TREATMENT AND OUTCOME OF A REAL-WORLD COHORT OF PATIENTS WITH ADVANCED, NON-SQUAMOUS NSCLC AND KRAS MUTATIONS WITH A SPECIAL FOCUS ON KRAS G12C

BACKGROUND

Lung cancer is the most common cancer worldwide, and non-small cell lung cancer (NSCLC) accounts for 85% of the cases. Mutations in the KRAS gene belong to the most frequent oncogenic driver mutations. Details on the current treatment and outcome of patients with advanced NSCLC and mutations in the KRAS gene in routine care are scarce and KRAS mutations have been long perceived as “undruggable”. Considering recent developments regarding specific small molecule inhibitors of the KRAS mutation subtype G12C, we analyzed patient characteristics, treatment reality and outcome in a representative advanced NSCLC cohort in Germany with KRAS G12C and non-G12C mutations.

METHODS

CRISP is a non-interventional, prospective, multi-center, national clinical research platform collecting representative data on molecular testing, treatment and outcome of patients with metastatic NSCLC in Germany. Patients with advanced, non-squamous (nsq) NSCLC and KRAS mutations were identified within the 3717 evaluable patients recruited by 73 sites (cancer centers, hospitals, and office-based oncology practices) into the registry CRISP from December 2015 to June 2019 in Germany. Details on patients’ characteristics, treatment and outcome were analyzed in subsamples of patients with advanced, non-squamous, non-G12C mutations with known KRAS mutations. KRAS G12C was present in 371 (5.9% of nsq / 4.4% of all) cases and non-KRAS G12C in 270 (9.2% of nsq / 7.9% of all) cases. The distribution of KRAS mutation subtypes is shown in Figure 1. Age and sex distribution were similar in patients with KRAS G12C and non-G12C mutations, with 45.0% and 46.3% female patients (Table 1). Median age at the start of 1st-line treatment of patients with KRAS G12C (non-G12C) mutations was 64 years, respectively. ECOG performance status was 0 in 36.8% of G12C patients and in 34.8% of non-G12C mutated patients. The proportion of current/former smokers was in the G12C group 94.6% (84.3% in the non-G12C group 84.1%); and most frequent metastatic sites were bones (35.3% / 27.0%), contralateral lung (29.2% / 24.4%), and brain (27.5% / 24.4%) (Table 1).

RESULTS

Patient and tumour characteristics

Until data cut on June 30, 2019, 4032 patients with advanced NSCLC were recruited into the CRISP registry, of which 3717 were evaluable. Of these, 454 had been tested for KRAS mutations and 511 test results had been positive. Patients with unknown mutations (n=65) and patients with squamous NSCLC (n=7) were excluded from the analysis, resulting in 444 patients with advanced, non-squamous NSCLC with known KRAS mutations. KRAS G12C was present in 271 (5.9% of nsq / 4.6% of all) cases and non-KRAS G12C in 270 (9.2% of nsq / 7.9% of all) cases. The distribution of KRAS mutation subtypes is shown in Figure 1. Age and sex distribution were similar in patients with KRAS G12C and non-G12C mutations, with 45.0% and 46.3% female patients (Table 1). Median age at the start of 1st-line treatment of patients with KRAS G12C (non-G12C) mutations was 64 years, respectively. ECOG performance status was 0 in 36.8% of G12C patients and in 34.8% of non-G12C mutated patients. The proportion of current/former smokers was in the G12C group 94.6% (84.3% in the non-G12C group 84.1%); and most frequent metastatic sites were bones (35.3% / 27.0%), contralateral lung (29.2% / 24.4%), and brain (27.5% / 24.4%) (Table 1).

Treatment of patients with KRAS mutations

In palliative 1st-line treatment, 48.5% patients with G12C mutation received a checkpoint inhibitor (CPI), either as single agent or combined with chemotherapy, while patients with other KRAS mutations received a CPI in 40.7% of cases (Figure 2). A total of 38.6% (G12C) and 47.4% (non-G12C) received platinum-combination therapies. So far, second-line treatments have been documented for 48 pts (G12C) and 93 pts (non-G12C) (Figure 2). Of these second-line treatments, 27 (56.3%) patients with G12C and 60 (63.8%) patients with non-G12C mutations received a checkpoint inhibitor (Figure 3). Since many patients had not completed 1st-line treatment at the time of analysis, patients with early disease progressions might be slightly overrepresented in the current 2nd-line treatment, which should be considered when interpreting the data.

Clinical outcome of patients with KRAS mutations

Survival was similar for patients with KRAS G12C and non-G12C mutations: median OS was 4.9 months (95% CI 3.2-6.6) vs. 4.8 months (95% CI 4.3-5.7) (Figure 4), median OS was 10.1 months (95% CI 7.0-13.2) vs. 9.6 months (95% CI 7.1-11.8) (Figure 5).