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INTERLINK-1: Phase 3 study of cetuximab ± monalizumab in participants with recurrent / metastatic head and neck squamous cell carcinoma with disease progression on / after platinum chemotherapy and previously treated with an immune checkpoint inhibitor

Dr Jérôme Fayette

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DECLARATION OF INTERESTS

Dr Jérôme Fayette

Consulting or advisory role: AstraZeneca, Bristol-Myers Squibb, Elevar, Hookipa, Innate Pharma, iTeos, Merck, Merck Sharp & Dohme, Rakuten, Roche and Seagen

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Introduction

- The first-line treatment recommended for R/M HNSCC* is ICI +/- chemotherapy[1] and, in some cases, cetuximab may be recommended[†,1]; however, treatment for R/M HNSCC which has previously been treated with an ICI and had disease progression on / after platinum-based chemotherapy is not clearly defined[1]
- In people with R/M HNSCC with disease progression on / after platinum-based therapy, the ORR for cetuximab monotherapy was 13%[2]
- Monalizumab is an ICI that targets NKG2A receptors on NK cells and CD8+ T cells[3]
- Preclinical data suggested that the addition of monalizumab to cetuximab may have antitumour activity[3]; in a Phase 2 study of participants with R/M HNSCC previously treated with platinum-based therapy and an ICI, the ORR for this combination was 20%[4]

INTERLINK-1 (NCT04590963) was a Phase 3, randomised, double-blind, placebo-controlled, multicentre global study evaluating the efficacy and safety of monalizumab plus cetuximab versus placebo plus cetuximab in participants with R/M HNSCC previously treated with platinum-based chemotherapy and an ICI

*Not amenable to curative radiotherapy or surgery. †In cases of contraindication to immunotherapy and unfit for platinum-based therapy.
ICI, immune checkpoint inhibitor; NK, natural killer; NKG2A, natural killer group 2 member A; ORR, objective response rate; R/M HNSCC, recurrent or metastatic head and neck squamous cell carcinoma.
1. Machiels J-P, et al. *Ann Oncol* 2020;31:1462–1475. 2. Vermorken JB, et al. *J Clin Oncol* 2007;25:2171–2177. 3. André P, et al. *Cell* 2018;175:1731–1743.e13. 4. Cohen RB, et al. *J Clin Oncol* 2020;38(suppl 15). Abs 6516.

Methods

Key eligibility criteria
- Confirmed R/M HNSCC of the oral cavity, oropharynx, hypopharynx or larynx
- 1 or 2 prior systemic regimens for R/M HNSCC
- Prior treatment with a PD-(L)1 inhibitor
- Prior platinum failure*
- ECOG PS 0 or 1
- No prior cetuximab therapy for R/M HNSCC
- Provision of fresh or recently acquired tumour tissue

Stratification factors
- HPV status (HPV-positive oropharyngeal cancer or HPV-unrelated†)
- ECOG PS (0 or 1)
- Number of prior lines of therapy in the R/M setting (1 or 2)

R (2:1)
N=~624

Monalizumab 750 mg IV Q2W +
cetuximab 400 mg/m^2 IV x 1 dose then 250 mg/m^2 IV QW‡
until disease progression or unacceptable toxicity

Placebo IV Q2W +
cetuximab 400 mg/m^2 IV x 1 dose then 250 mg/m^2 IV QW†
until disease progression or unacceptable toxicity

Primary objective
- OS in participants with HPV-unrelated HNSCC‡

Secondary objectives
- OS in all randomised participants
- PFS
- ORR
- DoR
- PROs/HRQoL
- Pharmacokinetics of monalizumab
- Assessment of biomarkers (HLA-E and NKp46+)
- Safety and tolerability

The protocol was updated to change the primary population of interest from the full analysis set to the HPV-unrelated analysis set. To allow for the change in population, the planned number of participants was increased, the hierarchical testing procedure was updated, and a futility analysis for OS was added.
*Platinum failure is defined as disease progression on / after treatment with a platinum-containing regimen for R/M disease, or recurrence / progression within 6 months of the last dose of platinum treatment as part of a multimodal therapy for locally advanced disease. †HPV-unrelated participants include participants with HPV-negative oropharyngeal cancer or participants with non-oropharyngeal cancer, regardless of HPV status. ‡As per label.
DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group; HLA-E, human leukocyte antigen E; HPV, human papillomavirus; HRQoL, health-related quality of life; IV, intravenous; NKp46, natural killer cell p46-related protein; ORR, objective response rate; OS, overall survival; PD-(L)1, programmed cell death (ligand)-1; PFS, progression-free survival; PRO, patient-reported outcome; PS, performance status; QW, once weekly; QXW, every X weeks; R, randomisation; R/M HNSCC, recurrent or metastatic head and neck squamous cell carcinoma.

Statistical analysis

Interim analysis 1

Performed after ~99 OS events in participants with HPV-unrelated HNSCC

Objective: to assess futility of treatment with monalizumab plus cetuximab versus placebo plus cetuximab in terms of OS in participants with HPV-negative oropharyngeal cancer or non-oropharyngeal cancer (HPV-unrelated analysis set)

The futility criteria were determined as OS HR >0.874, which corresponds to 20% conditional power assuming future data are consistent with the trend from interim analysis 1

Efficacy analysis data cut-off: 11 May 2022

Safety analysis data cut-off: 01 September 2022

The protocol was updated to change the primary population of interest from the full analysis set to the HPV-unrelated analysis set. To allow for the change in population, the planned number of participants was increased, the hierarchical testing procedure was updated, and a futility analysis for OS was added. For efficacy analyses, data cut-off was 11 May 2022, including participants who were randomised on / before 11 March 2022. For safety analysis, data-cut off was extended to 01 September 2022, including all participants who received at least one dose of any study treatment by 01 September 2022.

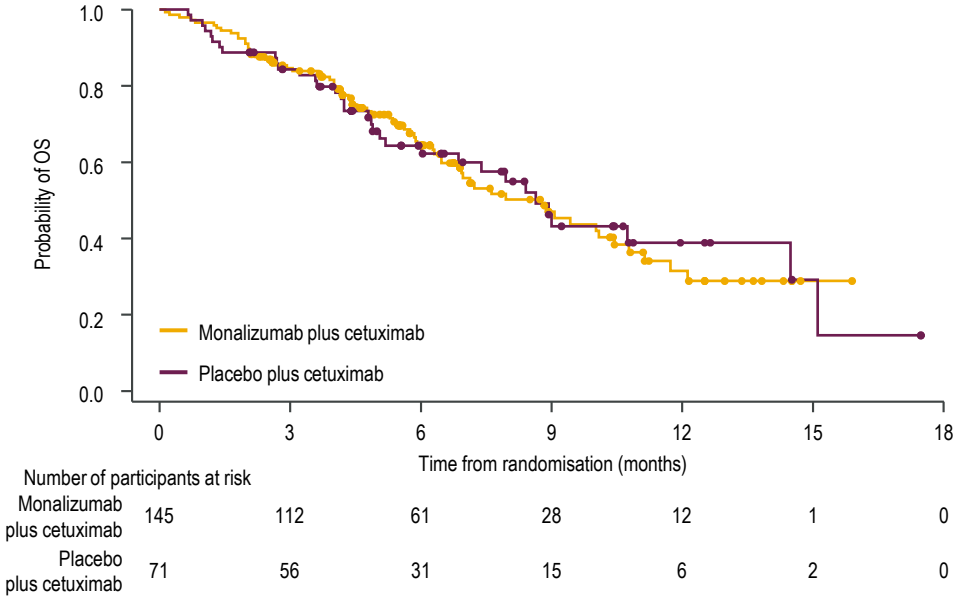
HNSCC, head and neck squamous cell carcinoma; HPV, human papillomavirus; HR, hazard ratio; OS, overall survival.

Participant demographics and baseline clinical characteristics

		HPV-unrelated analysis set (n=216)		Full analysis set (n=264)	
		Monalizumab plus cetuximab (n=145)	Placebo plus cetuximab (n=71)	Monalizumab plus cetuximab (n=175*)	Placebo plus cetuximab (n=89)
Median age, (range) years		63.0 (35–86)	61.0 (39–81)	63.0 (35–86)	61.0 (39–81)
Male sex, n (%)		119 (82.1)	55 (77.5)	146 (83.4)	70 (78.7)
HPV status in OPC, n/N (%)	**Positive**	0/23	0/11	30/53 (56.6)	18/29 (62.1)
	Negative	23/23 (100.0)	11/11 (100.0)	23/53 (43.4)	11/29 (37.9)
ECOG PS, n (%)	**0**	45 (31.0)	20 (28.2)	56 (32.0)	27 (30.3)
	1	100 (69.0)	51 (71.8)	118 (67.4)	62 (69.7)
Prior lines of therapy in the R/M setting, n (%)	**0**	0	0	1 (0.6)	0
	1	49 (33.8)	24 (33.8)	61 (34.9)	29 (32.6)
	2	95 (65.5)	46 (64.8)	111 (63.4)	57 (64.0)
	3	1 (0.7)	1 (1.4)	2 (1.1)	3 (3.4)

Data cut-off was 11 May 2022, including participants who were randomised on / before 11 March 2022.
*One randomised participant had an ECOG PS of 2 and was ineligible for treatment.
ECOG, Eastern Cooperative Oncology Group; HPV, human papillomavirus; OPC, oropharyngeal cancer; PS, performance status.

Primary endpoint: OS in the HPV-unrelated analysis set

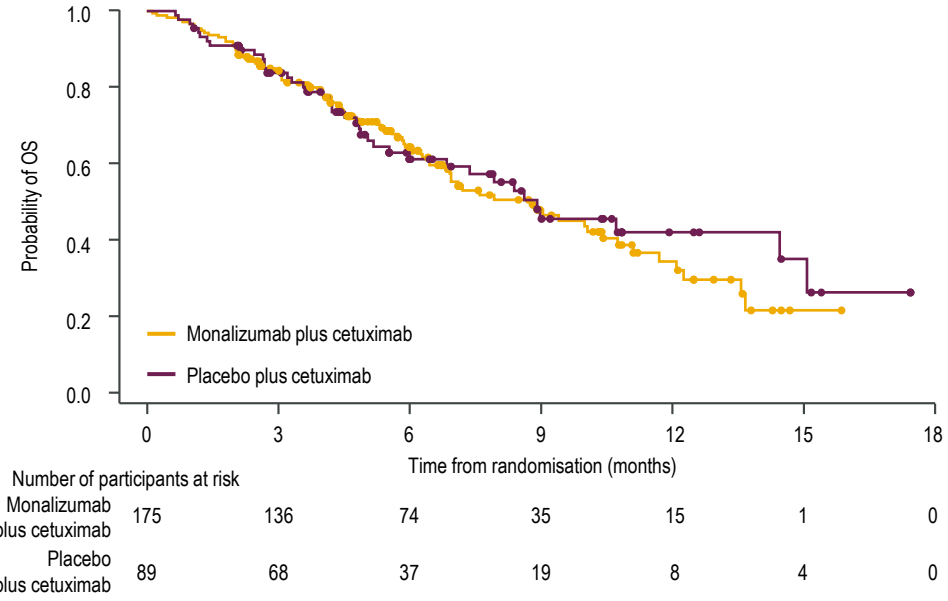


	HPV-unrelated analysis set (n=216)	
	Monalizumab plus cetuximab (n=145)	Placebo plus cetuximab (n=71)
OS events, n (%)	67 (46.2)	34 (47.9)
Median OS, months (95% CI)	8.8 (6.9–10.4)	8.6 (6.0–14.5)
HR (95% CI)	1.00 (0.66–1.54)	
Median DoFU, months (IQR)	7.2 (5.2–12.2)	8.4 (5.0–12.0)

- At the interim analysis of INTERLINK-1, there was no difference in OS observed between participants who received monalizumab plus cetuximab versus placebo plus cetuximab in the HPV-unrelated analysis set
- As the futility criteria (OS HR >0.874) were met, the study was stopped

Data cut-off was 11 May 2022, including participants who were randomised on / before 11 March 2022.
CI, confidence interval; DoFU, duration of follow-up; HPV, human papillomavirus; HR, hazard ratio; IQR, interquartile range; OS, overall survival.

Secondary endpoint: OS in the full analysis set



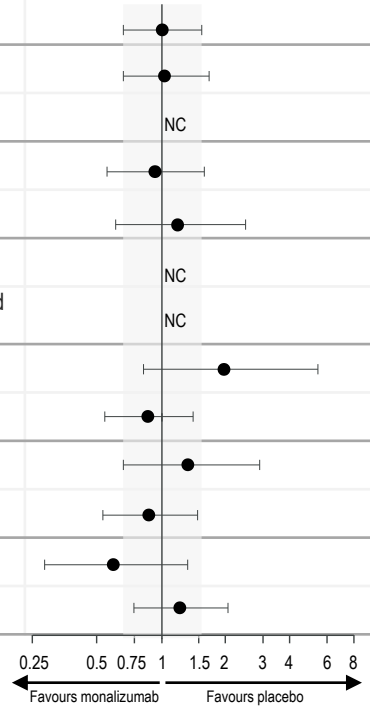
	Full analysis set (n=264)	
	Monalizumab plus cetuximab (n=175)	Placebo plus cetuximab (n=89)
OS events, n (%)	82 (46.9)	40 (44.9)
Median OS, months (95% CI)	8.8 (6.9–10.8)	8.9 (6.0–15.1)
HR (95% CI)	1.03 (0.70–1.53)	
Median DoFU, months (IQR)	7.2 (4.9–12.2)	8.4 (4.8–10.9)

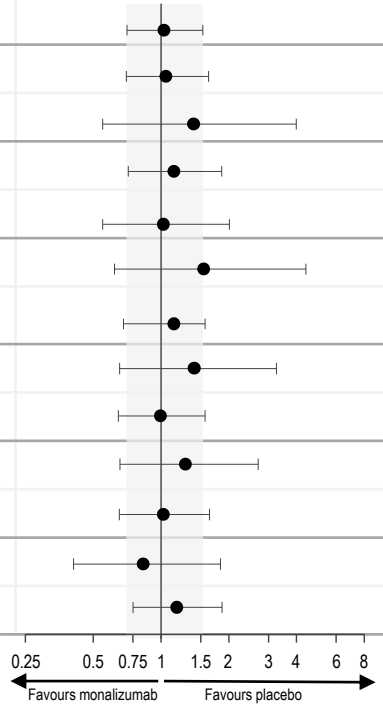
In this interim analysis of INTERLINK-1, there was no difference in OS observed between participants who received monalizumab plus cetuximab versus placebo plus cetuximab in the full analysis set

Data cut-off was 11 May 2022, including participants who were randomised on / before 11 March 2022.
CI, confidence interval; DoFU, duration of follow-up; HR, hazard ratio; IQR, interquartile range; OS, overall survival.

Subgroup analysis of OS in selected subgroups

		HPV-unrelated analysis set (n=216)	n	HR (95% CI)	Full analysis set (n=264)	n	HR (95% CI)
	All participants		216	1.00 (0.66–1.54)		264	1.03 (0.70–1.53)
Sex	Male		174	1.03 (0.66–1.66)		216	1.05 (0.70–1.62)
	Female	NC	42	NC*		48	1.39 (0.55–3.97)
Age at randomisation	<65 years		126	0.93 (0.55–1.58)		156	1.14 (0.71–1.85)
	≥65 years		90	1.18 (0.61–2.47)		108	1.02 (0.55–2.00)
HPV status	OPC HPV positive	NC	NA	NC*		48	1.54 (0.62–4.38)
	OPC HPV negative and non OPC	NC	NA	NC*		216	1.02 (0.68–1.56)
ECOG PS	Normal activity (0)		61	1.95 (0.82–5.38)		79	1.41 (0.66–3.25)
	Restricted activity (1)		155	0.86 (0.54–1.40)		185	1.00 (0.65–1.57)
Number of prior lines of therapy in the R/M setting	1		90	1.34 (0.67–2.91)		105	1.29 (0.66–2.70)
	2		124	0.88 (0.53–1.49)		156	1.03 (0.66–1.65)
Race	Asian		63	0.60 (0.29–1.34)		71	0.84 (0.41–1.84)
	Non-Asian†		153	1.23 (0.75–2.07)		193	1.18 (0.76–1.87)





Data cut-off was 11 May 2022, including participants who were randomised on / before 11 March 2022.

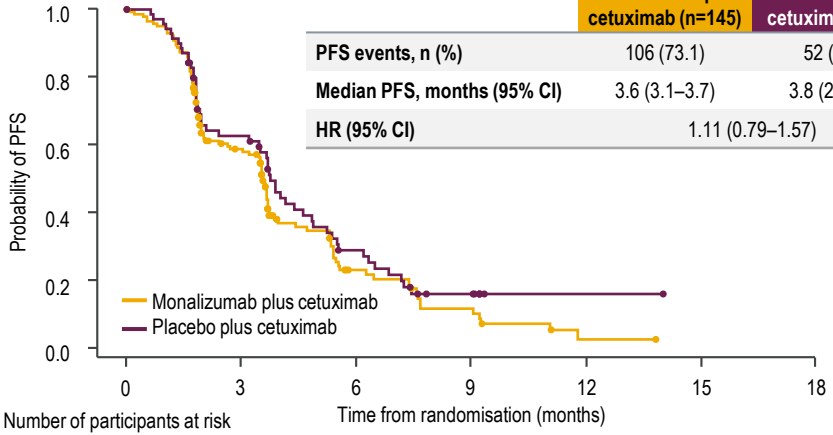
*The HR and 95% CI was not calculated if there were <20 events within the subgroup treatment comparison. †Non-Asian includes Black or African American participants, White participants, Other participants, and participants with race not reported.

CI, confidence interval; ECOG, Eastern Cooperative Oncology Group; HPV, human papillomavirus; HR, hazard ratio; NA, not applicable; NC, not calculated; OPC, oropharyngeal cancer; OS, overall survival; PS, performance status; R/M, recurrent or metastatic.

Secondary endpoint: PFS

PFS in the HPV-unrelated analysis set

	HPV-unrelated analysis set (n=216)	
	Monalizumab plus cetuximab (n=145)	Placebo plus cetuximab (n=71)
PFS events, n (%)	106 (73.1)	52 (73.2)
Median PFS, months (95% CI)	3.6 (3.1–3.7)	3.8 (2.4–4.9)
HR (95% CI)	1.11 (0.79–1.57)	

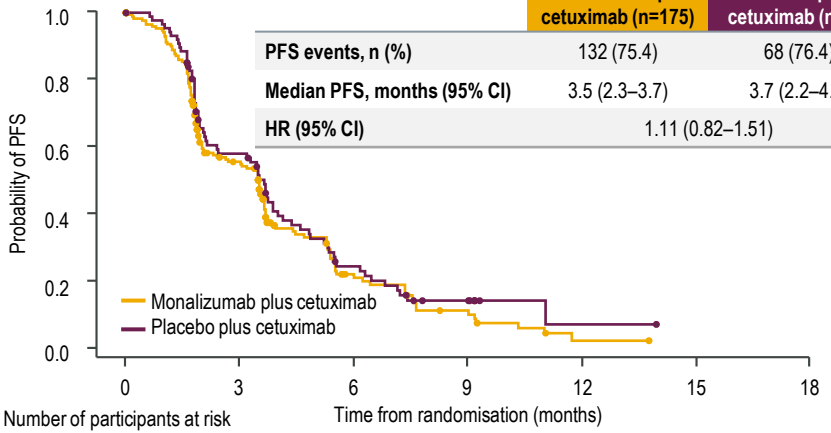


Number of participants at risk

Monalizumab plus cetuximab	145	72	17	8	1	0	0
Placebo plus cetuximab	71	40	16	6	1	0	0

PFS in the full analysis set

	Full analysis set (n=264)	
	Monalizumab plus cetuximab (n=175)	Placebo plus cetuximab (n=89)
PFS events, n (%)	132 (75.4)	68 (76.4)
Median PFS, months (95% CI)	3.5 (2.3–3.7)	3.7 (2.2–4.2)
HR (95% CI)	1.11 (0.82–1.51)	



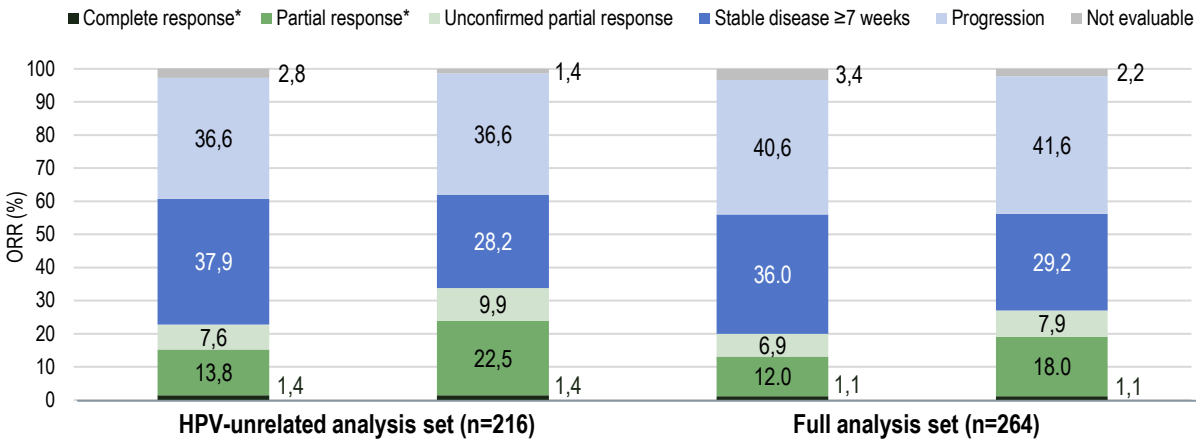
Number of participants at risk

Monalizumab plus cetuximab	175	83	21	9	1	0	0
Placebo plus cetuximab	89	46	17	7	1	0	0

Data cut-off was 11 May 2022, including participants who were randomised on / before 11 March 2022.
CI, confidence interval; ECOG, Eastern Cooperative Oncology Group; HPV, human papillomavirus; HR, hazard ratio; PFS, progression-free survival; PS, performance status.

Secondary endpoint: ORR

- The ORR with monalizumab plus cetuximab was not superior to placebo plus cetuximab
- The ORR with placebo plus cetuximab was higher than in previous reports[1–3]



	Monalizumab plus cetuximab (n=145)	Placebo plus cetuximab (n=71)	Monalizumab plus cetuximab (n=175)	Placebo plus cetuximab (n=89)
Confirmed response, n (ORR, %)	22 (15.2)	17 (23.9)	23 (13.1)	17 (19.1)
Odds ratio for response (95% CI)	0.56 (0.27–1.15), p=0.115		0.60 (0.30–1.23), p=0.162	
Median duration of response, months (IQR)	5.7 (5.5–8.1)	5.6 (4.4–NR)	5.7 (5.3–8.1)	5.6 (4.4–NR)
Median time to onset of response†, months (IQR)	1.9 (1.8–1.9)	1.8 (1.7–1.9)	1.9 (1.8–1.9)	1.8 (1.7–1.9)

Data cut-off was 11 May 2022, including participants who were randomised on / before 11 March 2022. All participants in the HPV-unrelated analysis set and full analysis set had measurable disease at baseline.
*Confirmed complete or partial response recorded at one visit then confirmed by repeat imaging at a visit no less than 4 weeks after, with no evidence of progression in between visits. †From randomisation.
CI, confidence interval; ECOG, Eastern Cooperative Oncology Group; HPV, human papillomavirus; IQR, interquartile range; NR, not reached; ORR, objective response rate; PS, performance status.
1. Vermorken JB, et al. *J Clin Oncol* 2007;25:2171–2177. 2. Seiwert TY, et al. *Ann Oncol* 2014;25:1813–1820. 3. Fayette J, et al. *Front Oncol* 2016;6:232.

Safety and tolerability: no differences in toxicity observed with monalizumab plus cetuximab versus placebo plus cetuximab

		Safety analysis set (n=368)	
		Monalizumab plus cetuximab (n=246)	Placebo plus cetuximab (n=122)
Any adverse event, n (%)		236 (95.9)	120 (98.4)
Any TRAE*, n (%)		198 (80.5)	102 (83.6)
Any maximum Grade 3/4 adverse event, n (%)		95 (38.6)	37 (30.3)
Any maximum Grade 3/4 TRAE*, n (%)		45 (18.3)	21 (17.2)
Any serious TRAE*, n (%)		24 (9.8)	12 (9.8)
Any TRAE* leading to death, n (%)		1 (0.4)	1 (0.8)
Any TRAE* leading to discontinuation of:	Monalizumab/placebo, n (%)	7 (2.8)	1 (0.8)
	Cetuximab, n (%)	12 (4.9)	3 (2.5)
	Monalizumab/placebo and cetuximab, n (%)	4 (1.6)	1 (0.8)
Any adverse event leading to cycle delay or dose interruption of monalizumab/placebo, n (%)		61 (24.8)	34 (27.9)
Any immune-mediated adverse event, n (%)		31 (12.6)	11 (9.0)
Any treatment-related immune-mediated adverse event, n (%)		31 (12.6)	11 (9.0)

Data cut-off was 01 September 2022, including all participants who received at least one dose of any study treatment by 01 September 2022. Participants with multiple events in the same category are counted only once in that category. Participants with events in more than one category are counted once in each of those categories.
*Treatment-related was assessed by the investigator.
TRAE, treatment-related adverse event.

Incidence of Grade 3/4 adverse events was low and similar between treatment arms

	Safety analysis set (n=368)	
	Monalizumab plus cetuximab (n=246)	Placebo plus cetuximab (n=122)
Anaemia, n (%)	11 (4.5)	0
Pneumonia, n (%)	10 (4.1)	6 (4.9)
Dermatitis acneiform, n (%)	5 (2.0)	4 (3.3)
Fatigue, n (%)	4 (1.6)	1 (0.8)
Stomatitis, n (%)	4 (1.6)	0
Dyspnoea, n (%)	3 (1.2)	1 (0.8)
Pneumonia aspiration, n (%)	3 (1.2)	1 (0.8)
Rash, n (%)	3 (1.2)	1 (0.8)
Hypocalcaemia, n (%)	3 (1.2)	0
Hypomagnesaemia, n (%)	2 (0.8)	3 (2.5)
Hypokalaemia, n (%)	2 (0.8)	2 (1.6)
Infusion-related reaction, n (%)	2 (0.8)	2 (1.6)
Syncope, n (%)	2 (0.8)	2 (1.6)
Pneumonitis, n (%)	1 (0.4)	2 (1.6)
Hypophosphataemia, n (%)	0	2 (1.6)

Participants with multiple events are counted once at the maximum reported Common Terminology Criteria for Adverse Events grade for each preferred term. Grade 3/4 adverse events with an incidence of >1% in either arm are shown.

Conclusions

- In the Phase 3 INTERLINK-1 study, which evaluated the efficacy and safety of monalizumab plus cetuximab in a large cohort of participants with R/M HNSCC previously treated with platinum-based chemotherapy and an ICI:
  - OS and PFS were not improved with monalizumab plus cetuximab versus placebo plus cetuximab
  - ORR in the placebo plus cetuximab arm was higher than in previous reports of participants with R/M HNSCC with progression on / after platinum therapy[1–3]
  - Monalizumab plus cetuximab had an acceptable safety profile
  - Exploratory biomarker analyses are ongoing to identify subpopulations that may benefit from monalizumab plus cetuximab treatment
- Monalizumab continues to be studied in combination with other treatments* in non-small cell lung cancer, small cell lung cancer, HER-2 positive breast cancer, colorectal cancer, and other advanced solid tumours

*Non-small cell lung cancer (PACIFIC-9 NCT05221840, COAST NCT03822351, NeoCOAST-2 NCT05061550), small cell lung cancer (MOZART NCT05903092), HER-2 positive breast cancer (MIMOSA NCT04307329) and other advanced solid tumours (NCT02671435).
ICI, immune checkpoint inhibitor; HLA-E, human leukocyte antigen E; NKp46, natural killer cell p46-related protein; ORR, objective response rate; OS, overall survival; R/M HNSCC, recurrent or metastatic head and neck squamous cell carcinoma.
1. Vermorken JB, et al. *J Clin Oncol* 2007;25:2171–2177. 2. Seiwert TY, et al. *Ann Oncol* 2014;25:1813–1820. 3. Fayette J, et al. *Front Oncol* 2016;6:232.

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Thank you for listening

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Supplementary material

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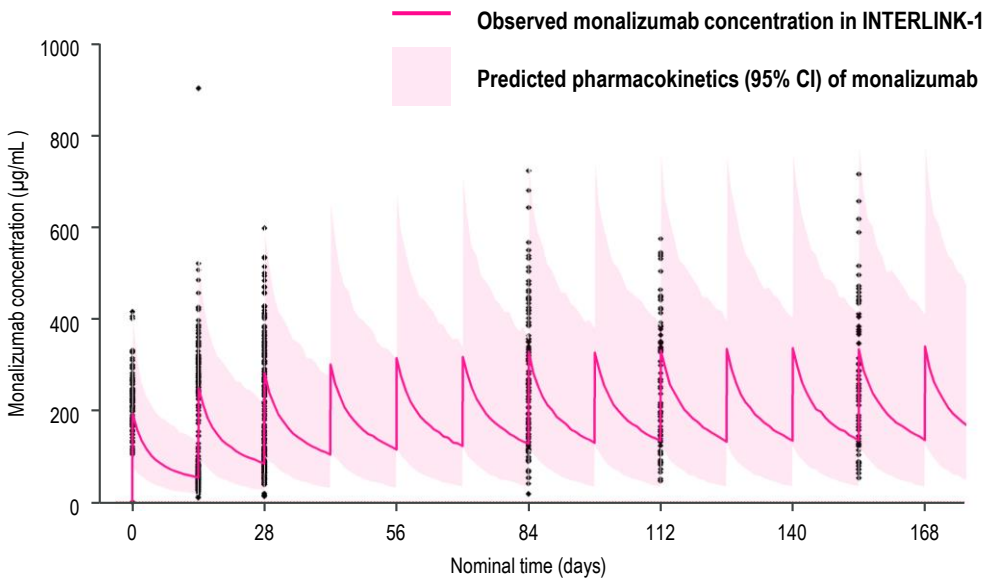
Participant disposition

	All randomised participants (N=306)			
	Monalizumab plus cetuximab (randomised n=203)		Placebo plus cetuximab (randomised n=103)	
	Monalizumab	Cetuximab	Placebo	Cetuximab
Full analysis set for the futility analysis*, n (%)	175 (86.2)		89 (86.4)	
Received treatment, n (%)	175 (86.2)	175 (86.2)	88 (85.4)	87 (84.5)
Ongoing treatment at data cut-off, n (%†)	30 (17.1)	30 (17.1)	21 (23.9)	20 (23.0)
Discontinued treatment, n (%†)	145 (82.9)	145 (82.9)	67 (76.1)	67 (77.0)
Reason for discontinuing, n (%†)				
Condition under investigation worsened	116 (66.3)	114 (65.1)	53 (60.2)	53 (60.9)
Death	12 (6.9)	12 (6.9)	7 (8.0)	7 (8.0)
Adverse event	9 (5.1)	10 (5.7)	1 (1.1)	2 (2.3)
Participant decision	5 (2.9)	5 (2.9)	3 (3.4)	2 (2.3)
Investigator decision	3 (1.7)	4 (2.3)	3 (3.4)	3 (3.4)

*Data cut-off was 11 May 2022, including participants who were randomised on / before 11 March 2022. †Percentage of participants who received treatment.

Secondary endpoint: pharmacokinetics of monalizumab



Median steady state C_{max} value at Cycle 7, µg/mL (SD)	352 (125)
Median steady state C_{min} value at Cycle 7, µg/mL (SD)	143 (76)

	Observed	Simulated
Estimated AUC last value at Cycle 12, day*µg/mL	36,900	29,200

- The pharmacokinetics of monalizumab in participants from INTERLINK-1 were consistent with the predicted pharmacokinetics of monalizumab in a population pharmacokinetic model[1]

Out of 1900 samples from 242 participants, 1113 samples were deemed suitable for analysis. After keeping only samples from within the first 12 cycles of dosing, 843 samples from 161 participants were included in the analysis.
AUC, area under the curve; CI, confidence interval
1. Hwang M, et al. *J Clin Pharm* 2023;63:817–829.

Secondary endpoint: anti-drug antibodies against monalizumab

ADA category	Monalizumab plus cetuximab
ADA evaluable participants	241
TE-ADA positive, n (%)	1 (0.4)
ADA positive at baseline only	0
Titer	–
ADA positive post-baseline,* n (%)	1 (0.4)
Titer	8

- The incidence of TE-ADA against monalizumab was very low
- These results are considered preliminary, and no definitive conclusions can be drawn

Data cut-off was 10 November 2022
Data was collected from 1327 samples
*Single subject with post-baseline ADA was positive only at the end of treatment visit
ADA, anti-drug antibody; TE-ADA, treatment-emergent anti-drug antibody

OS by biomarker expression level: preliminary exploratory results

		HPV-unrelated analysis set (n=51)		Full analysis set (n=64)	
		Monalizumab plus cetuximab (n=33)	Placebo plus cetuximab (n=18)	Monalizumab plus cetuximab (n=40)	Placebo plus cetuximab (n=24)
HLA-E expression level	**H-score ≥ median*, n**	17	10	19	14
	OS HR (95% CI)	1.36 (0.43–4.70)		1.07 (0.35–3.41)	
	H-score < median*, n	16	8	21	10
	OS HR (95% CI)	0.48 (0.14–1.80)		0.73 (0.23–2.59)	
NKp46+ expression level	**Density NKp46+ ≥ median†, n**	11	11	17	15
	OS HR (95% CI)	0.43 (0.09–1.71)		0.37 (0.10–1.18)	
	Density NKp46+ < median†, n	22	7	23	9
	OS HR (95% CI)	1.23 (0.38–4.81)		1.23 (0.38–4.81)	

- The sample size for the biomarker analyses was small; results are considered exploratory, and no definitive conclusions can be drawn
- Results do not adjust for baseline covariate imbalances. Further investigation is ongoing

Data cut-off was 11 May 2022, including participants who were randomised on / before 11 March 2022.
*H-score median value was 165.93. †Density NKp46+ median value was 36.75 cells/mm^2.
CI, confidence interval; HLA-E, human histocompatibility leukocyte antigen; HPV, human papillomavirus; HR, hazard ratio; OS, overall survival.

INTERLINK-1: Phase 3 study of cetuximab ± monalizumab in participants with recurrent / metastatic head and neck squamous cell carcinoma with disease progression on / after platinum chemotherapy and previously treated with an immune checkpoint inhibitor: Plain language summary

Why did we perform this research?

People who develop a specific type of cancer called head and neck squamous cell carcinoma (HNSCC) are typically treated with chemotherapy and immunotherapy (a type of treatment that targets the immune system to help the body fight cancer). The INTERLINK-1 study tested an immunotherapy called monalizumab (which blocks the activity of a protein called NKG2A) with another cancer drug called cetuximab (which blocks the activity of a protein called EGFR) in people whose previous chemotherapy and immunotherapy treatments did not work or stopped working. The goals of this study were to see if treatment with monalizumab and cetuximab could increase the length of time people with HNSCC lived, and to see the frequency and types of side effects people taking monalizumab and cetuximab experienced, compared with those who received placebo and cetuximab—especially in people whose cancer was not related to human papillomavirus (HPV) infection (the type of HNSCC caused by HPV infection has different characteristics to the cancers not related to HPV infection).

How did we perform this research?

Participants with HNSCC whose previous treatments did not work or had stopped working were given monalizumab and cetuximab or placebo and cetuximab. We looked at the results from all participants, but our primary focus was on participants whose cancer was not related to HPV infection. We measured the length of time participants were alive after being assigned to a treatment group; the length of time participants were alive without their cancer growing, spreading, or getting worse; and the side effects they experienced.

What were the findings of this research?

We examined the data partway through the study and found that participants who received monalizumab did not live longer than participants who received placebo. There was no difference in the length of time participants were alive without their cancer growing, spreading, or getting worse for participants treated with monalizumab versus placebo. Participants in both groups reported similar types and severity of side effects regardless of which treatment they received. Whether participants' cancer was related to HPV infection did not impact how well treatment worked.

What are the implications of this research?

We stopped this study early because monalizumab did not appear to work better than placebo for this group of people. Adding monalizumab to cetuximab did not appear to affect the severity of side effects compared with placebo and cetuximab. Monalizumab is being tested in combination with other drugs as a treatment for other cancers.

Where can I access more information?

More information about this clinical trial can be found here: https://clinicaltrials.gov/study/NCT04590963.