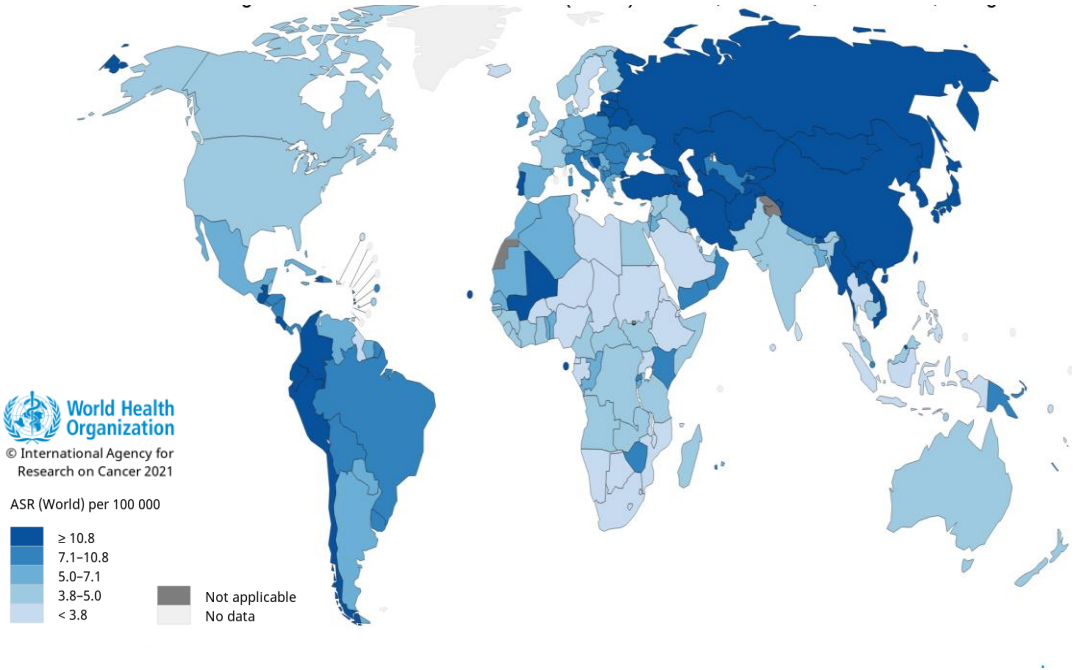
ALX ONCOLOGY

# SITC Conference Call

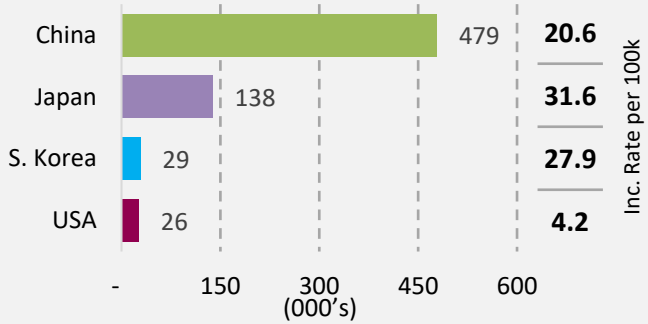
November 9, 2021

# Gastric Cancer Statistics

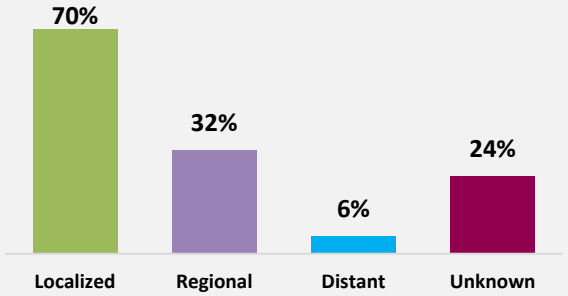
## Age-Standardized Incidence Rate (ASR)[1]




## Annual New Cases and ASR Incidence Per 100,000[1]




## 5-Year Survival by Stage at Diagnosis in US[2]




(1) WHO/IARC accessed October 22, 2021 for most recent year, 2020; (2) SEER Cancer Stats accessed October 22, 2021



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# Current HER2 positive GC Standards of Care (SOC) and Recent Studies

## Standards of care for HER2 positive gastric cancer

| 1st Line | 2nd Line | 3rd Line |
|---|---|---|
| **Trastuzumab + FP doublet*** <br>• FOLFOX, XELOX, SOX, XP, SP, CF | **Ramucirumab/Paclitaxel** <br>**Trastuzumab-deruxtecan (US)** <br>Paclitaxel <br>Docetaxel <br>Irinotecan | **Trastuzumab-deruxtecan** <br>**Trifluridine/tipiracil** <br>**Pembrolizumab (CPS≥1)** <br>**Nivolumab** <br>Irinotecan |

## Outcomes in recent studies

| HER2 GC Population | N | ORR (%) | DOR (m) [95% CI] | PFS (m) [95% CI] | OS (m) [95% CI] | 0S rate at 12 m |
|---|---|---|---|---|---|---|
| **≥2L Gastric ramucirumab/paclitaxel RAINBOW[1]** | **330** | **28** | **4.4 [IQR 2.8–7.5]** | **4.4 [4.2-5.3]** | **9.6 [8.5-10.8]** | **40%** |
| ≥2L Gastric trastuzumab/ram/paclitaxel[2] | 50 | 52 | 5.1 [3.3-6.9] | 7.4 [6.5-8.3] | 13.6 [9.6-17.5] | - |
| 2L Gastric trastuzumab-deruxtecan DESTINY 02[3] | 79 | 38 | 8.1 [4.1-NE] | 5.5 [4.2-7.3] | - | - |
| **≥3L Gastric trastuzumab-deruxtecan DESTINY 01[4]** | **126** | **41** | **11.3 [5.6-NE]** | **5.6 [4.3-6.9]** | **12.5 [9.6-14.3]** | **52%** |

[1]Wilke et al, Lancet October 2014, [2]Rha et al #4063 ASCO 2021, [3]Van Cutsem et al ESMO 2021, [4]Enhertu product insert, and Shitara et al, NEJM June 18, 2020; NE could not be estimated



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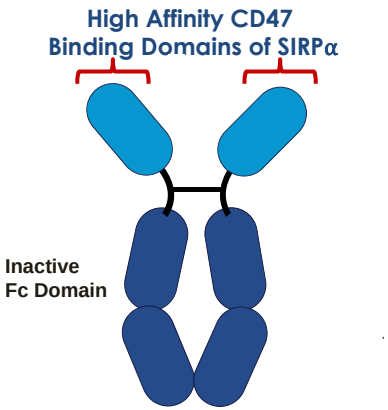
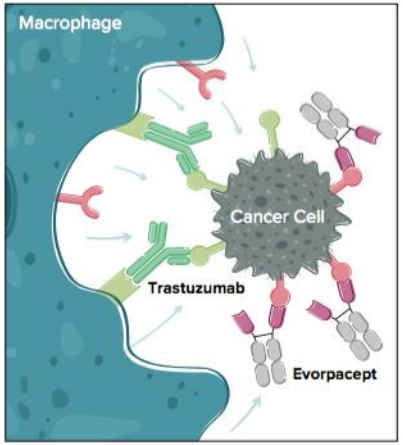
# Evorpacept: Targeting CD7 as A Myeloid Checkpoint

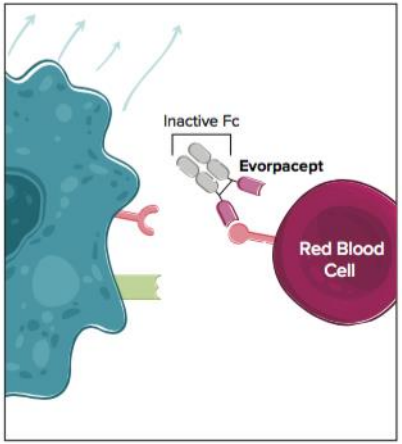
- **CD47, a marker of self, is upregulated by tumors to evade the immune system**
- **CD47-SIRPα signaling represents a myeloid checkpoint mechanism in cancer**
- **CD47 engages SIRPα and signals the macrophage to ignore the cell on which it is expressed**



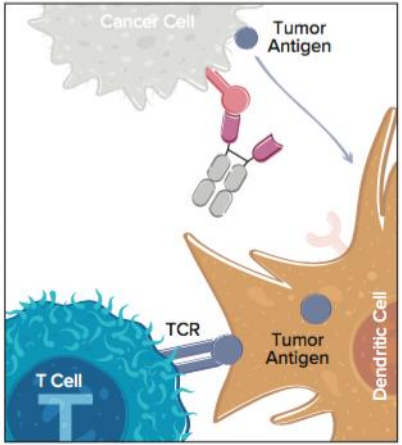

**Molecular weight half the size of a typical antibody**




Evorpacept with an inactive Fc binds and blocks CD47-SIRPα interaction enhancing anti-cancer antibody's ADCP activity




Evorpacept's inactive Fc spares normal blood cells from CD47 targeted ADCP activity




Evorpacept activates dendritic cells and enhances cross-priming of T cells



Kauder, SE. et al. PLoS ONE. 2018 August;13(8): e0201832

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# Evorpacept (ALX148), a CD47 myeloid checkpoint inhibitor, in patients with head and neck squamous cell carcinoma (HNSCC) and with gastric/gastroesophageal cancer (GC); ASPEN-01

Keun-Wook Lee,[1] Hyun Cheol Chung,[2] Tae Min Kim,[3] Nehal J Lakhani,[4] Wells Messersmith,[5] Rafael Santana-Davila,[6] Won Seog Kim,[7] Patricia LoRusso,[8] Yung-Jue Bang,[3] Laura QM Chow,[6*] Philip Fanning,[9] Pierre Squifflet,[10] Feng Jin,[9] Alison Forgie,[9] Hong Wan,[9] Jaume Pons,[9] Sophia S Randolph,[9] Justin Gainor[11]

[1]Seoul National University Bundang Hospital, Seoul National University College of Medicine, Seongnam, Korea; [2]Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, Korea; [3]Seoul National University College of Medicine, Seoul, Korea; [4]START Midwest, Grand Rapids, MI; [5]University of Colorado Cancer Center, Aurora, CO; [6]University of Washington, Seattle, WA; [7]Sungkyunkwan University School of Medicine, Samsung Medical Center, Seoul, Korea; [8]Yale Cancer Center, New Haven, CT; [9]ALX Oncology, South San Francisco, CA, USA, [10]International Drug Development Institute, Brussels, Belgium, [11]Massachusetts General Hospital Cancer Center, Boston, MA

*Dr. L Chow currently at University of Texas at Austin, TX.

Presented at the 2021 Society for Immunotherapy of Cancer Annual Meeting Nov 10-14,2021 Abstract #498



ALX ONCOLOGY

# ASPEN-01: Evorpacept administered in combination with trastuzumab, ramucirumab, and paclitaxel

**Primary Part 2 gastric cancer combination study objective:** Characterize evorpacept's safety profile in combination with

- trastuzumab (**T**) (8 mg/kg IV→6 mg/kg Q3W),
- ramucirumab (**R**) (8 mg/kg Days 1, 15 Q4W),
- paclitaxel (**P**) (80 mg/m2 Days 1, 8, 15 Q4W),

Preliminary data as of September 01, 2021.

| | | *evorpacept + trastuzumab + ramucirumab/paclitaxel ≥2L GC (N=18)* |
|---|---|---|
| ***Median age, years (range)*** | | 67.5 (36-83) |
| ***Sex, n*** | **M** | 13 |
| | **F** | 5 |
| ***Race, n*** | **Asian** | 15 |
| | **White** | 3 |
| ***ECOG PS, n*** | **0** | 8 |
| | **1** | 10 |
| ***Progressed upon prior anti-HER2 Therapy, n ( %)*** | | 17 (94) |
| ***Progressed upon ≥2 prior anti-HER2 therapy n (%)*** | | 2 (11.1) |
| ***Progressed upon prior CPI Therapy, n (%)*** | | 2 (11.1) |
| ***Visceral distant metastasis, n (%)*** | | 15 (83) |



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# ASPEN-01: Evorpacept + TRP Tolerability

| Evorpacept + Trastuzumab + Ramucirumab + Paclitaxel (N=18) / Adverse Event, n (%) | | | | | | |
|---|---|---|---|---|---|---|
| | ALL Causality | | | Evorpacept-Related | | |
| Evorpacept Dose QW | G1-2 | G3 | G4 | G1-2 | G3 | G4 |
| Neutrophil Count Decreased | 3 (17) | 5 (28) | 3 (17) | – | – | – |
| Epistaxis | 9 (50) | – | – | – | – | – |
| Peripheral Neuropathy / Peripheral Sensory Neuropathy | 8 (44) | 1 (6) | – | – | – | – |
| Decreased Appetite | 8 (44) | – | – | – | – | – |
| Fatigue | 7 (39) | 1 (6) | – | 2 (11) | – | – |
| Anemia | 3 (17) | 4 (22) | – | 1 (6) | – | – |
| Hypertension | – | 6 (33) | | – | – | – |
| Abdominal Pain / Abdominal Pain Upper | 5 (28) | – | – | 1 (6) | – | – |
| Headache | 5 (28) | – | – | 1 (6) | – | – |
| Stomatitis | 5 (28) | – | – | 1 (6) | – | – |
| Alanine Aminotransferase Increased | 4 (22) | – | – | – | – | – |
| Alopecia | 4 (22) | – | – | – | – | – |
| Aspartate Aminotransferase Increased | 3 (17) | 1 (6) | – | – | – | – |
| Asthenia | 3 (17) | 1 (6) | – | – | – | – |
| Diarrhea | 4 (22) | – | – | 3 (17) | – | – |
| Insomnia | 4 (22) | – | – | – | – | – |
| Rash/Dermatitis Acneiform | 4 (22) | – | – | 4 (22) | – | – |
| Pruritis | 3 (17) | – | – | 2 (11) | – | – |
| Urticaria | 3 (17) | – | – | 3 (17) | – | – |
| Back Pain | 2 (11) | – | – | 1 (6) | – | – |
| Diverticulitis | 1 (6) | 1 (6) | – | – | – | – |
| Dysphagia | 1 (6) | 1 (6) | – | – | – | – |
| Hypophosphatemia | 1 (6) | 1 (6) | – | – | – | – |
| Platelet Count Decreased | 1 (6) | 1 (6) | – | – | – | – |
| Hydronephrosis | – | 1 (6) | – | – | – | – |
| Lymphocyte Count Decreased | – | 1 (6) | – | – | 1 (6) | – |
| Non-Cardiac Chest Pain | – | 1 (6) | – | – | – | – |
| Urinary Tract Infection | – | 1 (6) | – | – | – | – |
| Vision Blurred | 1 (6) | – | – | 1 (6) | – | – |

Evorpacept: 10 mg/kg (n=3) & 15 mg/kg (n=15); All TEAEs occurring in ≥4 patients. For cases of TEAEs Grade ≥3 and any TRAE, all AEs are listed irrespective of patient numbers.

**Evorpacept in combination with trastuzumab, ramucirumab and paclitaxel was well tolerated**

**There were no dose limiting toxicities, on study deaths or evorpacept-related SAEs**



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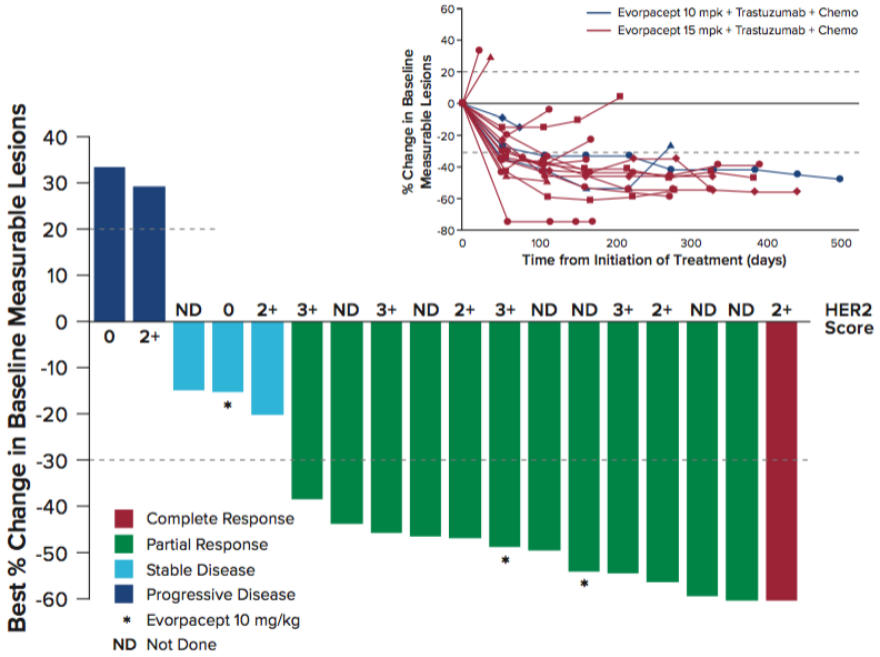
# Clinical activity of evorpacept + TRP in patients with ≥2L HER2 positive GC




| Population | N (EVAL) | OR Rate | Median DOR (m) (95% CI) | Median PFS (m) (95% CI) | Median OS (m) (95% CI) | OS Rate at 12 months | Follow Up (m) (95% CI) |
|---|---|---|---|---|---|---|---|
| **≥2L GC (evorpacept 10 mg/kg or 15 mg/kg + TRP)** | 18 | 72.2% | 14.8 (3.9; NR) | 17.1 (5.4; NR) | 17.1 (9.8; NR) | 79.0% | 14.5 (7.2; 19.0) |

TRP – Trastuzumab + Ramucirumab + Paclitaxel; NR – Not reached



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# Evorpacept's initial response benefit is reflected in survival-based endpoints in GC populations evaluated

- **Preliminary data suggests that evorpacept can be safety combined with TRP with no maximum tolerated dose reached.**
- **Preliminary pharmacokinetics analysis demonstrates no impact of the combination partners upon evorpacept exposure levels.**
- **Evorpacept demonstrates initial ORR of 72.2% with a 14.8m mDOR and a mOS of 17.1 months in patients with ≥2L HER2 positive GC in combination with TRP that compares favorably with the clinical experience of both ramucirumab + paclitaxel as well as trastuzumab-deruxtecan in similar populations.**

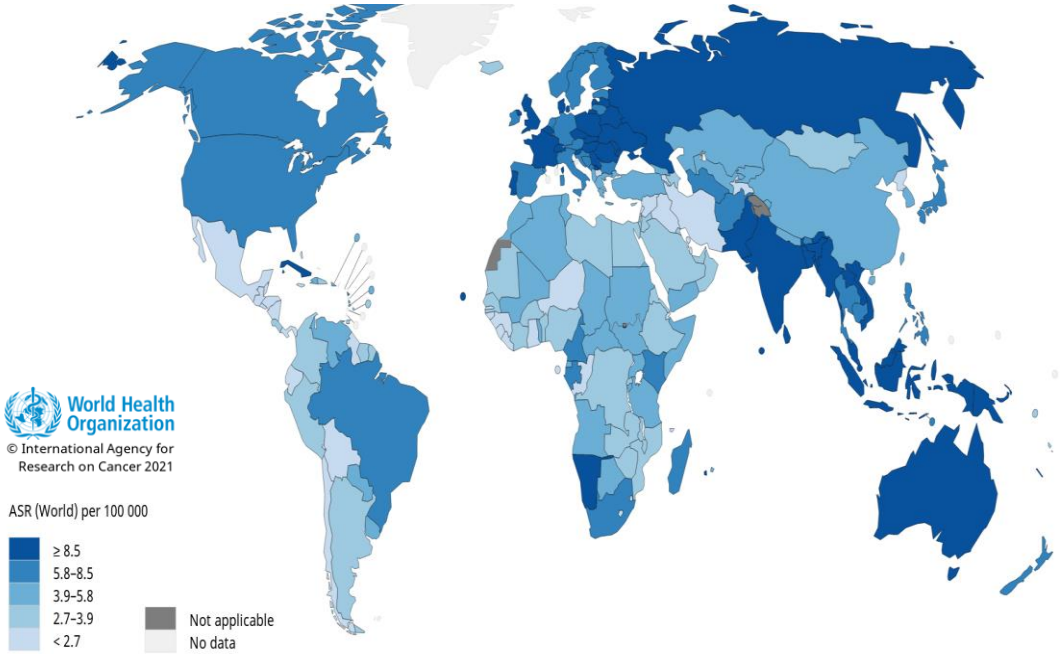
# Professor  Kevin Harrington, MBBS, PhD, MRCP, FRCP, FRCR

Professor Harrington is Professor of Biological Cancer Therapies and is the Head of the Division of Radiotherapy and Imaging at The Institute of Cancer Research.  He serves as a consultant oncologist at the Royal Marsden (RMH) and St George's Hospital and leads the Targeted Physical Therapies within the RMH/ICR Biomedical Research Centre.

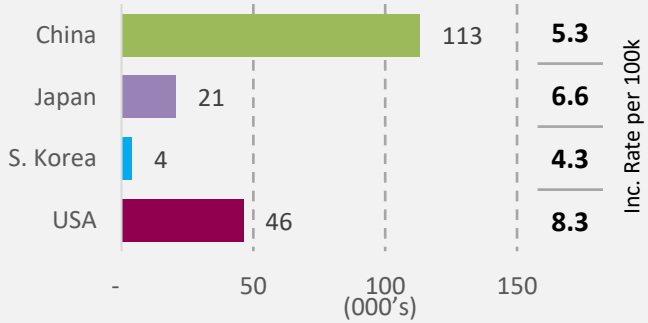
He is the national chair of the CRUK Advanced Radiotherapy Technologies Network Accelerator (ART-NET) and specializes in developing new treatments using biologically-targeted agents that selectively destroy cancer cells and activate anti-tumor immune responses.

# Head and Neck Cancer Statistics

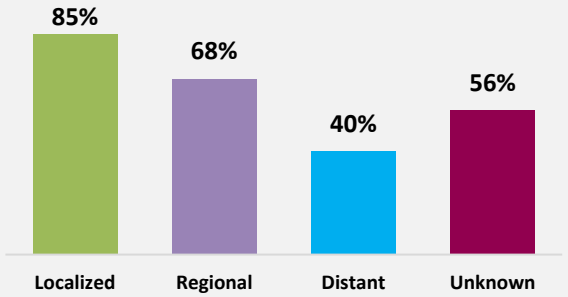
**Age-Standardized Incidence Rate (ASR)[1]**




**Annual New Cases and ASR Incidence Per 100,000[1]**




**5-Year Survival by Stage at Diagnosis in US[2]**




Oral cavity and pharynx. (1) WHO/IARC data accessed October 22, 2021 for most recent year, 2020; (2) SEER Cancer Stats accessed October 22, 2021



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# Pembrolizumab clinical standards of care in patients with 1L and 2L CPI naïve advanced HNSCC (total population)

| Population | N | ORR (%) | PFS (m) [95% CI] | OS (m) [95% CI] | OS Rate at 12 m | Follow Up (m) [95% CI] |
|---|---|---|---|---|---|---|
| **KN048: 1L HNSCC** pembrolizumab + 5FU/platinum | 281 | 36% | 4.9 [4.7–6.0] | 13.0 [10.9–14.7] | 53% | 13 [6.4–26.6] |
| **KN048: 1L HNSCC** cetuximab + 5FU/platinum | 300 | 36% | 5.1 [4.9–6.0] | 10.7 [9.3–11.7] | 44% | 10.7 [6.6–19.7] |
| **KN040: 2L HNSCC (CPI naïve)** pembrolizumab | 247 | 14.6% | 2.1 [2.1–2.3] | 8.4 [6.4–9.4] | 37% | 8.4 [3.3–14.5] |
| **KN040: 2L HNSCC (CPI naïve)** Phys Choice: methotrexate, docetaxel, or cetuximab | 248 | 10.1% | 2.3 [2.1–2.8] | 6.9 [5.9–8.0] | 26.5% | 7.1 [3.7-12.4] |

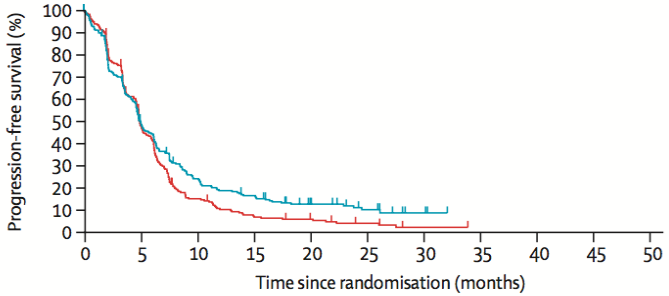


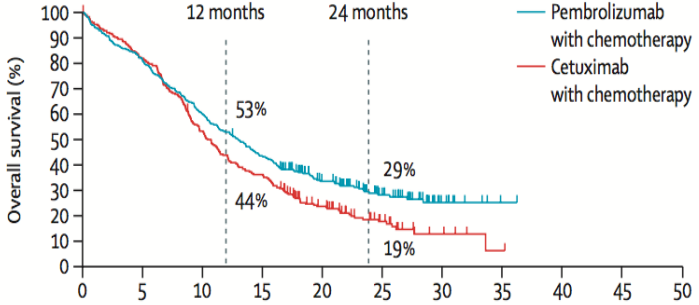
Burtness et al. Lancet 2019; Cohen et al. Lancet 2018

# Immuno-oncology agents in CPI naïve HNSCC populations: PFS and OS as endpoints in KN040 and KN048

Burtness et al. Lancet 2019

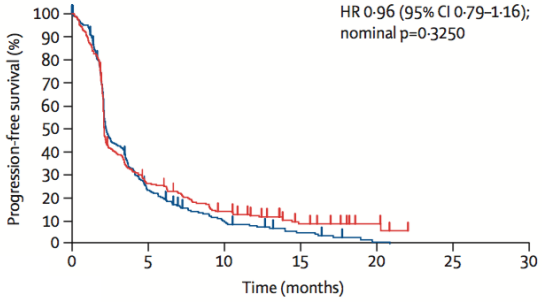
**KN048: OS and PFS K-M Curves at the Second Interim Analysis in the 1L HNSCC CPI Naïve Population**

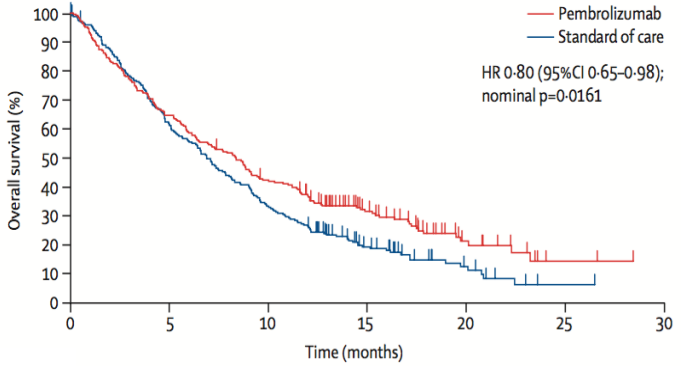



Cohen et al. Lancet 2018

**KN040: OS and PFS K-M Curves at the FA in the 2L HNSCC CPI Naïve Population**



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# Evorpacept (ALX148), a CD47 myeloid checkpoint inhibitor, in patients with head and neck squamous cell carcinoma (HNSCC) and with gastric/gastroesophageal cancer (GC); ASPEN-01

Keun-Wook Lee,[1] Hyun Cheol Chung,[2] Tae Min Kim,[3] Nehal J Lakhani,[4] Wells Messersmith,[5] Rafael Santana-Davila,[6] Won Seog Kim,[7] Patricia LoRusso,[8] Yung-Jue Bang,[3] Laura QM Chow,[6*] Philip Fanning,[9] Pierre Squifflet,[10] Feng Jin,[9] Alison Forgie,[9] Hong Wan,[9] Jaume Pons,[9] Sophia S Randolph,[9] Justin Gainor[11]

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ALX ONCOLOGY

# ASPEN-01: Evorpacept administered in combination with pembrolizumab with and without chemotherapy

**Primary Part 2 HNSCC combination study objective:**

Characterize evorpacept's safety profile in combination with:

- **pembrolizumab (200 mg IV Q3W) with/without**
- **cisplatin (100 mg/m2 Q3W x 6) or**
- **carboplatin (AUC 5 mg/ml/min Day 1 Q3W x 6), and**
- **5FU: 1000 mg/m2/day Days 1, 2, 3, 4 Q3W x 6)**

Preliminary data as of September 01, 2021.

| | | *evorpacept + pembrolizumab + chemo 1L HNSCC (N=13)* | *evorpacept + pembrolizumab ≥2L CPI naïve HNSCC (N=10)* |
|---|---|---|---|
| ***Median age, years (range)*** | | 61 (45-70) | 63 (35-81) |
| ***Sex, n*** | **M** | 12 | 7 |
| | **F** | 1 | 3 |
| ***Race, n*** | **Asian** | 10 | 5 |
| | **White** | 3 | 4 |
| | **Black** | - | 1 |
| ***ECOG PS, n*** | **0** | 8 | 3 |
| | **1** | 5 | 7 |
| ***Progressed upon prior CPI Therapy, n (%)*** | | 0 (0) | 0 (0) |
| ***Visceral distant metastasis, n (%)*** | | 7 (54) | 6 (60) |

# Evorpacept in combination with standard pembrolizumab + 5FU + Platinum was well tolerated

| Evorpacept + Pembrolizumab + 5FU + Platinum (N=13) / Adverse Event, n (%) | | | | | | |
|---|---|---|---|---|---|---|
| | ALL Causality | | | Evorpacept-Related | | |
| Evorpacept Dose QW | G1-2 | G3 | G4 | G1-2 | G3 | G4 |
| Anemia | 4 (31) | 4 (31) | – | – | 1 (8) | – |
| Nausea | 8 (62) | – | – | – | – | – |
| Stomatitis | 7 (54) | 1 (8) | – | – | – | – |
| Neutrophil Count Decreased / Neutropenia | 2 (15) | 5 (38) | – | 1 (8) | – | – |
| Platelet Count Decreased / Thrombocytopenia | 7 (54) | – | – | – | – | – |
| Fatigue | 5 (38) | – | – | 1 (8) | – | – |
| Alanine Aminotransferase Increased | 3 (23) | 1 (8) | – | – | – | – |
| Dysphagia | 1 (8) | 1 (8) | – | – | – | – |
| Hypersensitivity | 1 (8) | – | 1 (8) | – | – | 1 (8) |
| Pneumonia | 1 (8) | 1 (8) | – | – | – | – |
| Pneumonitis | 2 (15) | – | – | 1 (8) | – | – |
| Candida Infection | – | 1 (8) | – | – | – | – |
| Cardiac Tamponade | – | – | 1 (8) | – | – | – |
| Headache | – | 1 (8) | – | – | – | – |
| Pericarditis Constrictive | – | 1 (8) | – | – | – | – |
| Supraventricular Tachycardia | – | 1 (8) | – | – | – | – |
| Tracheal Obstruction | – | 1 (8) | – | – | – | – |

Evorpacept: 10 mg/kg (n=3) & 15 mg/kg (n=10); All TEAEs occurring in ≥ 4patients. For cases of TEAEs Grade ≥3 and any TRAE, all AEs are listed irrespective of patient numbers.

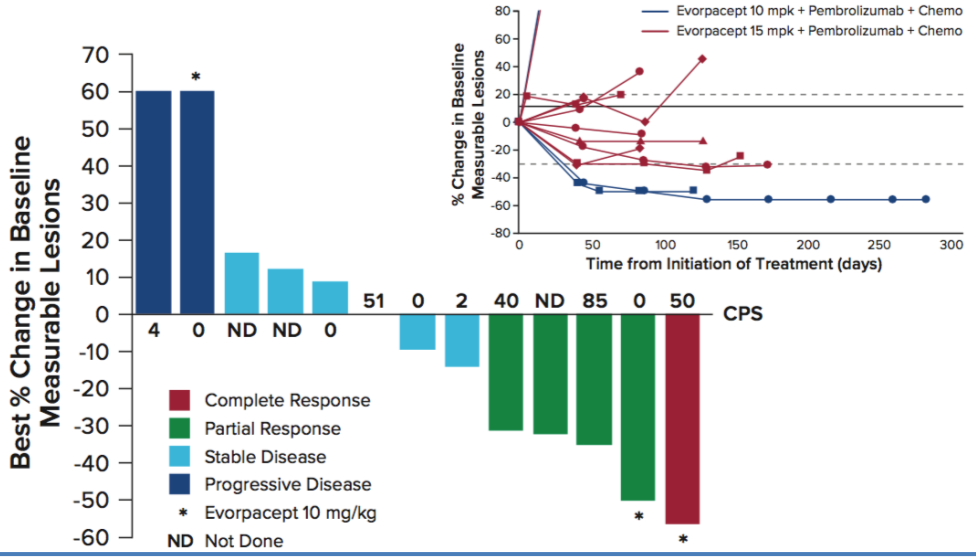
- **There were no dose limiting toxicities, on study deaths, or evorpacept-related SAEs**



ALX ONCOLOGY

# Clinical activity of evorpacept + pembrolizumab with and without chemotherapy in response evaluable patients with CPI naïve 1L HNSCC and ≥2L HNSCC

## Clinical activity of evorpacept + pembrolizumab + 5FU + platinum in patients with CPI naïve 1L HNSCC (N=13)




| Population | N (EVAL) | OR Rate | Median PFS (m) (95% CI) | Median OS (m) (95% CI) | OS Rate at 12 months | Follow Up (m) (95% CI) |
|---|---|---|---|---|---|---|
| **1L HNSCC (evorpacept 10 mg/kg or 15 mg/kg + pembrolizumab + chemo)** | 13 | 38.5% | 5.6 (3.6; NR) | NR | 87.5% | 6.2 (4.7; 10.6) |
| **≥2L HNSCC (CPI naïve) (evorpacept 10 mg/kg + pembrolizumab)** | 10 | 40% | 4.6 (0.5; 7.5) | 24.5 (3.1; NR) | 80% | 32.5 (26.9; NR) |

NR – Not reached



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# Evorpacept's initial response benefit is magnified in survival-based endpoints in HNSCC populations evaluated

- **Preliminary data suggests that evorpacept can be safety combined with the multi-agent chemotherapy regimens studied with no maximum tolerated dose reached.**

- **Evorpacept demonstrates initial ORR of 38.5% with median OS not reached, and 12 month OS rate of 87.5% in combination with pembrolizumab + 5FU + platinum in patients with 1L advanced HNSCC that compares favorably with standard pembrolizumab-based therapy in the 1L HNSCC setting.**

- **Updated follow up data from patients with CPI naïve ≥2L HNSCC receiving evorpacept + pembrolizumab demonstrates a median OS of 24.5 months with 12 month OS rate of 80% that compares favorably with standard pembrolizumab in patients with 2L CPI naïve HNSCC.**

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