Addendum to the Company Submission: Ceritinib for the treatment of ALK positive non-small cell lung cancer previously treated with crizotinib

Clarification

In the company submission (CS) for "Ceritinib for the treatment of ALK positive non-small cell lung cancer previously treated with crizotinib" a pooled median progression-free survival (PFS) for ceritinib is calculated using the median PFS from the ASCEND-1 and ASCEND-2 trials based on the Blinded Independent Review Committee (BIRC) assessment. This is reflected in table 28 and table 46 of the submission.

In three statements contained in the CS, the median PFS values from ASCEND-1 and ASCEND-2 studies from investigator assessments are reported, followed by the median pooled PFS value. It is felt that adding a statement also quoting the median PFS values calculated from the BIRC assessment would help the reader interpret the median pooled PFS value reported. Please refer to the table below for this clarification, where the added explanation text appears in red.

Page number	Current text	Version of text with added referencing to BIRC median PFS – added text in red
19	The median PFS for patients who received ceritinib was 5.7 months (95% CI: 5.4, 7.6) in ASCEND-2 and 6.9 months (95% CI: 5.6, 8.7) in ASCEND-1(9, 10). A pooled analysis of ASCEND-1 and ASCEND-2 resulted in a median PFS of 7.0 months [95% CE: 5.72,7.69]	The median PFS for patients who received ceritinib was 5.7 months (95% CI: 5.4, 7.6) in ASCEND-2 and 6.9 months (95% CI: 5.6, 8.7) in ASCEND-1 (from investigator assessment).(9, 10) The median PFS for patients who received ceritinib via BIRC assessment was 7.2 months (95% CI: 5.4, 9.0) in ASCEND-2 and 7.0 months (95% CI: 5.7, 8.6) in ASCEND-1.(7, 9) A pooled analysis of ASCEND-1 and ASCEND-2 median PFS values via BIRC assessment resulted in a median PFS of 7.0 months [95% CE: 5.72,7.69]
29	In a phase II clinical trial (ASCEND-2), median overall survival (OS) amongst 140 patients treated with ceritinib was 14.9 months (95% CI: 13.5, NE) and median progression-free survival (PFS) was 5.7 months (95% CI: 5.4, 7.6.(9).	In a phase II clinical trial (ASCEND-2), median overall survival (OS) amongst 140 patients treated with ceritinib was 14.9 months (95% CI: 13.5, NE) and median progression-free survival (PFS) was 5.7 months (95% CI: 5.4, 7.6) via investigator assessment.(9) Median PFS via BIRC

	Survival estimates were similar in a phase I trial of ceritinib (ASCEND-1) in which 163 patients treated with ceritinib experienced a median OS of 16.7 months (95% CI: 14.8, NE) and median PFS of 6.9 months (95% CI: 5.6, 8.7).(10, 14)	assessment was 7.2 months (95% CI: 5.4, 9.0).(9) Survival estimates were similar in a phase I trial of ceritinib (ASCEND-1) in which 163 patients treated with ceritinib experienced a median OS of 16.7 months (95% CI: 14.8, NE) and median PFS of 6.9 months (95% CI: 5.6, 8.7) (10, 14) via investigator assessment. Median PFS via BIRC assessment was 7.0 months (95% CI: 5.7, 8.6).(7)
Summary box - page 38	**Progression free survival (PFS) and overall survival (OS)** • **PFS by Investigator assessment:** The median PFS for patients who received ceritinib was 5.7 months (95% CI: 5.4, 7.6) in ASCEND-2 and 6.93 months (95% CI: 5.55, 8.67) in ASCEND-1. o A pooled analysis of ASCEND-2 and ASCEND-1 resulted in a median PFS of 7.0 months [95% CI: 5.72, 7.69].	**Progression free survival (PFS) and overall survival (OS)** • **PFS by Investigator assessment:** For patients who received ceritinib was 5.7 months (95% CI: 5.4, 7.6) in ASCEND-2 and 6.93 months (95% CI: 5.55, 8.67) in ASCEND-1.(9, 10) • **PFS by BIRC assessment**: the median PFS for patients who received ceritinib was 7.2 months (95% CI: 5.4, 9.0) in ASCEND-2 and 7.0 months (95% CI: 5.7, 8.6) in ASCEND-1 by BIRC assessment.(7, 9) o A pooled analysis of ASCEND-2 and ASCEND-1, based on BIRC assessment, resulted in a median PFS of 7.0 months [95% CI: 5.72, 7.69].