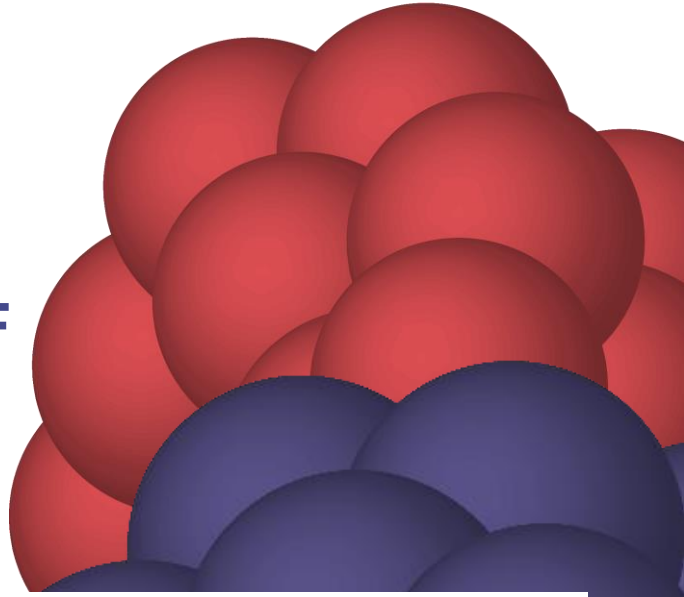
ESMO IMMUNO-ONCOLOGY

Onsite and Online Congress

MONALIZUMAB, CETUXIMAB AND DURVALUMAB IN FIRST LINE TREATMENT OF RECURRENT OR METASTATIC SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK (R/M SCCHN): A PHASE 2 TRIAL



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123MO Abstract #237

DECLARATION OF INTERESTS

A. Dimitrios Colevas

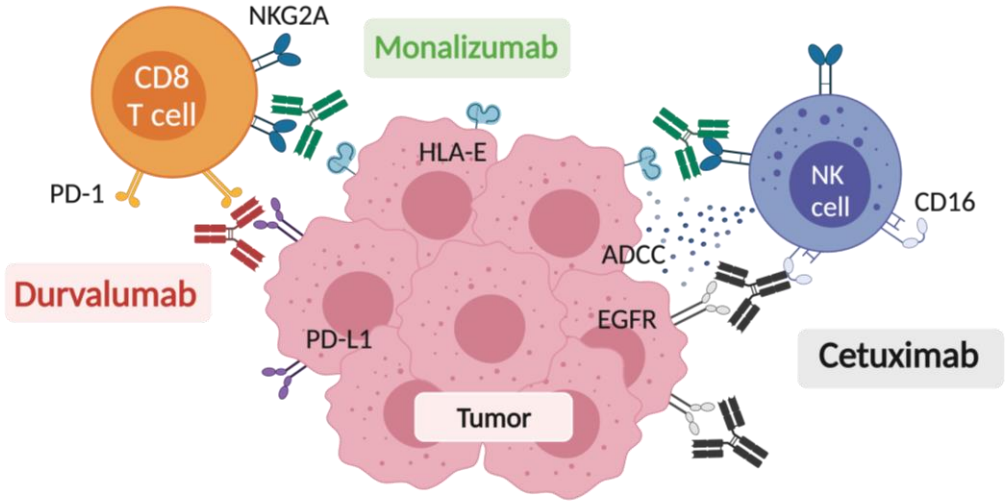
Clinical trials support: Innate, NRG, NCI, BioNTech, FDA, Replimune, Abbvie, Gilead, BMS, Tessa, CUE, Regeneron, Exelis, Viracta

Consulting: GrandRounds, Beigene, Clarion, Aravive, Clearview Oncology, Gilead, CUE

DSMB: PDS Biotech

TRIPLET ANTIBODY COMBINATION STATEGY BASED ON STRONG SCIENTIFIC RATIONALE

- **Monalizumab** is a first-in-class, humanized IgG4 checkpoint inhibitor targeting the CD94/NKG2A receptor, expressed on NK and tumor infiltrating CD8+ T cells. NKG2A is an inhibitory receptor for HLA-E[1].
- PD-L1, EGFR and HLA-E[1] are up-regulated on many cancer cells including H&N, and can suppress tumor immune response and/or contribute to tumor progression.
- Monalizumab in combination with **durvalumab** promotes anti-tumor immunity in preclinical models[1]. Monalizumab in combination with **cetuximab** showed promising clinical activity in patients with post-anti-PD(L)1 and post-platinum R/M HNSCC[2, 3].



- The triplet combination of **monalizumab, cetuximab and durvalumab** is here explored in the first line setting as it could optimize the anti-tumor activity based on the strong scientific rationale.

1. André P et al. Cell 2018: 175(7):1731-1743; 2. Fayette J, ESMO 2018; 3. Cohen RB, ASCO 2020

FIRST STUDY TO EVALUATE THE TRIPLET ANTIBODY COMBINATION

IPH2201-203 study is a multicenter, single arm, multi-cohort* phase II trial (NCT02643550). Cohort 3 is evaluating monalizumab, cetuximab and durvalumab in first line treatment of R/M SCCHN.

Patients

R/M SCCHM

No prior systemic treatment in the R/M setting

Regardless of PD-L1 or HPV status

Treatment

Monalizumab 1500 mg Q4W
Durvalumab 1500 mg Q4W
Cetuximab loading dose 400 then 250 mg/m² Q1W
until progression
or unacceptable toxicity

Primary endpoint

Objective Response Rate (ORR)
as per RECIST 1.1

Key secondary endpoints

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

*Dose escalation, cohorts 1 and 2 evaluating monalizumab and cetuximab in post anti-PD-(L)1 and post-platinum setting were previously presented (Cohen RB, AACR 2017; Fayette J, ESMO 2018; Cohen RB, ASCO 2020, Fayette J, ESMO-IO 2020)

COHORT 3 PATIENT CHARACTERISTICS IN 1L R/M SCCHN

Data cutoff:
1 Aug 2021

Patient Demographics		N=40 n(%)
Age, median [range]		65 [48-91]
Sex	Female	8 (20%)
	Male	32 (80%)
ECOG	0	17 (43%)
	1	23 (58%)
Tobacco	Never	11 (28%)
	Former	**22 (55%)**
	Current	**3 (8%)**
	Unknown	4 (10%)
Alcohol	Never	7 (18%)
	Former	15 (38%)
	Current	11 (28%)
	Unknown	7 (18%)

Disease and primary treatment Characteristics		N=40 n(%)
Tumor site	Oral cavity	14 (35%)
	Oropharynx HPV+	**12 (30%)**
	Oropharynx HPV- or unknown	3 (7.5%)
	Larynx	6 (15%)
	Hypopharynx	4 (10%)
	Nasopharynx	1 (2.5%)
PD-L1 status	**CPS≥1**	**25 (63%)**
	CPS<1	5 (13%)
	Unknown*	10 (25%)
Primary treatment	None	10 (25%)
	Radiotherapy	25 (62%)
	Surgery	19 (48%)
	Systemic	17 (43%)

* Tumor sample at baseline was not available or unsuitable for scoring

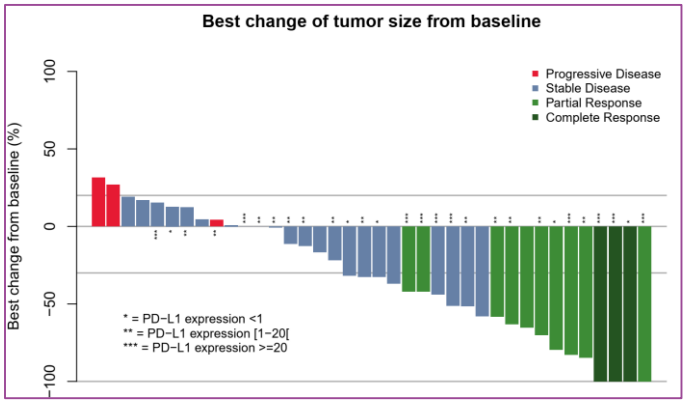
PROMISING ANTI-TUMOR ACTIVITY OF CHEMO-FREE REGIMEN

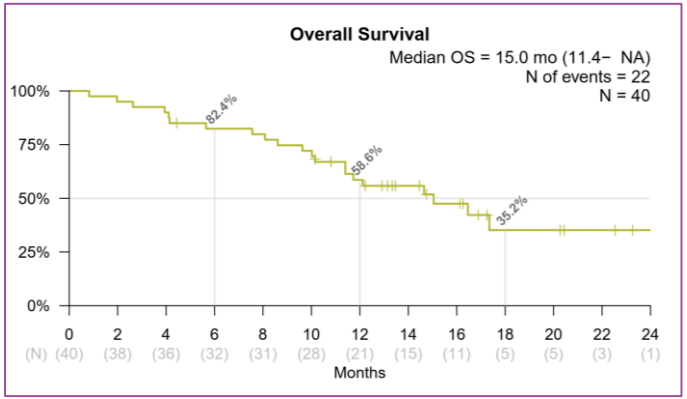
Data cutoff: 1 Aug 2021

	N=40
Confirmed ORR (95% CI), %	**32.5% (20-48)**
Confirmed + unconfirmed ORR (95% CI), %	50% (35-65)
Objective responses by RECIST, n (%)	
CR	3 (7.5%)
PR	10 (25%)
SD	22 (55%)
PD	4 (10%)
NE (early death)	1 (2.5%)
Median DoR (95% CI), months	NA (7.1-NA)
Median Time To Response (95% CI), months	1.8 (1.6-3.7)
Median PFS (95% CI), months	6.9 (4.4-9.3)
Median OS (95% CI), months	**15 (11.4-NA)**
12mo OS (95% CI), %	**58.6% (45-77)**

Median follow-up 16.3 months [4.4 - 25.7]

7 pts/13 still in response; 7.6+, 9.2+, 10.8+, 14.3+, 14.8+, 16.1+, 19.5+ months





CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease; DoR, duration of response;; NA, not available; ORR, objective response rate, CI, confidence interval; PFS, progression free survival; OS, overall survival

EXPLORATORY CPS SUBGROUP ANALYSES

Data cutoff:
1 Aug 2021

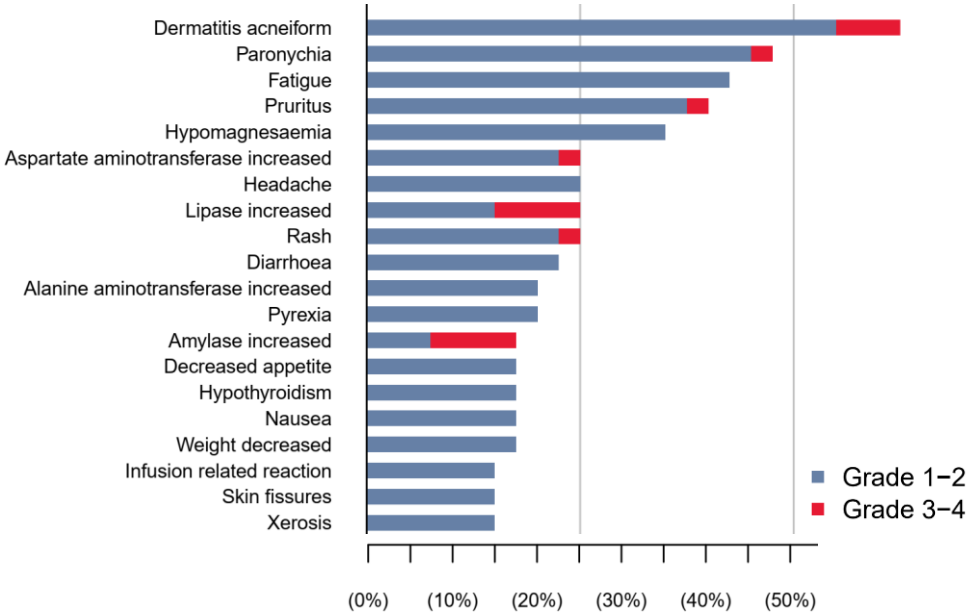
	All N=40	CPS≥1 N=25	CPS<1 N=5	CPS unknown N=10
Confirmed ORR (95% CI), %	32.5% (20-48)	**40% (23-59)**	40% (12-77)	10% (1-40)
Confirmed + unconfirmed ORR (95% CI), %	50% (35-65)	52% (34-70)	80% (37-99)	30% (11-60)
Objective responses by RECIST, n (%)				
CR	3 (7.5%)	2 (8%)	1 (20%)	0 (0%)
PR	10 (25%)	8 (32%)	1 (20%)	1 (10%)
SD	22 (55%)	12 (48%)	3 (60%)	7 (70%)
PD	4 (10%)	2 (8%)	0 (0%)	2 (20%)
NE (early death)	1 (2.5%)	1 (4%)	0 (0%)	0 (0%)
Median PFS (95% CI), months	6.9 (4.4-9.3)	**7.4 (4.1-NA)**	5.3 (4.4-NA)	4.9 (3.5-NA)
Median OS (95% CI), months	15 (11.4-NA)	**17.3 (14.7-NA)**	9.6 (8.6-NA)	11.4 (8.1-NA)

Evaluation of the activity according to CPS status was performed as an exploratory analysis. Due to sparse data resulting from the small subsets of patients (in particular, CPS<1 group n=5) and many patients with unknown CPS (n=10), the wide estimates above should be interpreted with caution. Further follow-up and analysis is needed.

ACCEPTABLE SAFETY PROFILE

Data cutoff:
1 Aug 2021

Most frequent (≥15%) AEs related to any drug



	N (%)
Any TEAEs	40 (100%)
Grade ≥3 TEAEs	29 (72%)
Drug-related Grade ≥3 AEs	19 (48%)
Drug-related SAEs	**3 (8%)**
AEs leading to any drug discontinuation	5 (12%)
AEs leading to all drug discontinuation*	**2 (5%)**
AEs leading to death**	3 (8%)
Drug related AEs leading to death	**0 (0%)**

* adrenal insufficiency, ASAT increased **recurrence of *Clostridium difficile* infection; distributive shock; pneumonia thought related to to hip fracture and subsequent medical procedures

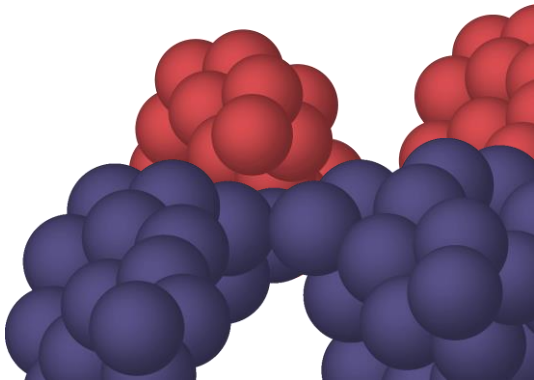
AE, adverse event; SAE, serious adverse event; TEAE, treatment-emergent adverse event; related AEs refer to AE related to any of the 3 drugs as per investigator assessment.

CONCLUSION

- The combination of monalizumab (anti-NKG2A), cetuximab (anti-EGFR) and durvalumab (anti-PD-L1) demonstrates promising activity in the first line R/M SCCHN setting.
- Safety of this chemotherapy free regimen is acceptable with a low rate of treatment discontinuation. There are no new safety signals identified.
- These data support further evaluation of this antibody triplet combination.

ACKNOWLEDGEMENTS

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



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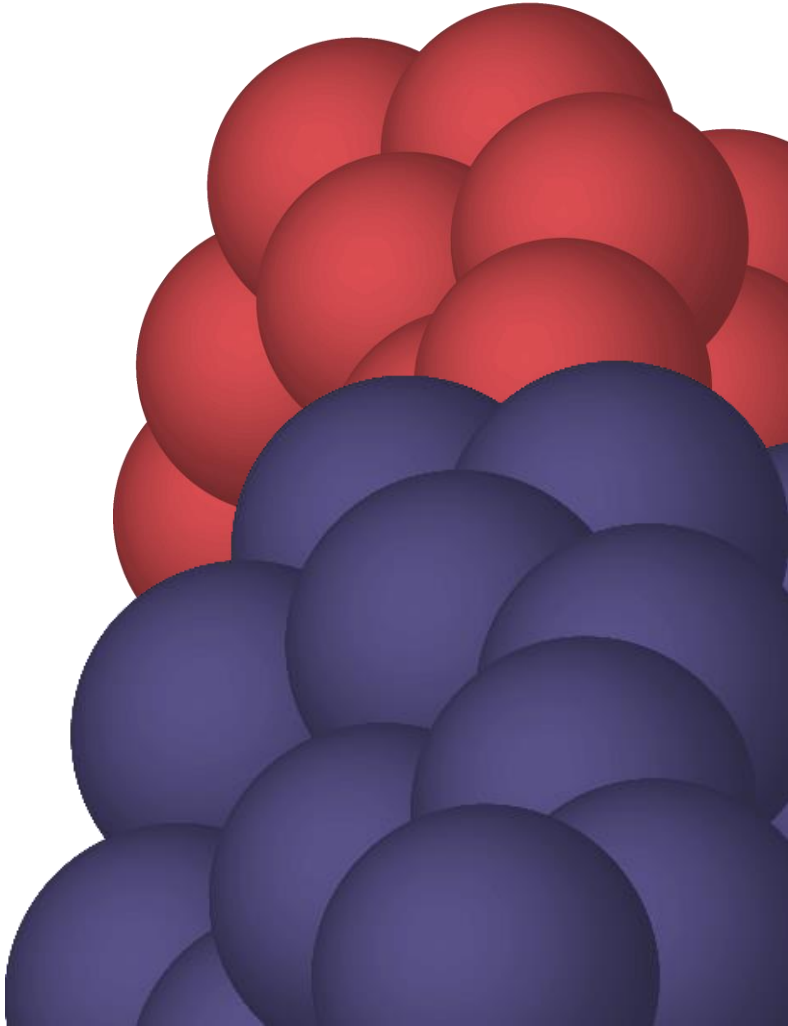

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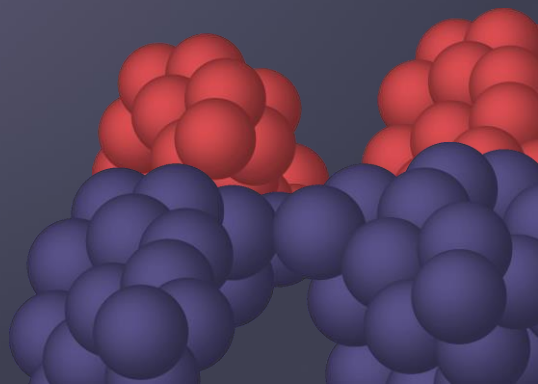
COMPLEMENTARY SLIDE

Keynote-048 results



COMPLEMENTARY SLIDE: KEYNOTE-048 RESULTS

	KN-048 Pembro All comers N=301	KN-048 Pembro+Platinum+5FU All comers N=281	KN-048 Pembro CPS ≥1 N=257	KN-048 Pembro+Platinum+5FU CPS ≥1
ORR % 95% CI	16.9%	36,3%	19.1%	37.2%
CR	4.7%	6%	5.4%	
PR	12.3%	29.5%	13.6%	
SD	27.2%	27.8%	28%	
PD	40.5%	17.1%	38.9%	
NE	11%	15%	10%	
DoR median % 95% CI	23.4 m	6.7 m	24.8 m	6.7 m
PFS median % 95% CI	2.3 m	4.9 m	3.2 m	5.1 m
OS median % 95% CI	11.5 m	13 m	12.3 m	13.6 m
12months OS % 95% CI	49%*	53%*	51%*	55%*

CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease; DoR, duration of response; NE not evaluable; NA, not available; ORR, objective response rate, c, confirmed;; CI, confidence interval; PFS, progression free survival, OS overall survival

**Keynote 048 from Burtness, Lancet 2019; 394: 1915–28 and Greil, ESMO 2020, 915MO*