675P - Patterns of radiological responses to anti-PD1 in patients (pts) with recurrent or metastatic head and neck squamous cell carcinoma (R/M HNSCC) in TOPNIVO (T) study

Caroline EVEN (Gustave Roussy, Villejuif), Alice BERNARD-TESSIER (Gustave Roussy, Villejuif), Matthieu TEXIER (Gustave Roussy, Villejuif), Oumaya BEN-SAID (Gustave Roussy, Villejuif), Mariana IACOB (Gustave Roussy, Villejuif), Amaury DASTE (CHU St André, Bordeaux), Jérôme FAYETTE (Centre Léon Bérard, Lyon), Sylvie ZANETTA (Centre Georges-François Leclerc, Dijon), Gautier LEFEBVRE (Centre Oscar Lambret Lille), Marie VINCHES (ICM, Montpellier), Alison JOHNSON (Centre François Baclesse, Caen), Laurence BOZEC (Institut Curie, Paris), Esma SAADA-BOUZID (Centre Antoine Lacassagne, Nice), Isabelle JALLUT (Unicancer, Paris), Florence GARIC (Unicancer, Paris), Laure Monard (Unicancer, Paris) Jean BOURHIS (Lausanne University Hospital), Joël GUIGAY (Centre Antoine Lacassagne, Nice), Anne AUPERIN (Gustave Roussy, Villejuif), Samy AMMARI (Gustave Roussy , Villejuif).

BACKGROUND

Nivolumab (N) is the standard of care in pts with platinum refractory R/M HNSCC. Novel patterns of response and progression to immunotherapy (hyperprogression (HP), pseudoprogression (PSPD), dissociated responses (DR)) have been described that have not been observed with conventional cytotoxic or targeted anticancer drugs. No prospective data have been reported for pts with R/M HNSCC.

OBJECTIVE

To describe the different patterns of radiological responses to anti-PD1 and their frequency in R/M HNSCC.

PATIENTS AND METHODS

T was a single-arm phase II trial
From 08/2017 to 11/2018, 343 pts with platinum refractory R/M HNSCC were treated with Nivolumab (3 mg/kg, Q2W) (Even et al Ann Oncol 2020).
Timing of studied CT scans for this study was: pre-baseline, baseline before N, 1st evaluation (E1) at week 8, 2nd evaluation (E2) at week 16. All CT scans were independently re-analyzed by two expert radiologists . Tumor response was evaluated by RECIST 1.1.
HP was evaluated using the 3 first CT by 2 different methods (Champiat et al Clin Cancer Res 2017 (C), Ferrara et al JAMA Oncol 2018 (F)).
PSPD was defined as progression at E1 and stabilization of tumor growth or response at E2.
DR was studied at E1 and defined as objective response (OR) in loco-regional (LR) site and no OR in metastatic (M) site or no OR in LR site and OR in M site

RESULTS

HYPERPROGRESSION

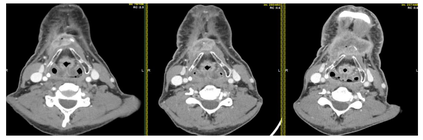
Of the 114 pts evaluable with C method, 15 (13%, 95% confidence interval (CI) 8-21) experienced hyperprogression

Of the 117 pts evaluable with F method, 9 (8%, 95%CI 4-14) experienced hyperprogression

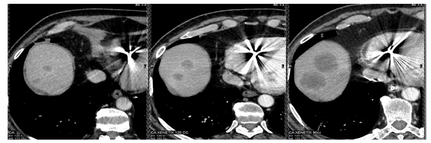
C Method	*Pts without hyperprogression N=99*	*Pts with hyperprogression N=15*
Sex		
Male	79 (80%)	14 (93%)
Female	20 (20%)	1 (7%)
Age		
Mean	65	61
Range	37 ; 87	39 ; 83
Pts older than 70		
Patients < 70 years old	67 (68%)	11 (73%)
Patients >= 70 years old	32 (32%)	4 (27%)
ECOG		
ECOG: 0	28 (28%)	2 (13%)
ECOG: 1	58 (59%)	10 (67%)
ECOG: 2	13 (13%)	3 (20%)
Type of relapse		
Loco regional disease	34 (34%)	9 (60%)
Metastatic disease	33 (33%)	2 (13%)
Both	32 (32%)	4 (27%)
Prior therapy (Th)		
No prior systemic Th	4 (4%)	1 (7%)
One prior systemic Th	54 (55%)	7 (47%)
Two or more systemic Th	41 (41%)	7 (47%)

F Method	*Pts without hyperprogression N=108*	*Pts with hyperprogression N=9*
Sex		
Male	88 (81%)	8 (89%)
Female	20 (19%)	1 (11%)
Age		
Mean	65	58
Range	37 ; 87	39 ; 70
Pts older than 70		
Patients < 70 years old	72 (67%)	8 (89%)
Patients >= 70 years old	36 (33%)	1 (11%)
ECOG		
ECOG: 0	41 (28%)	1 (11%)
ECOG: 1	39 (58%)	7 (78%)
ECOG: 2	15 (14%)	1 (11%)
Type of relapse		
Loco regional disease	37 (34%)	6 (67%)
Metastatic disease	37 (34%)	0 (0%)
Both	34 (31%)	3 (33%)
Prior therapy (Th)		
No prior systemic Th	3 (3%)	2 (22%)
One prior systemic Th	58 (54%)	5 (56%)
Two or more systemic Th	47 (44%)	2 (22%)

Champiat et al. = ratio TGR (TGR^1/TGR^{-1}) ≥2
Ferrara et al. = delta TGR (TGR^1-TGR^{-1}) > 50%



Pre-Baseline Baseline E1



Pre-Baseline Baseline E1

PSEUDOPROGRESSION

127 pts were evaluable for PSPD, 3 (2%, 95%CI 1-7) met the criteria

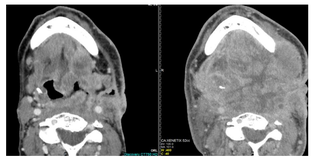
	Pts without pseudoprogression N=124	*Pts with Pseudoprogression N=3*
Sex		
Male	102 (82%)	2 (67%)
Female	22 (18%)	1 (33%)
Age		
Mean	64	58
Range	42 ; 87	52 ; 66
Pts older than 70		
Patients < 70 years old	91 (73%)	3 (100%)
Patients >= 70 years old	33 (27%)	0
ECOG		
ECOG: 0	38 (31%)	2 (67%)
ECOG: 1	72 (58%)	0
ECOG: 2	14 (11%)	1 (33%)
Type of relapse		
Loco regional disease	45 (36%)	1 (33%)
Metastatic disease	48 (39%)	1 (33%)
Both	31 (25%)	1 (33%)
Prior therapy		
No prior systemic therapy	5 (4%)	0
One prior systemic therapy	74 (60%)	2 (67%)
Two or more systemic therapies	45 (36%)	1 (33%)

Date of CT scan Last injection of N	*RECIST evaluation – site of PD*
Pt with PSPD n°1	
BL 23 JAN 18	HN and M sites
E1 20 MAR 18	PD on HN sites
E2 10 JUL 18	PR
Last N 16 AUG 19	
Pt with PSPD n°2	
BL 7 FEB 18	M sites
E1 4 APR 18	PD on M sites and new HN and M sites
E2 19 JUL 18	CR
Last N 09 JUL 18	
Pt with PSPD n°3	
BL 26 MAR 18	HN sites
E1 29 MAY 18	PD on HN sites
E2 31 JUL 18	CR
Last N 10 OCT 18	

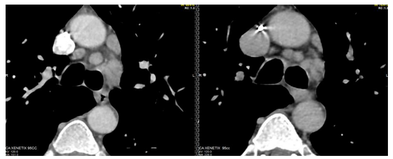
DISSOCIATED RESPONSE

208 pts had CT at baseline and at E1 with the following characteristics:
Male 83%, mean age 64 y (range 37-87), ECOG 0-1 88% - ECOG 2 12%,
No prior systemic therapy 6%, one line 55%, >=2 lines 40%.
146 pts had HN disease, OR in HN sites was observed in 9 pts (6%, 95%CI 3-12)
132 pts had M disease, OR in M sites was observed in 16 pts (13%, 95%CI 8-20)

In the 70 pts with disease in both LR and M sites, the DR rate was 19% (95%CI 10-31)
- In the 49 pts who previously received HN radiotherapy (RT), the rate of DR was 22% (11 pts) (95%CI 12-37)
- In the 14 pts without prior HN RT, the rate of DR was 7% (1 pt) (95%CI 0-34)

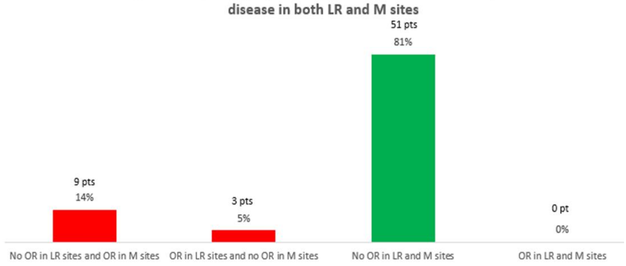


Baseline E1



Baseline E1

Rate of objective response (OR) according to sites of disease in 63 patients with disease in both LR and M sites



On the 70 pts with disease both in LR and M sites, DR was evaluable in 63 pts.

CONCLUSION

In this prospective study, we estimated the rate of R/M HNSCC pts with **hyperprogression** under Nivolumab between **4 and 21%.**
The rate of **pseudoprogression** is **very low**, which should be considered in our clinical practice.
No predictive factor for **hyperprogression** or **pseudoprogression** were identified.
19% (95%CI 10-31) of the pts presented **dissociated response,** mainly by absence of objective response in loco regional site while objective response occurred in metastatic site.