

NIVOLUMAB OUTCOMES IN OCTOGENARIAN PATIENTS WITH ADVANCED NON-SMALL CELL LUNG CANCER IN A FRENCH REAL-WORLD SETTING

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Introduction

- The introduction of immune checkpoint inhibitors represents a major advance in the treatment of lung cancer, allowing sustained recovery in a significant proportion of patients [1, 2].
- Nivolumab is a monoclonal anti-PD-1 antibody licensed for the treatment of locally advanced or metastatic non-small cell lung cancer (NSCLC) after prior chemotherapy in adults.
- Two large randomised studies in patients with advanced squamous and non-squamous NSCLC demonstrated that nivolumab was superior to docetaxel at extending overall survival (OS) [3, 4].
- However, in these clinical studies, very few patients aged >75 years were enrolled and experience with nivolumab in the elderly is still limited.
- Around 10% of patients newly diagnosed with NSCLC in France are octogenarian [5].
- The French Early Access Programme (EAP) provides a valuable source of information to examine use and outcomes of nivolumab in elderly patients aged ≥80 years.
- The objectives of the present study were as follows:
 - To describe the demographic and clinical characteristics of patients aged ≥80 years with advanced NSCLC treated with nivolumab in the French EAP.
 - To estimate time to nivolumab treatment discontinuation in these patients.
 - To estimate OS in these patients.

Methods

Patients and data source

- All participants in the French EAP were eligible.
- All patients with advanced NSCLC initiating nivolumab in 2015-2016 in second- or later-line setting were enrolled and followed until December 2017 with a minimum of 12 months follow-up
- Data were extracted from the French national hospital discharge database (PMSI) [6]
- Patients with advanced NSCLC were identified from the ICD code (C34*) in the hospitalisation discharge summary.

Data extraction

- All inpatient and outpatient hospitalisations between 1st January 2011 and 31st December 2017 were extracted from the database.
- Demographic variables were documented at the time of the first nivolumab administration.
- Lung cancer history duration was defined as the interval between first hospitalisation with lung cancer and first nivolumab administration.
- Comorbidities were identified from the ICD codes in the hospitalisation discharge summary for any hospital stay in the seven-year extraction period.
- Patients with non-squamous cell NSCLC were identified through the proxy measure of treatment with bevacizumab or pemetrexed, as previously described [7].
- The treatment duration of nivolumab was defined as the interval between the index hospital visit and discontinuation, defined as no new treatment for at least six weeks after the previous treatment (ie three missed treatments) or death, if the patient died. The date of discontinuation was defined as the last treatment date plus 14 days, or the date of death.
- Patients who died in hospital were identified and overall survival defined as the interval between the index hospitalisation and the date of death.

Statistical analysis

- Data presentation is principally descriptive.
- Patient characteristics were compared between patients aged ≥80 years and those aged <80 years using the χ^2 test for categorical variables or Student's t-test for continuous variables.
- Treatment discontinuation rates and overall survival rates were determined from Kaplan-Meier actuarial survival curves.

Results

Study population

- 10,452 patients with advanced NSCLC initiating nivolumab were enrolled in the EAP.
- Of these, 514 (4.9%) were aged ≥80 years (median age: 82.5 ± 2.4 years).
- Patient characteristics at baseline are compared between the two age groups in Table 1.
- Compared to younger patients, patients aged ≥80 years were more frequently men ($p < 0.001$) and had comorbid hypertension and diabetes ($p < 0.001$). They less frequently presented with non-squamous cell disease, cerebral metastasis, renal failure, chronic obstructive pulmonary disease (COPD), pulmonary insufficiency, malnutrition and other chronic pulmonary diseases ($p < 0.001$).

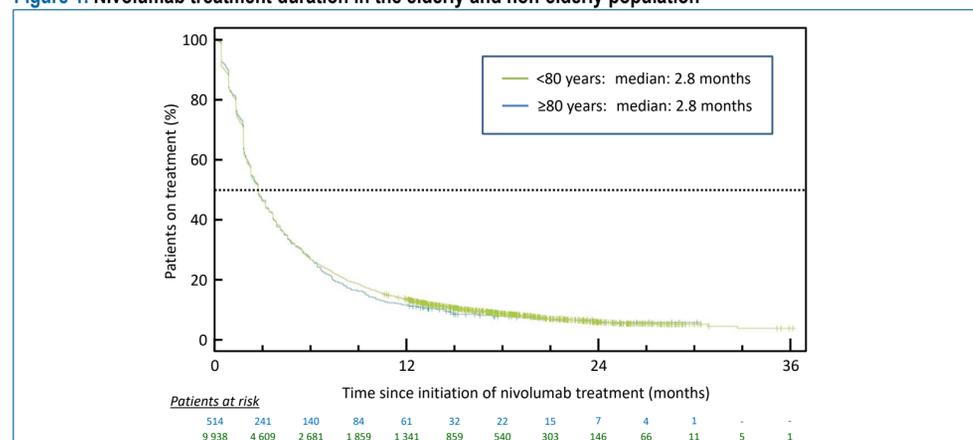
Table 1. Patient characteristics

Characteristics	< 80 years (N = 9 938)	≥ 80 years (N = 514)	P-value
Gender			
Men	7 019 (70.6%)	401 (78%)	<0.001
Age			
Median (years)	64	82	<0.001
Comorbidities			
Hypertension	1 844 (18.6 %)	142 (27.6 %)	<0.001
Diabetes	871 (8.8 %)	63 (12.3 %)	
Renal failure	460 (4.6 %)	19 (3.7 %)	
COPD	1 298 (13.1 %)	50 (9.7 %)	
Pulmonary insufficiency	149 (1.5 %)	4 (0.8 %)	
Other chronic pulmonary disease	870 (8.8 %)	33 (6.4 %)	
Cerebral metastasis	1 771 (17.8 %)	29 (5.6 %)	
Dementia, degenerative disease	24 (0.2 %)	5 (1.0 %)	
Malnutrition	1 880 (18.9 %)	79 (15.4 %)	
Lung cancer history			
Median duration (months)	12.4	14.2	0.002
Histological subtype			
Non-squamous NSCLC (%)	5 666 (57.0%)	139 (27.0%)	<0.001

Treatment duration

- The median treatment duration (Figure 1) was identical in both groups (2.8 months).
- Of the patients who discontinued nivolumab, 44.4% of patients aged ≥80 years subsequently started a second course of immunotherapy, compared to 53.8% of younger patients ($p < 0.001$),

Figure 1. Nivolumab treatment duration in the elderly and non-elderly population



Overall Survival

- One- and two- year OS rates were comparable in the two age groups (Table 2).
- Median OS was similar between elderly and non-elderly patients (Table 2; Figure 2).

Figure 2. Overall survival in the elderly and non-elderly population

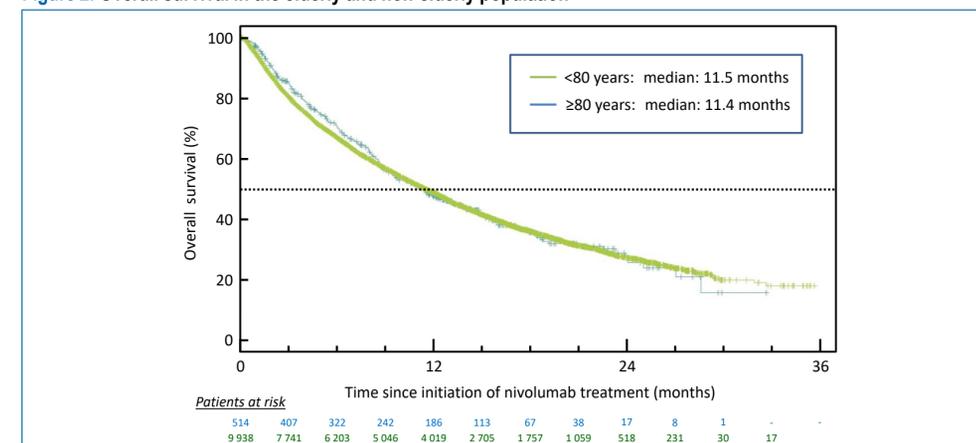


Table 2. Overall survival

Overall survival	< 80 years (N = 9 938)	≥ 80 years (N = 514)	P-value
12 month survival rate	49%	48%	NS
24 month survival rate	27%	26%	
Median (months)	11.5	11.4	

Conclusions

- Less than five percent of patients with advanced NSCLC treated with nivolumab were aged 80 years or over. This proportion is less than the 10% of patients diagnosed with advanced NSCLC in this age group expected from the literature [5].
- The rate of comorbidities in these patients treated with nivolumab is relatively low for a population of this age. This may suggest that clinicians have been cautious in their choice of elderly patients for treatment.
- The treatment duration in this elderly population is identical to that observed in younger patients, suggesting that no specific tolerability issue arose in this age group.
- Similarly, survival outcome is very comparable, suggesting that the effectiveness of nivolumab is maintained in elderly patients over eighty years of age.
- A limitation of the use of the PMSI database is that no data on treatment safety is available.

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