ASPEN-04: A Randomized Phase 2 Study of Evorpacept in Combination with Pembrolizumab and Chemotherapy in Patients with Recurrent, Unresectable or Metastatic (R/M) Head and Neck Squamous Cell Carcinoma (HNSCC)

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Disclosures / Conflicts of Interest

I have the following relevant financial relationships to disclose:

- Scientific Advisory Boards/Steering Committee memberships: ALX Oncology; Amgen; Arch Oncology; AstraZeneca; Beigene; Bicara; BMS; Boehringer-Ingelheim; Codiak; Eisai; GSK; Johnson and Johnson; Merck-Serono; Molecular Partners; MSD; Nanobiotix; Onchilles; One Carbon; Oncolys; PDS Biotech; Pfizer; PsiVac; Qbiotics; Replimune; VacV.
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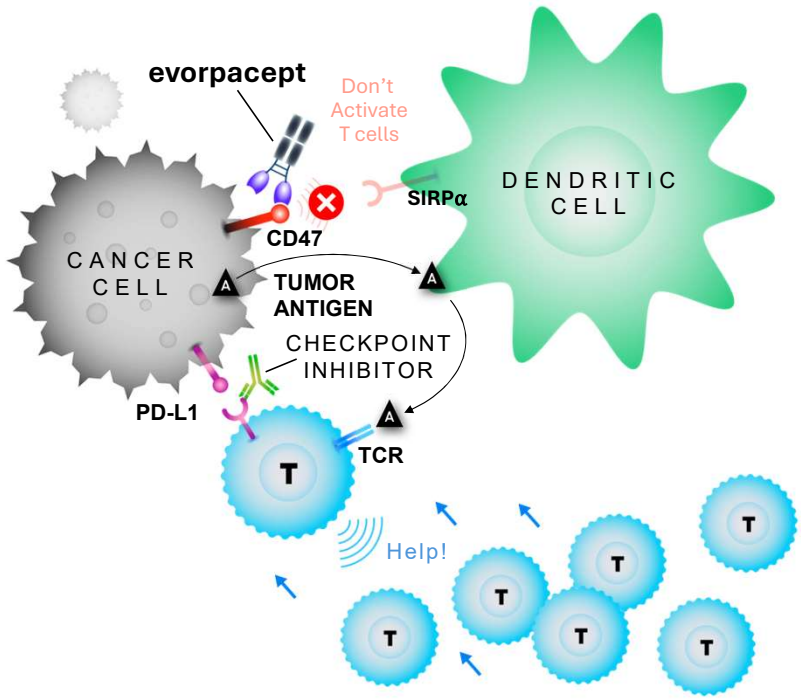
Evorpacept: A CD47 Inhibitor with an Inactive Fc Domain that Enables Anticancer Immune Activation

- Evorpacept blocks the immune evasive 'don't eat me' signal transmitted by CD47 on the surface of cancer cells
- Primary validated mechanism:
  - Evorpacept was designed with an inactive Fc domain to selectively target cancer cells and not healthy cells when combined with anti-cancer antibodies through ADCP
  - This mechanism has been validated in HER2-positive advanced Gastric/GEJ and metastatic breast cancer
- Potential secondary mechanism:
  - CD47 blockade may enhance T-cell priming by activating dendritic cells and stimulating the adaptive immune system
- CD47 expression **may** identify cancers that are responsive to evorpacept

Secondary CD47 Mechanism Investigated in ASPEN-04



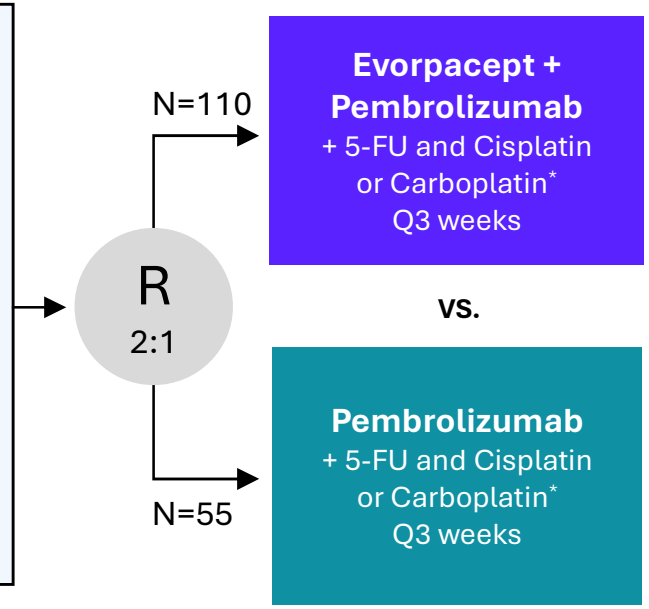
Hypothesis: CD47 blockade may enhance benefit from PD-1 inhibition

ADCP – Antibody dependent cellular phagocytosis.

ASPEN-04 is a Global, Open-Label, Randomized Phase 2 Study of Pembrolizumab and Chemotherapy with or without Evorpacept in Patients with Recurrent, Unresectable or Metastatic HNSCC (NCT04675333)

Key Eligibility Criteria

- Unresectable, recurrent and/or metastatic (R/M) HNSCC
- No prior treatment for R/M HNSCC
- Measurable disease (RECIST v1.1)
- Adequate organ function
- Age ≥ 18 years old
- ECOG PS ≤ 1
- No prior anti-CD47 or anti-SIRPα agent
- No prior anti-PD-1, anti-PD-L1/L2 agent or agent directed to other stimulatory or co-inhibitory T cell receptor



Primary Endpoints

- Objective response rate (ORR) by BICR
- Primary analysis compares ORR to historical control ORR of 36% (Burtness et al., 2019)

Secondary Endpoints

- ORR by investigator assessment, DCR, DOR, TTP, PFS, OS, Safety
- Secondary analysis compares ORR (BICR/inv) between treatment arms

Exploratory Analysis

- Preplanned biomarker analysis of CD47 vs efficacy endpoints

Minimization Factors

- Geography: Asia Pacific, Europe, North America
- PD-L1 CPS: CPS 0, CPS 1-19, CPS ≥20
- HPV (p16) Status: positive, negative, unknown, other
- Tobacco Habits: Current, Past, Non-user
- ECOG PS: 0, 1

*Dosing: evorpacept 45 mg/kg IV Q3W, pembrolizumab 200 mg IV Q3W (for a maximum of 35 cycles) and 5FU (1000 mg/m^2/day continuous infusion D1,2,3 and 4 Q3W x 6 cycles) and either carboplatin (AUC 5 mg/ml/min as a 60 min infusion D1 Q3W x 6 cycles) or cisplatin (100 mg/m^2 as a 60 min infusion D1 Q3W x 6 cycles); **BICR** – Blinded independent central review; **CPS** – Combined positive score; **DCR** – Disease control rate; **DOR** – Duration of response; **ECOG PS** – Eastern cooperative oncology group performance status; **HNSCC** – Head and neck squamous cell carcinoma; **HPV** – Human papilloma virus; **IV** – Intravenous; **PD-1** – Programmed cell death protein 1; **PD-L1** – Programmed death ligand 1; **PD-L2** – Programmed death ligand 2; **Pembro** – Pembrolizumab; **PFS** – Progression free survival; **OS** – Overall survival; **Q3W** – Every three weeks; **RECIST** – Response evaluation criteria in solid tumors; **SIRPα** – Signal regulatory protein alpha; **TTP** – Time to progression.

ASPEN-04: Patient Demographics and Baseline Characteristics

	Evorpacept + Pembrolizumab + Chemo (n=110)	Pembrolizumab + Chemo (n=55)
Median Age (range), Yrs	61.5 (26-78)	63.0 (19-76)
Male	81%	82%
Race: White, Asian, Other	54, 43%, 3%	53% , 44%, 3%
Region: North America, Europe, Asia	13%, 36%, 51%	15%, 34%, 51%
ECOG PS 0	34%	31%
Former or Current Smoker	66%, 10%	66%, 6%
PD-L1 CPS		
0	25%	25%
1-19	49%	46%
≥20	26%	29%
Disease Status		
Recurrent	27%	20%
Metastatic	73%	80%
Primary Tumor Location		
Oropharynx	40%	34%
Lip or Oral Cavity	24%	29%
Hypopharynx	13%	13%
Larynx	20%	18%
HPV Positive	32%	31%

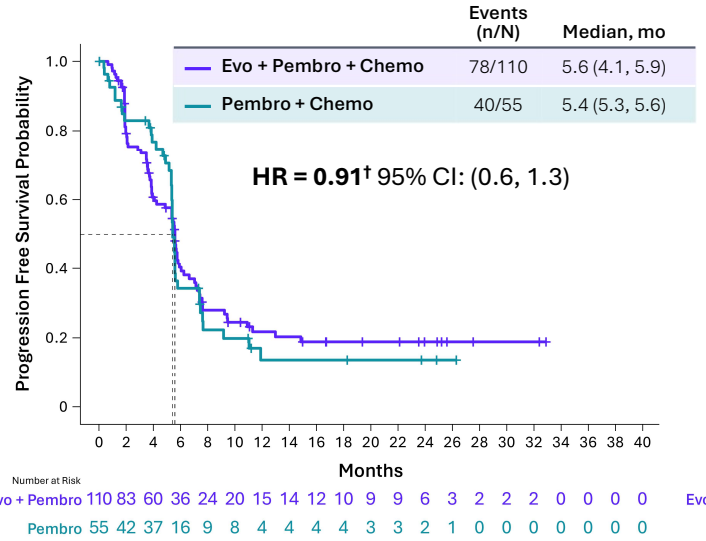
CPS – Combined positive score; **ECOG PS** – Eastern cooperative oncology group performance status; **HPV** – Human papilloma virus.

ASPEN-04: Overall Efficacy

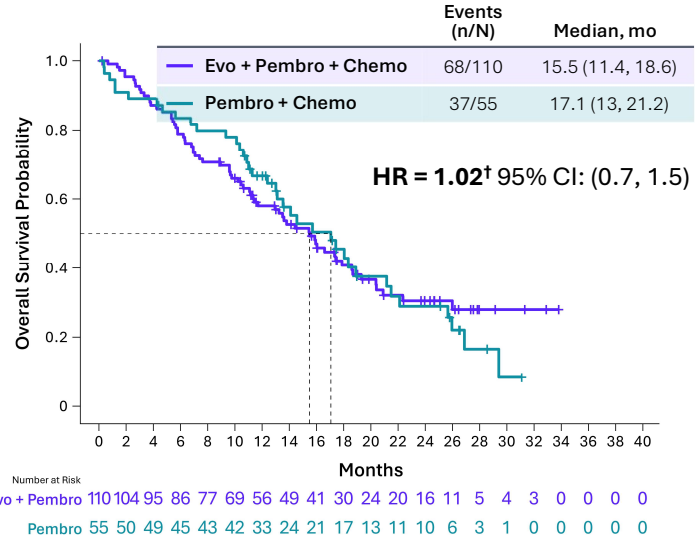
ORR and DOR by BICR

	Evorpacept + Pembrolizumab + Chemo (n=110)	Pembrolizumab + Chemo (n=55)
ORR, % (95% CI)	37.3 (28, 47)	45.5 (32, 59)
CR,%	16.4	9.1
PR, %	20.9	36.4
SD, %	31.8	30.9
PD, %	21.8	7.3
Other*, %	9.1	16.4
Median DOR, mo (95% CI)	7.7 (5.6, NE)	3.9 (3.6, 5.8)
Median Follow Up, mo	24.0	25.8

Progression Free Survival by BICR



Overall Survival



- ORR for evorpacept + pembrolizumab + chemo (37.3%) was not statistically different from ORR for historical control[1] (36.4%; 1-sided p = 0.425 vs α = 0.025)
- No difference in ORR, PFS and OS between treatment arms
- No differences were observed in outcomes based on CD47 expression

. †HR (Evo + Pembro + Chemotherapy vs. Pembro + Chemo) is from a stratified Cox proportional hazards model stratified by PD-L1 CPS per IRT. **BICR** – Blinded independent central review; **DOR** – Duration of response; **NE** – not estimable; **Evo** – Evorpacept; **mo** – Month; **ORR** – Objective response rate; **OS** – Overall survival; **Pembro** – Pembrolizumab; **PFS** – Progression free survival. **1.** Burtness et al. *Lancet* 2019;394:1915-28

ASPEN-04 Treatment-Emergent Adverse Events Occurring in >15% in Either Treatment Arm

	Evorpacept + Pembrolizumab + Chemo (n=109)		Pembrolizumab + Chemo (n=55)	
n (%)	Any Grade	≥Grade 3	Any Grade	≥Grade 3
Any TEAE	109 (100)	76 (69.7)	55 (100)	34 (61.8)
Nausea	56 (51.4)	1 (0.9)	28 (50.9)	0
Anemia	51 (46.8)	14 (12.8)	22 (40.0)	3 (5.5)
Constipation	50 (45.9)	0	19 (34.5)	0
Fatigue	34 (31.2)	1 (0.9)	22 (40.0)	0
Neutrophil Count Decreased	37 (33.9)	26 (23.9)	17 (30.9)	8 (14.5)
Stomatitis	35 (32.1)	8 (7.3)	18 (32.7)	2 (3.6)
Platelet Count Decreased	32 (29.4)	4 (3.7)	12 (21.8)	3 (5.5)
Mucosal Inflammation	31 (28.4)	5 (4.6)	16 (29.1)	1 (1.8)
Diarrhea	29 (26.6)	2 (1.8)	12 (21.8)	1 (1.8)
Neutropenia	21 (19.3)	13 (11.9)	10 (18.2)	4 (7.3)
Pyrexia	20 (18.3)	3 (2.8)	7 (12.7)	0
ALT Increased	20 (18.3)	3 (2.8)	4 (7.3)	0
AST Increased	20 (18.3)	2 (1.8)	4 (7.3)	0
Weight Decreased	19 (17.4)	3 (2.8)	6 (10.9)	0
Decreased Appetite	18 (16.5)	2 (1.8)	9 (16.4)	0
Oral Candidiasis	18 (16.5)	0	5 (9.1)	0
Hypokalemia	17 (15.6)	7 (6.4)	5 (9.1)	1 (1.8)

- EP + chemo was generally well tolerated, and no new safety signals were identified
- Treatment-emergent SAEs: 45.9% vs 36.4% for EP + chemo vs P + chemo
- Febrile neutropenia 9.2% vs 0% in EP + chemo vs P + chemo (Incidence of G3+ febrile neutropenia in KN-048 was 9.0%)[1]
- TEAEs leading to permanent discontinuation or delays:
  - D/C: 6.4% vs 9.1% EP + chemo vs P + chemo
  - Dose delays: 61.5% vs 41.8% EP + chemo vs P + chemo
- Grade 5 treatment-emergent AEs: 7 (6.4%) vs 3 (5.5%) for EP + chemo vs P + chemo
  - Related grade 5 events: 1 (0.9%) vs 1 (1.8%) for EP + chemo* vs P + chemo†

All treatment emergent fatal events: evorpacept + pembrolizumab + chemotherapy (N=7; 6.4%): disease progression N=2, drowning N=1, pleural effusion N=1; *Febrile neutropenia N=1, tumor hemorrhage N=1, death N=1; Pembrolizumab + chemotherapy (N=3; 5.5%): pneumonia aspiration N=1; †Septic shock N=1, death N=1; **E** – Evorpacept; **P** – Pembrolizumab. 1. Burtness *et al. Lancet* 2019;394:1915-28, suppl appendix.

Conclusions

- ASPEN-04 did not meet the primary endpoint when comparing the ORR of evorpacept, pembrolizumab and chemotherapy (37.3%) vs historical control for pembrolizumab and chemotherapy (36%)
- No difference was identified in the overall population between the two treatment arms for ORR, DOR, PFS, and OS
- The combination of evorpacept + pembrolizumab + chemo was generally well tolerated, and no new safety signals were identified
- The outcomes do not support advancing evorpacept in combination with pembrolizumab and chemotherapy in recurrent, unresectable or metastatic HNSCC

Thank you.

We would like to thank all the participating patients and their families as well as site research staff.

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