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NISCAHN: Phase II Study of Nivolumab in Patients With Progressive Recurrent or Metastatic Salivary Glands Carcinoma

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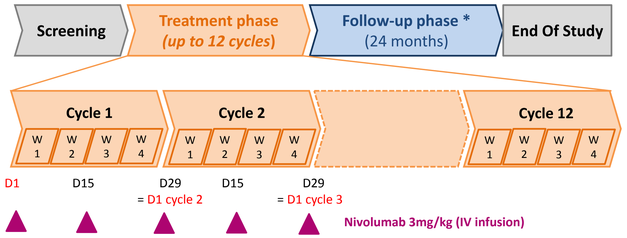
BACKGROUND

- **Salivary Glands Carcinoma of Head and Neck (SGCHN) are rare tumors with no standard systemic treatment for recurrent or Metastatic (R/M) patients.**
- **SCG include many histological subtypes such as Adenoid Cystic Carcinoma (ACC) and non-ACC.**
- **Targeting PDL-1 pathway could be effective in SGCHN as shown by biological studies and clinical case reports.**
- **We conducted a multicenter single arm phase II study to assess the antitumor activity of Nivolumab in ACC and non-ACC patients.**

TRIAL DESIGN

- **Centralised radiological review,** during screening process, **to confirm RECIST 1.1 progression at study entry.**



* If progression RECIST 1.1 during the Follow-up phase, patients can re-start Nivolumab, within the study, for 12 new cycles

STUDY ENDPOINTS

- **Primary endpoint: Non-Progression Rate at 6 months (NPR_{6m}) as per RECIST 1.1**
- **Main secondary endpoints**: ORR, PFS, OS, Safety (NCI CTCAE v4.03), Quality of life (EORTC-QLQ C-30 and H&N35), Tumor Growth Rate, biomarkers analysis

STATISTICAL CONSIDERATIONS

- Using a Fleming's single-stage design (alpha 5% unilateral, power=90%):
- Inacceptable NPR_{6m} is ≤ 20%, promising NPR_{6m} is ≥ 40%, 42 evaluable patients were required in each cohort. ACC and non-ACC results were analysed separately.

If ≤ 13 patients are non-progressive at 6 months => treatment is not effective enough

If ≥ 14 patients are non-progressive at 6 months => treatment is promising.

MAIN INCLUSION CRITERIA

- **R/M SGCHN histologically confirmed (ACC and non-ACC)**
- **Measurable disease using RECIST 1.1 criteria**
- **Progressive disease within 6 months before inclusion as assessed by CT-scan and/or MRI using at least 2 measurements (RECIST 1.1) and confirmed centrally.**
- **Unlimited prior therapy with a 28 days wash-out before starting Nivolumab**

ENROLLMENT

- **98 enrolled patients** between March-17 and March-18

Safety population: 98 patients (**46 ACC**, **52 Non-ACC**)

Efficacy population: 98 patients (**46 ACC**, **52 Non-ACC**), 3 were not evaluated at 6 months for Primary Endpoint.

PATIENTS CHARACTERISTICS		ACC (N = 46)	Non-ACC (N = 52)
Gender	M (%)	26 (56.5%)	29 (55.8%)
	F (%)	20 (43.5%)	23 (44.2%)
Age median (range)		59 (36-80)	63 (29-81)
Metastatic Disease at inclusion	Yes	42 (91.3%)	49 (94.2%)
	No	4 (8.7%)	3 (5.8%)
Locoregional relapse at inclusion	Yes	11 (23.9%)	16 (30.8%)
	No	35 (76.1%)	36 (69.2%)
Prior Treatments		46 (100%)	52 (100%)
Surgery		39 (84.8%)	47 (90.4%)
Radiotherapy		42 (91.3%)	47 (90.4%)
Metastatic Chemotherapy		23 (50%)	34 (65.4%)
Histology for non-ACC (as per local review)			
Mucoepidermoid carcinoma			6 (11.5%)
Adenocarcinoma			28 (53.8%)
Salivary duct carcinoma			2 (3.8%)
Other			16 (30.8%)

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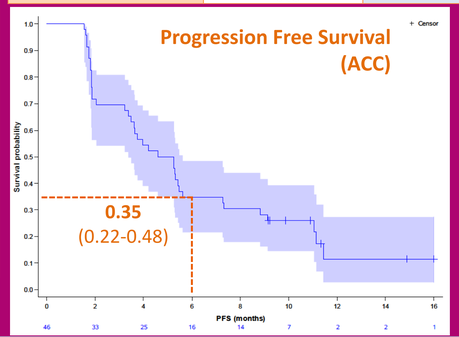
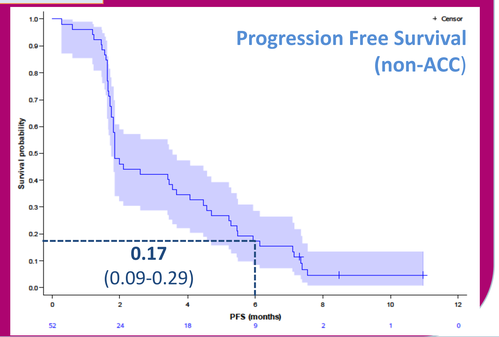
TREATMENT CHARACTERISTICS

	ACC (N = 46)		Non-ACC (N = 52)	
Treatment Status *(December 2018)*	N = 6 (ongoing)	N = 40 (interrupted)	N = 3 (ongoing)	N = 49 (interrupted)
Median Treatment Duration (range)	5.55 months (0.49 – 11.53 months)		3.25 months (0.26 – 11.47 months)	
Median Cycles Number (range)	6 (1 – 12)		4 (1 – 12)	
Median Perfusions Number (range)	12 (1 – 24)		7 (1 – 24)	
Reasons for End of Treatment	N = 40 (100 %)		N = 49 (100 %)	
End of first 12 cycles	5 (12.5%)		2 (4.1%)	
Progressive Disease	29 (72.5%)		40 (81.6%)	
Death	0 (0%)		5 (10.2%)	
Other	6, including 4 (10%) for Adverse Event, 1 (2.5%) for Physician decision and 1 other		Subject Withdrawal: 2 (4.1%)	

ACC	Primary Endpoint	Non-ACC
33.3% [90%CI: 21.8-46.6]	NPR_{6m}	14% [90%CI: 6.8-24.7]
N = 15 / 45	Pts alive without progression at 6 months	N = 7 / 50
N = 46	Secondary Endpoints	N = 52
4.9 [95%CI: 3.4-5.6]	Median PFS (in months)	1.8 [95%CI: 1,7-3,5]
18.1 [95%CI: 12.5-18.1]	Median OS (in months)	9.5 [95%CI: 7.2-NE]
10.77 [3.44- 17.41]	Median FU (in months) [min - max]	8.25 [3.32-14.85]
8.7% [95%CI:2.4-20.8]	Overall Response Rate	3.8% [95%CI:0.5-13.2]





EFFICACY RESULTS

BEST OVERALL RESPONSE	ACC (N = 46)	Non-ACC (N = 52)
Complete Response	0 (0%)	0 (0%)
Partial Response	4 (8.7%)	2 (3.8%)
Stable Disease	26 (56.5%)	22 (42.3%)
Progressive Disease	16 (34.8%)	28 (53.8%)

SAFETY ANALYSIS

- **14/46 ACC patients (30.4%)** and 20/52 (38.5%) non-ACC patients experienced clinical or biological adverse event of grade 3-4
- **36/46 ACC patients (78.3%)** and 26/52 (50%) non-ACC patients experienced at least one adverse event related to treatment, including:
  - **6 AE grade 3-4 in ACC cohort:** lipase increase (N=2), amylase increase, blood bilirubin increase, hypothyroidism, hepatic failure
  - **2 grade 3-4 in non-ACC cohort:** asthenia and amylase increase
- 15 SAE related to 9/46 ACC patients and 15 SAE related to 14/52 non-ACC patients were reported.

Main RELATED adverse events

NCI CTCAE V4.03	ACC N=46	Non-ACC N=52
Asthenia	14 (30.4%)	9 (17.3%)
Hyperthyroidism	8 (17.4%)	0
Diarrhoea	7 (15.2%)	2 (3.8%)
Rash	6 (13%)	3 (5.8%)
Hypothyroidism	5 (10.9%)	1 (1.9%)
Pruritus	5 (10.9%)	7 (13.5%)

CONCLUSION

- **Limited efficacy was observed with Nivolumab in R/M SGCHN patients.**
- **Nivolumab in combination might be of interest and deserves further exploration in ACC patients.**
- **No new safety signals.**

ACKNOWLEDGMENTS

- The patients and their families who accepted to participate in this study
- All the participating investigational sites
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