

Correlation between quality of life of patients treated with nivolumab in recurrent and/or metastatic squamous cell carcinoma of head and neck and their caregivers

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Introduction

Context

- Squamous cell carcinomas of the head and neck (SCCHNs) comprise >90% of head and neck cancers, and usually arise in the oral cavity, larynx and pharynx¹⁻³
- SCCHN is the fifth most common cancer in France, with 15,000 new cases and 4,000 deaths per year^{4,5}
- Patients with recurrent/metastatic SCCHN (R/M SCCHN) who progress within 6 months after platinum-based therapy generally have a poor prognosis and treatment options are limited^{3,6}
- R/M SCCHN patients tend to have a decreased quality of life (QoL)^{7,8}
- Nivolumab is a programmed death receptor-1-blocking monoclonal antibody and acts as an immune checkpoint inhibitor^{9,10}
- Based on the promising clinical efficacy and manageable safety profile demonstrated in the pivotal phase III CheckMate 141 trial (NCT02105636), nivolumab was approved in the United States in 2016 and in Europe in 2017 for the treatment of patients with R/M SCCHN with disease progression on or after platinum-based therapy⁶
- In CheckMate 141, nivolumab significantly improved overall survival (OS), improved response rates, reduced adverse events (AEs), and stabilized/slightly improved quality of life (QoL) at 1 year compared with the investigator’s choice of systemic therapy⁶

Study rationale

- While correlation between patients’ QoL questionnaire and their survival has been already assessed, the relationship between HRQoL of patients and caregivers has not been studied in this patient population^{11,12}
- The ProNIHN study evaluated the effectiveness and safety of nivolumab, as well as QoL of patients and caregivers, in patients with R/M SCCHN in routine clinical practice in France. Preliminary results have been reported previously¹³

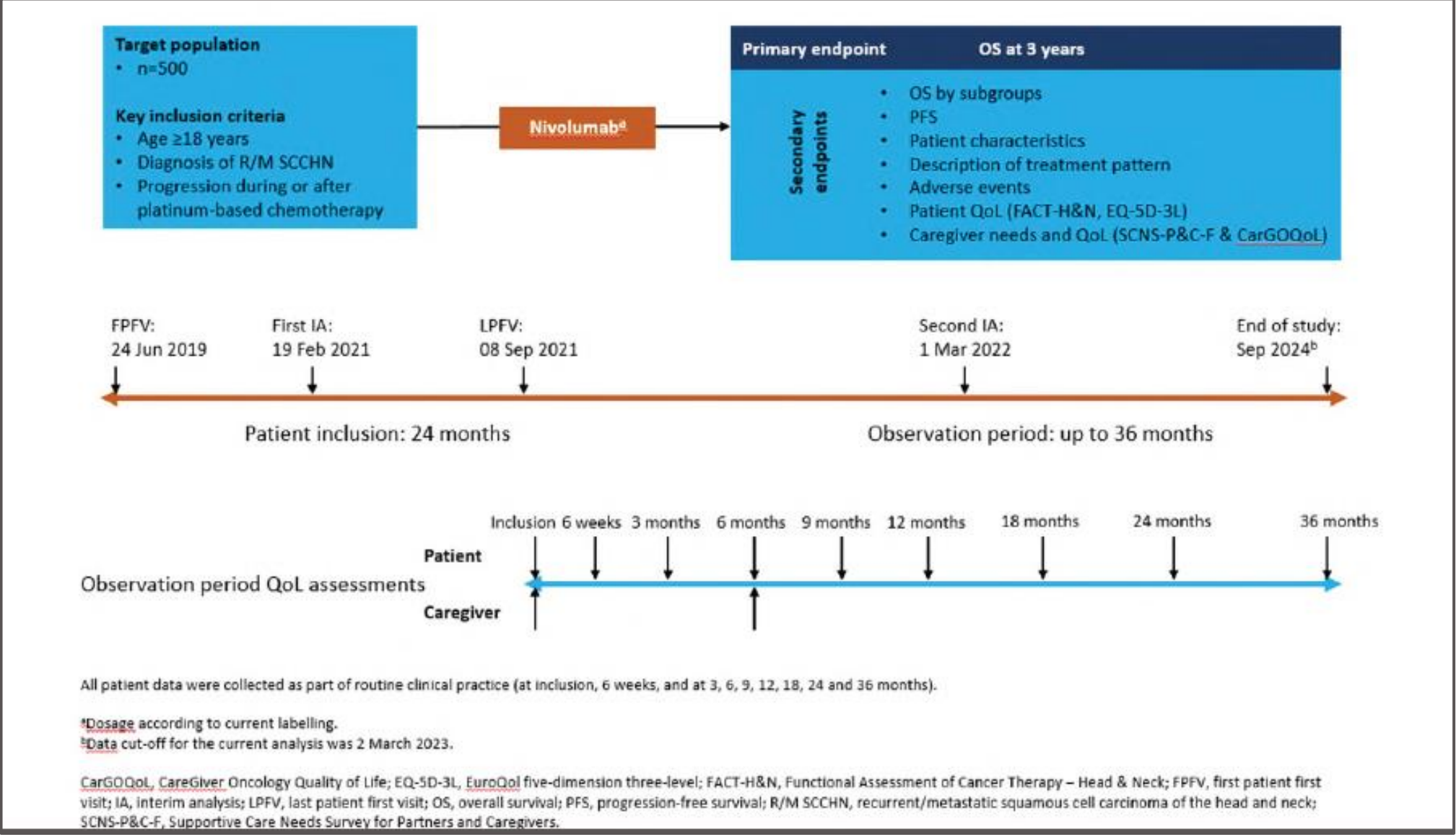
Objective

The objective of this study was to assess correlation between patient and caregiver QoL and its evolution over time.

Methods

- ProNIHN is an ongoing prospective, observational, non-interventional, national multicenter study including patients with R/M SCCHN and disease progression on or after platinum-based therapy (NCT0450761) (Figure 1)
- Patients have R/M SCCHN and disease progression on or after platinum-based therapy, and have not previously received nivolumab or any other treatment targeting T-cell costimulation or immune-checkpoint inhibitor

Figure 1. ProNIHN study design



HRQoL assessments

- QoL of patients was assessed at inclusion, week-6, mo-3, 6, 12 and 18 using the Functional Assessment of Cancer Therapy-Head and Neck (FACT-H&N), the EQ-5D-3L questionnaire and visual analogue scale (VAS)
 - FACT-H&N is composed of 27 core items (FACT-G) assessing patient function in four domains (physical, social/family, emotional and functional well-being) and 12 site specific items for head and neck related symptoms. Higher scores represent a better QoL
 - EQ-5D-3L is composed of 5 dimensions (mobility, self-care, usual activities, pain/discomfort, anxiety/depression) and three levels (no problem, some problem, extreme problems). Higher scores on the index represent a better QoL
 - VAS is a scale from 0 to 100. Higher scores represent a better QoL
- Caregivers needs and QoL were assessed at inclusion and 6 months using the Supportive Care Needs Survey for Partners and Caregivers (SCNS-P&C-F) and CareGiver Oncology Quality of Life (CarGOQoL) questionnaires, respectively
 - For SCNS-P&C-F, items are scored from 1 to 5, where higher scores indicate greater unmet needs
 - CarGOQoL is composed of ten dimensions (psychological, burden, relationship with healthcare, administration and finances, coping, physical, self-esteem, leisure time, social support and private life). Each domain range from 0 to 100, where higher scores indicate better QoL

Statistical analysis

- Continuous endpoints were compared between groups using the Student t-test (for variables with a normal distribution) or the non-parametric Wilcoxon Mann-Whitney test (for variables with a non-normal distribution)
- Dichotomous variables were compared using the McNemar’s test, and qualitative variables with more than two categories were compared using the Bowker’s test
- Minimally important score differences were set at 6 for the FACT-H&N scale, 0.08 for the EQ-5D-3L index and 7 for the EQ-5D VAS^{14,15}
- The Pearson correlation coefficient was used to report correlations between continuous variables
- All statistical analyses were performed using SAS® software (v.9.4, SAS Institute, NC, USA)

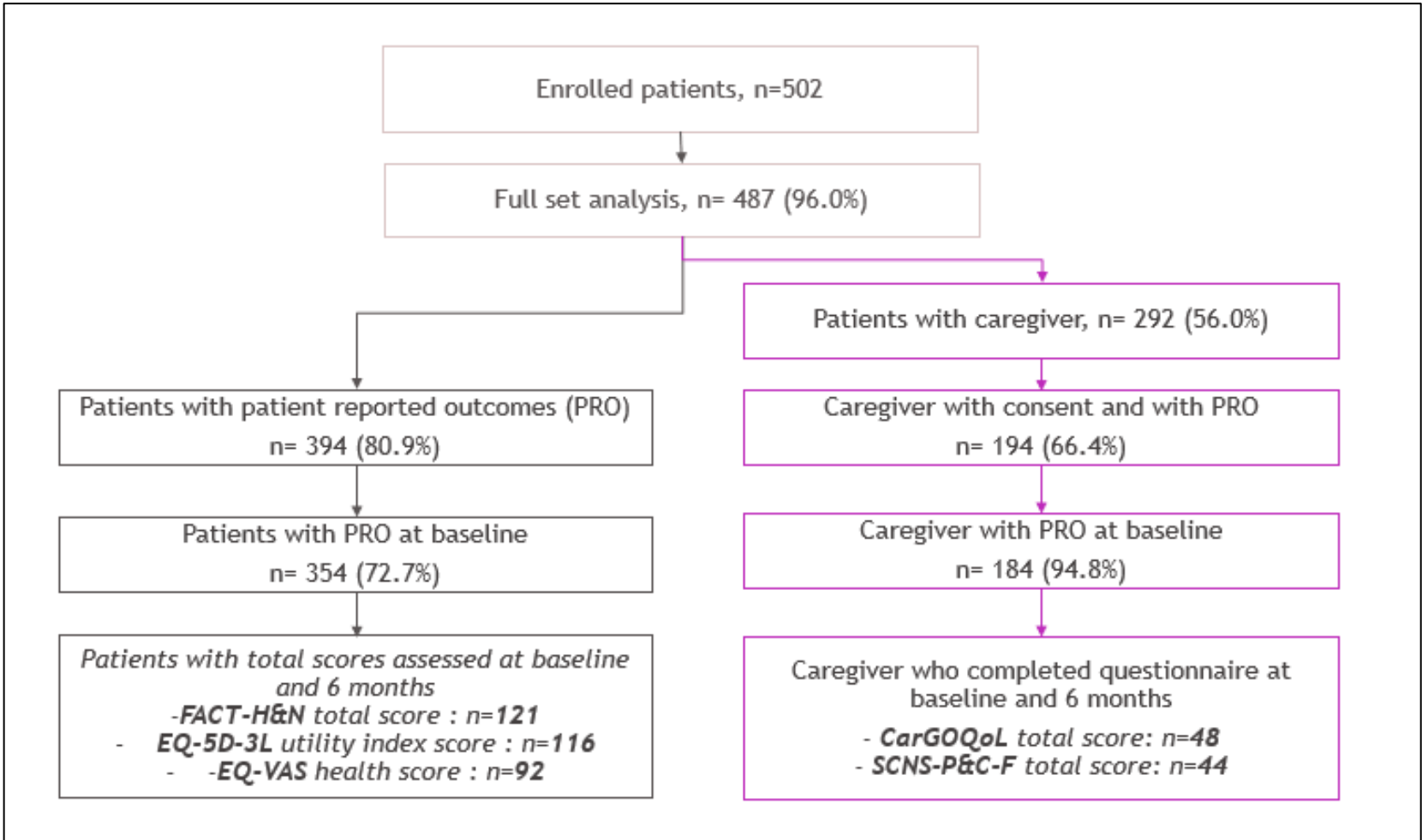
Results - Population and characteristics

- The full set analysis included 487 patients who were followed at least 17 months or until death (Figure 2)
- Patients’ characteristics are :
 - Median age 64.4 [Q1-Q3: 58.6-70.9] years; 28.3% aged ≥70 years
 - 81.5% male
 - 89.3% with a smoking history
 - 21.3% with Eastern Cooperative Oncology Group performance status (ECOG) ≥2
 - Primary tumour location was the oropharynx in 36.7% of patients, oral cavity in 28.9%, hypopharynx in 15.1%, larynx in 13.6%, and other/missing in 6.2%
- 292 patients (56.0%) mentioned having a caregiver
 - Mostly (71%) a spouse or significant other

- Of the 487 patients included, 354 had QoL data at baseline
- QoL questionnaires were completed at baseline and at 6 months by 127 patients
 - 121 patients completed the FACT-H&N at both times
 - 116 patients completed the EQ-5D-3L at both times
 - 92 patients completed the EQ-5D VAS at both times

- 253 caregivers gave their consent to participate to the study and 194 completed QoL questionnaires
- QoL questionnaires were completed at baseline and 6 months by:
 - 48 caregivers for the CarGOQoL
 - 44 caregivers for the SCNS-P&C-F

Figure 2. Patients and caregivers diagram



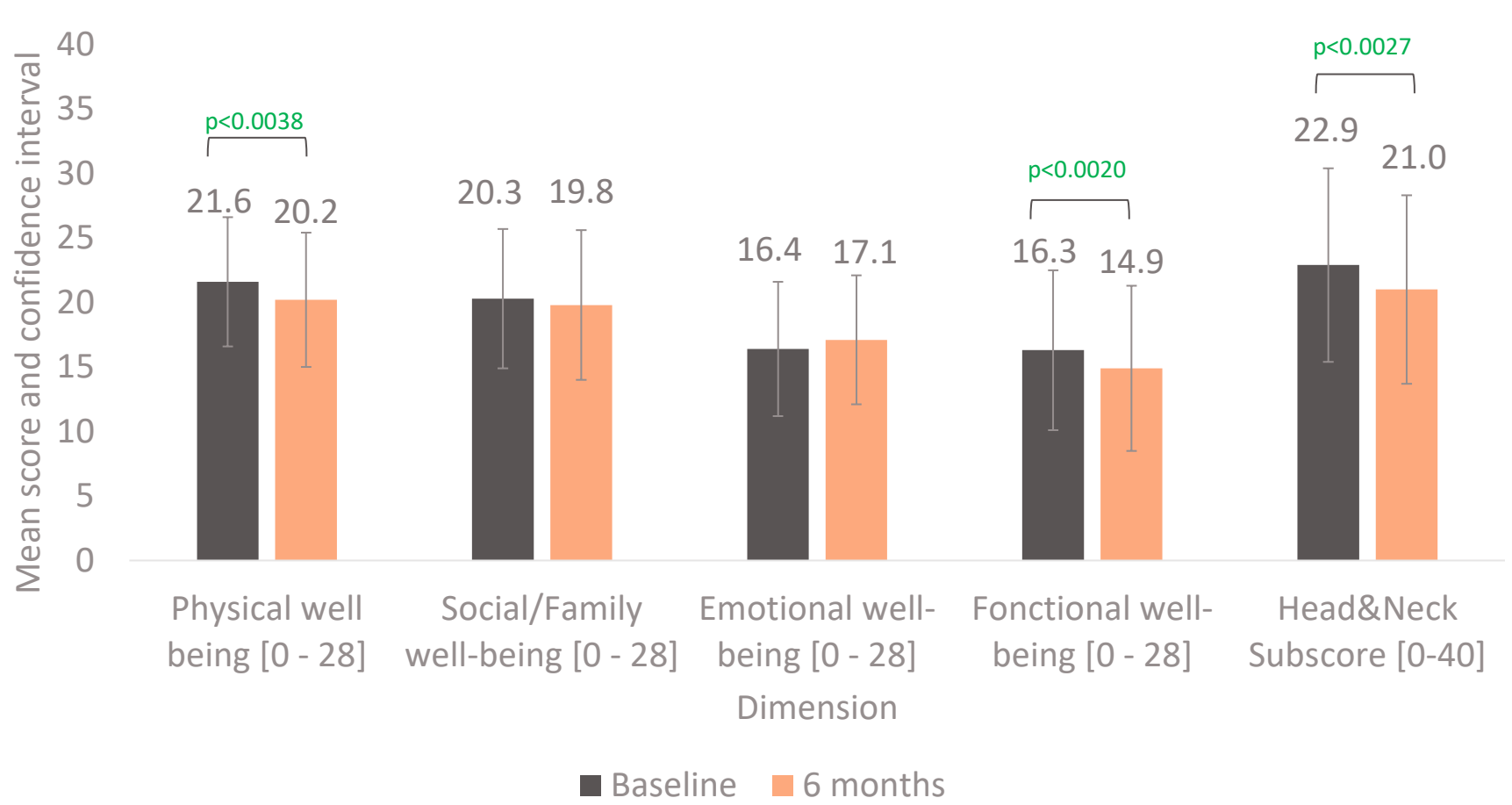
Quality of life evolution

Patients quality of life

- Fact-H&N total score decreased significantly between baseline and 6 months (mean: 97.6 vs. 93.0 ; p<0.0029)
 - A significant decrease was observed for the **physical well-being** dimension (mean: -1.5; p<0.0038) (Figure 3)
 - A significant decrease was observed for the **functional well-being** dimension (mean: -1.4; p<0.0020)
 - A significant decrease was observed for the **head & neck subscore** dimension (mean: -1.9; p<0.0027)

Figure 3. FACT-H&N evolution (n=121)

A higher score represent a better QoL



- EQ-5D-3L index score decreased significantly between baseline and 6 months (mean: 0.7 vs. 0.6; p<0.0039) (Table 1)
- EQ-VAS score was not significantly different between baseline and 6 months (mean : 62.0 vs. 62.3; p=0.88)

Table 1. EQ-5D-3L index score and VAS evolution

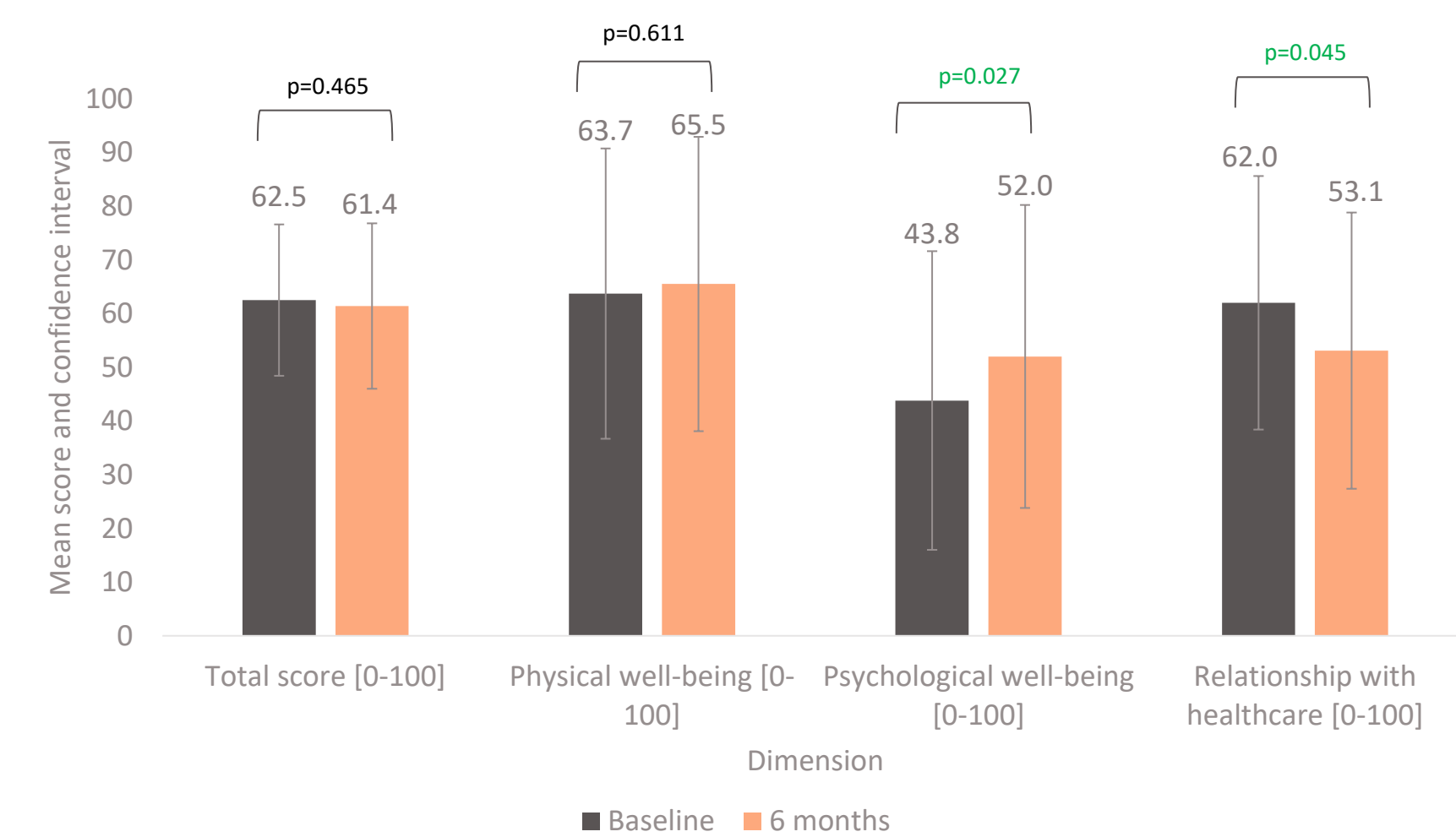
	Baseline	6 months	P-value
EQ-5D-3L index	n=116		
Mean (±SD)	0.7 (0.2)	0.6 (0.3)	0.004
EQ-5D-3L VAS	n=92		
Mean (±SD)	62.0 (17.5)	62.3 (16.6)	0.880

Caregiver quality of life and needs

- CarGOQoL total score did not change significantly between baseline and 6 months (Figure 4)
- Psychological well-being significantly increased while relationship with healthcare decreased

Figure 4. CarGOQoL score evolution (n=48)

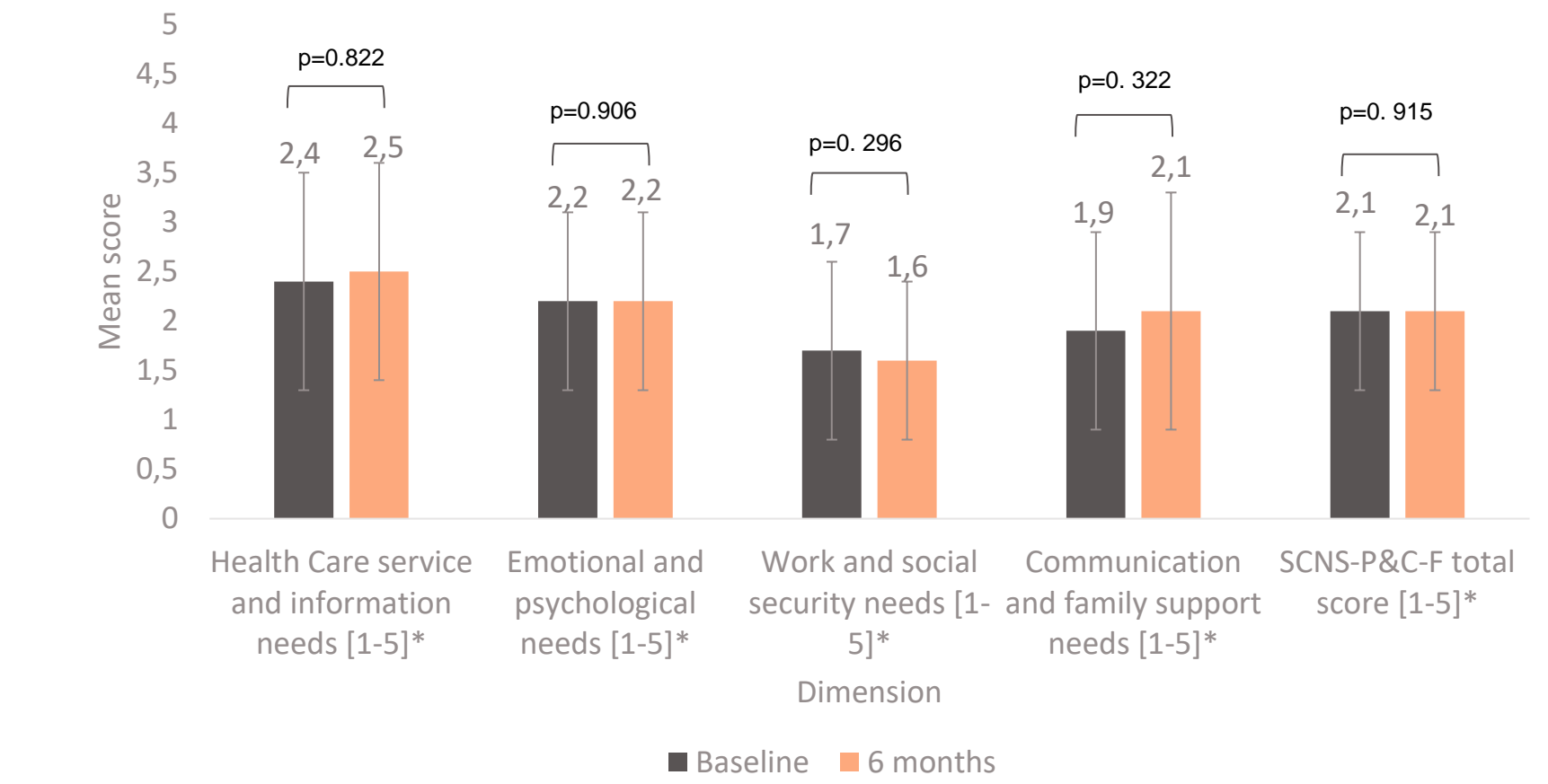
A higher score represent a better QoL



- There were no significant differences in caregiver needs between baseline and 6 months (Figure 5)

Figure 5. SCNS-P&C-F score evolution (n=44)

* A higher score means higher unmet need



Correlation

- Matched patients-FACT-H&N and caregivers-CarGOQoL results were:
 - weakly correlated at baseline (0.226; p<0.01)
 - weakly correlated at 6 months (0.363; p<0.01)
- Matched patients-FACT-H&N and caregivers-SCNS-P&C-F results were:
 - weakly inversely correlated at baseline (-0.170; p<0.05)
 - weakly inversely correlated at 6 months (-0.281; p<0.05)
- Matched patients-EQ-5D-3L utility index and caregivers-CarGOQoL results were:
 - weakly correlated at baseline (0.160; p<0.05)
 - moderately correlated at 6 months (0.489; p<0.001)
- Matched patients-EQ-5D-3L utility index score and caregivers-SCNS-P&C-F results were only weakly inversely correlated with results at 6 months (-0.361;p<0.01)
- Patients-EQ-5D-3L VAS results were not significantly correlated with caregiver-CarGOQoL. A moderate inverse correlation with SCNS-P&C-F was observed at 6 months (-0.413;p<0.01)

Table 2. Correlation between patients and caregivers total scores

	Spearman Correlation Coefficients [-1 ; 1] Prob > r under H0: Rho=0 Number of Observations	Caregiver total scores	
		At baseline	At 6 months
Patient total scores		CarGOQoL	SCNS P&C-F
FACT-H&N	0.22558 p=0.0032 n=169	-0.17026 p=0.0273 n=168	
FACT-H&N Trial Outcome Index (TOI)	0.15498 p=0.0430 n=171	-0.10473 p=0.1741 n=170	
FACT-G	0.27079 p=0.0004 n=169	-0.17056 p=0.0271 n=168	
EQ-5D index-based utility score	0.16014 p=0.0375 n=169	-0.08712 p=0.2615 n=168	
EQ-VAS	0.11832 p=0.1701 n=136	-0.09618 p=0.2672 n=135	
FACT-H&N			0.36243 p=0.0061 n=56
FACT-H&N Trial Outcome Index (TOI)			-0.28066 p=0.0460 n=51
FACT-G			0.26172 p=0.0514 n=56
EQ-5D index-based utility score			-0.27009 p=0.0553 n=51
EQ-VAS			-0.24049 p=0.0891 n=51
			0.48934 p=0.0003 n=51
			-0.36065 p=0.0118 n=48
			0.22018 p=0.1461 n=45
			-0.41334 p=0.0053 n=44

- Only psychological/emotional well-being and physical well-being of FACT-H&N and CarGOQoL could be assessed.
- Matched psychological/emotional patients-FACT-H&N and caregivers-CarGOQoL results were:
 - weakly correlated at baseline (0.164; p<0.04)
 - weakly correlated at 6 months (0.262; p=0.05)
- Matched physical patients-FACT-H&N and caregivers-CarGOQoL results were:
 - weakly correlated at baseline (0.208; p<0.01)
 - weakly correlated at 6 months (0.355; p<0.01)

Table 3. Correlation per dimension patients and caregivers questionnaires

	Spearman Correlation Coefficients [-1 ; 1] Prob > r under H0: Rho=0 Number of Observations	Caregiver total scores	
		At baseline	At 6 months
Patient subscores		CarGOQoL - Psychological well-being	CarGOQoL - Physical well-being
FACT-H&N - Emotional Well-being	0.16423 p=0.0313 n=172		
FACT-H&N - Physical Well-being		0.20825 p=0.0055 n=176	
FACT-H&N - Emotional Well-being			0.26186 p=0.0512 n=56
FACT-H&N - Physical Well-being			0.35526 p=0.0062 n=58

Conclusions

- Quality of life of patients and their caregivers as well as its evolution should be more widely studied
- In this study, quality of life of patients with R/M SCCHN decreased between inclusion and 6 months, especially on physical, functional and symptom dimensions
- The quality of life of caregivers significantly decreased only in the ‘relationship with healthcare’ dimension but their unmet needs did not significantly increase
- Correlation between patients and caregivers’ questionnaires results were weakly correlated at baseline and tended to be moderately correlated at 6 months
- Emotional/Psychological well-being and Physical well-being results between patients and caregivers seemed to be weakly correlated.

References

- Vigneswaran N, et al. *Oral Maxillofac Surg Clin North Am* 2014;26:123-141
- Ferris RL, et al *CA Cancer J Clin* 2018;68:394-424
- Samra B, et al. *J Invest Med* 2018; 66:1023-1030
- Defossez G, et al. Available from: <https://www.cancer.fr/Expertises-et-publications/Catalogue-des-publications/Severely-impaired-quality-of-life-in-patients-with-recurrent-or-metastatic-squamous-cell-carcinoma-of-the-head-and-neck>, 1990-04-20182, Published July 2019, Accessed 14 August 2023.
- Institut National du Cancer. Panorama des cancers en France. Edition 2023
- Ferris RL, et al. *N Engl J Med* 2016;375:1856-1867.
- Melo Filho MR, et al. *Braz J Otorhinolaryngol* 2013;79(1):82-8
- Singh P, et al. *BMC Cancer* 2021;21(1):854
- OPDIVO (nivolumab) [prescribing information]. Princeton, NJ: Bristol-Myers Squibb Company; 2020.
- European Medicines Agency. OPDIVO (nivolumab) summary of product characteristics. EMEA/H/C/003985.
- Etalidi R, et al. *Eur Arch Otorhinolaryngol* 2021;278(7):2437-2445
- Gomes APA, et al *J Dent* 2020;211(1):31-41
- Le Tourneau C, et al. *Ann Oncol* 2021;32(Suppl.5):S812-S813.
- Ringash J, et al. *Cancer* 2007;110:196-202.
- Pickard AS, et al. *Health Qual Life Outcomes* 2007;5:70.

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Disclosure

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