Phase II Study of Neoadjuvant Cemiplimab Prior to Surgery in Patients with Stage III/IV (M0) Cutaneous Squamous Cell Carcinoma of the Head and Neck (CSCC-HN)

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Background

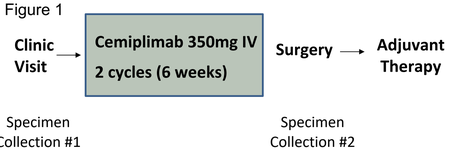
- Cutaneous squamous cell carcinoma (CSCC) harbors a high tumor mutation burden (TMB) due to ultraviolet light-mediated DNA damage, and is highly immune-responsive.
- Cemiplimab, a monoclonal antibody directed against programmed death 1 (PD-1), is approved by the FDA and EMA as treatment for advanced CSCC patients who are not candidates for curative surgery.
- Here we explore the efficacy of neoadjuvant cemiplimab in CSCC- head and neck (HN) patients for whom surgery and radiation was planned.

Methods

- Patients with stage III/IV (M0) (AJCC 8th Ed) radiation-naive CSCC-HN received 2 doses of cemiplimab 350mg IV q3 weeks prior to surgery.
- The primary endpoint was overall response rate (ORR) per RECIST v1.1.
- Secondary endpoints included pathologic response rate (blinded review at MDACC), safety and tolerability (NCI CTCAE v4.03), and analysis of candidate biomarkers from pre- and post-treatment blood and tumor specimens.

Study Schema

Figure 1



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Study Population and Adverse Events

Table 1

Patient #	Gender	Age	Clinical TNM	Clinical Stage	AE* Grade	AE* Details
1	M	88	TxN2b	IV	0	
2	M	64	TxN1	III	1 2	Rash Myalgia
3	M	69	rT2N1	III	1	Rash
4	M	83	rT1N2b	IV	2	Fatigue
5	M	76	T3N2b	IV	0	
6	M	69	TxN2b	IV	1	Pruritis
7	M	62	TxN1	III	0	
8	M	70	rT4N0	IV	0	
9	M	66	TxN2b	IV	0	
10	M	77	rT3N0	III	0	
11	M	66	rT3N0	III	1 2 2	Pruritis Joint Pain Myalgia
12	M	64	T3N0	III	0	
13	M	80	TxN2b	IV	0	
14	M	76	T3N0	III	0	
15	F	71	rT1N2c	IV	1	Rash/Pruritis
16	M	65	TxN2b	IV	0	
17	F	47	T4aN2b	IV	0	
18	M	71	TxN1	III	1	Pruritis
19	M	42	rT3N2b	IV	0	
20	M	61	TxN3b	IV	0	

Responses and Outcomes

Table 2

Imaging Response	Pathologic Response	Adjuvant Therapy	Disease Status
PR	**MPR**	RT**	NED
SD	**pCR**	None	NED
SD	**pCR**	None	NED
PR	**pCR**	None	NED
SD	**MPR**	None	NED
PD	pPR	CRT	NED
PR	**pCR**	None	NED
PD	pSD/PD	RT	NED
PR	pPR	RT	NED
SD	**pCR**	RT	NED
SD	**pCR**	None	NED
PR	**pCR**	None	NED
SD	**pCR**	None	NED
SD	**pCR**	None	NED
SD	pSD/PD	RT	NED
SD	pSD/PD	CRT**	**Progression**
SD	**pCR**	None	NED
SD	pPR	RT	NED
PR	**MPR**	RT	NED

Pathologic Complete Response (pCR)	11/20	55%
Major Pathologic Response (MPR)	3/20	15%
Total	14/20	70%

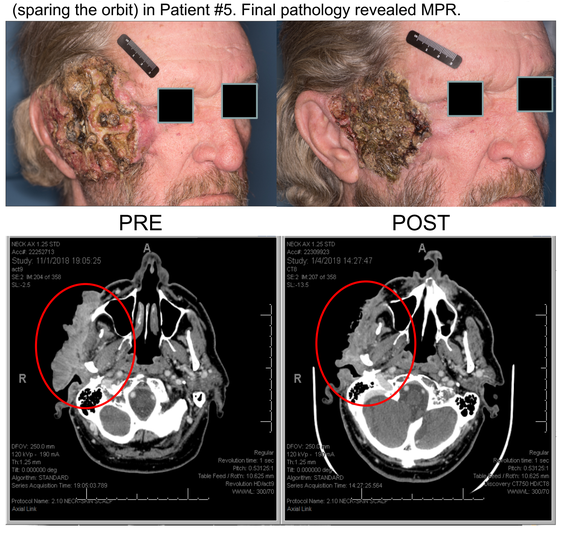
Definitions

Pathologic complete response (pCR); 0% viable
Major pathologic response (MPR): ≤ 10% viable
Pathologic partial response (pPR): 11-50% viable
Pathologic stable /progressive disease (pSD/PD): >50% viable

M, male; F, Female; T, tumor; N, nodal; AE, adverse event; PR, partial response; SD, stable disease, PD, progressive disease; RT, radiation therapy; CRT, chemoradiation; NED, no evidence of disease;
* Treatment-related; ** Did not complete therapy

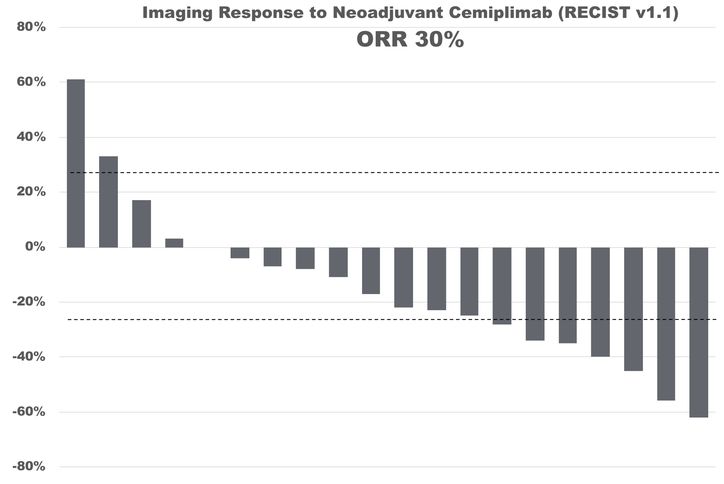
Clinical Response

Figure 2: Significant reduction in tumor allowed for less extensive surgery (sparing the orbit) in Patient #5. Final pathology revealed MPR.



Imaging Responses

Figure 3



Results

From Jul-2018 to Apr-2019, 20 patients (18M, 2F) were enrolled and analyzed by intention-to-treat with median age 69 years (range: 42-88) and stage III (n = 8) or IV (n= 12) disease. Seven (35%) patients experienced grade 1 or 2 adverse events (AEs); 6 (30%) grade 1 rash/pruritis, 2 (10%) grade 2 myalgia, and 1 (5%) grade 2 fatigue. There were no grade ≥ 3 AEs, no surgical delays and no loss of opportunity for curative surgery. ORR by RECIST was 30% (6 partial response, 12 stable disease, 2 progressive disease). pCR was observed in 11 (55%) patients and MPR in an additional 3 (15%) patients. Eleven (55%) patients did not receive planned radiotherapy after surgery based on the pathologic responses. One patient progressed despite surgery and chemoradiation, and was treated palliatively. No other treatment failures have been observed with a median follow up of 3.8 months (range: 1.5-11.2). (Data cutoff 1-Aug-2019) Correlative analyses are in process.

Conclusions

- Neoadjuvant cemiplimab was well-tolerated and induced a pCR or MPR in 70% of stage III/IV (M0) CSCC patients.
  - 55% did not received planned adjuvant radiation based on response.
- A multicenter phase II study is planned to confirm these results and to describe the ability of neoadjuvant cemiplimab to allow less extensive treatment.

Conflicts

Ferarrotto- advisory board (Ayala, Sanofi-Regeneron), consultant (Ayala, Medscape)
Yuan- consultant (Boehringer Ingelheim, Servier, Amgen, Salzman group, Midas Medical Tech)
Glisson- research funding (Pfizer, ISA)
Wong- advisory board (EMD-Serano, Pfizer, Merck, Regeneron)
Rosenthal- advisory board (Merck)
Migden- research support (Regeneron)
Gross- research support (Regeneron), advisory board (PDS Biotechnology, Regeneron)