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Original article

Characteristics, management, and healthcare resources of patients with advanced non–small-cell lung cancer surviving 5 years after nivolumab treatment initiation: A national database analysis



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ABSTRACT

Background: Data on long-term survivors with advanced non-small-cell lung cancer (NSCLC) treated with nivolumab are available from randomized trials. Characteristics, management, and healthcare resources of those patients need to be confirmed with real-world data.

Methods: The UNIVOC retrospective observational study included all patients with advanced NSCLC recorded in the French national hospital database starting nivolumab in 2015 and followed them until December 2020. The Kaplan-Meier method estimated the overall survival (OS). A machine learning approach identified patients with similar treatment sequences.

Results: Within the 3,050 patients who had nivolumab initiation, 5-year OS rate was 14.6 % (95 % CI 13.3 %–16.2 %). In total, data covering at least 5 years of follow-up were retrieved for 231 surviving patients. Survivors were younger, often female and had fewer comorbidities than non-survivors. Three clusters of patients with different nivolumab treatment durations were identified: 1/ Continuous nivolumab treatment; 2/ Long period of nivolumab treatment followed by chemotherapy or no treatment; 3/ Short period of nivolumab treatment then chemotherapy or no treatment. At 5 years, 61.0 % of survivors were no longer receiving systemic therapy, 26.4 % were treated with nivolumab, 8.7 % chemotherapy, and 3.9 % other immunotherapies. Among 5-y survivor patients, the average number of hospitalisations per patient decreased from 23.4 to 12.8 between the 1st and the 5th year. In the 5th year, 46 % of patients had no more hospitalization for lung cancer.

Conclusions: This large nationwide study confirms the long-term benefit of nivolumab treatment for advanced NSCLC patients in the real-world setting, with a 5-year survival rate similar to that reported in clinical trials.

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Introduction

In 2020, with 2.2 million new lung cancer cases diagnosed, the disease was the second most frequent cancer in the world [1]. In France, in 2018, there were more than 46,000 estimated new lung cancer cases and 33,000 estimated deaths [2]. Furthermore, 88 % of new lung cancer cases of known histology were non–small-cell lung cancers (NSCLC) [3].

Immunotherapy is a standard of care in first line as monotherapy and in combination with chemotherapy for metastatic NSCLC. Immune checkpoint inhibitors (ICI) have changed lung cancer management. In France, pembrolizumab, atezolizumab and cemiplimab are considered a standard first-line option for patients with advanced NSCLC and PD-1 expression ≥ 50 % in absence of contraindications to use of immunotherapy [4,5]. Combination of pembrolizumab and platin doublet chemotherapy is a therapeutic option in patients with performance status 0–1. Nivolumab, an anti-PD-(L)1, demonstrated its efficacy in extending overall survival (OS) in patients with locally advanced or metastatic NSCLC after chemotherapy in large

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randomized trials [6,7]. Based on these results, in 2015, nivolumab became the first anti-PD-1 treatment approved for previously treated NSCLC [8]. In a long-term extension of these trials, the 5-year survival rate of NSCLC patients treated with nivolumab was 13.4 % compared to 2.6 % with docetaxel [9].

Ensuing real-world studies observed 2- and 3-year OS close to those reported in pivotal clinical trials [8,10,11]. However, data on long-term survival in the real-world setting are still limited.

Using a machine learning analysis, Chouaïd et al. presented the therapeutic management over the 2 years following nivolumab initiation [12]. They identified four distinct clusters of patients: (1) patients almost continuously treated with nivolumab; (2) patients with long-term nivolumab treatment followed by chemotherapy or a systemic treatment-free interval; patients with a short or medium nivolumab treatment, followed by (3) a long systemic treatment-free interval or (4) a long chemotherapy. However, the study did not report information beyond 2 years of follow-up.

To date, economic studies of advanced NSCLC mostly focus on cytotoxic chemotherapies. Data show that, for patients treated with cytotoxic chemotherapy, costs usually increase over treatment lines until death [13]. The situation may be different for patients treated with immunotherapy, whose treatment costs tend to decrease over the long term [14]. Likewise, there are little economic data 5 years after nivolumab initiation.

The aims of this study were to describe patients' characteristics, management, and healthcare resources of advanced NSCLC patients alive 5 years after initiating a treatment with nivolumab in a real-world setting.

Methods

Study design and data sources

The UNIVOC study cohort design and data sources have been described [11,12,15]. It was a retrospective, longitudinal, observational study based on the hospital discharge database (PMSI, *Programme de Médicalisation des Systèmes d'Information*) of the French National Health Data System (SNDS, *Système National des Données de Santé*) [16]. It contains comprehensive data on healthcare resource consumption on all hospital stays in France (both in the public and private sectors). The PMSI offers information on hospital stay (reason for hospitalization, medical procedures, comorbidities requiring care during the hospital stay, expensive drugs dispensing, and medical devices implant), at-home hospitalization, and in follow-up and rehabilitation facilities.

Study population and study period

Selection criteria

All patients with a hospital stay with an ICD-10 code for lung cancer (C34) in 2015, with a unique social security number, and initiating nivolumab that year were included. At that time, nivolumab was the only ICI authorized for advanced NSCLC as second line and later treatment. There were no exclusion criteria.

Study period

The inclusion period lasted from January 1, 2015 until December 31, 2015. The index date was defined as the date of the first treatment with nivolumab (Appendix Figure A. 1). Each patient was followed until the end of the study (December 31, 2020) or death, whichever occurred first.

The analysis was restricted to patients alive 5 years after the index date.

Data extraction

For each patient, information was documented at the time of initial nivolumab administration on sex, age, and ecological social deprivation index (FDep99) an index developed at the city area level (only available for metropolitan France) [17] combining median household revenue, percentage of people 15 years old and above with high school diploma, percentage of blue-collar workers in the labor workforce, and the unemployment rate. Time since diagnosis was computed as time between the first hospitalization for NSCLC and the index date. The presence of significant chronic comorbidities (hypertension, diabetes mellitus, renal insufficiency, chronic obstructive pulmonary disease, pulmonary insufficiency, other chronic lung diseases, and brain metastases) identified in the patient discharge record during the year prior to inclusion was investigated.

All hospital stays during the 1st and the last year of follow-up were identified. Healthcare resource utilizations were classified as: ambulatory, inpatient stays, at-home hospitalization, and in follow-up and rehabilitation facilities.

Four therapeutic options were identified: nivolumab, other immunotherapies, chemotherapies, and absence of systemic treatment. Treatments were summarized in three ways: the proportion of patients with each type of treatment every 6 months, the treatment sequences over 5 years, and the proportion of patients with each type of treatment at the end of the 5 years.

The treatment duration was defined as the interval between the index date and treatment discontinuation (defined as no new treatment for at least 6 weeks [42 days] after the previous treatment, or death).

Mortality corresponds to all-cause hospital mortality as cause of death is not documented in the PMSI. The bias introduced by this limitation of the PMSI should be limited as 86 % of lung cancer patients die at the hospital [13].

Study outcomes

The OS was estimated, and healthcare resource utilization was analyzed as follows: the percentage of patients requiring at least one medical visit or hospitalization, the total number of hospital visits per patient for the 1st and the last year of follow-up as well as the number per category of stay.

Statistical methods

Continuous data were summarized by their mean, standard deviation (SD), median, and first (Q1) and third (Q3) quartiles. Continuous variables were analyzed with Student's *t*-test. Categorical data were summarized by percentage. χ^2 test was used for analysis of categorical data. The Kaplan-Meier method was used to estimate the OS after nivolumab initiation. It was defined as the time between the initiation of the nivolumab treatment and the last hospital stay (in-hospital death or the day of the last documented hospital stay).

Given that all hospital healthcare resources are reported in the database, no replacement of missing values was performed.

All applicable statistical tests were two-sided and were performed at a 5 % significance level.

Statistical analyses were performed using SAS version 9.4.

A machine learning approach was used to provide a data visualization of the management sequences and to identify patients with similar 5-year treatment sequences. The method has been detailed elsewhere [12]. In brief, patients are initially sorted according to first continuous nivolumab treatment duration. Then, a clustering technique, called the Time sequence Analysis through K-clustering (TAK), was applied. Patients' treatment sequence (vectors) were clustered using an unsupervised hierarchical Ward's clustering method, a two-step algorithm [18]. First, a matrix of pairwise distances between all

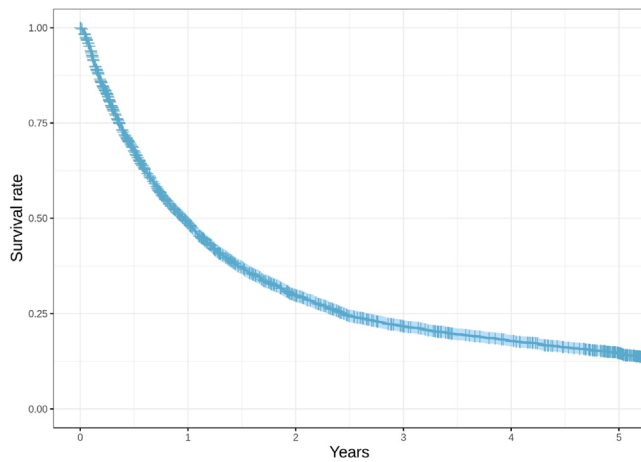


Fig. 1. Overall survival of all advanced non-small-lung cancer patients who started nivolumab treatment in 2015 (3050 patients).

patients was computed. Second, the Ward's linkage method was used to build patient clusters with the goal of minimizing the distance between patients within the cluster. The final step is to filter noise and artefacts to polish the visual output.

Results

Study participants characteristics and survival

Among the 3050 advanced NSCLC patients who initiated nivolumab in 2015 and considered for the study the 5-year OS was 14.6 % (95 %CI 13.3 % to 16.2 %) (Fig. 1). Data covering at least 5 years of follow-up were retrieved for 231 patients.

Patients who were still alive 5 years after starting nivolumab were younger (mean age of 61.5 vs 63.3 years, respectively $p = 0.008$), more frequently women (36.8% vs 29.7 %, $p = 0.029$), and had fewer

comorbidities compared to patients who did not survive at least 5 years ($p = 0.014$) (Table 1). Five-year survivors and non-survivors had similar distribution across strata of the social deprivation index.

Treatments

In the patients alive at 5-years ($n = 231$), the median time to treatment discontinuation was 16.6 months (Q1-Q3: 4.8 – 33.4 months). As the years since nivolumab initiation passed by, the proportion of patients still treated with nivolumab decreased from 79.7 % at 6-month to 24.2 % the fifth year and the proportion of patients with no systemic treatment increased from 13.4 % at 6-month to 64.1 % the last year (Fig. 2).

Patients were initially sorted according to first continuous nivolumab treatment duration (Fig. 3A). After applying the TAK method, three treatment clusters were identified (Fig. 3B) and differed in nivolumab treatment durations. The largest cluster (48 % of patients) included patients treated with nivolumab for a long period (> 6 months) but finally stopped for a systemic treatment-free period or for chemotherapy. The second cluster (39 % of patients) included patients exclusively treated with nivolumab, for at least 4 years. Patients in the third cluster (13 % of patients) were shortly treated with nivolumab (< 6 months) followed by a chemotherapy or another immunotherapy.

At the end of the follow-up, 61.0 % of patients were no longer receiving any systemic treatment (Table 2). Their median nivolumab treatment duration was 18.9 months (Q1-Q3: 10.0-37.9 months). The other patients were being treated with nivolumab (26.4 %), chemotherapy (8.7 %), or another immunotherapy (3.9 %). In those patients, the median nivolumab treatment duration were 59.2 months, 23.7 months, and 11.1 months, respectively. Of the nine patients treated with another immunotherapy, 6 patients received pembrolizumab and 3 patients received atezolizumab.

Healthcare resource utilization

During the first year of the nivolumab treatment, all 5-year survivor patients were hospitalized at least once for lung cancer and 91 % of patients were admitted more than 10 times to the hospital. The mean number of hospital stays was 23.4 per patient (Table 3).

During the fifth year 46 % of patients were not hospitalized at all for lung cancer and 35 % of patients had more than 10

Table 1
Study participants characteristics.

	5-year survivors (n = 231)	5-year non-survivors (n = 2819)	P-value
Male, n (%)	146 (63.2 %)	1982 (70.3 %)	0.029
Female, n (%)	85 (36.8 %)	837 (29.7 %)	
Mean age at inclusion (years) ±SD	61.5 ± 9.8	63.3 ± 9.4	0.008
Meantime since lung cancer diagnosis (months) ±SD	22.4 ± 19.7	21.4 ± 20.9	0.068
Comorbidities during the year before inclusion			0.014
Hypertension	22 (9.5 %)	497 (17.6 %)	
Diabetes	15 (6.5 %)	231 (8.2 %)	
Renal failure	7 (3.0 %)	130 (4.6 %)	
Chronic obstructive pulmonary disease	21 (9.1 %)	327 (11.6 %)	
Pulmonary insufficiency	2 (0.9 %)	43 (1.5 %)	
Other chronic lung diseases	23 (10.0 %)	258 (9.2 %)	
Brain metastases	46 (19.9 %)	484 (17.2 %)	
Auto-immune diseases	0 (0.0 %)	9 (0.3 %)	
Undernutrition	23 (10.0 %)	477 (16.9 %)	
Dementia, degenerative diseases	0 (0.0 %)	8 (0.3 %)	
Connective tissue disease	1 (0.4 %)	17 (0.6 %)	
Social deprivation index			0.053
Most deprived	34 (14.7 %)	618 (21.9 %)	
Deprived	74 (32.0 %)	741 (26.3 %)	
Privileged	49 (21.2 %)	651 (23.1 %)	
Most privileged	72 (31.2 %)	795 (28.2 %)	

SD: standard deviation.

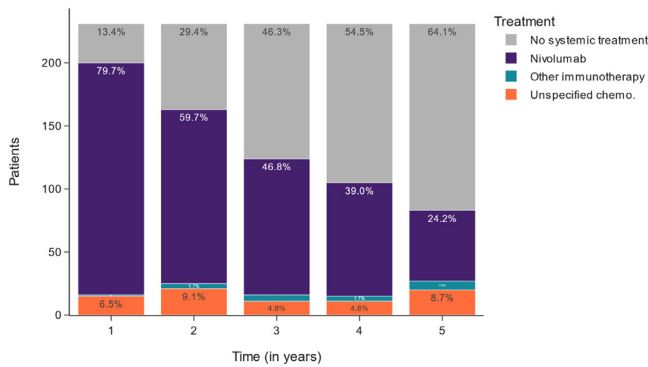


Fig. 2. Distribution of treatments over time of advanced non-small-lung cancer patients surviving 5 years after nivolumab treatment initiation (231 patients) The proportion of patients with each type of treatment is the proportion at each mid-year (i.e., at 6 months, 1.5 year, 2.5 years, 3.5 years, and 4.5 years).

hospitalizations. The mean number of hospital stays was 12.8 per patient. Among 5-year survivors' patients,

All patients had at least one-day stay during the first year of the nivolumab treatment, but only 54.1 % during the fifth year. The proportion of patients with at least one inpatient admission and one intensive care unit admission remained stable between the first and fifth years: 34.2 % and 37.7 % and 3.0 % and 3.9 %, respectively.

Discussion

To our knowledge, this is the largest observational study with a 5-year follow-up after nivolumab treatment for advanced NSCLC, providing unparalleled information regarding long-term outcomes, treatment, and healthcare utilization. Out of the 3050 patients with advanced NSCLC who started a nivolumab treatment in 2015 in France, 231 were retrieved alive 5 years later and uncensored in the PMSI, corresponding to a 5-year Kaplan-Meier estimate survival rate of 14.6 %. Surviving patients were younger and had fewer comorbidities than those who had died. The proportion of women was also higher among 5-year survivors. The therapeutic management of patients could be summarized by three treatment sequences, including 23 % of patients treated for <1 year with nivolumab. Five years after nivolumab initiation, 61 % of patients were no longer receiving systemic therapy and 26 % were still being treated with nivolumab. The mean number of hospital stays per patient decreased over time (mainly driven by the decline in 1-day hospital stays) and in the fifth year, almost half of patients did not go to the hospital for lung cancer at all.

The 5-year survival rate observed in this unselected and broader study population validate the findings of a pooled analysis of CheckMate 017 and 057 clinical trials (5-y survival 13.4 % [95 % CI 10.4 to 16.9]) [9]. In these trials, pooled OS rates at 5 years were similar regardless of squamous or non-squamous histology, irrespective of tumor PD-L1 expression, and it was observed across several subgroups of patients. Patients who were progression-free at 2, 3, and

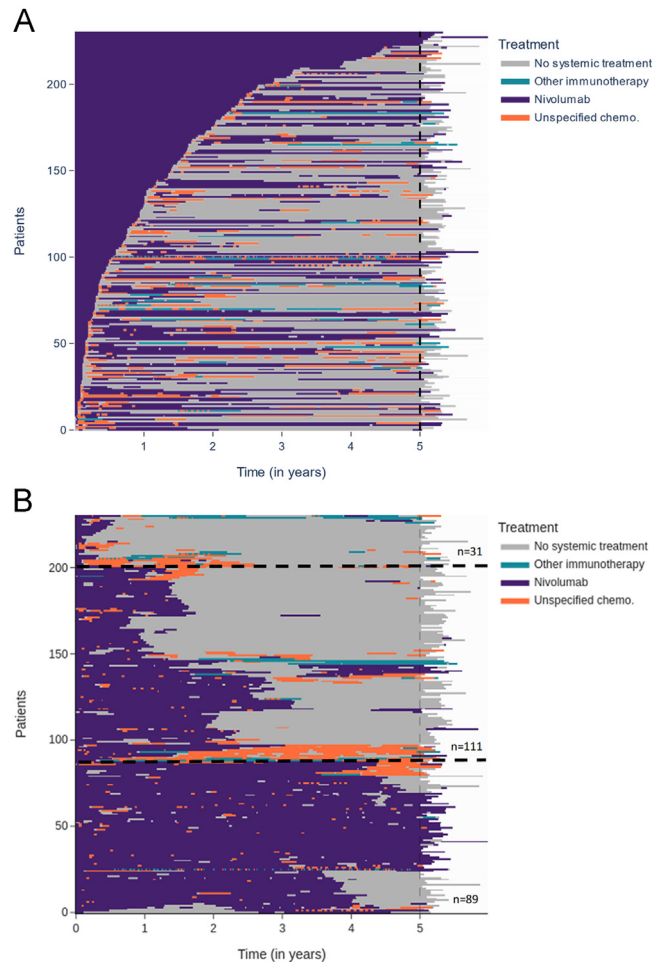


Fig. 3. (A) Treatment sequences of patients sorted by first continuous nivolumab treatment duration (231 patients) (B) Treatment sequences over time of patients with advanced non-small-lung cancer patients alive 5-years after nivolumab initiation (231 patients).

4 years had an increased probability (59.6 %, 78.3 %, and 87.5 %, respectively) of still being progression-free at 5 years, as well as a chance to survive of 82.0 %, 93.0 %, and 100.0 %, respectively.

In our study, the 1-year survival rate was identical to that of a pooled observational study in France, Germany, and Canada (49 %) but superior to results from a systematic literature review of real-world effectiveness of immunotherapies in second lines and later settings [19]. In a Dutch study in routine clinical care, overall survival rates after 2 and 3 years were 23.8 % and 17.1 %, respectively [10], similar to survival rates found in the pooled analysis of CheckMate 017 and 057 (26.9 % and 17.1 %, respectively) [9] and lower than our findings. Overall, our study reported higher 2-year survival rate than previous real-world study [19]. Similar 3-year survival rates have

Table 2

Nivolumab treatment duration according to the management at the end of the follow-up period in advanced non-small-cell lung cancer 5-year survivors (231 patients).

Nivolumab treatment Duration (months)	No systemic treatment n = 141 (61.0 %)	Nivolumab n = 61 (26.4 %)	Chemotherapy n = 20 (8.7 %)	Other immunotherapy n = 9 (3.9 %)	Total n = 231 (100 %)
Mean (±SD)	23.4 (±16.2)	51.4 (±15.6)	24.5 (±16.0)	16.9 (±15.0)	30.6 (±20.3)
Q1	10.0	48.9	11.3	4.7	12.7
Median	18.9	59.2	23.7	11.1	28.0
Q3	37.9	62.1	34.3	25.3	49.2

Other immunotherapies: 6 patients (66.7 %) were treated with pembrolizumab, and 3 patients (33.3 %) were treated with atezolizumab.

Table 3
Number of hospital stays for lung cancer and number of patients with at least one hospital stay for lung cancer during the first and fifth years after nivolumab treatment initiation in 5-year survivors.

	1st year (n = 231)	5th year (n = 231)	P-value*
Ambulatory			
Mean (±SD)	22.81 (±5.82)	8.68 (±9.90)	<0.0001
No. of patients with at least one visit (%)	231 (100)	151 (65.4)	
Nivolumab administration			
Mean (±SD)	20.33 (±6.78)	4.82 (±7.68)	<0.0001
No. of patients with at least one visit (%)	231 (100)	84 (36.4)	
Chemotherapy administration			
Mean (±SD)	1.48 (±3.54)	2.44 (±6.09)	0.428
No. of patients with at least one visit (%)	78 (33.8)	48 (20.8)	
Ambulatory (none of the above)			
Mean (±SD)	1.0 (±2.64)	1.43 (±3.87)	0.098
No. of patients with at least one visit (%)	82 (35.5)	88 (38.1)	
Hospital stays			
Mean (±SD)	0.54 (±0.93)	0.74 (±1.30)	0.083
No. of patients with at least one visit (%)	79 (34.2)	87 (37.7)	
with Intensive care or Resuscitation Department hospital stay			
Mean (±SD)	0.03 (±0.21)	0.10 (±0.44)	0.053
No. of patients with at least one visit (%)	7 (3.0)	16 (6.9)	
At-home hospitalization			
Mean (±SD)	0.01 (±0.11)	0.10 (±1.14)	0.285
No. of patients with at least one visit (%)	3 (1.3)	6 (2.6)	
Follow-up and rehabilitation facility			
Mean (±SD)	0.02 (±0.17)	0.06 (±0.30)	0.085
No. of patients with at least one visit (%)	4 (1.7)	12 (5.2)	
Any hospital stays for lung cancer**			
Mean (±SD)	23.42 (±5.55)	9.69 (±10.33)	<0.0001
No. of patients with at least one visit (%)	231 (100.0)	175 (75.8)	

* Signed rank Wilcoxon test.

** Excluding doctors' appointments at the hospital
SD: standard deviation.

also been shown in the real-world setting with atezolizumab, with efficacy comparable to that of nivolumab [20].

The earlier machine learning analysis of treatment sequences of all French patients alive 2 years after initiating nivolumab for advanced NSCLC in 2015–2016 found four clusters of treatment sequences [12]. In the 2-year study, those treated for <1 year with nivolumab represented 40 % of patients but 23 % in our 5-year study. In this analysis at 5 years, we found only three clusters, with very different nivolumab treatment durations. While a quarter of the patients were continuously under nivolumab treatment, the majority (61 %) had no more systemic treatment at 5 years. For the latter patients, the mean nivolumab treatment duration was around 2 years. The third cluster is composed of patients who are undergoing treatment chemotherapy at the end of the 5-year study, also with a mean nivolumab treatment duration of about 2 years.

The optimal immunotherapy duration, in any line of therapy, remains a debated issue. In detail, some products such as pembrolizumab have been developed with limited duration of administration (2 years) unlike nivolumab or atezolizumab in second line and later settings both prescribed until progression or toxicity. In the KEYNOTE 010 study [21], the 5-year OS rates of pembrolizumab and docetaxel were 25 % and 8.2 %, respectively, in patients with PD-L1 TPS (programmed death ligand 1 tumor proportion score) ≥ 50 %, while it was 15.6 % and 6.5 %, respectively, in those with PD-L1 TPS ≥ 1 %. In the 79 patients who completed 35 cycles/2 years of pembrolizumab, the 3-year OS rate was 83 %. The practice of providing lifetime immunotherapy for advanced NSCLC has been investigated in the

CheckMate 153 study [22]. In an exploratory analysis focusing on those who had received nivolumab for 1 year, patients were randomly assigned to continue nivolumab or to interrupt it. The median PFS (progression-free survival) and OS were longer for patients who continued the treatment, as opposed to those who ceased it (24.7 versus 9.4 months, [HR: 0.56; 95 % CI: 0.37–0.84]) and not reached vs. 28.8 months; HR: 0.62; 95 % CI: 0.42–0.92). However, this exploratory analysis was not pre-planned, and therefore, the sample size was not determined in advance, patients were not stratified according to the response at the time of randomization and randomization was not blinded. Unfortunately, apart from this trial, we only have mostly retrospective, heterogeneous studies, with limited sample size, which do not allow definitive conclusions to be drawn [23]. It should be noted that the PMSI does not contain the causes of immunotherapy discontinuation (i.e., progression vs toxicity).

The cost of NSCLC patients care represents currently one of the most challenging public healthcare issues worldwide and is an obstacle to the accessibility of cancer healthcare. In this context, it is important to measure the impact on healthcare consumption of patients who have a long-term benefit after new cancer therapies. The analysis shows that almost half of the long survivors at 5 years (46 %) have no hospitalization for lung cancer during the 5th year, clearly showing a decrease in healthcare care consumption over time.

The greatest strength of this study lies in the exhaustivity of the patient selection: all patients with advanced NSCLC treated with nivolumab in France in 2015, which prevents any issues of

representativeness of the study population. This large observational study neatly complements the clinical trials. Patients are accurately identified in the database using drug administration codes in the hospital database. As this is a retrospective study, there is no patient recruitment bias. Finally, this study is one with the longest follow-up in real-life on patients treated with nivolumab for NSCLC. The limitations relate to the absence of information on clinical decision-making, outcome and quality of life in the claims database. Notably, no data are available on Eastern Cooperative Oncology Group performance status, smoking status, epidermal growth factor receptor mutation status, treatment-related adverse events, certain comorbidities or concomitant medications that may influence survival [10]. Furthermore, the reasons for treatment withdrawal or treatment switch, disease progression, performance status, outcomes other than in-hospital death were not available either. Other limitations include caveats of the definition of “time of diagnosis” (it is a proxy based on the interval between the first hospitalization for NSCLC and the index date) and possible lack of comparability of our results with other studies with different definition of “time of diagnosis” and patient inclusion criteria (e.g., the rank of the treatment line for nivolumab). The number of clusters is decided by clinical experts based on preliminary TAK outputs and clinical practice. Lastly, to improve readability, immunotherapies other than nivolumab were combined into one group even though they are not clinically equivalent.

Conclusion

This study confirms the long-term benefit of nivolumab treatment for advanced NSCLC patients in the real-world setting, with a 5-year survival rate similar to that reported in clinical trials. The number of hospital stays decreased over the years, driven by the decline in one-day hospital stays. In year 5, almost half of patients were not hospitalized and 61 % had no systemic treatment, suggesting possible remission or at least the end of the active treatment period and persistent treatment response.

Authors' contributions

Anne-Françoise Gaudin, Valentine Grumberg and François-Emery Cotté initiated this study. All authors contributed to the study conception and design. Material preparation, data management and analysis were performed by Ronan Jolivel. Jean-Baptiste Assié, Christos Chouaïd, Dorothee Reynaud, François-Emery Cotté and Valentine Grumberg oversaw data collection, analysis and interpretation. Jean-Baptiste Assié, Valentine Grumberg, and Christos Chouaïd commented on versions of the manuscript. All authors read and approved the final manuscript.

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Data availability

The data supporting the study findings are part of the National health data system (SNDS, *Système national des Données de Santé*) and are available from the HDH (*Health Data Hub* <https://www.health-data-hub.fr/>). Restrictions apply to the availability of these data containing potentially identifying and sensitive patient information.

Declaration of Competing Interest

JBA report no conflict of interest CC reports AZ, BI, GSK, Roche, Sanofi Aventis, BMS, MSD, Lilly, Novartis, Pfizer, Takeda, Bayer, Janssen, Viatrix, Chugai, and Amgen for Advisory Board, research funding,

honoraria, and travels AB, RJ and BJ work for Heva, the CRO which conducted the study on behalf of BRISTOL MYERS SQUIBB. VG has a PhD contract partly funded by Bristol Myers Squibb AFG, DR and FEC are employees of Bristol Myers Squibb

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Ethics approval

Since this was a retrospective study of an anonymized database and had no influence on patient care, ethics committee approval was not required. The study was performed according to the MR-006 guideline of the French data protection agency (CNIL, Commission Nationale de l'Informatique et des Libertés). This framework allows pharmaceutical industries to access PMSI data under strict conditions. The study must be of public interest (i.e., examining in the real-world setting the characteristics and healthcare use of long-term NSCLC survivors treated with nivolumab). The data controllers — BRISTOL MYERS SQUIBB — must declare the study process in an activity registry supervised by the SNDS (declaration No. F20210623164242). Patient anonymity and data confidentiality must be guaranteed; patient data linkage with other datasets is impossible. Access to the data is only possible through certified third-party research consultancy/laboratories — Heva. The third-party must comply with a reference system set by the CNIL (Decree of July 17, 2017), is independently audited every third year, and complies with the ban on prohibited purposes.

Consent

This study is a retrospective study based on claims data. Patient consent was not necessary (article R.1461-9 of the French Public Health Code).

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.resmer.2023.101051](https://doi.org/10.1016/j.resmer.2023.101051).

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