Nivolumab in patients with recurrent and/or metastatic squamous cell carcinoma of head and neck (R/M SCCHN) progressing on/or after a platinum-based therapy: interim analysis of a prospective French real-world study (ProNiHN)

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Introduction

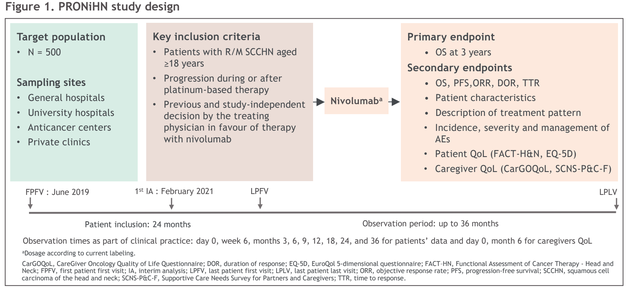
- Globally, head and neck cancer was the seventh most common cancer in 2018, causing an estimated 450,000 deaths[1]
- Patients frequently present with locoregional advanced disease, and recurrence within 3 years is seen in >50% of patients[2-4]
- Nivolumab is a fully human IgG4 monoclonal antibody that blocks the programmed cell death-1 receptor and acts as a immune checkpoint inhibitor[2,3]
- Nivolumab is approved in Europe and in the USA for the treatment of patients with recurrent or metastatic squamous cell carcinoma of the head and neck (R/M SCCHN) with disease progression on or after platinum-based therapy; this approval was based on the survival benefits and manageable safety profile demonstrated in the phase III CheckMate 141[2,5,6]
- The pivotal phase III trial CheckMate 141 demonstrated that treatment with nivolumab significantly improved overall survival (OS) and response rates, and reduced adverse events (AEs) in patients with R/M SCCHN compared with the investigator's choice of systemic therapy (methotrexate, docetaxel or cetuximab)[2]
- Data from large real-world studies provide complementary evidence to preclinical and clinical studies, and are important for making informed decisions in routine clinical practice
- The objective of the real-world ProNiHN study was to describe the clinical characteristics of SCCHN patients treated with nivolumab in France and to assess effectiveness and safety of nivolumab in these patients

Methods

Study design

- ProNiHN is an ongoing prospective, observational, non-interventional longitudinal study conducted in 91 sites in France with representative national medical practices in patients with R/M SCCHN and disease progression on or after platinum-based therapy (ClinicalTrials.gov identifier: NCT04050761) (**Figure 1**)
- All participants initiated intravenous nivolumab, with dosage and administration as per the approved label
- Patients will be followed for 3 years and evaluated according to routine clinical practice
- The primary objective of the study is assessment of OS at 3 years
  - Secondary objectives include progression-free survival (PFS) and objective response rate (ORR) assessed by investigator, safety, description of socio-demographic, clinical characteristics, patient-reported outcomes and management of patients

Figure 1. PRONiHN study design



Observation times as part of clinical practice: day 0, week 6, months 3, 6, 9, 12, 18, 24, and 36 for patients' data and day 0, month 6 for caregivers QoL

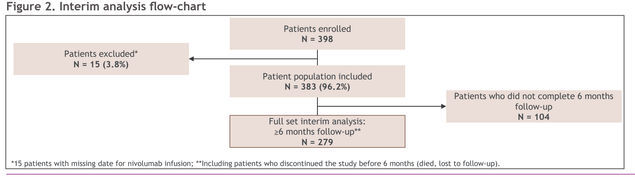
[a]Dosage according to current labeling.

CarGOQoL, CareGiver Oncology Quality of Life Questionnaire; DOR, duration of response; EQ-5D, EuroQol 5-dimensional questionnaire; FACT-HN, Functional Assessment of Cancer Therapy - Head and Neck; FPFV, first patient first visit; IA, interim analysis; LPFV, last patient first visit; LPLV, last patient last visit; ORR, objective response rate; PFS, progression-free survival; SCCHN, squamous cell carcinoma of the head and neck; SCNS-P&C-F, Supportive Care Needs Survey for Partners and Caregivers; TTR, time to response.

First Interim Analysis

- Patients were prospectively enrolled at 80 centres in France between 26 June 2019 and 19 February 2021 (data cut-off date)
- As of this interim analysis, 279 patients were followed-up for a minimum of 6 months
- Descriptive statistics and Kaplan-Meier analysis were used to estimate OS and PFS and Cox proportional-hazards regression model was used to assess the association between baseline patient characteristics and survival

Figure 2. Interim analysis flow-chart



*15 patients with missing date for nivolumab infusion; **Including patients who discontinued the study before 6 months (died, lost to follow-up).

Results

Patient baseline and clinical characteristics

- Of the 383 patients included in the study at data cut-off, the first interim analysis comprised of 279 patients who had a follow-up of >6 months (**Table1**)

Table 1. Patient baseline characteristics

	All population (N = 383)	Patients analysed (N = 279)
Age at nivolumab initiation		
Median (range), years	65 (31–94)	65 (32–94)
≥70 years, n (%)	116 (30.3)	88 (31.5)
Male, n (%)	311 (81.2)	226 (81.0)
Smoking status, n(%)		
Current/former smoker	322 (84.1)	237 (85.0)
Alcohol status, n (%)		
Non-drinker	209 (54.6)	155 (55.5)
Active drinker	113 (29.5)	80 (28.7)
Unknown	61 (15.9)	44 (15.8)

Table 2. Clinical characteristics

	All population (N = 383)	Patients analysed (N = 279)
Location of primary tumour, n (%)		
Oral cavity	109 (28.5)	78 (28.0)
Oropharynx	133 (34.7)	94 (33.7)
Hypopharynx	54 (14.1)	42 (15.1)
Larynx	49 (12.8)	39 (14.0)
Trachea	0	0
Nasal cavity	5 (1.3)	1 (0.4)
Paranasal sinuses	6 (1.6)	5 (1.8)
Nasopharynx	6 (1.6)	4 (1.4)
Other	16 (4.2)	14 (5.0)
Unknown	5 (1.3)	2 (0.7)
HPV status for patients with oropharyngeal cancer, n (%)*	**61 (45.2)**	**45 (44.1)**
HPV+	19 (31.2)	13 (28.9)
HPV-	42 (68.9)	32 (71.1)
Tumour localisation at nivolumab first infusion, n (%)		
Locoregional recurrence only	162 (42.3)	121 (43.4)
Both locoregional recurrence and distant metastases	114 (29.8)	91 (32.6)
Distant metastases only	71 (18.5)	44 (15.8)
Missing	36 (9.4)	23 (8.2)
Location of metastases, n (%)		
Lungs	162 (80.6)	118 (81.9)
Bone	47 (23.4)	35 (24.3)
Liver	29 (14.4)	20 (13.9)
Adrenal gland	10 (5.0)	8 (5.6)
Brain	3 (1.5)	1 (0.7)
Other	57 (28.4)	42 (29.2)
ECOG PS at inclusion, n (%)		
0	54 (14.1)	33 (11.8)
1	219 (57.2)	156 (55.9)
2	65 (17.0)	54 (19.4)
3	7 (1.8)	7 (2.5)
4	0	0
Unknown/missing	38 (9.9)	29 (10.4)
Timing of progression in relation to prior platinum-based therapy, n (%)		
<3 months	181 (47.3)	139 (49.8)
3-6 months	59 (15.4)	37 (13.3)
>6 months	88 (23.0)	65 (23.3)
Missing	55 (14.4)	38 (13.6)

*Percentage has been calculated on the basis of patients who had HPV test performed.
ECOG PS, Eastern Cooperative Oncology Group performance status; HPV, Human papillomavirus.

Table 3. Treatment characteristics

	All population (N = 383)	Patients analysed (N = 279)
Nivolumab LOT, n (%)		
1	44 (11.5)	32 (11.5)
2	263 (68.7)	185 (66.3)
3	65 (16.9)	51 (18.3)
≥4	11 (2.9)	11 (3.9)
Prior therapy, n (%)		
Surgery	176 (45.9)	133 (47.7)
Radiation therapy	330 (86.1)	241 (86.4)
Targeted therapy	168 (43.8)	124 (44.4)
Chemotherapy	353 (92.2)	255 (91.4)
Direct prior systemic treatment to nivolumab for R/M SCCHN, n (%)[a]	**316 (82.5)[b]**	**234 (83.9)[c]**
EXTREME: platinum-based therapy (carboplatin or cisplatin) + 5 F-U + cetuximab	89 (28.2)	73 (31.2)
Cetuximab monotherapy	69 (21.8)	49 (20.9)
Carboplatin + cetuximab	33 (10.4)	24 (10.3)
Carboplatin + paclitaxel	26 (8.2)	18 (7.7)
PCC: Carboplatin + paclitaxel + cetuximab	18 (5.7)	14 (5.9)
TPEX: platinum-based therapy (carboplatin or cisplatin) + taxane + cetuximab	13 (4.1)	10 (4.3)
Platinum-based therapy alone or other platinum based combination[d]	49 (15.5)	37 (15.8)
Other	19 (6.1)	9 (3.8)
Direct subsequent systemic treatment to nivolumab, n (%)[e]	**124 (32.8)**	**113 (40.5)**
Chemotherapy	88 (71)	80 (70.8)
Platinum-based therapy[f]	10 (8.1)	9 (7.9)
Taxanes	49 (39.5)[g]	44 (38.9)[h]
Methotrexate	18 (14.5)	17 (15.0)
Cetuximab	5 (4.0)	4 (3.5)
Immunotherapy	1 (0.1)	1 (0.1)

[a]Excluding patients who received nivolumab in first line and patients with no chemotherapy records, or chemotherapy records with missing start and stop dates; [b]n=23 patients who received nivolumab in second line or beyond and were missing prior chemotherapy information; [c]n=13 patients who received nivolumab in second line or beyond and were missing prior chemotherapy information; [d]Other combination refers to combination with platinum-based therapy that are not mentioned in the table; [e]Patients with subsequent therapy information; [f]All patients received carboplatin; [g]47 patients received paclitaxel and 2 received docetaxel; [h]42 patients received paclitaxel and 2 received docetaxel.
LOT, line of therapy; 5-FU, 5-fluorouracil.

Median follow-up and nivolumab treatment pattern

- As of this interim analysis, 279 patients were followed-up for a median of 6 months (range 0.03–18.0)
- The median duration of nivolumab treatment was 2.3 months (maximum 18.2 months)
- As of February 2021, 141 patients (50.5%) had discontinued treatment with nivolumab
  - 127 patients (90.1%) discontinued due to disease progression and 6 (4.3%) discontinued due to drug-related toxicity

Overall Survival (OS)

- The median OS was 8.6 months (95% CI, 6.7–9.7), with an estimated survival probability of 60% (95% CI, 40–66) at 6 months and 31% (95% CI, 24–39) at 12 months (**Figure 3**)
- The OS was analysed on the basis of the following subgroups: LOT for nivolumab, platinum sensitivity, ECOG PS, age and type of recurrence

OS according to nivolumab LOT

- Median OS for patients treated with nivolumab as the first LOT was 8.0 months (95% CI, 3.5–not estimable [NE]), 8.6 months (95% CI, 6.3-10.4) for second LOT and 8.8 months (95% CI, 5.5-9.7) for third LOT or beyond (**Figure 4**). In univariate Cox regression models, the hazard ratio (HR) for death vs second LOT was 1.03 (95% CI, 0.59, 1.70; p=0.9029) for first LOT and 1.09 (95% CI, 0.73, 1.59; p=0.6596) for third LOT

Figure 3. OS of overall population

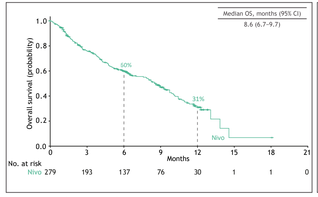
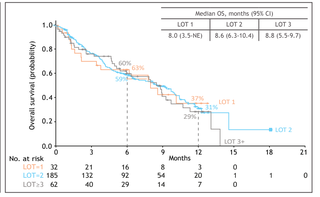


Figure 4. OS by nivolumab LOT



OS according to platinum sensitivity

- Median OS was longer but not significantly different for patients with platinum-sensitivity (progression >6 months of prior platinum therapy; 10.0 months [95% CI, 6.4–10.4]) vs platinum-refractory patients (progression ≤6 months of prior platinum therapy; 8.2 months [95% CI, 6.2–9.3]) HR (95% CI) for difference, 0.86 (0.56,1.26; p=0.4449) (**Figure 5**)

OS according to ECOG PS

- Median OS ranged from 9.9 months (95% CI, 8.5–11.3) for patients with an ECOG PS <2 to 3.7 months (95% CI, 2.0–5.5) for patients with an ECOG PS of ≥2; HR (95% CI) for difference, 2.47 (1.70, 3.54); p<0.001 (**Figure 6**)

Figure 5. OS by platinum sensitivity

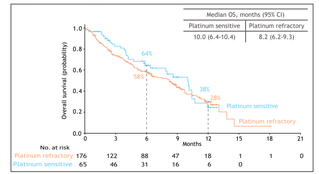
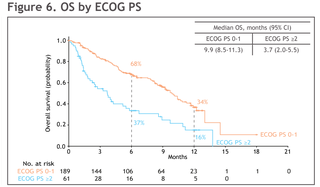


Figure 6. OS by ECOG PS



OS according to age

- Median OS did not differ between patients aged <70 years (8.4 months [95% CI, 6.2–10.1]) and those aged ≥70 years (8.9 months [95% CI, 6.5–NE]); HR (95% CI) for difference, 0.83 (0.57, 1.18); p=0.3020 (**Figure 7**)

OS according to type of recurrence

- Median OS was longer but not significantly different for patients with only distant metastases (9.7 months [95% CI, 4.0–NE]), followed by 8.6 months (95% CI, 7.8–10.5) for patients with only a locoregional recurrence, and 6.5 months (95% CI, 5.2–9.9) for those with both distant metastases and a locoregional recurrence (**Figure 8**). HR (95% CI) versus distant metastases only was 1.19 (0.73, 2.01); p=0.5104 for locoregional recurrence only and 1.45 (0.88, 2.48); p=0.1561 for both metastases/locoregional recurrence

Figure 7. OS by age (<70 vs ≥70 years)

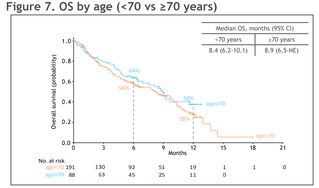
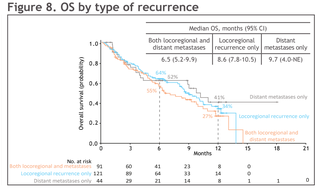


Figure 8. OS by type of recurrence



Progression-free survival

- Median PFS was 3.1 months (95% CI, 2.8–3.7) for all patients in this interim analysis

Safety

- Treatment-related adverse events (TRAEs) occurred in 18.6% of patients, with 12.3% having grade 3 TRAEs and 3.7% having grade 4 and no grade 5 was reported
- Grade 3 and 4 AEs included skin toxicity, diarrhoea, asthenia, duodenitis, peripheral sensory neuropathy, cerebellar syndrome, renal failure, hypercalcemia, malaise, disease progression and general physical health deterioration
- Two patients died; one due to disease progression and the other due to hypercalcaemia/renal failure

Conclusions

- Preliminary ProNiHN results are consistent with Checkmate 141 for patients with R/M SCCHN treated with nivolumab in routine clinical practice in France and provide complementary information on additional subgroups
- Median OS was consistent in subgroups based on age, type of recurrence, line of nivolumab therapy and sensitivity to platinum therapy, but was longer in patients with ECOG PS of 0–1 (9.9 months) versus ≥2 (3.7 months)
- Most TRAEs were grade 1 or 2, and no grade 5 TRAEs occurred. No new safety signals were identified

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Disclosures

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