Comparative Efficacy of Brigatinib versus Ceritinib and Alectinib in Patients with Crizotinib-Refractory Anaplastic Lymphoma Kinase–Positive Non-Small Cell Lung Cancer

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Supplementary Material

Supplementary Table 1. Comparison of trial designs

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|   | **Brigatinib** | **Ceritinib** | **Alectinib** |
| **ALTA** | **ASCEND-1** | **ASCEND-2** | **NP28761** | **NP28673** |
| Design | Phase 2, randomized, open-label, multicenter | Phase 1, open-label, multicenter | Phase 2, single-arm, open-label, multicenter | Phase 2, single-arm, open-label, multicenter | Phase 2, single-arm, open-label, multicenter |
| Sample size | 110 | 163 (crizotinib-resistant subgroup) | 140 | 87 | 138 |
| Age category | ≥ 18 years | ≥ 18 years | ≥ 18 years | ≥ 18 years | ≥ 18 years |
| Diagnosis | Histologically or cytologically confirmed locally advanced or metastatic NSCLC that is ALK+, progressed while on crizotinib | ALK+ NSCLC, locally advanced or metastatic NSCLC that had progressed despite therapy, or for which no effective standard therapy existed | Locally advanced or metastatic ALK+ NSCLC, progressed while on crizotinib | Histologically confirmed, locally advanced not amenable to curative therapy, or metastatic ALK+ NSCLC, crizotinib resistant | Locally advanced or metastatic NSCLC, ALK+, crizotinib resistant |
| ECOG performance status | 0-2 | 0-2 | 0-2 | 0-2 | 0-2 |
| Tumor response measure | RECIST v1.1 | RECIST v1.0 | RECIST v1.1 | RECIST v1.1 | RECIST v1.1 |
| Assessment | INV, IRC | INV | IRC | IRC | IRC |
| Geography | North America, Europe, Asia, Australia | North America, Europe, Asia, Australia | North America, Europe, Asia, Australia | North America | North America, Europe, Asia, Australia |
| **ALK Rearrangement** |
| Documented rearrangement | x | x | x | x | x |
| Ascertained with an FDA-approved test | x |   | x | x | x |
| FISH test | x |   | x | x | x |
| **Prior Treatment** |
| Treated with crizotinib | x | x | x | x | x |
| Progressed on crizotinib | x | x | x | x | x |

Abbreviations: ALK, Anaplastic lymphoma kinase; ECOG, Eastern Cooperative Oncology Group; FDA, Food and Drug Administration; INV, Investigator; IRC, Independent review committee; NSCLC, Non-small cell lung cancer

Supplementary Table 2. Comparison of duration of response outcomes before and after matching

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|  | **ASCEND-1+** | **ASCEND-2** | **NP28761** | **NP28673** |
|  | **Ceritinib ASCEND-1** | **Brigatinib Pre-Match** | **Brigatinib Post-Match** | **Ceritinib ASCEND-2** | **Brigatinib Pre-Match** | **Brigatinib Post-Match** | **Alectinib NP28761** | **Brigatinib Pre-Match** | **Brigatinib Post-Match** | **Alectinib NP28673** | **Brigatinib Pre-Match** | **Brigatinib Post-Match** |
|  | **N=92** | **N=61** | **ESS=40.5** | **N=50** | **N=60** | **ESS=27.8** | NA | **N=62** | **N=60** | **ESS=38.2** |
| Number of events | 62 | 35 | 23.6 | 26 | 26 | 9.3 | 36 | 26 | 15.7 |
| Median duration of response (95% CI), months | 7.7\*(6.2, 9.4) | 13.8 (10.2, 17.6) | 13.8(9.9, 19.3) | 11.1\*(6.0, 13.1) | 14.8 (12.7, NR) | NR(3.0, NR) | 16.4\* (11.1, NR) | 14.8(12.7, NR) | 15.6 (12.7, NR) |
| HR (95% CI) | ‒ | 0.45 (0.29, 0.69) | 0.44 (0.27, 0.73) | ‒ | 0.45 (0.25, 0.80) | 0.28(0.13, 0.61) | ‒ | 1.10 (0.66, 1.84) | 0.95 (0.52, 1.73) |
| P-value |  | <0.001 | 0.001 |  | 0.007 | 0.001 |  | 0.714 | 0.871 |

HR<1 suggests better outcome from brigatinib trial

+ALK TKI-pretreated cohort, \*Estimated from VPL data

Abbreviations: CI, Confidence interval; ESS, Effective sample size; HR, Hazard ratio; NA, Not available; NR, Not reached; VPL, Virtual patient-level.

Supplementary Figure. Pre-match-adjusted and post-match-adjusted duration of response comparison. (A) Kaplan-Meier estimates of brigatinib ALTA vs ceritinib ASCEND-1 duration of response. (B) Kaplan-Meier estimates of brigatinib ALTA vs ceritinib ASCEND-2 duration of response. (C) Kaplan-Meier estimates of brigatinib ALTA vs alectinib NP28673 duration of response.

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| (A) Duration of Response: Brigatinib (ALTA) vs. Ceritinib (ASCEND-1) | (B) Duration of Response: Brigatinib (ALTA) vs. Ceritinib (ASCEND-2) |

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| --- | --- |
| (C) Duration of Response: Brigatinib (ALTA) vs. Alectinib (NP28673) |  |