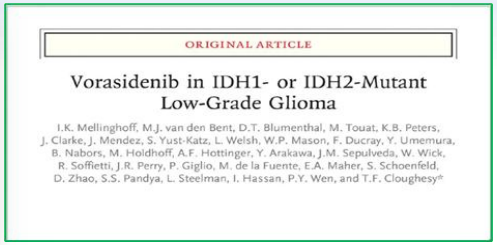
VII SIMPOSIO NACIONAL
de ONCOLOGÍA de PRECISIÓN
Vigo, 20 y 21 de febrero de 2025

LO MEJOR DE 2024:
CABEZA y CUELLO, SNC y TIROIDES

Dr. Edel del Barco Morillo
Servicio de Oncología Médica
CAUSA-IBSAL

VII SIMPOSIO NACIONAL de ONCOLOGÍA de PRECISIÓN

SNC 2023



ORIGINAL ARTICLE

Vorasidenib in IDH1- or IDH2-Mutant Low-Grade Glioma

I.K. Mellinghoff, M.J. van den Bent, D.T. Blumenthal, M. Touat, K.B. Peters, J. Clarke, J. Mendez, S. Yust-Katz, L. Welsh, W.P. Mason, F. Ducray, Y. Umemura, B. Nabors, M. Holdhoff, A.F. Hottinger, Y. Arakawa, J.M. Sepulveda, W. Wick, R. Soffietti, J.R. Perry, P. Giglio, M. de la Fuente, E.A. Maher, S. Schoenfeld, D. Zhao, S.S. Pandya, L. Steelman, I. Hassan, P.Y. Wen, and T.F. Cloughesy*

SNC 2024

✔ Phase II/III Clinical Trial Results for Paxalisib in Glioblastoma

Estudio PLATAFORMA_GBM AGILE .

Paxalisib (60 mg/día). **Inhibidor selectivo PI3K/mTOR inhibitor. Pasa la barrera hematoencefálica**.

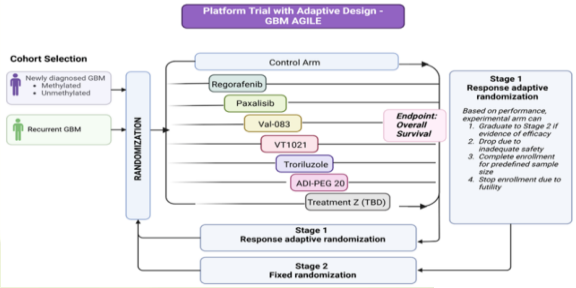
Población: 313 p. con GBM MGMT no metilado.

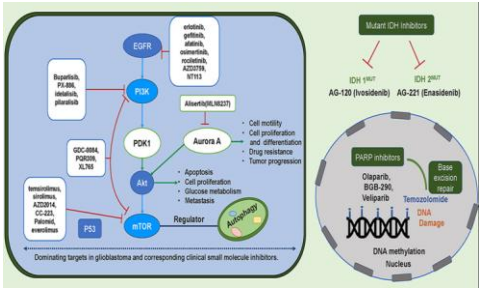
Sin datos de toxicidad grave

EN 1L: MEJORA SP en 3.6 meses. (15.54 meses vs 11,8 meses_temozolamida)

-- > **En Enf. Recurrente: No diferencias frente al estándar de cuidado.**

Datos concordantes con fase II (Wen 2022) mediana de SG fue de 15,7 meses en comparación con los 12,7 meses informados históricamente con temozolomida en este grupo de pacientes





FDA (Estados Unidos):

Designación de Medicamento Huérfano.

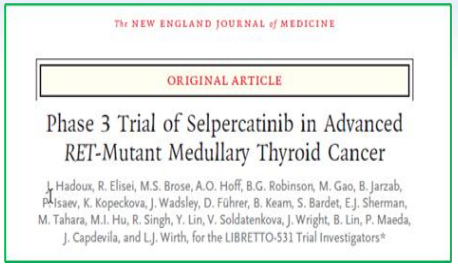
Designación de Vía Rápida: Glioblastoma Metastásico

Designación de Enfermedad Pediátrica Rara

Agencia Europea del Medicamento (EMA):No

VII SIMPOSIO NACIONAL
de ONCOLOGÍA de PRECISIÓN

TIROIDES 2023


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Phase 3 Trial of Selpercatinib in Advanced *RET*-Mutant Medullary Thyroid Cancer

J. Hadoux, R. Elisei, M.S. Brose, A.O. Hoff, B.G. Robinson, M. Gao, B. Jarzab, P. Isaev, K. Kopeckova, J. Wadsley, D. Führer, B. Keam, S. Bardet, E.J. Sherman, M. Tahara, M.I. Hu, R. Singh, Y. Lin, V. Soldatenkova, J. Wright, B. Lin, P. Maeda, J. Capdevila, and L.J. Wirth, for the LIBRETTO-531 Trial Investigators*

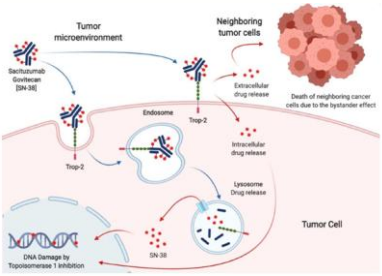
TIROIDES 2024

✔ **Diferenciado de tiroides refractario al radioyodo.**

ESMO 2024. DATOS VIDA REAL EN 337 pacinetes

Se refuerza el uso de lenvatinib, estudio SELECT. (vs placebo)

SLE 18 vs 3.6 MESES. **TR 65% vs 1.5%.** **RC 20%**



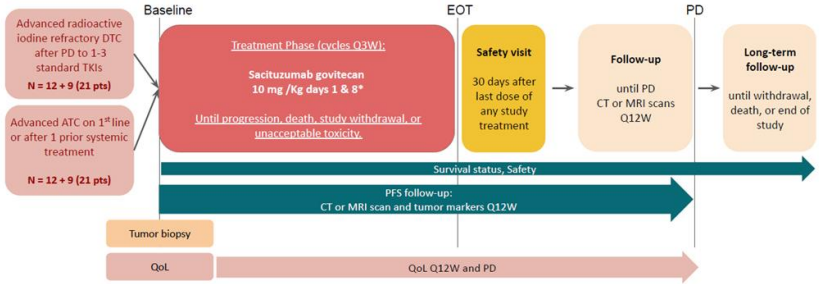
✔ DISEÑO **ESTUDIO SETTHY. FASE II.**

GETNE-T2318

POSTER ASCO 2024. Grupo Dr. Capdevilla

AC CONJUGADO: Sacituzumab govitecan

Carcinoma de tiroides refractario al yodo radiactivo avanzado o metastásico
Carcinoma de tiroides anaplásico



Primary endpoint: Objective Response Rate (ORR) according to RECIST 1.1

Secondary endpoints: Disease control rate (DCR), Duration of Response (DoR), Progression-free Survival (PFS), Overall Survival (OS), Safety, Patient reported outcomes, Translational research

SALIVARES

✔ MYTHOS. FASE II. **TRASTUZUMAB-DERUXTECAN**

Cáncer poco frecuente (8 % de los cánceres de HN)

Mala respuesta modesta al QT

Sobreexpresión de HER2 en algunos subtipos histológicos: más alta en el carcinoma de los conductos salivales (43,0 %)

Las terapias dirigidas a HER2, como trastuzumab + docetaxel, muestran resultados prometedores, con una aprobación limitada.

Sin experiencia a la progresión a terapias previas de HER2 y baja expresión de HER2 .

MYTHOS Trial: Study design

Open-label, multi-center, investigator-initiated phase II trial of T-DXd for HER2 expressing SGC

HER2 screening
(central assessment)
Archive or biopsy sample
IHC 1+ ~ 3+

→ Registration

Cohort 1 (N = 19)
HER2-positive
IHC 3+, IHC 2+/ISH +*

Cohort 2 (N = 33)
HER2-low expression
IHC 2+/ISH -, IHC 1+

T-DXd
5.4 mg/kg Q3W IV

- Trial sites: 5 hospitals in Japan
- Enrollment: Jan 2022 to Oct 2022 for cohort 1 (19 patients enrolled)

Study population:
- Recurrent or metastatic salivary gland cancer
- HER2 expressing (IHC 1+ ~ 3+) by central assessment
- Prior anti-HER2 treatment was allowed
- Excluded patients with a history of ILD/pneumonitis

Primary endpoint:
- Confirmed ORR by ICR

Secondary endpoint:
- PFS, OS, ORR by investigator, DCR, Safety, etc.

Primary analysis of ORR by ICR in cohort 1
- Data cutoff: Oct 11, 2023 (Median follow-up:15.0 months)

Statistical consideration for cohort 1:
- Planned sample size: 19 patients
- A threshold ORR of 25%, an expected ORR of 65%, 90% power, and a two-sided alpha of 0.05 using the binomial test, assuming 2 dropout patients.

Abbreviations: T-DXd, trastuzumab deruxtecan; SGC, salivary gland cancer; IHC, immunohistochemistry; ISH, In situ hybridization; ILD, interstitial lung disease; ICR, independent central review; ORR, objective response rate; DCR, disease control rate; PFS, progression-free survival; OS, overall survival
*IHC staining used Ventana Ultraview Pathway HER2 (4B5), and ISH (FISH) used the PATHVISION® HER-2 DNA Probe Kit with the ASCO-CAP 2018 algorithm for breast cancer.

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✔ MYTHOS. FASE II. TRASTUZUMAB-DERUXTECAN

Se presentan datos de altos expresores de HER2

Tasa RO en 19 pacientes: 68%. RC 10%. TASA DE CONTROL: 82% SIN PROGRESIONES

8 pacientes ya habían recibido TRASTUZUMAB

SALIVARES

Best objective response (FAS* of cohort 1)

Response assessment	By ICR N = 19	By investigator N = 19
Response, n (%)		
confirmed CR	2 (10.5)	2 (10.5)
confirmed PR	11 (57.9)	13 (68.4)
SD	6 (31.6)	4 (21.1)
PD	0 (0)	0 (0)
NE	0 (0)	0 (0)
Confirmed ORR, % (95% CI)	68.4 (43.4, 87.4)**	78.9 (54.4, 93.9)
DCR, % (95% CI)	100 (82.4, 100)	100 (82.4, 100)

Abbreviations: FAS, full set analysis; ICR, independent central review; CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease; NE, not evaluable; ORR, objective response rate (CR + PR); DCR, disease control rate (CR + PR + SD); CI, confidence interval.
*Patients who were enrolled and received at least one dose of the investigational drug, excluding those with major protocol deviations, GCP violations, or post-enrollment ineligibility were defined as FAS (N = 19). Efficacy analysis was performed on the FAS. **The lower 95% CI limit for ORR was above the threshold of 25%.

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Overall safety summary (SAS*)

n (%)	All patients (N = 19)
TEAEs	19 (100%)
Drug-related	19 (100%)
Grade ≥ 3 TEAEs	9 (47.4%)
Drug-related	9 (47.4%)
Serious TEAEs, n (%)	4 (21.1%)
Drug-related	3 (15.8%)
TEAEs leading to T-DXd discontinuation	5 (26.3%)
ILD/Pneumonitis**	5 (26.3%)
Drug-related	5 (26.3%)
TEAEs leading to dose reduction	7 (36.8%)
Drug-related	7 (36.8%)
TEAEs leading to dose interruption	10 (52.6%)
Drug-related	7 (36.8%)
TEAEs leading to death	0 (0%)
Drug-related	0 (0%)

Abbreviations: SAS, safety analysis set; TEAEs, treatment-emergent adverse events; T-DXd, trastuzumab deruxtecan; ILD, interstitial lung disease.
*Patients who received at least one dose of the investigational drug were defined as SAS (N =19). Safety analysis was performed on the SAS.
**Assessed by investigator.

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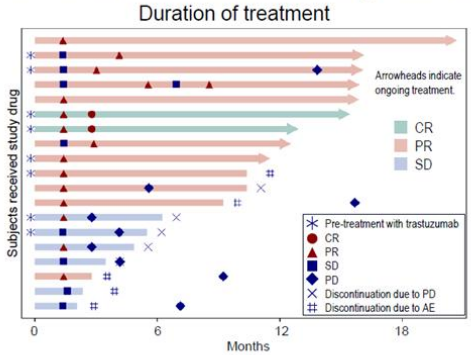
Duration of treatment (duration of response by ICR) (FAS†)



Median duration of treatment (DOT)* (n = 19): 10.4 months (range, 2.1-20.7)

Median duration of response (DOR)** (n = 15): 14.3 months (95%CI, 4.2-NE)

Abbreviations: ICR, independent central review; FAS, full set analysis; CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease; AE, adverse effect; DOT, duration of treatment; DOR, duration of response; CI, confidence interval; NE, not estimable.

†Patients who were enrolled and received at least one dose of the investigational drug, excluding those with major protocol deviations, GCP violations, or post-enrollment ineligibility were defined as FAS (N = 19).
*DOT was measured from the initiation of the treatment until its discontinuation.
**DOR was measured from the time of initial response (PR/CR) to the first occurrence of PD, clinical progression or death, whichever occurred first and assessed by ICR. The DOR analysis comprised 15 patients, including two who had SD but initially achieved PR and then experienced PD before PR confirmation.

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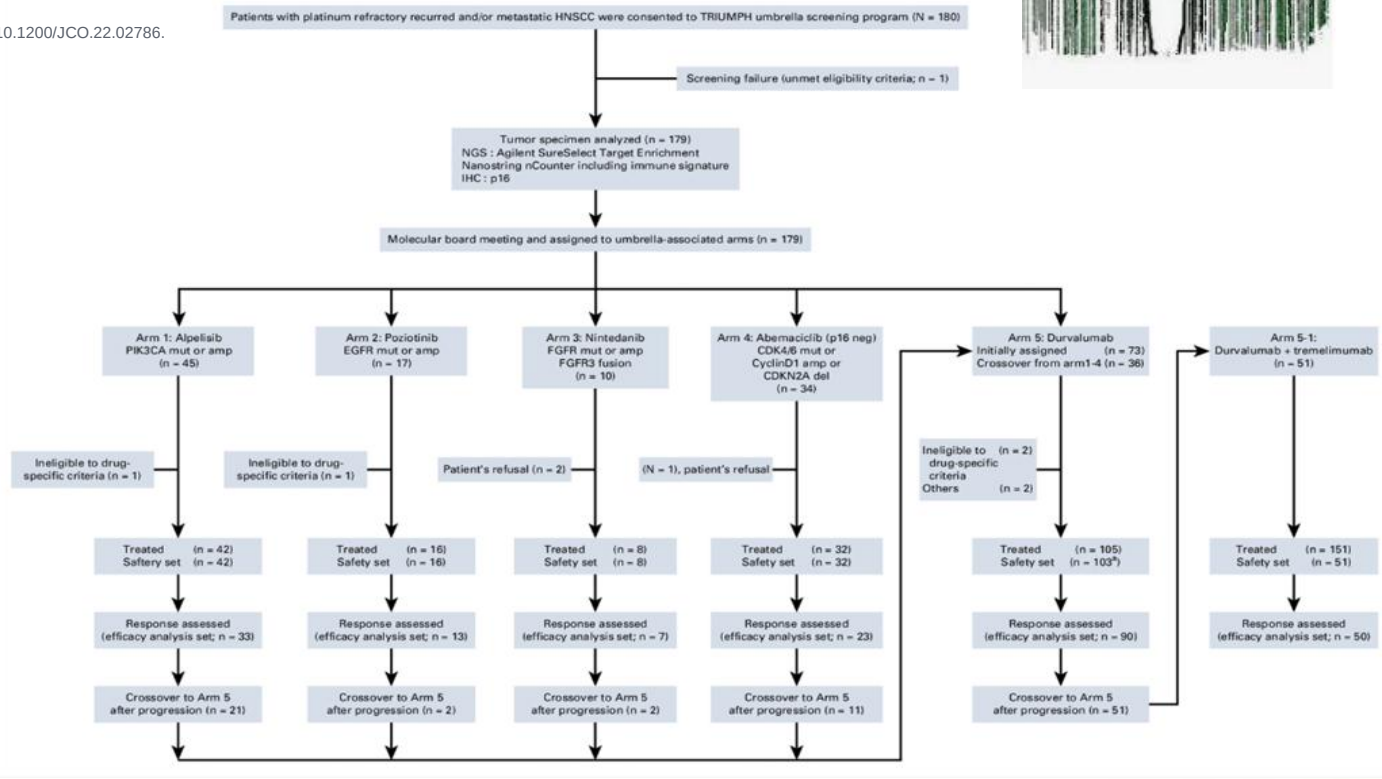
CABEZA y CUELLO

J Clin Oncol. 2024 Feb 10;42(5):507-517. doi: 10.1200/JCO.22.02786.

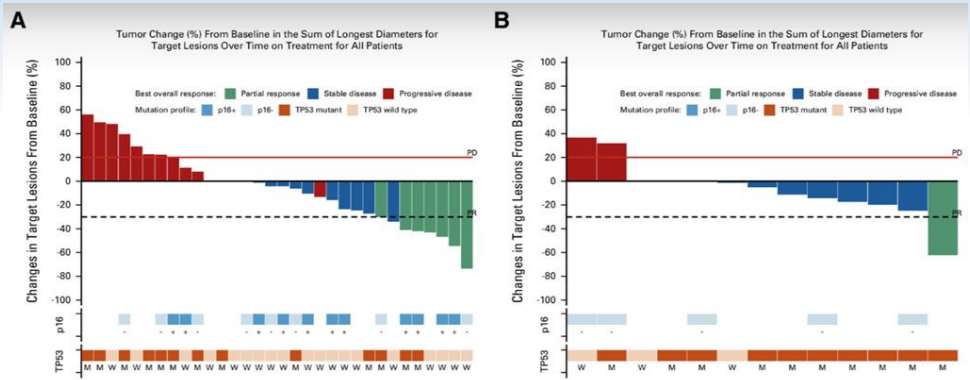
Personalized

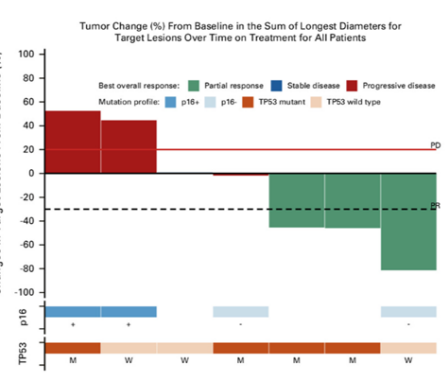
Biomarker Based Umbrella Trial

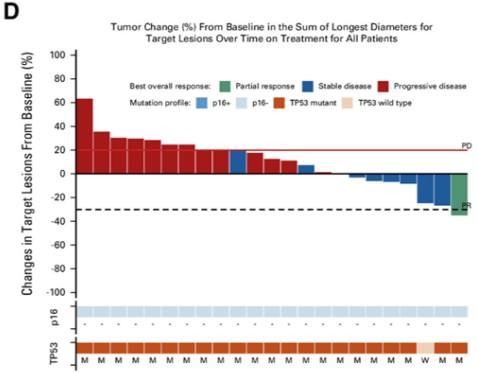
for Patients With Recurrent or Metastatic Head and Neck Squamous Cell Carcinoma: KCSG HN 15-16 TRIUMPH Trial

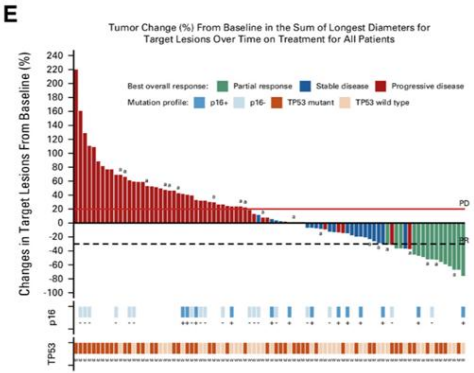


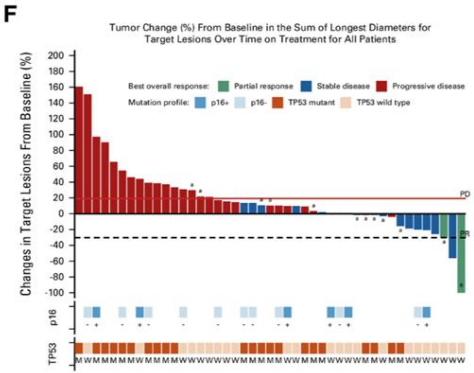
Octubre de 2017 y agosto de 2020. Screening molecular a 180 pacientes HN recurrente/M platinoR











TASA DE RP:

21%	ALPELISIB (PIK3CA)
0%	POZIOTINIB (EGFR)
43%	NINTEDANIB (FGFR)
0%	AMEBACICLIB (CICLINAS)
15%	DURVALUMAB
2 %	DURVA-TREME

For Squamous Cancers, the Streetlamps Shine on Occasional Keys, Most Baskets Are Empty, and the Umbrellas Cannot Keep Us Dry: A Call for New Models in Precision Oncology

D. Neil Hayes, MD, MPH[1]; Oluchukwu Oluoha, MD[2]; and David L. Schwartz, MD[1]

DOI https://doi.org/10.1200/JCO.23.01758

Sesgo molecular
En el caso de generar resultados, son relevantes solo para una pequeña proporción de pacientes
No abordan la necesidad terapéutica del resto de pacientes

Complejidad logística:
centralización de pruebas
asignación a múltiples brazos terapéuticos

Riesgo de sobreinterpretar resultados positivos en subgrupos reducidos

DIANAS NO MOLECULARES

CABEZA y CUELLO_ESCAMOSO

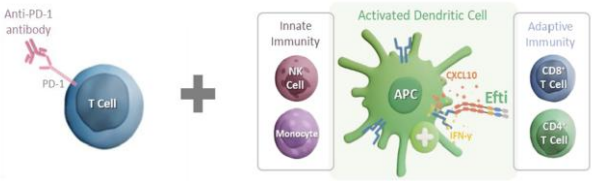
EFTILAGIMOD

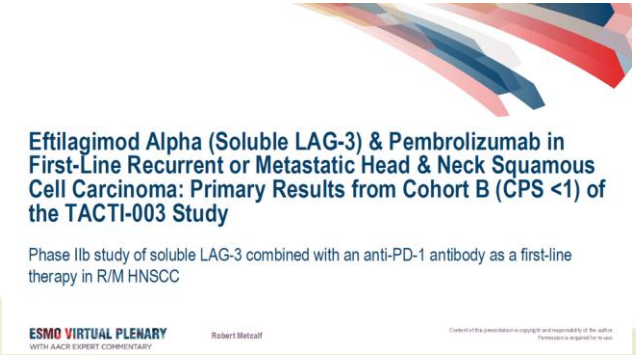
Inmunomodulador **agonista de LAG-3**

Interactúa con las moléculas MHC de clase II en las células dendríticas.

Estimula la activación de células dendríticas.

Promueve la proliferación de linfocitos T CD8+ citotóxicos,
POTENCIA la respuesta inmune antitumoral




Eftilagimod Alpha (Soluble LAG-3) & Pembrolizumab in First-Line Recurrent or Metastatic Head & Neck Squamous Cell Carcinoma: Primary Results from Cohort B (CPS <1) of the TACTI-003 Study

Phase IIb study of soluble LAG-3 combined with an anti-PD-1 antibody as a first-line therapy in R/M HNSCC

ESMO VIRTUAL PLENARY
WITH AACR EXPERT COMMENTARY

Robert Metcalf


European Society for Medical Oncology (ESMO) Congress 2024

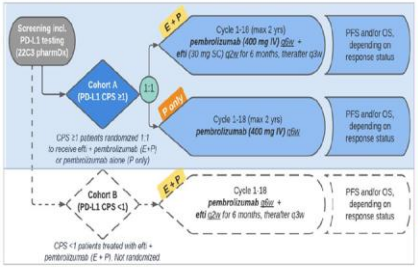
Proffered Paper Oral Presentation

Primary Results from TACTI-003: A Randomized Phase IIb Trial Comparing Eftilagimod Alpha (soluble LAG-3) Plus Pembrolizumab Versus Pembrolizumab Alone in First-Line Recurrent or Metastatic Head and Neck Squamous Cell Carcinoma with CPS ≥1

Phase IIb study of a soluble LAG-3 protein combined with an anti-PD-1 antibody in R/M 1L HNSCC

Barcelona, September 15, 2024

Patient Population: R/M HNSCC patients eligible to 1st line therapy with PD-L1 results available[1]



Primary endpoint: ORR* by RECIST 1.1 (imaging Q9W for 36 wks then Q12W) in evaluable patients.

Secondary endpoints: ORR by iRECIST, DoR, TTR, safety, PFS, OS, immunogenicity & QoL.

*Investigator assessment in patients with ≥1 evaluable post-baseline scan.

[1] https://clinicaltrials.gov/study/NCT04811027
CPS: combined positive score; OS: overall survival; PD-L1: programmed cell death ligand 1; PFS: progression free survival; Q2,3..)W: every (2,3..) weeks; Note: 1 cycle = 6 weeks.

Tumour Response Summary

Best Overall Response (BOR); N (%)	E+P N=58	P alone N=60
Complete response	4 (6.9)	3 (5.0)
Partial response	15 (25.9)	13 (21.7)
Stable disease	23 (39.7)	22 (36.7)
Progressive disease	16 (27.6)	22 (36.7)
ORR; N (%) [90% CI][1]	**19 (32.8)**, [22.6–44.3]	**16 (26.7)**, [17.5–37.6]
DCR; N (%)	**42 (72.4)**	**38 (63.3)**
Median DOR; months	**17.5**	**17.1**

[1] Calculated using Clopper-Pearson method.

An additional partial response was reported in E+P arm after data cut-off. Updated ORR of 34.5% (N=20) for E+P.

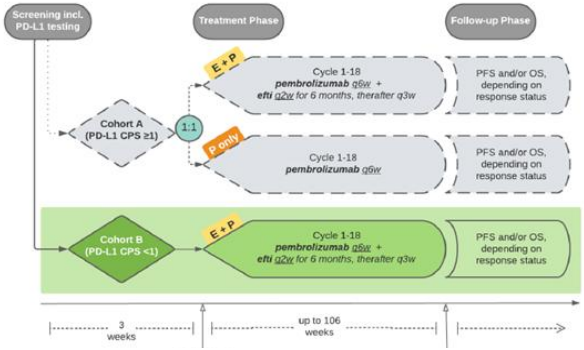
- Numerically higher ORR[1] & DCR[1] in E+P compared to P alone patients with CPS ≥1.
- Comparable results by iRECIST.
- Excellent median duration of response (DOR) of 17.5 months (E+P) and 17.1 months (P alone).

Data cut-off date: March 11, 2024

STUDY DESIGN

TACTI-003: a multicentre, randomized, open-label Phase IIb trial with 2 cohorts:

- Cohort A*: CPS ≥1 patients randomized 1:1 to receive eftilagimod plus pembrolizumab or pembrolizumab alone.
- **Cohort B**: CPS <1 patients treated with eftilagimod and pembrolizumab.**



TUMOUR RESPONSE SUMMARY

Best objective response[1], n (%)	RECIST 1.1 N=31	iRECIST N=31
Complete response	3 (9.7)	3 (9.7)
Partial response	8 (25.8)	9 (29.0)
Stable disease	7 (22.6)	8 (25.8)
Progressive disease	13 (41.9)	11 (35.5)
ORR, [95% CI][2]	**11 (35.5)** [19.2-54.6]	**12 (38.7)** [21.8-57.8]
DCR, [95% CI][2]	**18 (58.1)** [39.1-75.5]	**20 (64.5)** [45.4-80.8]

[1] unconfirmed responses per Investigator read.
[2] calculated using Clopper-Pearson method.
[3] per RECIST 1.1.
[4] per iRECIST.

- ORR[1,3] of 35.5% and DCR[1,3] of 58.1%, including ~10% complete responses.
- 10 responses[4] were confirmed until data cut-off.
- Responses are observed regardless of HPV status* (1/4 HPV-positive and 2/7 HPV-negative patients were responders).

*in patients with primary oropharyngeal tumours only.
Data cut-off date: March 11, 2024

PEMBRO SIN QT EN PDL1 <1: RO 4.5% SP 8 MESES

EFECTOS ADV INMUNOMEDIADOS

EFTI (LAG-3) MONOTERAPIA: 40% GRADO ≥3: 9%

COMBINACIÓN EFTI (LAG-3) + PEMBRO: 56% GRADO ≥3: 10%

Safety Overview

Summary[5,6]

Safety parameters, n (%)	E+P N=69	P alone N=68
Any TEARs	39 (56.5)	41 (60.3)
Any TEARs with Grade ≥3	7 (10.1)	8 (11.8)
Any TEARs Leading to Discontinuation of Study Treatment[1]	3 (4.3)[2]	3 (4.4)[3]
Any Immune-mediated Adverse Reaction (imAR)	17 (24.6)	29 (42.6)
Any kind of Local Injection Site Reaction (LISR)	9 (13.0)[4]	0

[1] Study treatment: efti and/or pembrolizumab.
[2] Total 5 events: Immune-mediated myositis (G3) & Myasthenic syndrome (G3) in 1 patient; Anaphylactic reaction (G4) and later Immune-mediated enterocolitis (G4) in 1 patient. General physical health deterioration (G2) in 1 patient.
[3] Myocarditis (G3), Erythema multiforme (G3), Rash maculo-papular (G2) in 1 patient each.
[4] All Grade 1-2.
[5] Safety population includes all patients who were treated (N=137). 1 patient was enrolled, but not treated.
[6] TEARs – treatment emergent adverse events at least possibly related to efti and/or pembrolizumab.

Most frequent (≥5%), related adverse events[5,6]

Preferred term, n (%)	E+P N=69	P alone N=68
Hypothyroidism	5 (7.2)	15 (22.1)
Fatigue	9 (13.0)	8 (11.8)
Pruritus	5 (7.2)	5 (7.4)
Diarrhea	5 (7.2)	3 (4.4)
Rash	0	6 (8.8)
Rash maculo-popular	0	4 (5.9)
Injection site reaction	5 (7.2)	0

- No fatal TEARs & no new safety signals.
- Well-balanced Grade ≥3 TEARs between arms.

Summary of TEARs (Safety population)

Safety parameters, n (%)	N=33
Any TEARs	24 (72.7)
Any TEARs with Grade ≥3	5 (15.2)
Any TEARs Leading to Discontinuation of Study Treatment[1]	3 (9.1)[2]

- No new safety signals were observed.
- Immune-mediated adverse reactions were seen in 39.4% of patients, Grade 1-2 (30.4%) and Grade 3 (9.1%).
- Local injection site reactions were observed in 18.2% of patients (all Grade 1).

[1] Study treatment: efti/agimod and/or pembrolizumab.
[2] Immune thrombocytopenia (G4), Immune-mediated hepatitis (G3), Laryngeal obstruction (G4).
TEAE: treatment-emergent adverse event; TEAR: treatment-emergent adverse reaction.

Most frequent TEAEs (Safety population)

Preferred term (incidence ≥15%), n (%)	N=33
Fatigue	7 (21.2)
Weight decreased	6 (18.2)
Hypothyroidism	6 (18.2)
Pyrexia	5 (15.2)
Arthralgia	5 (15.2)
Gamma-glutamyltransferase increased	5 (15.2)
Anaemia	5 (15.2)

Data cut-off date: March 11, 2024

RX LOCALES PUNTO DE INYECCIÓN SC: 13-18% LEVES

Head and Neck Cancer

Breaking Ground in Recurrent or Metastatic Head and Neck Squamous Cell Carcinoma: Novel Therapies Beyond PD-L1 Immunotherapy

Ari J. Rosenberg, MD[1]; Cesar A. Perez, MD[2]; Wenji Guo, MD[1]; Jose Monteiro de Oliveira Novaes, MD[3]; Kamilla F. Oliveira da Silva Reis, MD[4]; Patrick W. McGarrah, MD[5]; and Katharine A.R. Price, MD[5]

DOI https://doi.org/10.1200/EDBK_433330

CABEZA y CUELLO_ESCAMOSO

✔**AC CONJUGADOS**

TISOTUMAB VEDOTIN (Tissue factor CD 142- MMAE_ monomethyl auristatin)

31 pacientes. Fase II en 2ª L o más.

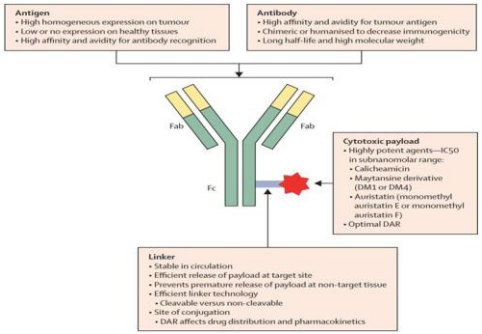
TR: 30%. TR en 2ªL: 40%.

ENFORTUMAB VEDOTIN (nectina 4-MMAE_ monomethyl auristatin)

46 pacientes. Ensayo de fase II. En 2ª L.

RO. 23, 9%. Tasa control enfermedad: 56,5%

Tox. antimicrotúbulo: Neuropatía periférica y ocular, hiperglucemia, neutropenia



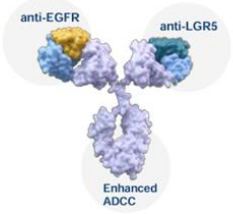
✔**AC BIESPECÍFICOS**: **PETOSEMTAMAB**

PETOSEMTAMAB (EGFR y LGR5)

EGFR and WNT signaling are oncogenic and mitogenic drivers in several cancer types, including HNSCC

MCLA-158 is a first-in-class molecule with enhanced ADCC activity and high target affinity

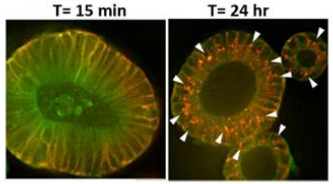
Blocks EGFR signaling, inducing potent growth inhibition



Significant MCLA-158-induced internalization of EGFR and LGR5 results in EGFR degradation[1]

MCLA-158 has potent antitumor activity in patient-derived HNSCC xenograft models[1]

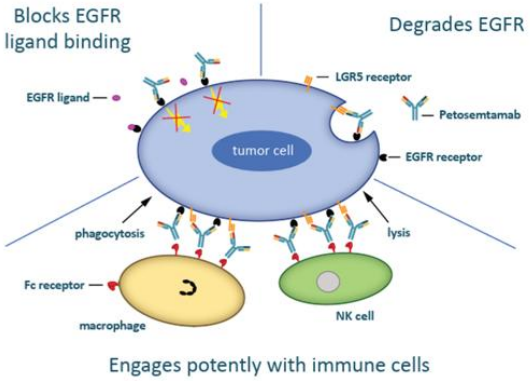
Recurrent/metastatic HNSCC has a poor prognosis, with ~15% ORR and median OS ~8 months in 2nd line[2-4]



EGFR MCLA-158

High magnification images of P18T organoids shows that after 24h exposure, MCLA-158 (red) is localized intracellularly in speckle-like patterns and overall EGFR expression (green) is strongly reduced.

1. Argiles et al. J Clin Oncol. 39, no. 3_suppl (Jan 2021) Abst 62. 2. Cohen E et al. Lancet 2019;393:156-67
3. Ferris et al. N Engl J Med 2016;375:1856-67. 4. Larkins et al. Oncologist 2017; 22:873-78



Mechanism of action[1]

Inhibición de la señalización dependiente de EGFR

Mayor internalización y degradación de EGFR

Mejora la citotoxidad y fagocitosis dependiente de AC

SINGAPORE 2024 ESMO ASIA

Petosemtamab (MCLA-158) Monotherapy in Previously Treated (2L+) Recurrent/Metastatic (r/m) Head and Neck Squamous Cell Carcinoma (HNSCC): Phase 2 Trial

Presenter: Christophe Le Tourneau MD, PhD,
Senior Medical Oncologist Institut Curie, Professor of Medicine Paris-Saclay University

Christophe Le Tourneau,[1] Jérôme Fayette,[2] Caroline Even,[3] Assuntina G. Sacco,[4] Amaury Daste,[5] Irene Braña,[6] Carla M. L. van Herpen,[7] Thibault Mazard,[8] Stephane Henry,[9] Michael Saerens,[10] Fabian Zohren,[11] Eduardo Pennella,[11] Yu-Ming Shen,[11] Kees Bol,[11] Lokesh Jain,[11] Marina Magin Ferrer,[11] Renée de Leeuw,[11] Antoine Hollebecque[5]

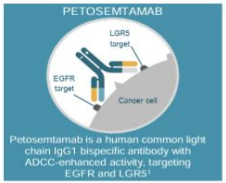
[1]Department of Drug Development and Innovation (D3i), Institut Curie, INSERM U900 Research Unit, Paris-Saclay University, Paris, France; [2]Department of Medical Oncology, Léon Bérard Center, University of Lyon, Lyon, France; [3]Department of Medical Oncology, Institut Gustave Roussy, Villejuif, France; [4]Department of Internal Medicine, Division of Hematology-Oncology, UC San Diego Health, La Jolla, CA, USA; [5]Oncology, Centre Hospitalier Universitaire de Bordeaux, Bordeaux, France; [6]Vall d'Hebron Hospital Campus and Institute of Oncology (VHIO), IOB-Quirón, UVic-UCC, Barcelona, Spain; [7]Department of Medical Oncology, Radboud Institute for Medical Innovation, Radboud University Medical Center, Nijmegen, Netherlands; [8]Institut Régional du Cancer de Montpellier (ICM), Montpellier, France; [9]Department of Oncology-Hematology, Radiotherapy, and Nuclear Medicine, CHU UCL Namur, Namur, Belgium; [10]Department of Medical Oncology, Ghent University Hospital, Ghent, Belgium; [11]Merus N.V., Utrecht, Netherlands.

Singapore; Saturday, December 7, 2024

SINGAPORE 2024 ESMO ASIA

Petosemtamab Monotherapy in 2L+ r/m HNSCC

MoA and Phase 2 Trial Design (NCT03526835)



Key HNSCC inclusion criteria
- 2L+ r/m HNSCC
- ECOG PS 0–1
- Measurable disease

Single-arm cohort: Petosemtamab 1500 mg (n=54)[a] IV, Q2W; 28-day cycle — Initial cohort presented[2]

Dose-comparison cohort: Petosemtamab 1500 mg (n=28) IV, Q2W; 28-day cycle; Petosemtamab 1100 mg (n=28) IV, Q2W; 28-day cycle

Key objectives
- **Efficacy:** ORR (RECIST v1.1 per investigator), DOR, PFS, OS
- **Safety**, tolerability, and PK characterization
- **Efficacy evaluable population:** patients with ≥2 treatment cycles and ≥1 postbaseline tumor assessment or who discontinued early due to PD or death

Enrollment and analysis population

Data cutoff date: July 5, 2024
Enrollment at 1500 mg: N=82
Enrollment at 1100 mg: N=28

1500 mg efficacy evaluable population
- 75 patients
- 7 patients excluded[b]

1100 mg efficacy evaluable population
- 27 patients
- 1 patient excluded[c]

5-13% ORR
median OS ~6 months

in 2ndline with cetuximab, docetaxel or methotrexate

SINGAPORE 2024 ESMO ASIA

Petosemtamab Antitumor Activity in 2L+ HNSCC

Petosemtamab 1500 mg Q2W, efficacy evaluable population (N=75)

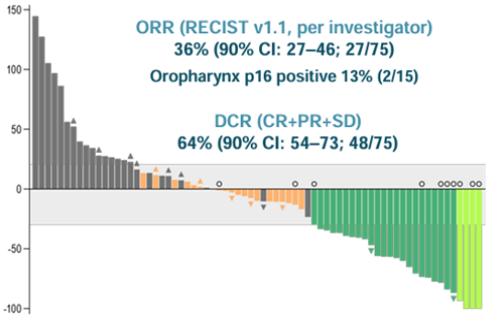
Tumor Biomarkers	N=49
EGFR	
• H-score[3], median (range) (n=35)	170 (0 - 300)
PD-L1	
• Positive (CPS[3] ≥1) / negative	20 (41%) / 9 (18%)
• Unknown[4]	20 (41%)
p16 status: oropharynx	**N=17**
• p16 positive / negative[3]	6 (35%) / 3 (18%)
• Unknown[4]	8 (47%)

SINGAPORE 2024 ESMO ASIA

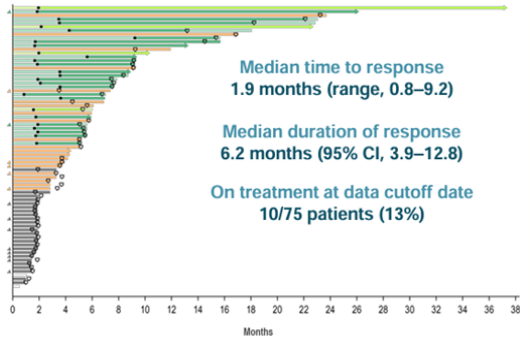
Baseline Characteristics,

Baseline characteristics	1500 mg Q2W (N=82)[a]	1100 mg Q2W (N=28)
Age (years), median (range)	60 (31–77)	64 (39–80)
Male / female, n (%)	65 (79) / 17 (21)	22 (79) / 6 (21)
ECOG PS 0 / 1, n (%)	25 (31) / 57 (70)	7 (25) / 21 (75)
Main tumor location, n (%)		
Oropharynx	37 (45)	6 (21)
Oral cavity	25 (31)	11 (39)
Hypopharynx	10 (12)	2 (7)
Larynx	5 (6)	8 (29)
Other[b]	3 (4)	1 (4)
p16 (HPV) status[c] (oropharynx), n (%)		
Positive / negative / unknown	17 (46) / 17 (46) / 3 (8)	1 (17) / 5 (83) / 0 (0)
EGFR (IHC) H-score, median (range)	200 (0–300)	255 (0–300)
Prior systemic therapy, median (range)	2 (1–4)	2 (1–4)
Prior platinum chemotherapy, n (%)	78 (95)	26 (93)
PD-(L)1 inhibitor, n (%)	80 (98)	28 (100)

Best percentage change in sum of target lesions from baseline (N=75)[a]



Time to response and duration of exposure (N=75)



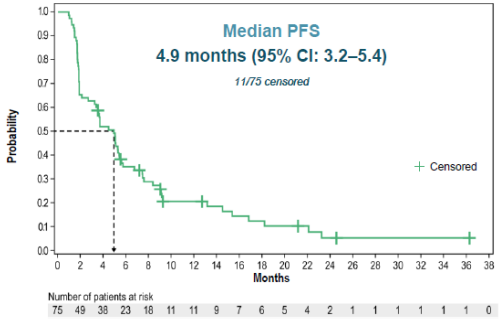
5-13% ORR

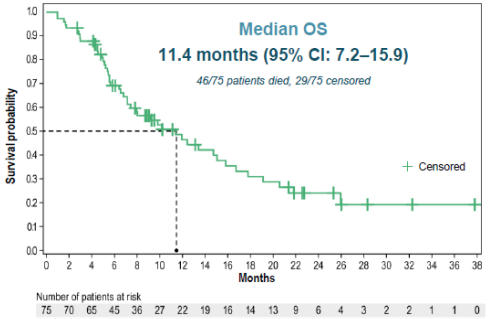
median OS ~6 months

in 2ndline with cetuximab, docetaxel or methotrexate

RX RELACIONADAS CON EGFR

RX INFUSIONALES





Petosemtamab Safety and Pharmacokinetics in 2L+ HNSCC

Petosemtamab 1500 mg Q2W, safety-evaluable population (N=82)

AEs irrespective of causality (>20% of patients)

Preferred Term	1500 mg Q2W N=82	
	All grades, n (%)	Grade ≥3, n (%)
At least one TEAE	82 (100)	48 (59)
Dermatitis acneiform	34 (41)	3 (4)
Blood magnesium decreased	32 (39)	7 (9)
Rash	24 (29)	0
Fatigue	22 (27)	1 (1)
Nausea	21 (26)	0
Hypotension	20 (24)	4 (5)
Pruritus	20 (24)	1 (1)

Infusion-related reactions (>10% of patients)

Preferred Term	Prior administration regimen N=49		Updated administration regimen N=33	
	All grades, n (%)	Grade 3–4, n (%)	All grades, n (%)	Grade 3, n (%)
At least one TEAE of IRR	33 (67)	12 (24)	15 (45)	3 (9)
Infusion-related reaction	12 (24)	7 (14)	7 (21)	2 (6)
Hypotension	10 (20)	4 (8)	4 (12)	0
Flushing	8 (16)	2 (4)	2 (6)	1 (3)
Nausea	6 (12)	0	2 (6)	0
Dyspnea	5 (10)	1 (2)	0	0
Erythema	5 (10)	0	0	0

Safety

- Petosemtamab 1500 mg Q2W in HNSCC was well tolerated with a manageable safety profile
- IRRs were generally only seen on day 1 of cycle 1; the IRR mitigation strategy reduced the severity and frequency of IRRs

Pharmacokinetics

- Geometric mean steady state C_{trough} was 68% higher with 1500 mg Q2W vs. 1100 mg Q2W
  - No positive exposure–safety (Grade ≥3 TEAE) relationship was observed
- 1500 mg Q2W was projected to achieve superior target engagement (*i.e.* ≥98%) for EGFR compared with 1100 mg Q2W dose

In the single-arm cohort, initially presented at AACR 2023[1], among 48 evaluable patients[a], the median DOR, PFS, and OS were 6.7, 5.2, and 12.5 months, respectively

RX RELACIONADAS CON LA INFUSIÓN

67 % 24% Grade 3-4

Durante la primera infusión

Se resuelven

6 pacientes suspenden por RX grado 3-4 y el resto se retrata

IRRs manejable con profilaxis + infusión prolongada (sobretodo en ciclo 1)

2024 ASCO® ANNUAL MEETING

Petosemtamab plus pembrolizumab in 1L r/m HNSCC: Phase 2 data (NCT03526835)

Phase 2 study (NCT03526835)

1L petosemtamab in combination with pembrolizumab

Key HNSCC inclusion criteria
- 1L r/m PD-L1+ HNSCC*
- ECOG PS 0-1
- Measurable disease

Treatment plan
- Petosemtamab 1500 mg IV, Q2W (28-day cycle) with pembrolizumab 400 mg IV Q6W
- Until PD or toxicity
- Tumor assessment Q8W

Follow-up
- Survival follow-up for up to 3 years

Objectives

- **Primary objectives:** ORR using RECIST 1.1 per investigator, and safety and tolerability
- **Secondary objectives:** DOR and PFS (per investigator and central review), ORR (per central review), OS, PK, immunogenicity, and biomarkers
- **Efficacy evaluable population:** Patients treated as of the abstract cutoff date (who had the opportunity for ≥4 months follow-up), with ≥2 treatment cycles and ≥1 post-baseline tumor assessment, or who discontinued early due to disease progression or death

Enrollment and analysis

Data cutoff date
06-Mar-2024

Enrollment
45 patients

Efficacy evaluable population
24 patients
- 19 patients enrolled after abstract cutoff date
- 2 patients were excluded per protocol:
  - 1 patient withdrew consent prior to first tumor assessment
  - 1 patient discontinued due to toxicity with <2 cycles of treatment

*PD-L1+ is defined as a patient with a PD-L1 CPS ≥1.
CPS, combined positive score; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; IV, intravenous; OS, overall survival; PD, progressive disease; PD-L1, programmed cell death-ligand 1; PFS, progression-free survival; PK, pharmacokinetics; Q2W, every 2 weeks; Q6W, every 6 weeks; Q8W, every 8 weeks; RECIST, response evaluation criteria in solid tumors.

PRESENTED BY: Dr. Jérôme Fayette

Merus

Patient demographics and disposition

Safety set (N=45)

Demographics and disease features	
Age (years), median (range)	64 (23-80)
Male / female, n (%)	35 (78) / 10 (22)
ECOG PS 0 / 1, n (%)	16 (36) / 29 (64)
Main tumor location, n (%)	
Oral cavity	17 (38)
Oropharynx	14 (31)
Larynx	7 (16)
Hypopharynx	5 (11)
Other*	2 (4)
PD-L1 status (local), n (%)	
PD-L1 positive	45 (100)
CPS 1-19 / ≥20	19 (42) / 25 (56)
p16 (HPV) status (local): Oropharynx (n=14), n (%)	
p16 positive	8 (57)
p16 negative	5 (36)
p16 unknown	1 (7)
IHC H-score (EGFR), n (%)†	
0 - <100	6 (13)
100 - <200	7 (16)
200 - 300	28 (62)

Patient disposition	
Petosemtamab treatment, n (%)	
Treatment ongoing	32 (71)
Treatment discontinuation	13 (29)
Disease progression	9 (20)
Withdrawal of consent	2 (4)
Death (unrelated to treatment)	1 (2)
Related AE‡	1 (2)
Petosemtamab exposure duration (months), median (range)	3.32 (0.5-10.3)
Duration of follow-up (months), median (range)	3.58 (0.5-10.3)

*One patient with HNSCC from unknown primary tumor location, one patient with HNSCC from sinonasal primary tumor;
†4 patients had no IHC H-score (EGFR) available; ‡Patient discontinued due to adverse events (asthenia, diarrhea, creatinine increase; all Grade <3).
AE, adverse event; HPV, human papillomavirus; IHC, immunohistochemistry.

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VII SIMPOSIO NACIONAL de ONCOLOGÍA de PRECISIÓN

2024 ASCO® ANNUAL MEETING

QT+PEMBRO o QT+CETUXI → RO 36%

CPS>20, QT+PEMBRO → RO 43%

Petosemtamab plus pembrolizumab in 1L r/m HNSCC: Phase 2 data (NCT03526835)

PHASE 2 TRIAL INTERIM DATA: 2024 ASCO®

Overall response rate (RECIST v1.1, per investigator)

Best percent change in sum of target lesions from baseline (N=24)[7]

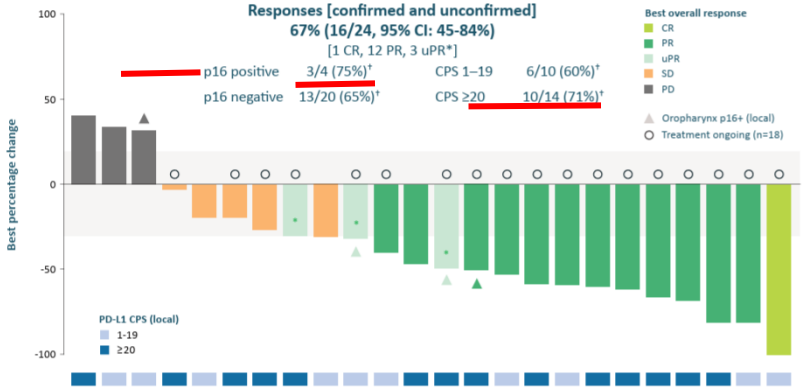

Figure 3 | Petosemtamab plus pembrolizumab in 1L r/m HNSCC: Phase 2 data (NCT03526835)

Petosemtamab plus pembrolizumab was observed to have a favorable safety profile including manageable infusion-related reactions[7]

Safety profile

Overall safety

- Treatment-emergent AEs (TEAEs) were reported in 45 patients; most were Grade 1 or 2
- Treatment-related TEAEs* led to study discontinuation in 2 patients (4%), both were Grade 1-2
- Grade ≥3 TEAEs occurred in 18 (40%) patients, 11 (24%) of which were treatment related
- No significant overlapping toxicities

IRRs (composite term)†

RX RELACIONADAS CON LA INFUSIÓN

38% % Grade 1-4 7% GRADO 3. 0% GRADO 4

NINGÚN PACIENTE SUSPENDIÓ EL TTO

Preferred term	Irrespective of causality (>15% of patients) (N=45)	
	All Grades, n (%)	Grades 3-5, n (%)
At least 1 TEAE[‡§]	**45 (100)**	**18 (40)**
Acneiform dermatitis	20 (44)	1 (2)
Rash	18 (40)	0
Asthenia	16 (36)	3 (7)
Skin fissures	15 (33)	0
Constipation	12 (27)	0
Folliculitis	12 (27)	0
Nausea	12 (27)	1 (2)
Blood magnesium decreased	10 (22)	1 (2)
[illegible]	10 (22)	1 (2)
[illegible]	10 (22)	0
[illegible]	10 (22)	0
[illegible]	10 (22)	1 (2)
[illegible]	7 (16)	0
[illegible]	7 (16)	1 (2)
[illegible] reaction	7 (16)	1 (2)
Paronychia	7 (16)	0
Tumor pain	7 (16)	1 (2)

*One patient had asthenia (Grade 2), diarrhea (Grade 1), and creatinine increase (Grade 1); one patient had dyspnea, tachycardia, nausea, and IRR (all Grade 2); †IRR is a composite term for one or multiple signs/symptoms during the 24-hour period after initiating the petosemtamab infusion, judged by investigators as an IRR; ‡Most common (>15% of patients) TEAEs, irrespective of causality, are listed; §TEAEs are defined as AEs with onset date on or after date of first administration of study drug and ≤30 days post-treatment. IRR, infusion-related reaction.

8

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LiGeR-HN2 PHASE 3 TRIAL DESIGN

LiGeR-HN2 is a phase 3, open-label, randomized, controlled, multicenter trial to compare petosemtamab vs. investigator's choice monotherapy in patients with HNSCC for the 2L and 3L treatment of incurable metastatic/recurrent disease

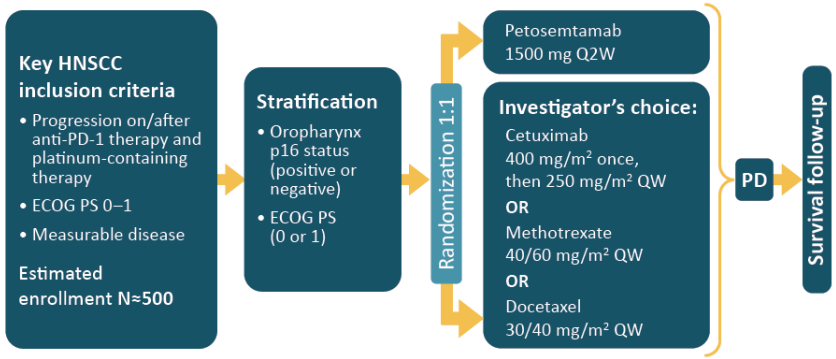


Figure 2 | LiGeR-HN2 trial design

No crossover is permitted. 2L: second line; 3L: third line; ECOG PS: Eastern Cooperative Oncology Group performance status; PD: progressive disease; Q2W: once every 2 weeks; QW: once weekly.

LiGeR-HN1 PHASE 3 TRIAL DESIGN

LiGeR-HN1 is a randomized, open-label, phase 3 trial to evaluate the efficacy and safety of petosemtamab plus pembrolizumab vs. pembrolizumab monotherapy in patients with 1L r/m PD-L1+ HNSCC

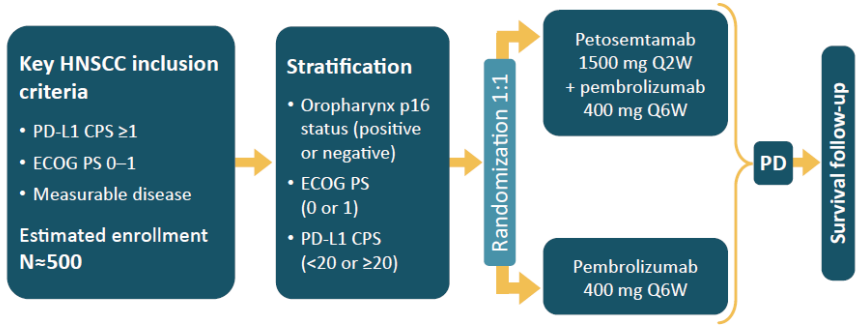
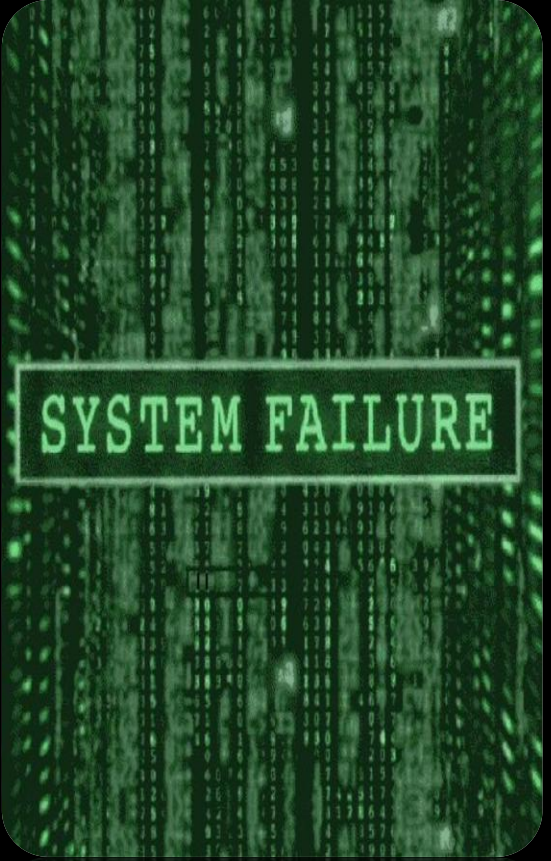


Figure 2 | LiGeR-HN1 trial design

No crossover is permitted. CPS: combined positive score; ECOG PS: Eastern Cooperative Oncology Group performance status; PD: progressive disease; Q2W: once every 2 weeks; Q6W: once every 6 weeks.

Primary outcome measures

- Objective response rate as assessed by BICR
- Overall survival



Dr. Edel del Barco Morillo

CAUSA-IBSAL
Salamanca

delbarco@usal.es

GRACIAS