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Data visualization of treatment patterns in Adults with BRAF^{V600E} Mutant mNSCLC in Real-World Settings

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Context and objectives

BRAF mutations are found in 1-8% of non-small cell lung cancer (NSCLC) patients, primarily in lung adenocarcinomas[1-5]. Of these, BRAF^{V600E} is the most common variant. Due to its rarity, clinical characteristics and real-world treatment practices for patients with BRAF^{V600E} mutant (BRAF MT) metastatic NSCLC (mNSCLC) are often not well described.

The OCTOPUS study aims to describe real-world treatment patterns, including treatment persistence and median treatment duration and effectiveness, safety, BRAF testing and quality of life in real-world settings among adult patients with BRAF^{V600E}-mutant mNSCLC.

This project also aims to explore various data visualization based on interim outputs to enable easier interpretation of results within the scientific community. The focus of this work is based on treatment patterns, effectiveness and BRAF testing practices.

Methods

OCTOPUS is an ambispective, multicenter study in adult patients from Germany, France, Italy, Spain, and the UK, who initiated a first systemic treatment for mNSCLC from 01 December 2017 and prior to study entry for the retrospective cohort (n=152 patients) and from 5 July 2022 until 31 January 2024 for the prospective cohort (n=14 patients).

This interim analysis focused on retrospective patients (n=152) with data collected until the cut-off on 4 April 2024.

Data on patient and clinical characteristics, BRAF mutation testing practices, treatment patterns, safety and effectiveness were collected.

Here, results are presented using advanced data visualization techniques:

- Patients' treatment pathways are represented on a Sankey diagram.
- Treatment sequences and duration of systemic treatments are showed through time sequence analysis with K-clustering (TAK).
- Patient characteristics are plotted on a radar chart according to the 1st line of treatment (LoT) received.

Real-world progression-free survival (rwPFS) is presented in a table, showing outcomes at 6 and 12 months according to the 1st LoT received.

Conclusion

These findings highlight the varied treatment management patterns in real-world settings. They also underscore the lack of clear treatment sequences, despite the availability of recommendations in international guidelines, with 24.3% of the study population not receiving a targeted therapy in any line.

Advanced visualization techniques reveal insights into clinical practices, pathways, and how patient characteristics differ by type of treatment.

However, treatment sequences may have been impacted by the availability of treatments especially targeted therapies. Similarly, the time to access BRAF testing results might affect therapies provided in 1st LoT.

References

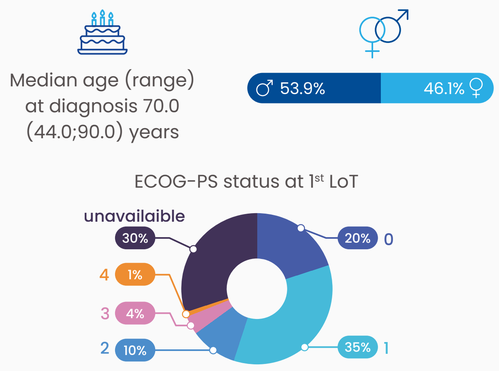
1. Baik CS, Myall NJ, Wakelee HA. Targeting BRAF-Mutant Non-Small Cell Lung Cancer: From Molecular Profiling to Rationally Designed Therapy. Oncologist. 2017;22(7):786-796. ; 2. Barlesi F, Mazieres J, Merlio JP, et al. Routine molecular profiling of patients with advanced non-small-cell lung cancer: results of a 1-year nationwide programme of the French Cooperative Thoracic Intergroup (IFCT). Lancet. 2016;387(10026):1415-1426. ; 3. Cardarella S, Ogino A, Nishino M, et al. Clinical, pathologic, and biologic features associated with BRAF mutations in non-small cell lung cancer. Clin Cancer Res. 2013;19(16):4532-4540. ; 4. Davies H, Bignell GR, Cox C, et al. Mutations of the BRAF gene in human cancer. Nature.2002;417(6892):949-954.; 5. Lin Y, Wang X, Jin H. EGFR-TKI resistance in NSCLC patients: mechanisms and strategies. Am J Cancer Res. 2014;4(5):411-435.

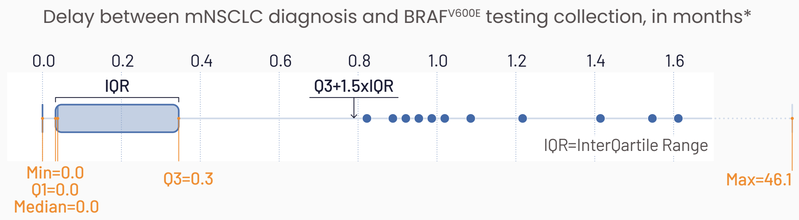
Glossary

Chemo: Chemotherapy ; **ECOG-PS:** Eastern Cooperative Oncology Group Performance Status ; **IO:** Immunotherapy ; **LoT:** Line of treatment ; **mNSCLC:** metastatic Non-Small Cell Lung Cancer ; **NSCLC:** Non-Small Cell Lung Cancer ; **rwPFS:** real-world Progression-Free Survival ; **TAK:** Time sequence Analysis through K-clustering ; **TT:** Targeted therapy

RESULTS

Patients disposition (n=152 patients)





*A total of 133 patients had a date of BRAF testing collection available. However, the estimation was performed on n=114 patients whose mNSCLC diagnosis preceded the BRAF testing collection (19 patients had testing collected before diagnosis). Additionally, 13 patients are not shown in the plot to simplify visualization, as their time to testing exceeds the upper limit of the graph.

Characteristics of patients according to 1st LoT received

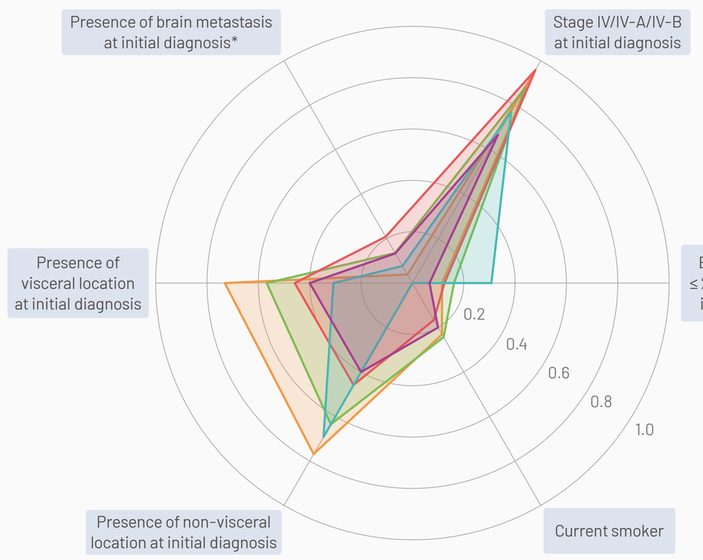


Fig. 1 Radar chart of patient characteristics, according to 1st LoT received

How to interpret this figure

This radar chart represents patient's clinical characteristics reported in each group according to the 1st LoT received. Distance from the center indicates the strength of the characteristic in the group, with outer points reflecting higher prevalence.

- Targeted Therapy** (n=74)
- Other (n=13)***
- Chemotherapy** (n=24)
- Immunotherapy** (n=15)
- Chemotherapy + Immunotherapy (n=26)

*Confirmation of brain metastasis presence through medical imaging was done as per routine clinical practice, and not mandated in the study protocol. Therefore, the presence of brain metastasis may not have been confirmed with medical imaging for all patients.

**Only single therapeutic class used.

***Chemo + ALK inhibitor, Chemo + BRAF inhibitor + MEK inhibitor, Chemo + IO + BRAF inhibitor + MEK inhibitor, Chemo + IO + VEGF inhibitor, Chemo + VEGF inhibitor, IO + BRAF inhibitor + MEK inhibitor. been confirmed with medical imaging for all patients.

Description of treatment patterns

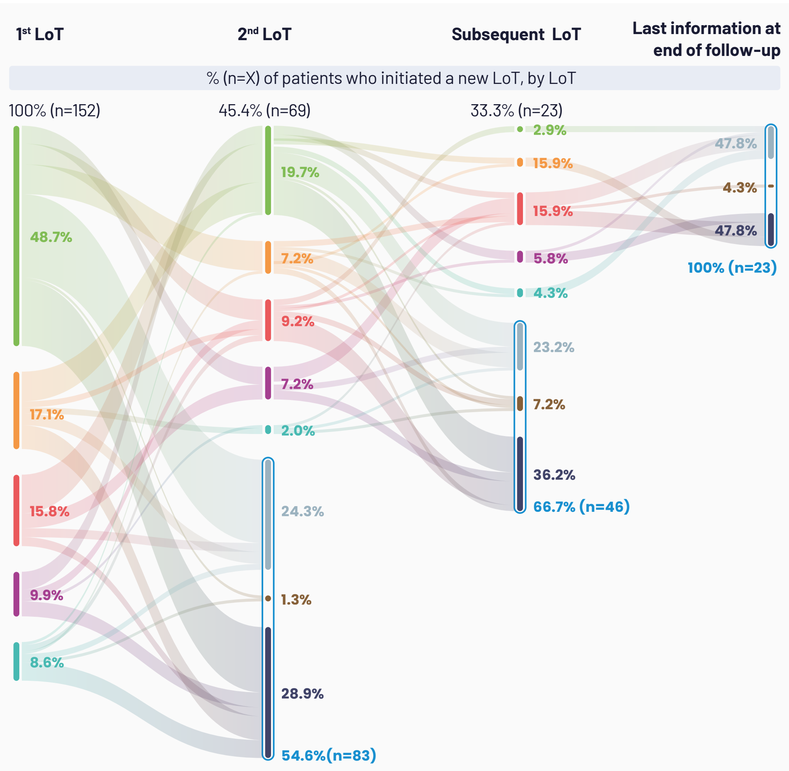


Fig. 2 Treatment sequences observed among BRAF^{V600E} mutant mNSCLC patients who initiated a first systemic treatment represented with a Sankey diagram

How to interpret this figure

Visualization with Sankey diagram provided an overview of the diversity of treatment sequences observed from 1st LoT up to subsequent LoT. Attrition rates and transition can be easily vizualized with this kind of representation.

Key results - treatment sequences (fig. 2)

Among patients who received a 1st LoT, 45.4% (n=69) received a 2nd LoT, 24.3% (n=37) were still under 1st LoT, and 15.1% (n=23) received a subsequent LoT during the follow-up period. 74 patients received TT in 1st LoT, 30 in 2nd LoT and 2 in subsequent LoT. 24.3% (n=37) of the patients did not receive TT during the follow-up.*

At the end of the follow-up period, 42.1% (n=64) of the patients were still receiving an ongoing treatment line, 52.6% (n=80) died and 5.3% (n=8) were lost to follow-up.

- Chemotherapy + Immunotherapy
- Other
- Death
- Immunotherapy**
- Ongoing
- Lost to follow-up
- Chemotherapy**
- Targeted Therapy**
- Attrition rate

*9 patients received TT but were classified in "Other" as TT was combined with another therapeutic class

**Only single therapeutic class used

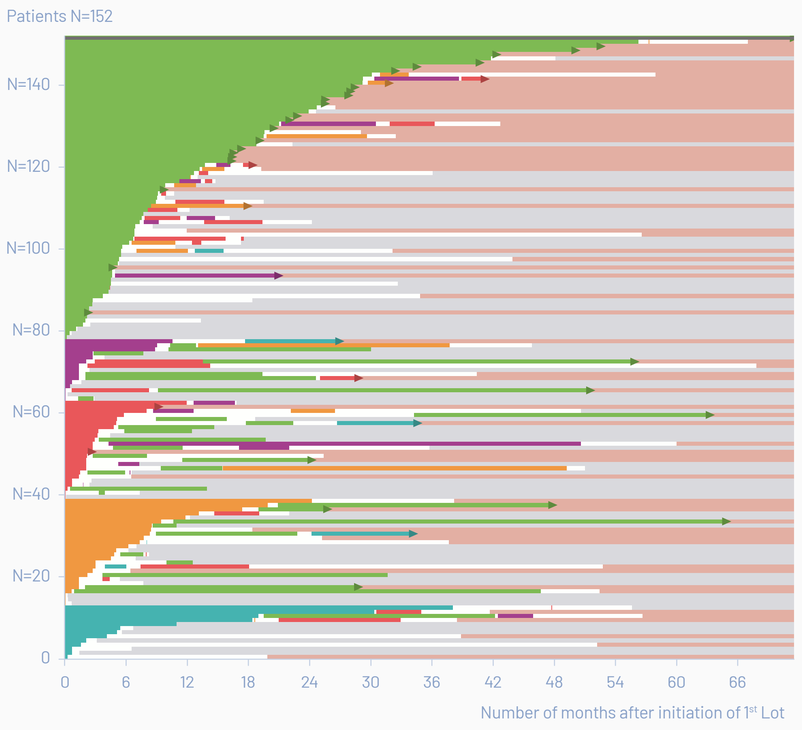


Fig. 3 Treatment patterns observed among BRAF^{V600E} mutant mNSCLC patients who initiated a first systemic treatment represented with a time-sequence analysis

How to interpret this figure

Each line represents a patient and time is represented as x-axis. Thus, the TAK provides a more detailed overwiew of treatment sequences with the type and duration of each treatment received. Death and end of follow-up are also represented. The arrow represents patients that were still treated at the time of interim analysis. Patients ranking was determined by type of 1st LoT received and its duration.

Key results - treatment patterns and duration (fig. 3)

Median duration (q1;q3) of 1st LoT was the longest in the TT group with 11.9 (5.4;25.4) month while IO, Chemo, Chemo-IO and Other groups had shorter durations of 1.4 (0.6;2.8), 2.7 (1.5;4.9), 5.7 (1.6;9.2), and 5.1 (2.9;19.7) months, respectively.

- Chemotherapy + Immunotherapy
- End of study*
- Death
- Chemotherapy**
- Targeted Therapy**
- Immunotherapy**
- ▶ Still treated at end of follow up
- No treatment
- Other

*End of study = Lost to follow-up (n=8 patients) and/or going (n=64 patients)

**Only single therapeutic class used.

rwPFS percentage rates (95% CI) of patients according to 1st LoT received

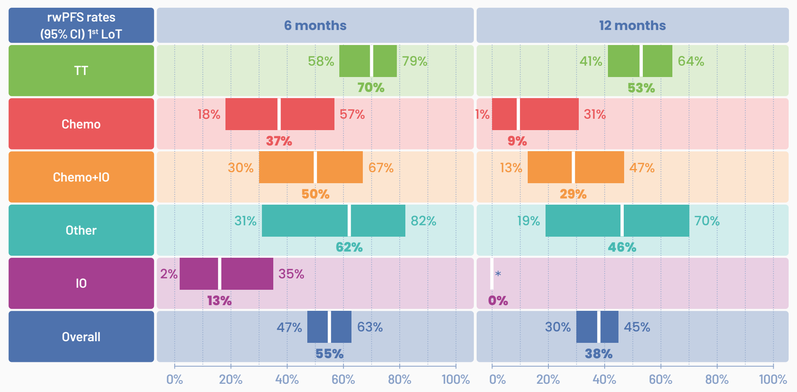


Fig. 4 rwPFS among BRAF^{V600E} mutant mNSCLC patients who initiated a first systemic treatment according to 1st LoT received

Key results - rwPFS (fig. 4)

Among patient who received TT as 1st LoT, rwPFS percentage rates (95% CI) were 70% (58%;79%) at 6 months and 53% (41%;64%) at 12 months. Overall, rwPFS percentage rates were 55% (47%;63%) and 38% (30%;45%) at 6 and 12 months respectively.

*Maximum time to rwPFS in this group was 9.1 months