# *KRAS* alterations in advanced non-small cell lung cancer: temporal trends in testing patterns and targeted treatment use across Europe between 2018 and 2024

EPH155

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*At the time the study was conducted.

## Background

- *KRAS* alterations are found in 25%–30% of all non-squamous non-small cell lung cancer (NSCLC) cases, with the *KRAS*$^{G12C}$ alteration representing ~42% of all *KRAS* alterations[1]
- Since 2023, European Society for Medical Oncology (ESMO) guidelines have recommended *KRAS* alteration testing as part of a comprehensive molecular diagnostic panel for advanced NSCLC[2]
- Until recently, there were no licensed second-line treatment options for *KRAS*$^{G12C}$-positive NSCLC; however, ESMO guidelines now recommend sotorasib after failure of prior therapy[2]
- Sotorasib is currently the only reimbursed targeted therapy for *KRAS*$^{G12C}$-positive NSCLC in Europe, with adagrasib recently receiving conditional authorization from the European Medicines Agency, and other *KRAS*$^{G12C}$ inhibitors currently under investigation[3-6]
- National guidelines and reimbursement decisions vary across Europe, influencing biomarker testing rates and associated access to treatment[7,8]
- As such, there is an interest in assessing variability in country-specific implementation of *KRAS*/*KRAS*$^{G12C}$ alteration testing and uptake of associated targeted therapy
- As part of the Onco-Optimise (formerly I-O Optimise) international collaborative research initiative,[9] we describe temporal patterns of *KRAS* and *KRAS*$^{G12C}$ alteration testing, positivity, and treatment use in patients with advanced NSCLC in Europe between 2018 and 2024

## Methods

### Study design

- The study used the Oncology Dynamics database, a syndicated survey collecting comprehensive oncology data, to identify sample populations of patients with drug-treated advanced NSCLC (including locally advanced or metastatic NSCLC) at centers in France, Germany, Italy, Spain, and the UK
- Participating countries were selected based on available representative data and having a leading role in reimbursement decisions, adoption of innovative medicines, and implementation of novel biomarker testing
- Data from physician questionnaires collected in the Oncology Dynamics database were used to estimate rates of *KRAS* and *KRAS*$^{G12C}$ alteration testing, positivity, and treatment use on a quarterly cross-sectional basis between 2018 and 2024
- Projection methodology was used to estimate patient numbers at a national level. Reported cases underwent quality checks and were used to estimate the prevalence of drug-treated patients based on physician workload data
- All data on rates of testing, positivity, and treatment use are presented at the national level (after projection)

## Results

### Patient numbers

- Sample population numbers ranged from 12,945 (Spain) to 20,148 (Italy)
- Total projected patient numbers were 314,313 in Germany, 258,227 in Italy, 222,678 in France, 215,757 in the UK, and 114,269 in Spain

### Projected *KRAS* testing rates

- *KRAS* testing rates in the overall projected population increased between 2018 (range, 11% [Italy] to 64% [France]) and 2024 (range, 51% [Spain] to 78% [Germany]) in all countries, with the greatest increase observed in the UK (from 16% to 63%; **Figure 1**)
- Testing rates were consistently higher in France and Germany compared with Italy, Spain, and the UK (**Figure 1**)

### Projected *KRAS*$^{G12C}$ testing rates

- *KRAS*$^{G12C}$ testing rates in the overall projected population increased between 2020 (range, 1% [UK] to 6% [France]) and 2024 (range, 5% [Germany and Italy] to 14% [France]) in all countries except Germany, with the greatest increases observed for France (from 6% to 14%) and the UK (from 1% to 9%; **Figure 2**)
- In Germany, projected *KRAS*$^{G12C}$ testing rates increased from 3% in 2020 to 8% in 2023, but the rate dropped to 5% in 2024 (**Figure 2**)
- Testing rates were consistently higher in France compared with the other countries (**Figure 2**)

### Projected *KRAS* and *KRAS*$^{G12C}$ positivity rates

- Although there was some variation in the projected *KRAS* positivity rates among the *KRAS*-tested population over the study period, there were no observational trends in any country (**Table 1**)
- Similarly, despite some variability, projected rates of *KRAS*$^{G12C}$ positivity in patients with *KRAS*-positive NSCLC and a known *KRAS*$^{G12C}$ status showed no observable trends over the study period in France, Germany, Italy, and Spain (**Table 1**)
- In the UK, an annual increase in the projected rate of *KRAS*$^{G12C}$ positivity was observed in patients with *KRAS*-positive NSCLC and a known *KRAS*$^{G12C}$ status (**Table 1**)

### Treatment patterns in patients with *KRAS*$^{G12C}$ alterations

- Programmed death-(ligand) 1 (PD-[L]1) immune checkpoint inhibitors (ICIs), alone or in combination with other agents, were the most common first-line treatments over the entire study period in all countries (**Figure 3**)
- From 2022, there was an increase in the proportion of patients receiving second-line single-agent targeted therapy (**Figure 3**)
- Increased use of second-line targeted therapy was seen over time in all countries, regardless of whether patients had received first-line anti-PD-(L)1 ICIs (data not shown)
- Despite some variability in the specific treatments used, there were no major differences in treatment practices between countries (**Figure 3**)

## Strengths and limitations

### Strengths

- The Oncology Dynamics database captures *KRAS* and *KRAS*$^{G12C}$ testing across a range of clinical settings, enabling a comprehensive assessment of testing rates
- Data are collected via standardized questionnaires with more than 400 quality controls, ensuring consistency and reliability across participating countries
- Longitudinal data collection enabled evaluation of evolving testing rates, positivity rates, and treatment patterns over time

**Figure 1. Projected *KRAS* testing rates by year and country**

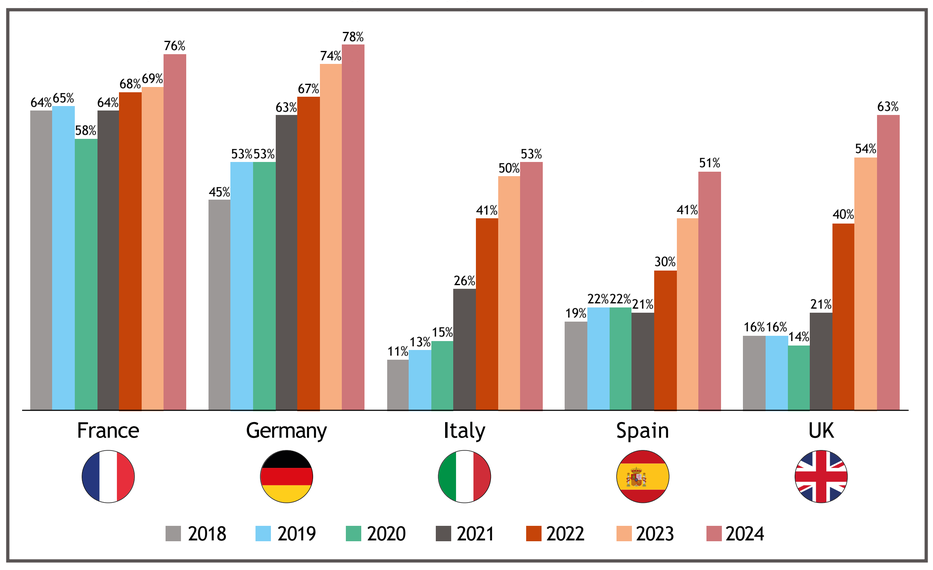
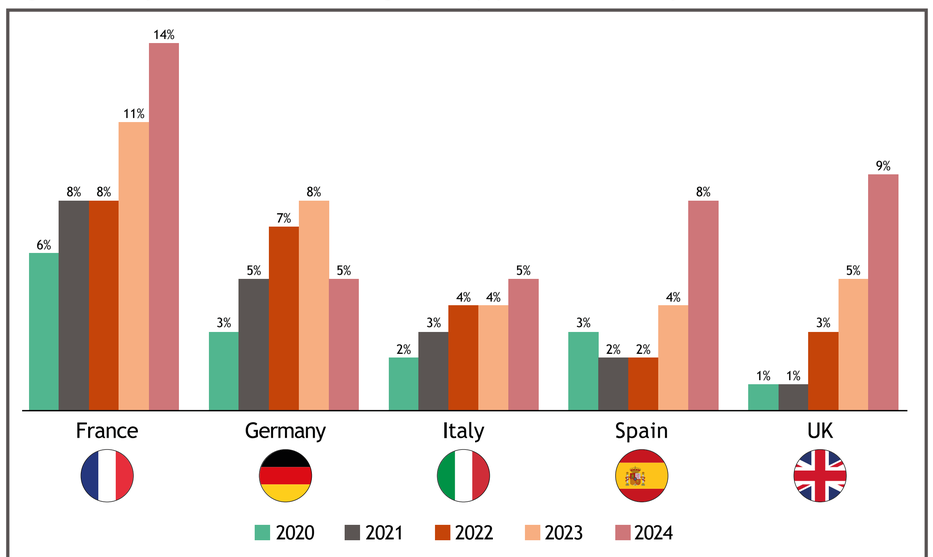



**Figure 2. Projected *KRAS*$^{G12C}$ testing rates by year and country**




*KRAS*$^{G12C}$ data were not captured in the Oncology Dynamics database for 2018 and 2019. *KRAS*$^{G12C}$ testing rates were calculated for each year/country by dividing the projected number of patients with *KRAS*-positive NSCLC and a known *KRAS*$^{G12C}$ status by the projected total NSCLC population. As data on *KRAS*$^{G12C}$ status were only collected in the questionnaires for patients with *KRAS*-positive NSCLC, this calculation assumes that patients with wild-type *KRAS* were not specifically screened for a *KRAS*$^{G12C}$ alteration.

**Table 1. Projected number and percentage of patients testing positive for *KRAS* and *KRAS*$^{G12C}$ alterations by year and country[a]**

| Patients, n (%) | | 2018 | 2019 | 2020 | 2021 | 2022 | 2023 | 2024 |
|---|---|---|---|---|---|---|---|---|
| ***KRAS* (as a % of all *KRAS*-tested patients)** | France | 4569 (22) | 3388 (17) | 2736 (15) | 2957 (15) | 2562 (12) | 3432 (16) | 4344 (19) |
| | Germany | 3128 (15) | 3892 (17) | 2927 (12) | 3632 (13) | 4887 (17) | 5401 (17) | 4736 (13) |
| | Italy | 731 (19) | 1022 (21) | 731 (14) | 1141 (12) | 1387 (9) | 1330 (7) | 1847 (10) |
| | Spain | 413 (14) | 467 (14) | 635 (18) | 411 (12) | 351 (7) | 773 (11) | 1415 (16) |
| | UK | 879 (18) | 850 (18) | 769 (18) | 569 (8) | 1036 (8) | 1778 (11) | 2633 (15) |
| ***KRAS*$^{G12C}$ (as a % of all patients with *KRAS*-positive NSCLC and a known *KRAS*$^{G12C}$ status)** | France | - | - | 1216 (62) | 1257 (49) | 1662 (68) | 1922 (57) | 2073 (49) |
| | Germany | - | - | 496 (33) | 1207 (56) | 2130 (68) | 1998 (57) | 1327 (59) |
| | Italy | - | - | 246 (34) | 644 (56) | 844 (61) | 724 (54) | 981 (53) |
| | Spain | - | - | 247 (53) | 167 (56) | 135 (40) | 264 (37) | 567 (40) |
| | UK | - | - | 108 (51) | 169 (63) | 679 (68) | 1167 (69) | 1898 (74) |

[a]Patient numbers provided were nationally projected. *KRAS*$^{G12C}$ data were not captured in the Oncology Dynamics database for 2018 and 2019. Positivity rates for *KRAS*$^{G12C}$ should be interpreted with caution as *KRAS*$^{G12C}$ positivity/negativity status was unknown for some patients in the overall *KRAS*-tested population. Patients with an unknown status were excluded from the *KRAS*$^{G12C}$ positivity rate analysis (2020 range, n = 0 [Italy] to 1403 [Germany]; 2021 range, n = 0 [Italy] to 1478 [Germany]; 2022 range, n = 0 [Italy] to 1759 [Germany]; 2023 range, n = 0 [Italy] to 1916 [Germany]; 2024 range, n = 0 [Italy and Spain] to 2490 [Germany].

### Limitations

- The study used physician-reported data and may be subject to bias, inconsistencies, and issues with data completeness
- Projections were derived from relatively small sample sizes, particularly for *KRAS*$^{G12C}$ testing, and data should be interpreted with caution
- The prevalence and impact of the *KRAS*$^{G12C}$ alteration may be underestimated due to low testing rates
- There were missing *KRAS*$^{G12C}$ data for Germany, as some physician panelists consistently reported patients as having an unknown *KRAS*$^{G12C}$ status. This resulted in *KRAS*$^{G12C}$ testing rates that were lower than expected in Germany (**Figure 2**). These panelists are under review. After exclusion of data from these panelists, *KRAS*$^{G12C}$ testing rates for Germany were 3% in 2020, 6% in 2021, 9% in 2022, 9% in 2023, and 6% in 2024

## References

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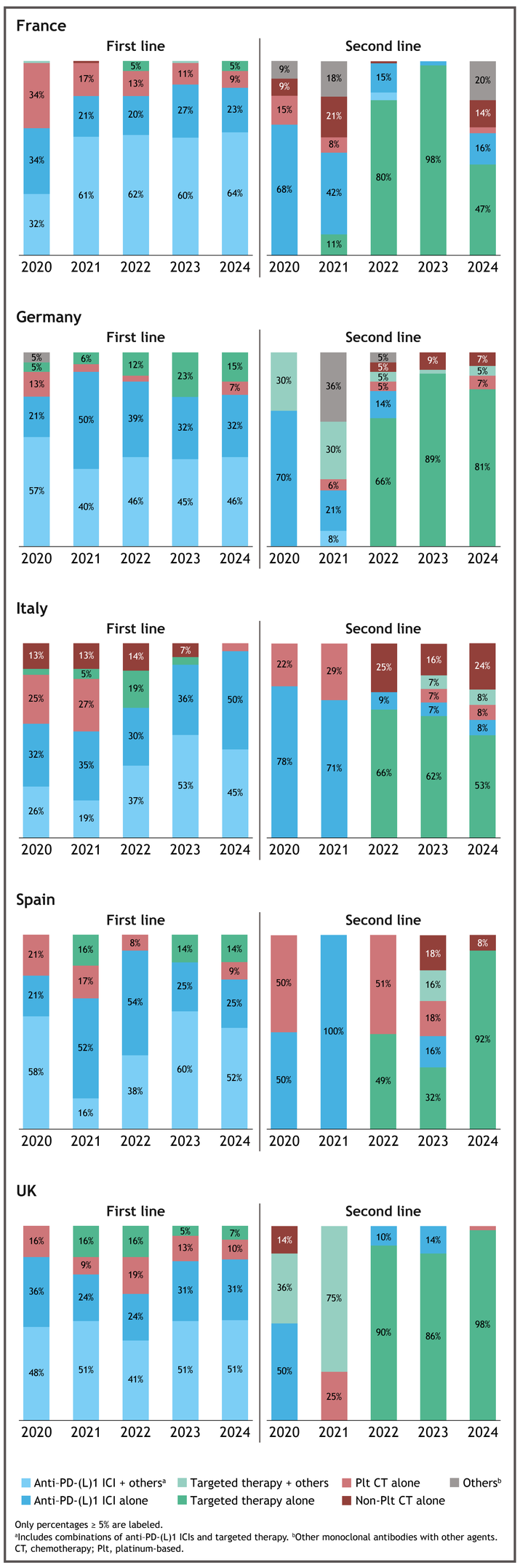
## Acknowledgments

- This work was funded by Bristol Myers Squibb
- All authors contributed to and approved the presentation; professional writing and editorial assistance were provided by Richard Daniel, PhD, of Parexel, funded by Bristol Myers Squibb

**Figure 3. Projected temporal changes in treatment among patients with *KRAS*$^{G12C}$-positive advanced NSCLC by country**




Only percentages ≥ 5% are labeled.
[a]Includes combinations of anti-PD-(L)1 ICIs and targeted therapy. [b]Other monoclonal antibodies with other agents.
CT, chemotherapy; Plt, platinum-based.

## Conclusions

- *KRAS* testing rates increased between 2018 and 2024 in all participating countries, identifying a population of patients with advanced NSCLC who may benefit from KRAS-targeted therapy
- *KRAS*$^{G12C}$ testing rates also increased over time, reflecting the evolution of the ESMO guidelines; however, testing among the overall advanced NSCLC study population was limited in all countries
- Observed differences in testing rates between countries likely reflect variability in international guideline adoption and reimbursement approval
- Although there was variability in *KRAS* and *KRAS*$^{G12C}$ positivity rates over the study period, there were no observable trends in most countries
- Treatment regimens were largely consistent across countries, with anti-PD-(L)1 ICIs, alone or in combination with other agents, dominating first-line therapy
  - From 2022, there was a notable rise in second-line targeted therapy use, aligning with the timing of sotorasib approval
- Given the limited European real-world data on *KRAS* and *KRAS*$^{G12C}$ testing and treatment, this study provides valuable insights into testing trends, prevalence of alterations, and associated regimen use among patients with advanced NSCLC

Presented at International Society for Pharmacoeconomics and Outcomes Research (ISPOR) Europe 2025; November 9-12; Glasgow, UK

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