may be conducted at any visit during the treatment period until the discontinuation or completion of this study if it is not possible to conduct it at the time of screening.
9) In the case of subjects whose RE is healed by general treatment and after that give informed consent and are enrolled in this study on the same day, the results of test conducted on randomisation day are available, these data may be used with the consent of subject even if obtained before informed consent.
10) In the case of subjects whose RE is healed by the initial treatment in the preceding study (D961HC00002) and enrolled in this study, the EGD data at the end of preceding study (D961HC00002) are used as the baseline data in this study.
11) In the case of subjects whose RE has prospects (or was confirmed) to be healed by general treatment and enrolled in this study, the duration of the treatment period with PPI by general treatment should be within 12 weeks at Visit 2 (randomisation day) (see Section 3.3.2).
12) When recurrence of RE is observed by EGD, this study is discontinued.

Revised text:

Table 1 Study plan

	Screening		**Study Treatment**					
		Randomisation						
Visit	**1[1)]**	**2**	**3** **Week 4**	**4** **Week 8**	**5** **Week 12**	**6** **Week 16**	**7** **Week 20**	**8 (or at discontinuation)** **Week 24**
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Time window (days)	**-**	**-**	**±4**	**±4**	**±4[13)]**	**±4[13)]**	**±4[13)]**	**±4[13)]**
Informed consent [2)]	X							
Inclusion/exclusion criteria	X	X[11)]						
Demographic data	X							
Medical/surgical history	X							
Underlying diseases	X	X						
Physical examination	X	X	X	X	X	X	X	X
Vital signs	X		X	X	X	X	X	X
Clinical laboratory tests [3)]	X		X		X			X
Pregnancy test (urine) [4)]	X							
Hp test (IgG antibody)	X[8)]							
Genetic test for CYP2C19	X[8)]							
GERD symptoms assessed by the investigator [5)]		X	X	X	X	X	X	X
EGD [6)]		X[9), 10)]	X[12)]		X[12)]			X
Randomisation		X						

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Time window (days)	**-**	**-**	**±4**	**±4**	**±4[13)]**	**±4[13)]**	**±4[13)]**	**±4[13)]**
Dispense investigational products		X	X	X	X	X	X	
Review/Collect returned investigational products			X	X	X	X	X	X
Check concomitant medications	←							→
AEs [7)]	←							→

1) In the case of subjects whose RE is healed by the initial treatment in the preceding study (D961HC00002) and enrolled in this study, the data at the end of preceding study (D961HC00002) (the data obtained at the latest visit after Visit 3 [Visit 1, if RE healed at Week 4] of the preceding study [D961HC00002] for the laboratory test values) are used as the Visit 1 data (excluding the pregnancy test. Refer to footnotes 3, 4 and 10 also.).
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11) In the case of subjects whose RE has prospects (or was confirmed) to be healed by general treatment and enrolled in this study, the duration of the treatment period with PPI by general treatment should be within 12 weeks at Visit 2 (randomisation day) (see Section 3.3.2).
12) When recurrence of RE is observed by EGD, this study is discontinued.
13) The visit window can be extended to ±7d only if a subject cannot visit within ±4d.

Reason for Amendment:

Since the visit window (±4d) of this clinical study has been causing a huge impact on conducting the study in many study sites where there have been difficulties in EGD reservations, the visit window of Week 12 and Week 24, at which EGD is scheduled, could be extended to ±7d to facilitate the clinical study conduct.

The visit window of Week 16 and Week 20, at which EGD is not mandatory, could also be extended to ±7d, because putting back the next visit as scheduled will be difficult once it occurs, considering that the visits will presumably occur on the same day of the week in a 28-day cycle.

Persons who initiated the Amendment:

Study Delivery Team Leader