STUDY REPORT SYNOPSIS	
Study Title	LUMINIST: Lung cancer Molecular Insights Non Interventional Study
AstraZeneca Study Number	D1532R00004
Medicinal Products	Not applicable
Background	Lung cancer is the most frequent form of cancer worldwide. Non-small cell lung cancer (NSCLC) is the most common type of lung cancer and it accounts for 85% of lung cancer cases in the United States. Several mutations have been identified in the different NSCLC histologies. The most prevalent mutations are found in the epidermal growth factor receptor (EGFR), and v-Ki-ras2 Kirsten Rat Sarcoma Viral Oncogene Homolog (KRAS), which codes for the RAS protein. In most NSCLC cases, EGFR mutations do not overlap with other mutations such as KRAS mutations or anaplastic lymphoma kinase (ALK) rearrangement (found aberrant in approximately 3% to 7% of lung cancers). The recent development of therapies targeting new biomarkers and mutations is changing the standards of care and prognosis of patients with advanced NSCLC, but very few data are currently available on these emerging biomarkers. Determining the patient characteristics, treatment, and outcomes of patients stratified by emerging biomarkers is extremely beneficial.
Objectives	**Primary Objective:** 1. To estimate the overall survival (OS) of advanced NSCLC patient populations by line of therapy (LOT). **Secondary Objectives:** 1. To estimate progression free survival (PFS) and time to disease progression (TTP) (as reported by the Physician). 2. To estimate the duration of response (DOR) to standards of care as reported by physicians. 3. To estimate the overall response rate (ORR) to standards of care as reported by physicians. 4. To estimate the healthcare resource utilization (HRU). 5. To characterise the patients by LOT with respect to demographics (age, gender), smoking status, known mutations and tumour stage.
Study Design	This study was an observational prospective cohort study of patients who failed screening for a randomised clinical trial (SELECT-1), and were receiving treatment for advanced NSCLC under routine clinical practice. Patients not eligible, or who chose not to enter SELECT-1 and SELECT-2 selumetinib randomized clinical trials were invited to participate in LUMINIST. A total of 763 patients from 79 sites in Australia, Europe, Russia, Northern and Southern America, and the Middle East were enrolled between 01 December 2014 and 31 March 2016, and followed until study closure (i.e., 3 months after the last patient in), death or discontinuation, whichever occurred first. The study primary outcome was OS, and the secondary outcomes included PFS, TTP, DOR, ORR, and HRU.

STUDY REPORT SYNOPSIS	
Inclusion Criteria and Statistical Methods	Patients were eligible for LUMINIST if they fulfilled all of the following inclusion criteria: 1. Provision of informed consent from the patient or next-of-kin for deceased patients at study entry, where this was mandated/allowed by local regulations. 2. Female and male adult (according to each country regulations for age of majority). 3. Patient was not eligible or chose not to enter selumetinib SELECT-1 or SELECT-2 trials. 4. Patient with confirmed histological diagnosis of NSCLC. Patients were not eligible if involved in the planning and/or conduct of this study. This exclusion criteria applied to both AstraZeneca staff and staff at the study site. Analyses were descriptive and exploratory in nature. Event time endpoints were analysed using the Kaplan-Meier method.
Data Collection Procedures	After obtaining informed consent from the patient, where applicable (or the patient's next-of-kin for patients deceased, where applicable), the Physician abstracted data from the patients' medical records every 3 months until study closure (i.e., 3 months after the last patient in), and recorded anonymized patient data in the study electronic case report form via a secure web-based data capture system.
Results	**Patient Characteristics** The LUMINIST study enrolled a total of 763 patients, 3 patients from SELECT-2 screen failures and the remaining from SELECT-1. Most of the enrolled patients were male (n/N=519/763, 68.0%), non-Hispanic/non-Latino (n/N=709/759, 93.4%), White (n/N=728/759, 95.9%), and had a mean age at diagnosis of 61.6 (standard deviation [SD] 8.56) years (n=632). A total of 460 of 763 patients reported at least 1 ongoing comorbidity at baseline (60.3%) with vascular disorders as the most frequently reported by 50.0% of patients (n/N=230/460). **Cancer Characteristics** Adenocarcinoma and squamous cell carcinoma were the most frequently reported histology types, found in 59.0% (n/N=448/759) and 34.3% of patients (n/N=260/759), respectively. In 21.9% (n/N=162/741) and 21.7% of patients (n/N=161/741) the tumour was assessed as poorly (G3) or moderately differentiated (G2), respectively. As per the American Joint Committee on Cancer staging system, cancer was diagnosed at Stage IV in 66.8% (n/N=466/698) and Stage IIIB in 16.3% of patients (n/N=114/698). Most patients were considered restricted in physically strenuous activities (n/N=290/443, 65.5%), and 38.1% of patients (n/N=169/443) were considered fully active, according to the World Health Organization/Eastern Cooperative Oncology Group performance status classification at diagnosis. A total of 283 patients (n/N=283/762, 37.1%) had experienced cancer recurrence at LUMINIST baseline, defined as the first point in time of data collection (i.e. when the patient was enrolled in LUMINIST).

STUDY REPORT SYNOPSIS	
	Line of Treatment The most frequent treatments used at LOT1 were cisplatin+pemetrexed (n=130/694, 18.7%), carboplatin+gemcitabine (n=102/694, 14.7%), carboplatin+paclitaxel (n=89/694, 12.8%), carboplatin+pemetrexed (n=62/694, 8.9%) and cisplatin+gemcitabine (n=60/694, 8.6%). At LOT2, docetaxel and nivolumab were the most frequently used treatments by 28.9% (n=71/246) and 12.2% of patients (n=30/246), respectively. At LOT3, nivolumab and docetaxel were the most frequently reported treatments by 24.4% (n=19/78) and 21.8% of patients (n=17/780), respectively. **Overall Survival** The median OS (95% confidence interval [CI]) from first LOT (LOT1) (N=694) was estimated at 20.27 (18.27, 22.70) months. The cumulative survival rate (95% CI) was 87.5% (84.8, 89.8) at 6 months from start of LOT1 (86 deaths) and declined to 69.0% (65.4, 72.4) at 12 months (123 deaths). The final cumulative survival rate (95% CI) was 8.3% (2.2, 19.7), at 96 months. From second LOT (LOT2) (N=246), the median OS (95% CI) was estimated at 9.89 (8.3, 12.49) months, with the most marked decrease in survival observed between Day 1 and 12 months. The cumulative survival rate (95% CI) was estimated at 65.3% (58.7, 71.1) at 6 months (80 deaths) and 43.9% (36.7, 50.9) at 12 months (36 deaths). The median OS (95% CI) from third LOT (LOT3) (N=78) was estimated at 5.39 (4.07, 9.17) months. More than 40% of patients at risk died within 6 months of LOT3, with a cumulative survival rate (95% CI) of 47.8% (34.5, 59.8) at this point in time (33 deaths). The last death was observed at 36 months, resulting in a final cumulative survival rate (95% CI) of 15.9% (4.1, 34.6). **Progression Free Survival and Time to Progression** The median PFS (95% CI) from LOT1 (N=652) was estimated at 12.06 (10.87, 13.17) months, with most patients progressing or dying within 18 months of the start of LOT1. The median TTP (95% CI) was estimated at 14.06 (13.01, 15.44) months (N=542). The majority of patients progressed within 18 months from therapy initiation. From LOT2 (N=229), the median PFS (95% CI) was estimated at 4.24 (3.38, 4.93) months. The median TTP (95% CI) was estimated at 5.58 (4.20, 7.23) months (n=170). The median PFS (95% CI) from LOT3 (N=64) was estimated at 2.86 (1.91, 3.78) months. The median TTP (95% CI) was estimated at 3.35 (1.9, 11.8) months (N=44). **Duration of Response and Overall Response Rate to Standards of Care** Among the 434 patients with at least 1 tumour assessment at LOT1, 111 patients (ORR=25.6%) were assessed by the Physician as having a complete response (CR) or partial response (PR), with a median DOR of 4.0 (Q1, Q3: 2.5, 6.5; min, max: 0.8, 16.5) months and a mean of 5.2 (SD 3.76) months.

STUDY REPORT SYNOPSIS	
	At LOT2, 25 of 152 patients with at least 1 tumour assessment (ORR=16.5%) were assessed as having a CR or PR, with a median DOR of 4.9 (Q1, Q3: 2.3, 6.6; min, max: 1.4, 6.9) months with a mean of 4.5 (SD 2.35) months. Only five of 46 patients with at least 1 tumour assessment (ORR=10.9%) at LOT3 were assessed as having a CR or PR. **Healthcare Resource Utilization** Among the 762 patients with available data, 319 patients (41.9%) reported the use of at least 1 healthcare resource. The most frequently used healthcare resource was hospitalisation (n/N=209/319, 65.5%), and oncology was the main type of care received at both outpatient and inpatient visits (n/N=137/245, 55.9%). The median duration of stay was 7.0 (Q1, Q3: 2.0, 16.0; min, max: 1, 1135) days for 286 patients with information available, and the primary sign or symptom leading to the visit or hospitalisation was a general cancer symptom in 58.6% of patients (n/N=187/319). Fifty-nine of 762 patients (7.7%) reported a caregiver at home for a median duration of 162.3 (Q1, Q3: 87.3, 324.0; min, max: 29, 1886) days (N=44).
Conclusion	The LUMINIST population was generally treated according to recommended treatment guidelines. Further investigations are planned, notably investigations of emerging biomarkers.