Monalizumab in combination with cetuximab in patients (pts) with recurrent or metastatic (R/M) head and neck cancer (SCCHN) previously treated or not with PD-(L)1 inhibitors (IO): 1-year survival data.

ID: 1134P

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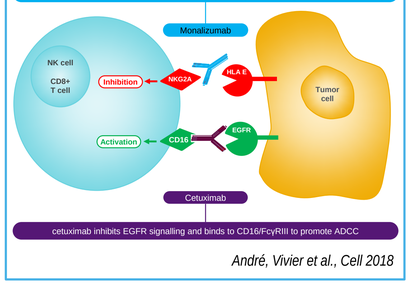
Background

Monalizumab is a first-in-class humanized IgG4 checkpoint inhibitor targeting NKG2A receptors expressed on subsets of CD8+ T cells & NK cells.

Cetuximab inhibits oncogenic EGFR signaling and binds to CD16/FcγRIII to promote ADCC.

NK cell stimulation with Monalizumab may enhance ADCC induced by cetuximab and thereby provide greater antitumor activity than cetuximab alone. [1-5]

Blocking NKG2A and triggering CD16 constitutes a novel form of dual immunotherapy that includes blockade of a novel immune checkpoint.



André, Vivier et al., Cell 2018

Patient and disease Characteristics

Patient and disease Characteristics		All n=40 n (%)	IO Naive n=22 n (%)	IO Pretreated n=18 n (%)
Age, median [range]		64 [34-76]	61 [34-75]	66 [52-76]
Sex	Female	12 (30%)	10 (45%)	2 (11%)
	Male	28 (70%)	12 (55%)	16 (89%)
ECOG	0	14 (35%)	7 (32%)	7 (39%)
	1	26 (65%)	15 (68%)	11 (61%)
HPV status	Positive	6 (15%)	0 (0%)	6 (33%)
	Negative	30 (75%)	19 (86%)	11 (61%)
	Unknown	4 (10%)	3 (14%)	1 (6%)
Tobacco	Never	7 (18%)	4 (18%)	3 (17%)
	Former	28 (70%)	14 (64%)	14 (78%)
	Current	5 (12%)	4 (18%)	1 (6%)
Alcohol	Never	7 (18%)	4 (18%)	3 (17%)
	Former	19 (48%)	9 (41%)	10 (56%)
	Current	14 (35%)	9 (41%)	5 (28%)
Tumor site	Oral cavity	17 (42.%)	12 (55%)	5 (28%)
	Oropharynx	13 (33.%)	5 (23%)	8 (44%)
	Larynx	6 (15%)	3 (15%)	3 (17%)
	Hypopharynx	3 (8%)	2 (9%)	1 (6%)
	Nasopharynx	1 (2.%)	0 (0%)	1 (6%)
Type of recurrence	Local	19 (48%)	14 (64%)	5 (28%)
	Distant	21 (52%)	8 (36%)	13 (72%)
Number of previous lines	1	19 (48%)	19 (86%)	0 (0%)
	2	14 (35%)	3 (14%)	11 (61%)
	≥3	7 (18%)	0 (0%)	7 (39%)

Study Design

Multicenter single arm phase II trial to evaluate the combination of monalizumab and cetuximab in patients with recurrent and/or metastatic squamous cell carcinoma of the head and neck cancer (R/M SCCHN) (NCT02643550).

Key eligibility criteria

- R/M SCCHN histologically confirmed, HPV (+) or HPV (-)
- Progression (PD) after platinum-based chemotherapy
- Maximum of 2 prior systemic treatment regimens for R/M disease
- Prior IO allowed
- Prior cetuximab allowed if for locally advanced disease with no PD for at least 4 months

Treatment

Monalizumab (10 mg/kg Q2W) + Cetuximab (approved dosage) until progression or unacceptable toxicity

Primary objective

- Objective Response Rate (ORR) RECIST 1.1

Secondary objectives

- Duration of Response (DoR)
- Progression Free Survival (PFS)
- Overall Survival (OS)
- Safety

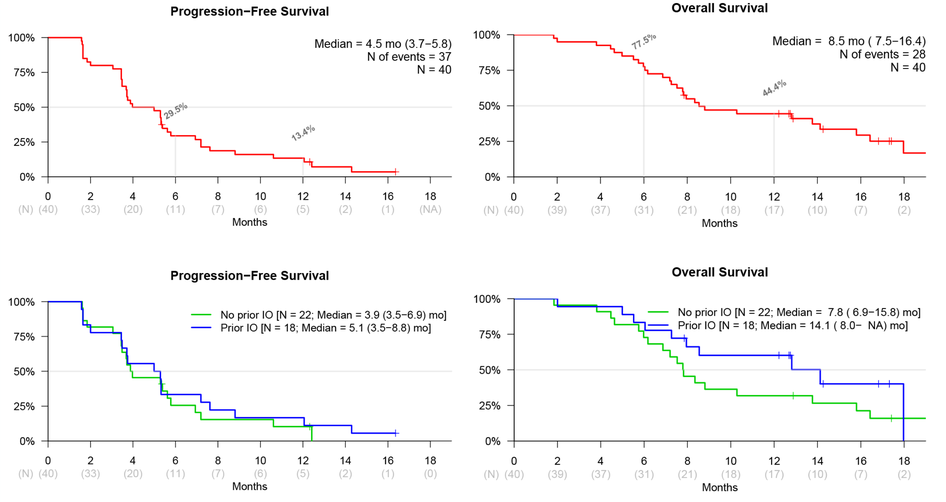
Exploratory objectives

- Translational analyses

Main results

- As of April 30, 2019, 40 patients were enrolled in France and US.
- The predefined number of at least 8 responses to declare the trial positive was reached with an ORR of 27.5% (36% and 17% in IO naïve and IO pretreated pts, respectively)[8].
- Responses were observed in platinum-resistant patients, HPV positive and negative patients, and IO naïve and IO pretreated patients.
- With a median follow-up of 17 months (mo), median OS is 8.5 mo with a trend for improved survival in IO-pretreated pts (14.1 mo in IO-pretreated pts and 7.8 in IO naïve pts, respectively), and 12 mo OS rate of 44% (60% in IO-pretreated and 32% in IO naïve pts, respectively).
- Cross-trial comparisons should be exercised with caution; however, numerically these figures compare favorably with historical data in patients with R/M SCCHN for cetuximab alone [6-7] (ORR, 12.6%, median PFS 2.3 mo, median OS 5.6 mo).

PFS and OS in all patients and by previous IO



Acknowledgments

- We thank the patients who participated in the IPH2201-203 study and their families, the referring physicians, co-investigators and clinical study site staff at the participating institutions.

Efficacy results

	All n=40	IO Naïve n=22	IO Pretreated n=18
Best overall response			
Complete Response n (%)	1 (2.5%)	1 (4.5%)	0 (0%)
Partial response n (%)	10 (25%)	7 (32%)	3 (17%)
Stable disease n (%)	22 (55%)	10 (45.5%)	12 (66%)
Progressive disease n (%)	7 (17.5%)	4 (18%)	3 (17%)
Overall Response Rate % [95%CI]	27.5% [16-43]	36% [20-57]	17% [6-39]
Disease Control Rate at 24 weeks [95%CI]	37.5% [24-53]	36% [20-57]	39% [20-61]
Median Time to Response [95%CI]	1.6 months [1.5- 3.9]	1.7 months [1.5- 3.9]	1.6 months [1.6- 3.1]
Median Duration of Response [95%CI]	5.6 months [4.2-NR]	5.3 months [4.2-NR]	5.6 months [3.7-NR]
Median progression free survival [95%CI]	4.5 months [3.5-5.8]	3.9 months [3.5-6.9]	5.1 months [3.5-8.8]
Median overall survival (OS) [95%CI]	8.5 months [7.5.-16.4]	7.8 months [6.9-15.8]	14.1 months [8.0.-NR]
12 months OS [95%CI]	44% [31-63]	32% [17-59]	60% [41-88]

Safety results

- Most adverse events (AEs) (91%) were Grade 1-2 in severity.
- There were no fatal AEs.
- The most common (> 10% of patients) AEs related to monalizumab or cetuximab were dermatitis acneiform, hypomagnesemia, skin fissures, paronychia, dry skin, pruritus, fatigue, hypophosphatemia, stomatitis, rash, headache, diarrhea, and hypokalemia.
- 8 patients (20%) experienced a Grade 3-4 AE deemed to be related to monalizumab (3 hypophophatemia, 1 stomatitis, 1 headache, 1 skin fissure, 1 colitis/interstitial lung disease, 1 lymphocyte count decrease).
- There was no potentiation of cetuximab side-effects.

Conclusions

- In a cohort of 40 patients of heavily pretreated SCCHN patients, monalizumab and cetuximab combination demonstrated an acceptable safety profile, a high response rate (27.5%), and promising OS (median 8.5 mo and 12 mo survival rate 44%).
- An additional cohort of 40 patients with R/M SCCHN who have received both platinum-based chemotherapy and anti-PD(L)1 is being enrolled in this study to confirm the preliminary results seen in this subgroup, a population with a continued high unmet medical need.

The study is sponsored by Innate Pharma and supported by AstraZeneca.

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