type (Del19 or L858R) and brain metastases (presence/absence). There were 3 co-primary endpoints: progression free survival (PFS) by independent review, time to treatment failure (TTF) and overall survival (OS). Secondary endpoints included objective response rate (ORR), disease control rate, tumour shrinkage and safety.

Results: Pts received daily afatinib (40 mg; n = 160) or gefitinib (250 mg; n = 159) until radiological disease progression or beyond if deemed beneficial by investigator. Baseline characteristics were balanced in treatment arms (Asian: 58.8% vs 55.3%, *EGFR* Del19: 57.5% vs 58.5%), respectively, with slightly more females in the gefitinib arm (56.9% vs 66.7%). PFS was significantly improved with afatinib vs gefitinib (HR = 0.73; 95% CI, 0.57–0.95; p = 0.017), as was TTF (HR = 0.73; 95% CI, 0.58–0.92; p = 0.007). Consistent treatment benefit was seen across the subgroups including mutation type and race. Independently assessed ORR was significantly higher with afatinib vs gefitinib (70% vs 56%, p = 0.008). OS data are not mature. Common grade $\geqslant$3 related adverse events (AEs) were: diarrhoea (12.5%) and rash/acne (9.4%) with afatinib, and alanine aminotransferase increase (8.2%) with gefitinib. There was no drug-related interstitial lung disease for afatinib (vs 4 gefitinib pts; 2.5%). Discontinuation due to drug-related AEs was the same in each arm (6.3%).

Conclusions: Afatinib significantly improved PFS compared with gefitinib as first-line treatment of *EGFR* m+ pts. Afatinib treatment benefit was also seen for TTF and ORR. The AE profiles for both drugs were manageable and discontinuation due to AEs was equally low.

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Legal entity responsible for the study: Boehringer Ingelheim

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141PD

Whole body and intracranial efficacy of ceritinib in patients (pts) with crizotinib (CRZ) pretreated, ALK-rearranged (ALK+) non-small cell lung cancer (NSCLC) and baseline brain metastases (BM): Results from ASCEND-1 and ASCEND-2 trials

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Background: BM are a common site of disease progression in pts with ALK+ NSCLC, including those who have received CRZ. Ceritinib is a selective oral ALK inhibitor with a 20-fold greater potency than CRZ in vitro. Here we present efficacy outcomes in pts with CRZ pretreated ALK+ NSCLC and baseline BM, treated with ceritinib in the ASCEND-1 (phase 1) and ASCEND-2 (phase 2) trials.

Methods: In both trials, pts with CRZ pretreated, ALK+ NSCLC and clinically / neurologically stable baseline BM received oral ceritinib 750 mg/day; the majority of pts had also received chemotherapy. CT/MRI scans were performed in pts at baseline and every 6 (ASCEND-1) or 8 (ASCEND-2) weeks thereafter. Efficacy analyses (by Blinded Independent Review Committee [BIRC]) assessed whole body responses according to Response Evaluation Criteria in Solid Tumors (RECIST) 1.0 and 1.1 criteria for ASCEND-1 and ASCEND-2, respectively. Pooled intracranial responses, by BIRC, were evaluated (retrospectively in ASCEND-1; prospectively in ASCEND-2) in pts with measureable BM at baseline according to RECIST 1.1 criteria.

Results: Of the 98 and 100 CRZ pretreated pts with baseline BM enrolled in the ASCEND-1 and ASCEND-2 trials, respectively, 69.4% and 72.0% had received prior radiotherapy to the brain. Ceritinib showed efficacy in the whole body and in brain metastases (Table 1). Tolerability was acceptable. The most common AEs (any grade, regardless of study drug relationship) were (ASCEND-1; ASCEND-2) nausea (83.7%; 82.0%), diarrhea (76.5%; 82.0%) and vomiting (60.2%; 64.0%); 10 and 7 pts discontinued due to AEs from ASCEND-1 and ASCEND-2, respectively.

Conclusions: Ceritinib treatment resulted in clinically meaningful whole body and intracranial activity with an acceptable tolerability profile in pts with CRZ pretreated, ALK+ NSCLC and baseline BM.

Clinical trial identification: NCT01283516 (ASCEND-1); NCT01685060 (ASCEND-2)

Legal entity responsible for the study: Novartis Pharmaceuticals Corporation

Funding: Novartis Pharmaceuticals Corporation

Table 1 (abstract 141PD).

	ASCEND-1	ASCEND-2	
Data cut-off	14 Apr 2014	13 Aug 2014	
Number of patients with BM at baseline	98	100	
Duration of follow-up, months (range)	9.8 (0.1–22.2)	11.2 (0.2–18.9)	
Whole body response per BIRC			
Overall response rate, % [95% CI]	41.8 [31.9, 52.2]	32.0 [23.0, 42.1]	
Disease control rate, % [95% CI]	69.4 [59.3, 78.3]	64.0 [53.8, 73.4]	
Median duration of response[a], months [95% CI]	8.2 [5.6, 13.1]	9.3 [5.5, 12.9]	
Median progression-free survival, months [95% CI]	6.7 [5.4, 9.5]	6.8 [5.4, 7.4]	
Intracranial response per BIRC			Pooled
Number of patients with measurable BM at baseline	28	33	61
Overall intracranial response rate, % [95% CI]	35.7 [18.6, 55.9]	39.4 [22.9, 57.9]	37.7 [25.6, 51.0]
Intracranial disease control rate, % [95% CI]	60.7 [40.6, 78.5]	84.8 [68.1, 94.9]	73.8 [60.9, 84.2]
Median intracranial duration of response[a], months [95% CI]	11.1 [2.8, NE]	12.8 [4.0, 13.2]	12.8 [6.9, NE]

NE, non-evaluable.
[a] Duration of response calculated for patients with confirmed complete or partial response CI, confidence interval.

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142PD

The impacts on work productivity from ceritinib compared with chemotherapy for crizotinib-experienced ALK+ non-small cell lung cancer

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Background: Ceritinib has demonstrated rapid and durable antitumor activity in ALK+ non-small cell lung cancer (NSCLC). This study projected the work productivity gain and its associated societal impact of ceritinib as compared to chemotherapy for patients with crizotinib-experienced ALK+ NSCLC in the EU5 countries.

Methods: An economic model was built to estimate the probabilities of ALK+ NSCLC patients being at stable, progressive disease, or death state in each monthly cycle based on efficacy inputs from clinical trials for ceritinib and from literature for chemotherapy. Labor costs and probabilities of restoring work productivity, based on inputs from public databases or publications, were incorporated to calculate work productivity for patients and their informal caregivers, and compared between patients initiating ceritinib vs. chemotherapy over a 5-year time horizon. Model parameters were varied in one-way sensitivity analyses.

Results: Compared to chemotherapy, ceritinib treatment was associated with 65 (Italy) to 70 (UK) additional working days per patient (including associated caregiver) over 5 years. Societal cost savings per patient due to work productivity gain ranged from €11,058 (Spain) to €18,641 (France). Across countries, 54–61% of these gains occurred for treated patients, while the remainder occurred for their informal caregivers. At the country level, the societal savings from ceritinib ranged from €3.5 to 10.2 million. The results were robust under sensitivity analyses.

Conclusions: Ceritinib treatment for crizotinib-experienced ALK+ NSCLC was associated with greater work productivity for patients and their informal caregivers compared to treatment with chemotherapy. These savings represent an economic benefit of ceritinib treatment from the societal perspective, which would occur in addition to clinical and quality-of-life benefits and impacts on medical expenditures.

Legal entity responsible for the study: Novartis Pharmaceuticals Corporation

Table (abstract 142PD): Per-patient and total societal impacts on productivity of ceritinib vs. chemotherapy for the EU5 countries over 5 years

	UK	France	Germany	Italy	Spain
Productivity gain per patient (working day)	70	67	68	65	65
Societal cost saving per patient (2014 euro)	€ 12,420	€ 18,641	€ 17,150	€ 14,656	€ 11,058
Total societal productivity gain (working day)	33,528	31,989	40,734	29,422	20,495
Total societal saving (2014 euro)	€ 5,981,367	€ 8,854,670	€ 10,232,265	€ 6,661,244	€ 3,492,396