POSTER
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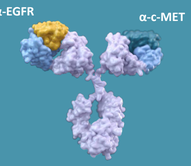
Efficacy and safety of MCLA-129, an anti-EGFR/c-MET bispecific antibody, in head and neck squamous cell carcinoma (HNSCC)



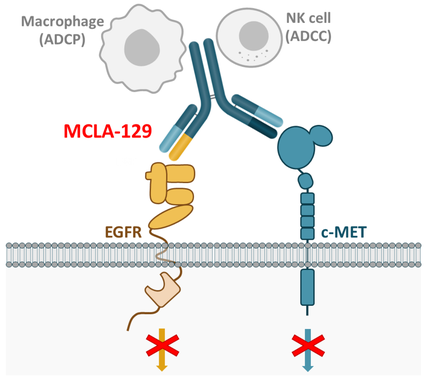
Paolo Bossi,[1] Gabriele Minuti,[2] **Irene Braña**,[3] Victor Moreno Garcia,[4] Valentina Boni,[5] Philippe Jamme,[6] Justin Call,[7] Benjamin A. Barasa,[8] Chris Yan,[8] Petra Doze,[8] Andrew K. Joe,[8] Gianluca Laus,[8] Amaury Daste[9]

[1]IRCCS Humanitas Research Hospital, Rozzano, Italy; [2]Istituto Nazionale Tumori "Regina Elena", Roma, Italy; [3]Vall d'Hebron University Hospital/Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain; [4]START Madrid-FJD, Hospital Fundación Jiménez Díaz, Madrid, Spain; [5]Hospital Universitario Quirónsalud, Madrid, Spain; [6]Hôpital Albert Calmette, Lille, France; [7]Mountain Region Family Medicine, PC, West Valley City, UT, USA; [8]Merus N.V., Utrecht, The Netherlands; [9]CHU Hopitaux de Bordeaux – Hôpital Saint-André, Bordeaux, France.

INTRODUCTION

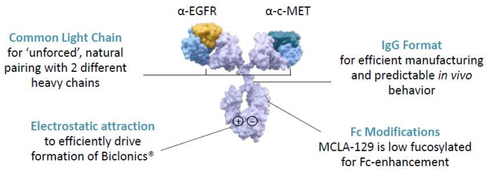
- Dysregulation of the epidermal growth factor receptor (EGFR) and the hepatocyte growth factor receptor (c-MET) drives cancer cell proliferation, survival, and invasion in many cancer types (**Figure 1**), including head and neck squamous cell carcinoma (HNSCC)[1-2]
- MCLA-129 is a humanized bispecific antibody targeting EGFR and c-MET, with multiple mechanisms of action, including inhibition of EGFR and c-MET signaling (**Figure 1** and **Figure 2**), antibody-dependent cellular phagocytosis (ADCP), and enhanced antibody-dependent cellular cytotoxicity (ADCC)[3]
- In a Phase 1/2 trial (ClinicalTrials.gov Identifier: NCT04868877), the initial recommended Phase 2 dose (RP2D) of MCLA-129 was established at 1500 mg intravenously (IV) every 2 weeks (Q2W) with 28-day cycles[4]
- Here, MCLA-129 is being further explored as a monotherapy in patients with recurrent or metastatic (RM) HNSCC

Figure 1 | MCLA-129 mechanism of action



ADCC: enhanced antibody-dependent cellular cytotoxicity; ADCP: antibody-dependent cellular phagocytosis; c-MET: hepatocyte growth factor receptor; EGFR: epidermal growth factor receptor; NK: natural killer cell.
EGFR and c-MET activate similar intracellular signal transduction pathways to drive cancer cell proliferation, survival, and invasion. MCLA-129 inhibits ligand-dependent phosphorylation of EGFR and c-MET to inhibit downstream signaling pathways and recruits immune effector cells that drive ADCP and ADCC.

Figure 2 | MCLA-129 structure

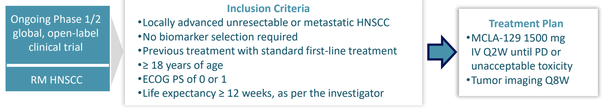


c-MET: hepatocyte growth factor receptor; EGFR: epidermal growth factor receptor; Fc: fragment crystallizable; IgG: immunoglobulin G.

TRIAL DESIGN AND OBJECTIVES

- This is an ongoing, Phase 1/2, global, open-label, multicenter trial in adult patients with locally advanced unresectable or metastatic solid tumors, including HNSCC (**Figure 3**)
  - Eligible patients had a clinical diagnosis of RM HNSCC and had previously relapsed on or were not candidates for approved therapies

Figure 3 | MCLA-129 development program



Endpoints and Population

Primary endpoint
ORR[a] using RECIST v1.1 per investigator assessment

Secondary endpoints
DoR, DCR,[b] PFS, OS, and safety[c]

Primary analysis population
≥ 2 MCLA-129 cycles, measurable disease at baseline, and ≥ 1 postbaseline scan

Enrollment and Analysis

Data cutoff date
August 10, 2023

Primary efficacy analysis population
20 patients with RM HNSCC

Enrollment
22 patients with RM HNSCC

2 patients without a postbaseline scan and who discontinued the study due to reasons other than PD were excluded

AE: adverse event; CR: complete response; CTCAE: Common Terminology Criteria for Adverse Events; DCR: disease control rate; DOR: duration of response; ECOG PS: Eastern Cooperative Oncology Group performance status; HNSCC: head and neck squamous cell cancer; IV: intravenous; MedDRA: *Medical Dictionary for Regulatory Activities*; ORR: overall response rate; OS: overall survival; PFS: progression-free survival; PD: progressive disease; PR: partial response; Q2W: every 2 weeks; Q8W: every 8 weeks; RECIST: Response Evaluation Criteria in Solid Tumors; RM: recurrent or metastatic; SD: stable disease.
[a]Defined as the proportion of patients with a best overall response of CR or PR per RECIST v1.1 based on investigator assessment in patients with measurable disease at baseline.
[b]Defined as the proportion of patients with CR, PR, or SD as the best overall response per RECIST v1.1 based on investigator assessment.
[c]AEs were coded using MedDRA v24.1 and graded using CTCAE v5.0.

PATIENTS WITH RM HNSCC

- As of the data cutoff date of August 10, 2023, 22 patients with RM HNSCC were treated with MCLA-129
- Patient demographic and disease characteristics are shown in **Table 1**
- Median age was 62 years (range, 32–73)
- Primary tumor locations were nasal cavity/sinus (14%), oropharynx (14%), hypopharynx (10%), larynx (14%), oral cavity (10%), nasopharynx (4%), and other (36%)
- Patients had a median of 3 prior systemic therapies, including anti-PD-(L)1 (91%) and platinum-based chemotherapy (100%)
  - 8 (36%) patients received cetuximab in the RM setting
- 6 (27%) patients were continuing treatment at the data cutoff date

Table 1 | Demographic and baseline disease characteristics

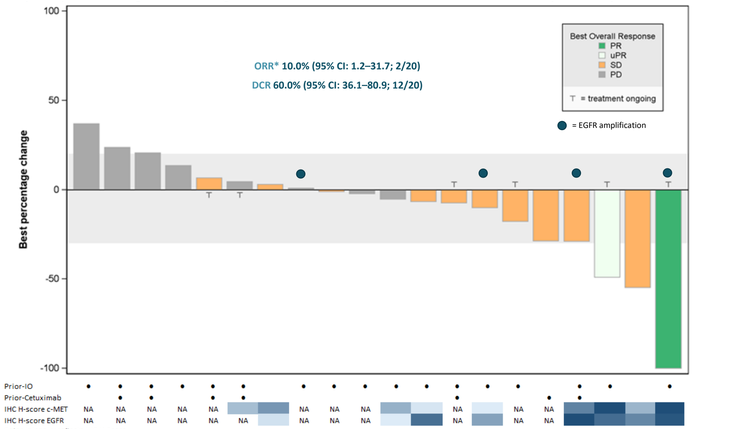
Characteristic	N = 22
Age, median (range), years	62 (32–73)
Gender, male / female, n (%)	17 (77) / 5 (23)
Race, White / other, n (%)	16 (73) / 6 (27)
ECOG PS, 0 / 1, n (%)	10 (45) / 12 (55)
Number of metastatic disease sites, median (range)[a]	2.5 (1–6)
Prior lines of systemic therapy, median (range)	3 (1–7)
Prior platinum-based chemotherapy, n (%)	22 (100)
Prior-IO (anti-PD(L)-1), n (%)	20 (91)
Prior cetuximab in the RM setting, n (%)	8 (36)

ECOG PS: Eastern Cooperative Oncology Group performance status; IO: immuno-oncology; PD-(L): programmed cell death-ligand; RM: recurrent or metastatic.
[a]In 16 evaluable patients.

ANTITUMOR ACTIVITY IN RM HNSCC

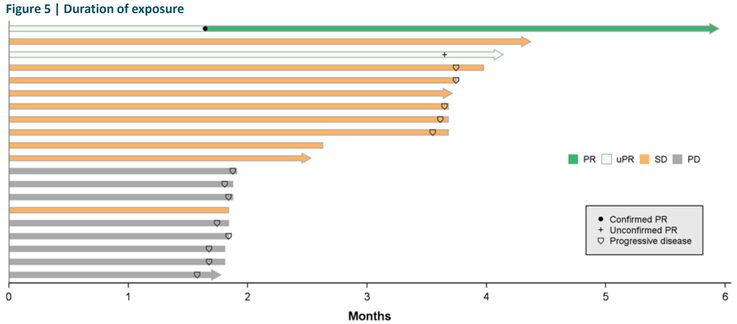
- Of 20 evaluable patients, partial response (PR) was observed in 2 (10%) patients (**Figure 4**):
  - 1 confirmed PR, still receiving treatment at data cutoff date; The duration of response (DOR) was 3.4+ months (**Figure 5**)
  - 1 unconfirmed PR, confirmed after the data cutoff date; treatment still ongoing
  - The disease control rate (DCR) was 60% (95% CI: 36–81) by RECIST v1.1 per investigator assessment
- High EGFR and c-MET expression was observed in baseline tissue from 2 patients with PR. EGFR amplification was detected by next-generation sequencing of baseline circulating-tumor DNA in 4 patients, including the patient with confirmed PR (**Figure 4**). Further biomarker analysis is ongoing

Figure 4 | Best percent change in sum of target lesion diameter from baseline and EGFR and c-MET expression by IHC



CI: confidence interval; DCR: disease control rate; IHC: immuno-histochemistry; IO: immuno-oncology; NA: not available; ORR: overall response rate; PD: progressive disease; PR: partial response; SD, stable disease; uPR: unconfirmed partial response (initial assessment of PR for a patient on treatment). *ORR is the proportion of confirmed and unconfirmed responders out of the primary efficacy analysis population.

Figure 5 | Duration of exposure



PD: progressive disease; PR: partial response; SD, stable disease; uPR: unconfirmed partial response.

SAFETY PROFILE

- Among 22 patients treated with MCLA-129, 16 (73%) patients experienced infusion-related reactions (IRRs, composite term), 3 (14%) patients with grade ≥3 IRRs; all IRRs occurred on Day 1 of Cycle 1 (C1D1; **Table 2**)
- Skin toxicity (composite term) was common, occurring in 19 (86%) patients, with only 3 (14%) patients experiencing grade ≥ 3 events
- No cases of interstitial lung disease were reported
- No treatment-emergent adverse events (TEAEs) of grade 5 were observed
- Among patients evaluable for immunogenicity (n = 12), no anti-MCLA-129 antibodies were detected

Table 2 | Safety profile in patients with RM HNSCC (N = 22)

	Treatment-related TEAEs[a] n (%)		TEAEs irrespective of causality >10%, n (%)	
	All grades	Grade ≥3	All grades	Grade ≥3
≥1 TEAE	**21 (95)**	**6 (27)**	**22 (100)**	**8 (36)**
Folliculitis	9 (41)	1 (5)	9 (41)	1 (5)
Nausea	7 (32)	0	7 (32)	0
Erythema	7 (32)	0	7 (32)	0
Hypotension	6 (27)	1 (5)	6 (27)	1 (5)
Rash	5 (23)	1 (5)	5 (23)	1 (5)
Dermatitis acneiform	4 (18)	0	5 (23)	0
Hypoalbuminemia	3 (14)	0	5 (23)	0
Epistaxis	3 (14)	0	4 (18)	0
Blood calcium decreased	3 (14)	0	4 (18)	0
Vomiting	2 (9)	0	4 (18)	0
Edema peripheral	1 (5)	1 (5)	3 (14)	1 (5)
Mucosal inflammation	3 (14)	0	3 (14)	0
Maculopapular rash	3 (14)	0	3 (14)	0
Skin fissures	3 (14)	0	3 (14)	0
Protein total decreased	3 (14)	0	3 (14)	0
Anemia	2 (9)	0	3 (14)	0
ALT increased	2 (9)	0	3 (14)	0
Amylase increased	2 (9)	0	3 (14)	0
Skin ulcer	2 (9)	0	3 (14)	0
Asthenia	1 (5)	0	3 (14)	0
Cough	1 (5)	0	3 (14)	0
Constipation	1 (5)	0	3 (14)	0

ALT: alanine aminotransferase; HNSCC: head and neck squamous cell cancer; RM: recurrent or metastatic; TEAE: treatment-emergent adverse event.
[a]Related TEAEs include TEAEs with relationship missing, related, or possibly related.

CONCLUSIONS

- **MCLA-129 demonstrated single-agent efficacy in heavily pretreated HNSCC on par with a variety of EGFR inhibitors approved and in clinical development:**
  - Among 20 patients observed, 1 confirmed PR and 1 unconfirmed PR were observed (10%)
  - DCR: 60% (95% CI: 36–81; n = 12)
  - Median duration of exposure: 2.2 months (0.5–6.0)
- **This cohort confirmed the well-tolerated safety profile of MCLA-129 monotherapy**

References

1. Kalyankrishna S, Grandis JR. *J Clin Oncol*. 2006;24(17):2666-2672.
2. Raj S, et al. *Mol Cancer*. 2022;21(1):31.
3. De Gorter DJ, et al. *Cancer Res*. 2021;81(13 suppl):952.
4. Ou SH, et al. *Eur J Cancer*. 2022;174(suppl 1):S122.

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