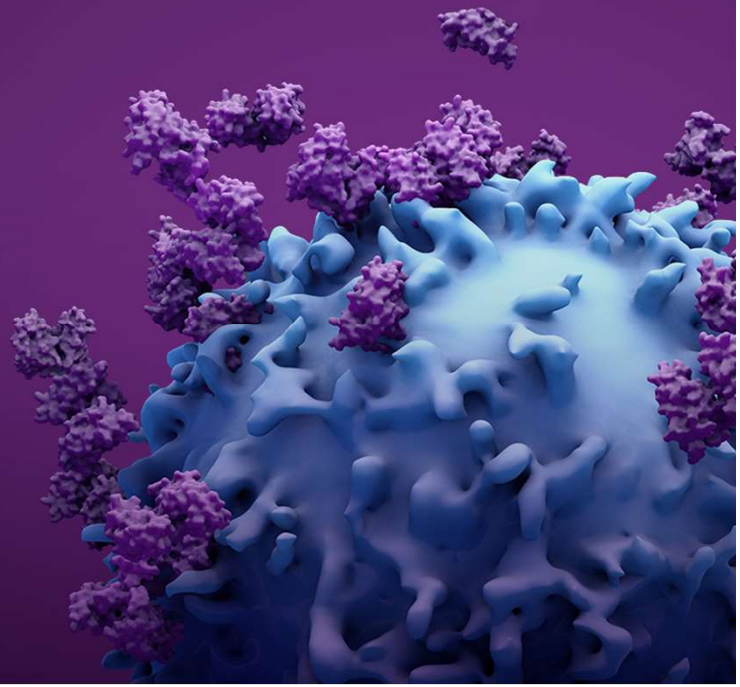
PrimO
Practical Recommendations in Immuno & Molecular Oncology
ADC Summit

Antibody–Drug Conjugates in Development for Non-small Cell Lung Cancer, Gastric Cancer, and Colorectal Cancer

H. Jack West, MD
Associate Clinical Professor in Medical Oncology
City of Hope Comprehensive Cancer Center
Duarte, CA

Suresh S. Ramalingam, MD, FACP, FASCO
Professor of Hematology and Medical Oncology
Emory University School of Medicine
Atlanta, GA

Rachna Shroff, MD, MS
Associate Professor of Medicine
University of Arizona Cancer Center (UACC)
Tucson, AZ



Learning Objectives

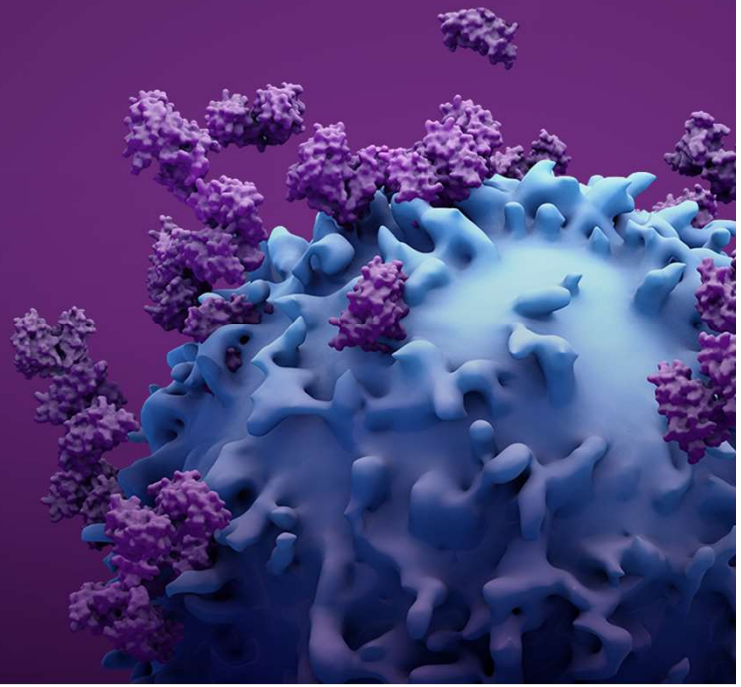
Review ADCs in development for NSCLC, GI cancers, and CRC

- Analyze the unmet need in patients with these NSCLC, GI cancers, and CRC
- Discuss their mechanisms of action
- Analyze available clinical data and discuss ongoing clinical trials

ADC, antibody–drug conjugate; CRC, colorectal cancer; GI, gastrointestinal; NSCLC, non-small cell lung cancer.

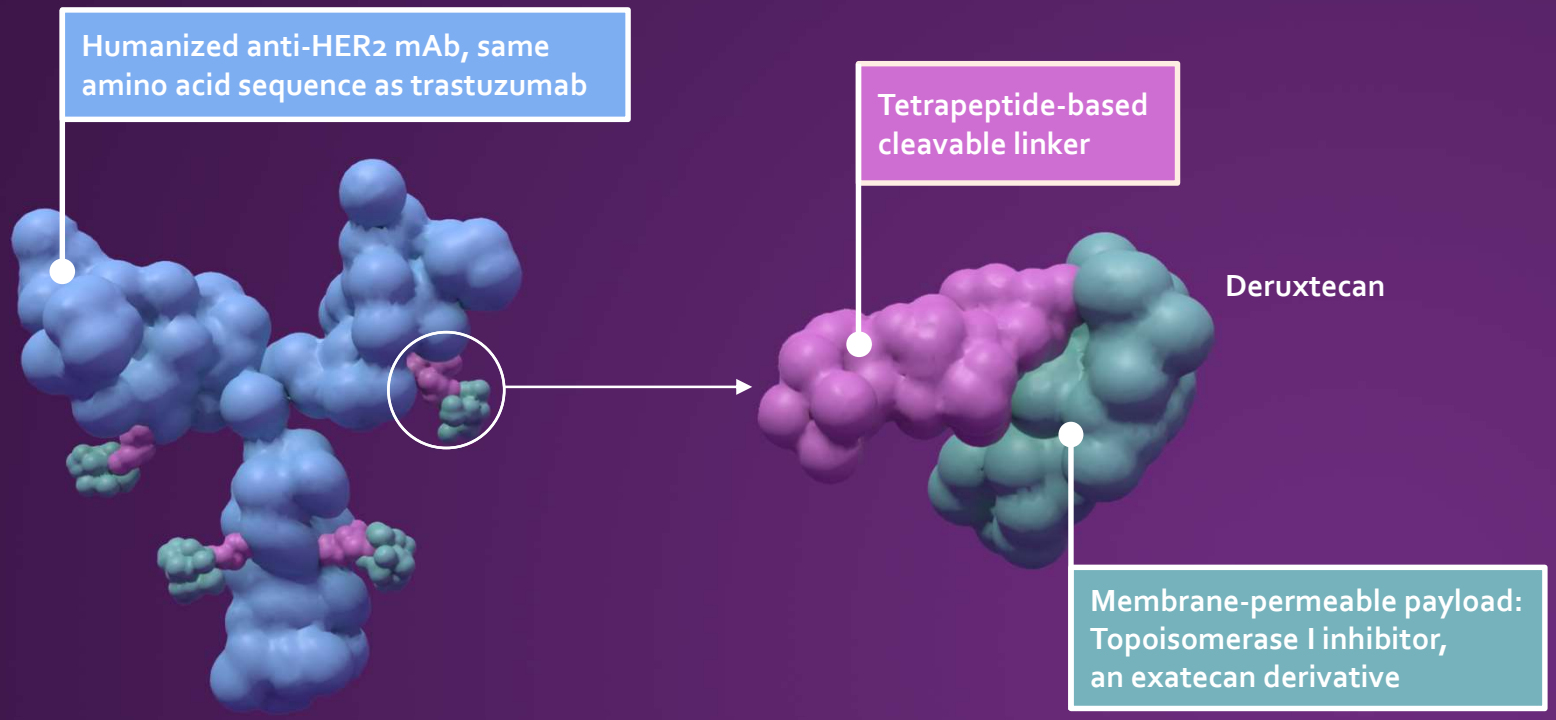
PrimO
Practical Recommendations in Immuno & Molecular Oncology
ADC Summit

ADCs in NSCLC



PrimO
Practical Recommendations in Immuno & Molecular Oncology
ADC Summit

Trastuzumab Deruxtecan (T-DXd)



mAB, monoclonal antibody.

Smit EF et al. Trastuzumab Deruxtecan (T-DXd; DS-8201) in patients with HER2-mutated metastatic non-small cell lung cancer: interim results of DESTINY-Lung01. Presented at: American Society for Clinical Oncology 2020 Virtual Scientific Program; May 29 – 31. Accessed November 6, 2020. https://meetinglibrary.asco.org/session/12667

DESTINY-Lung01: Phase 2, Multicenter, Open-Label, 2-Cohort Non-Randomized Study of T-DXd for HER2-Overexpressing or HER2-Mutated NSCLC[1,2]

PATIENTS

- Unresectable and/or metastatic NSQ NSCLC
- Relapsed/refractory to standard treatment
- HER2-expressing or HER2-activating mutation
- No prior HER2-targeted therapy, except pan-HER TKIs

STUDY DESIGN

Cohort 1 (n=42)
HER2 expressing (IHC 3+ or IHC 2+)

Cohort 2 (n=42)
HER2 mutated

T-DXd 6.4 mg/kg q3w

ENDPOINTS

1°

ORR

Select 2°

- DOR
- PFS
- OS

DOR, duration of response; HER, human epidermal growth factor receptor; IHC, immunohistochemistry; NSQ, nonsquamous; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; q3w, 3 times per week; TKI, tyrosine kinase inhibitor.

1. Smit EF et al. Trastuzumab Deruxtecan (T-DXd; DS-8201) in patients with HER2-mutated metastatic non-small cell lung cancer: interim results of DESTINY-Lung01. Presented at: American Society for Clinical Oncology 2020 Virtual Scientific Program; May 29 – 31. Accessed November 6, 2020. https://meetinglibrary.asco.org/session/12667; 2. U.S. National Library of Medicine Clinicaltrials.gov. URL: https://clinicaltrials.gov/ct2/show/NCT03505710. Accessed November 8, 2020. Last updated: September 11, 2020.

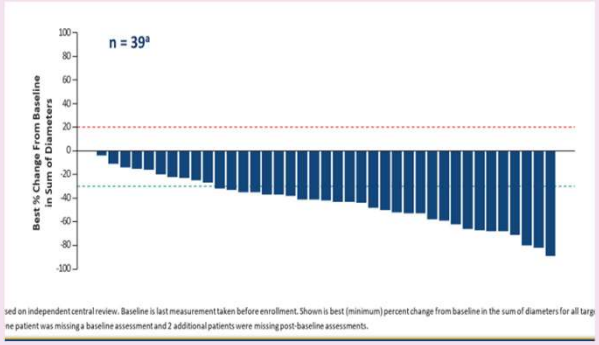
PrimO Practical Recommendations in Immuno & Molecular Oncology ADC Summit

T-DXd Demonstrated a High ORR and a Durable Response in Patients With HER2-Mutated NSCLC

ANTITUMOR ACTIVITY

	Patients (n=42)
Confirmed ORR by ICR	**61.9% (n=26)** (95% CI, 45.6%-76.4%
CR	2.4% (n=1)
PR	59.5% (n=25)
SD	28.6% (n=12)
PD	4.8% (n=2)
Not evaluable	4.8% (n=2)
DCR	90.5% (95% CI, 77.4%-97.3%)
DOR, medium	Not reached (95% CI, 5.3 months-NE)
PFS, median	14.0 mo (95% CI, 6.4-14.0 months)

Best Change in Tumor Size



SAFETY RESULTS

- The safety was consistent with the ph 1 trial and expansion in mTNBC
- Febrile neutropenia in 2 patients was the major gr 3 or 4 treatment-related SAE, but it was manageable
- A low frequency (7%) of grade ≥3 diarrhea was observed
- Discontinuation of treatment because of TRAEs occurred in 2 patients (4%)
- No treatment-related deaths occurred
- 49% of patients experienced a modest 25% dose reduction

CI, confidence interval; CR, complete response; DCR, disease control rate; gr, grade; ICR, Independent Central Review; mo, month; mTNBC, metastatic triple-negative breast cancer; PD, progression of disease; ph, phase; PR, partial response; SAE, serious adverse event; SD, standard deviation; TRAE, treatment-related adverse event;.

Smit EF et al. Trastuzumab Deruxtecan (T-DXd; DS-8201) in patients with HER2-mutated metastatic non-small cell lung cancer: interim results of DESTINY-Lung01. Presented at: American Society for Clinical Oncology 2020 Virtual Scientific Program; May 29 – 31. Accessed November 6, 2020. https://meetinglibrary.asco.org/session/12667

PrimO Practical Recommendations in Immuno & Molecular Oncology ADC Summit

Additional Ongoing Studies With T-DXd in NSCLC

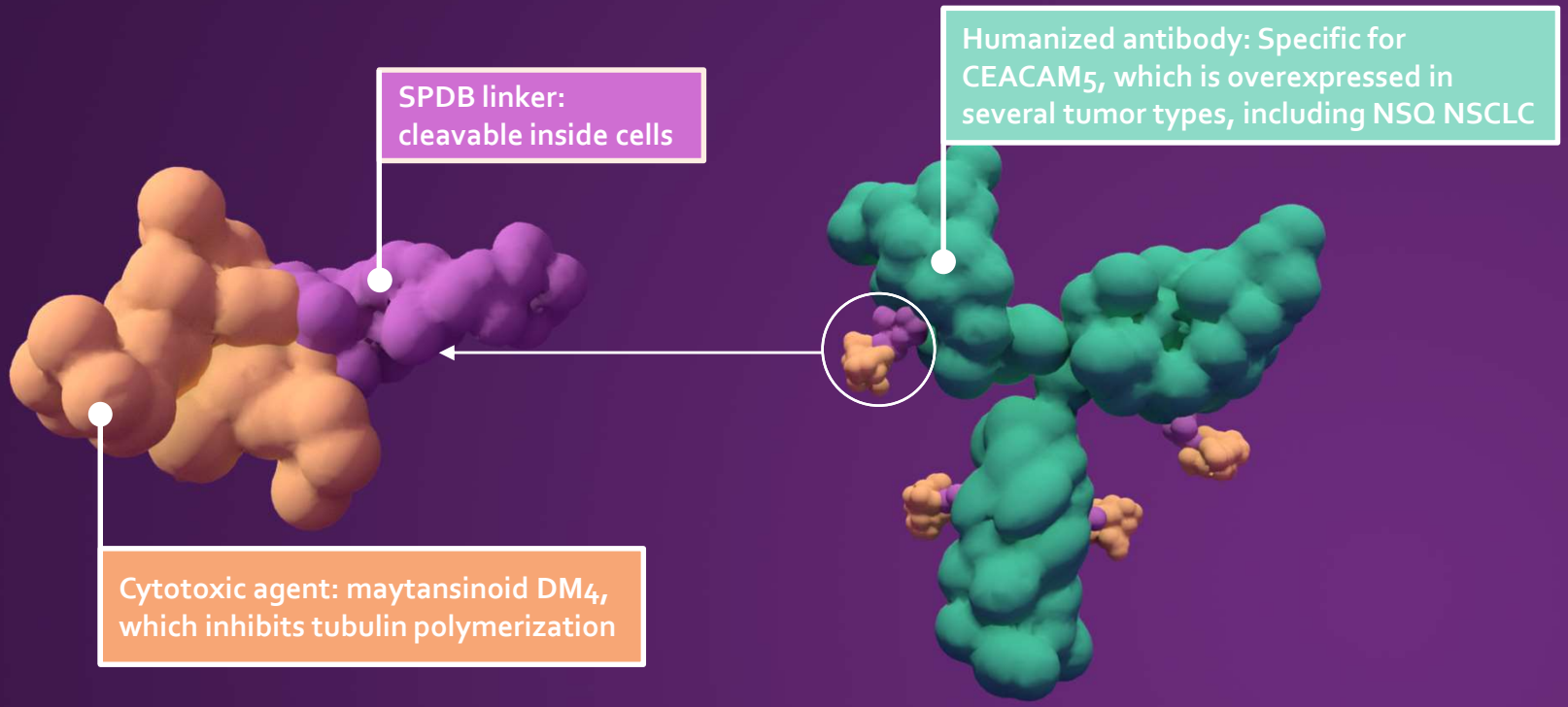
	Ph	Patients	N	Arms	1° EP	Est Study Completion
NCT04042701	1B	• Cohort 3: adults with locally advanced/metastatic HER2-expressing NSCLC • Cohort 4: adults with locally advanced/metastatic HER2-mutant NSCLC	115	• Dose escalation: trastuzumab deruxtecan + pembrolizumab • Dose expansion includes 2 NSCLC cohorts: HER2-expressing and HER2-mutated	DLT (2° EPs: DOR, DCR, PFS, TTR, OS)	04/2022

T-DXd granted Breakthrough Therapy Designation in the US

DCR, disease control rate; DLT, dose-limiting toxicity; EP, endpoint; Est, estimated; TTR, time to response.
U.S. National Library of Medicine Clinicaltrials.gov URL: https://clinicaltrials.gov/ct2/show/NCT04042701. Accessed: November 8, 2020. Last updated: August 6, 2020.

PrimO Practical Recommendations in Immuno & Molecular Oncology ADC Summit

SAR408701



Gazzah A et al. Efficacy and safety of the antibody-drug conjugate (ADC) SAR408701 in patients (pts) with non-squamous non-small cell lung cancer (NSQ NSCLC) expressing carcinoembryonic antigen-related cell adhesion molecule 5 (CEACAM5). Presented at: American Society for Clinical Oncology 2020 Virtual Scientific Program; May 29 – 31. Accessed November 8, 2020. https://meetinglibrary.asco.org/record/187279/abstract.

TED13751: Phase 1/2, Non-Randomized, Parallel Assignment Study Evaluation of SAR408701 in Patients With Advanced Solid Tumors[1,2]

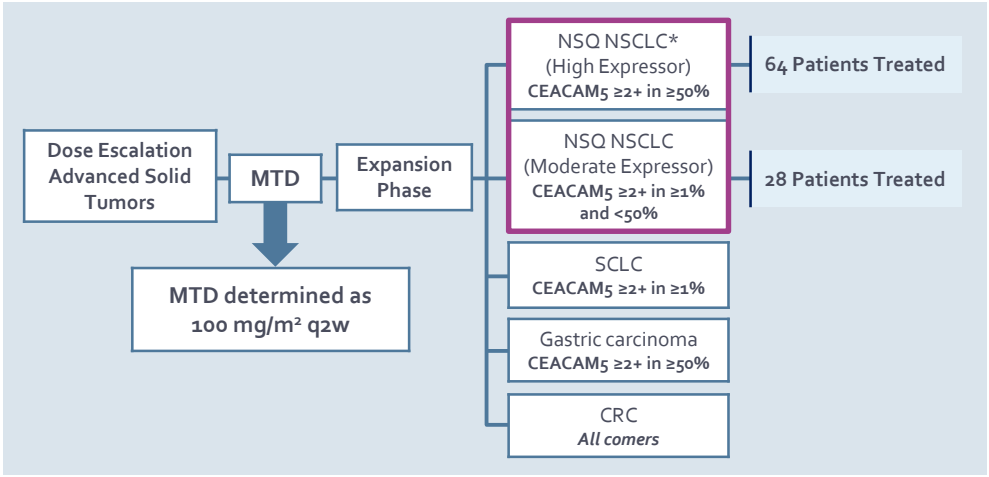
First-in-Human Study Evaluating the Safety, PK, and Antitumor Activity of SAR408701 in Pts With Advanced Solid Tumors

PATIENTS

Adults with locally advanced/metastatic solid malignant tumors for which no standard alternative therapy was available.

- **Dose Escalation Cohorts**: pts with tumors expressing/likely expressing CEACAM5 (eg, CRC, NSQ NSCLC, and gastric adenocarcinoma)
- **Expansion Phase cohorts**: pts with CRC or CEACAM5+ NSQ NSCLC, SCLC, or gastric carcinoma
  - High expression cohort: CEACAM5 ≥50% at ≥2+ intensity (20% of NSQ NSCLC)
  - Moderate expression cohort: CEACAM5 between ≥1% and <50% at ≥2+ intensity (24% of NSQ NSCLC)

STUDY DESIGN



ENDPOINTS

1°

- DLT (escalation phase)
- ORR (expansion phase)

Select 2°

- Safety
- DOR

MTD, maximum tolerated dose; PK, pharmacokinetics; pts, patients; Q2W, every 2 weeks; SCLC, small cell lung cancer.

1. Gazzah A et al. Efficacy and safety of the antibody-drug conjugate (ADC) SAR408701 in patients (pts) with non-squamous non-small cell lung cancer (NSQ NSCLC) expressing carcinoembryonic antigen-related cell adhesion molecule 5 (CEACAM5). Presented at: American Society for Clinical Oncology 2020 Virtual Scientific Program; May 29 – 31. Accessed November 8, 2020. https://meetinglibrary.asco.org/record/187279/abstract; 2. U.S. National Library of Medicine Clinicaltrials.gov. URL: https://clinicaltrials.gov/ct2/show/NCT02187848. Accessed: November 8, 2020. Last updated: April 30, 2020.

PrimO Practical Recommendations in Immuno & Molecular Oncology ADC Summit

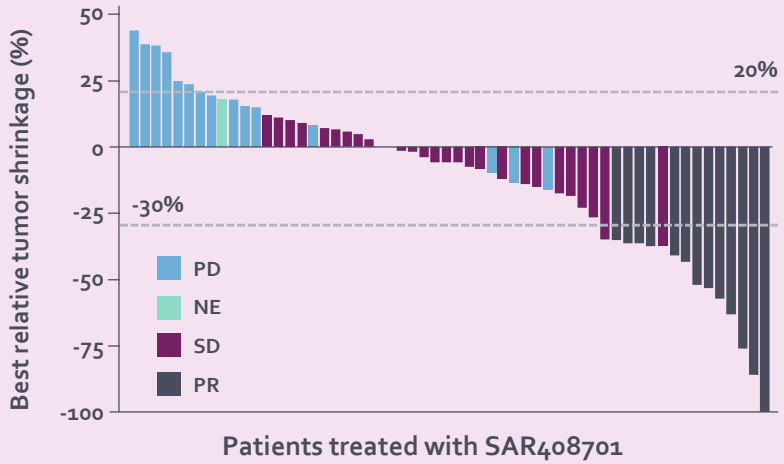
SAR408701 Was Well Tolerated, Showed Promising Antitumor Activity in Patients With Heavily Pretreated, Advanced NSQ NSCLC With High CEACAM5 Expression

ANTITUMOR ACTIVITY

Overall Population

Response, n (%)	High expression (n=64)
ORR	13 (20.3%) [12.27-31.71]
Confirmed PR	13 (20.3%)
SD	28 (43.8%)
DCR	41 (64.1%)
PD	21 (32.8%)

Best Relative Tumor Shrinkage – High Expressor Cohort



SAFETY RESULTS

- Most common TEAEs grade ≥3 were keratopathy/keratitis (10.9%) and dyspnea (10.9%)
- A total of 25 (27.2%) pts had corneal TEAEs leading to dose modification, and 1 pt discontinued treatment
- Ocular events are manageable with dose delay or reduction; primary prophylaxis was not effective

TEAE, treatment-emergent adverse event.

Gazzah A et al. Efficacy and safety of the antibody-drug conjugate (ADC) SAR408701 in patients (pts) with non-squamous non-small cell lung cancer (NSQ NSCLC) expressing carcinoembryonic antigen-related cell adhesion molecule 5 (CEACAM5). Presented at: American Society for Clinical Oncology 2020 Virtual Scientific Program; May 29 – 31. Accessed November 8, 2020. https://meetinglibrary.asco.org/record/187279/abstract.

PrimO Practical Recommendations in Immuno & Molecular Oncology ADC Summit

Ongoing Clinical Studies With SAR408701

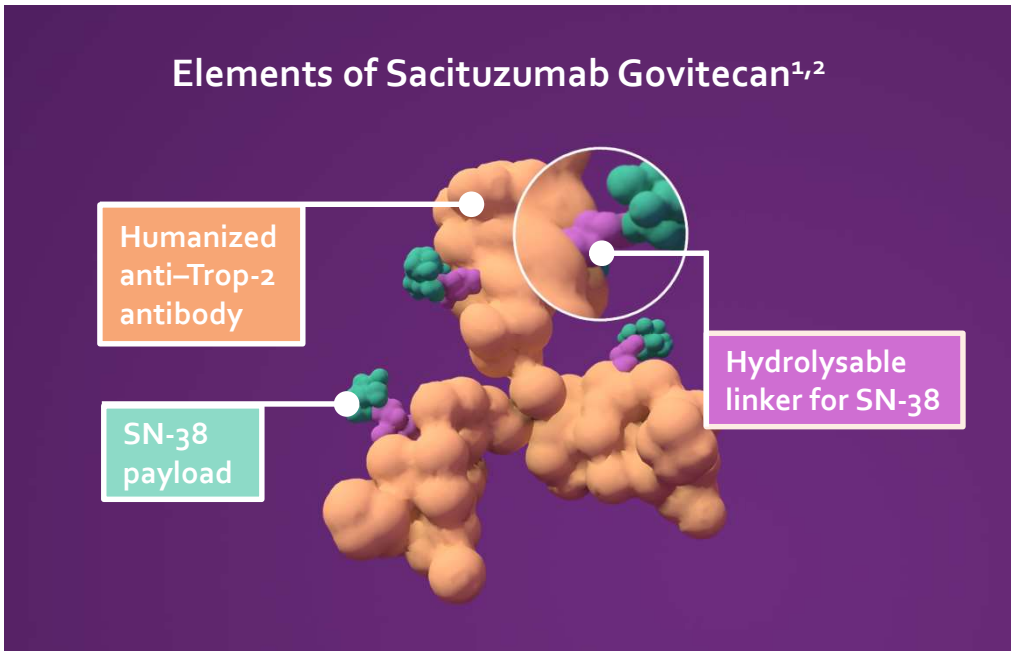
	Ph	Patients	N	Arms	1° EP	Est Study Completion
CARMEN-LC04 (NCT04394624)[1]	**2**	• Metastatic NSQ NSCLC • CEACAM5 expression confirmed via IHC • After 1 prior line of chemo in a metastatic setting or metastatic disease during/within 6 mo of (neo)adjuvant treatment • After/during Pt-based chemo and 1 ICI	**36**	Single arm; IV SAR408701 + IV ramucirumab	DLT	03/2022
CARMEN-LC03 (NCT04154956)[2]	**3**	• Adults with histologically or cytologically proven metastatic NSQ NSCLC • Progression after Pt-based chemo and ICI • CEACAM5 expression confirmed via IHC	**554**	Randomized; SAR408701 vs docetaxel	PFS, OS	03/2024

Regulatory application for 2L or greater treatment of NSCLC is expected in 2022.

2L, second line; ICI, immune checkpoint inhibitor; IV, intravenous; Pt, platinum.

1. U.S. National Library of Medicine Clinicaltrials.gov. URL: https://clinicaltrials.gov/ct2/show/NCT04394624. Accessed: November 8, 2020. Last updated: October 28, 2020;
2. U.S. National Library of Medicine Clinicaltrials.gov. URL: https://clinicaltrials.gov/ct2/show/NCT04154956. Accessed: November 8, 2020. Last updated: October 28, 2020.

PrimO
Practical Recommendations in Immuno & Molecular Oncology
ADC Summit



- SN-38 is the active metabolite of irinotecan, a topoisomerase I inhibitor that interferes with cell growth and spread[1]
- Sacituzumab govitecan delivers ≤136x more SN-38 than irinotecan[2]
- Inhibition of topoisomerase I by SN-38 leads to apoptosis[1]

Mechanism of Sacituzumab Govitecan (IMMU-132)

1. Bardia A et al. *J Clin Oncol*. 2017;35(19):2141-2148; 2. Goldenberg DM et al. *Oncotarget*. 2015;6(26):22496–22512.

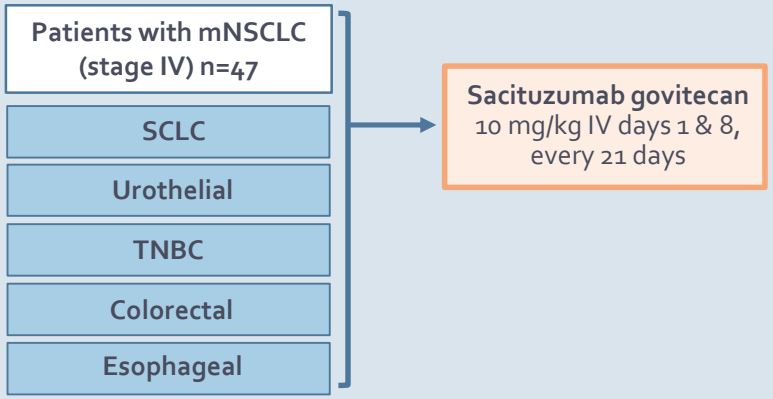
PrimO Practical Recommendations in Immuno & Molecular Oncology ADC Summit

Phase 1/2 Open-Label, Basket-Design, Single-Arm, Multicenter Study of Sacituzumab Govitecan in Patients With Epithelial Cancers[1-3]

PATIENTS

Basket Trial
Patients with relapsed/refractory metastatic epithelial cancer who received ≥1 standard therapeutic regimen

STUDY DESIGN



ENDPOINTS

1°

- ORR

Select 2°

- DOR
- PFS
- OS

Anticipated Study Completion: 08/2020

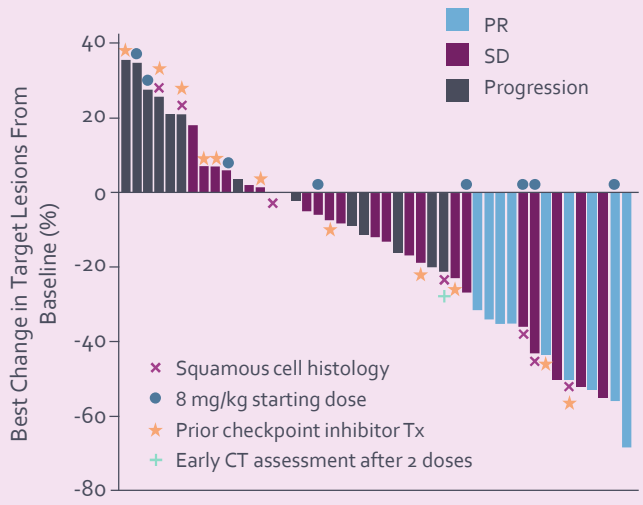
mNSCLC, metastatic non-small cell lung cancer;

1. Heist RS et al. *J Clin Oncol*. 2017;35(24):2790-2797; 2. Goldenberg DM et al. *Oncotarget*. 2015;6(26):22496–22512; 3. U.S. National Library of Medicine Clinicaltrials.gov. URL: https://clinicaltrials.gov/ct2/show/NCT01631552. Accessed: November 8, 2020. Last updated: September 9, 2020.

PrimO Practical Recommendations in Immuno & Molecular Oncology ADC Summit

Sacituzumab Govitecan Is Therapeutically Active in Patients With Diverse Metastatic Epithelial Tumors, With Manageable Neutropenia as the Major Toxicity[1,2]

ANTITUMOR ACTIVITY



Response	No. (%)
All patients	
Best overall response (n=47)	
PR	9 (19)
SD	23 (49)
PD	15 (32)
Objective response duration, months	
Median (95% CI)	6.0 (4.8 to 8.3)
Clinical benefit (PR + SD ≥ 4 months)	20 (43)
PFS (n=54), months	
Median (95% CI)	5.2 (3.2 to 7.1)
OS (n=54), months	
Median (95% CI)	9.5 (5.9 to 16.7)

SAFETY RESULTS

- The safety was consistent with the ph 1 trial and expansion in mTNBC
- Febrile neutropenia in 2 patients was the major grade 3 or 4 treatment-related SAE, but it was manageable
- A low frequency (7%) of grade ≥3 diarrhea was observed
- Discontinuation of treatment because of TRAEs occurred in 2 patients (4%)
- No treatment-related deaths occurred
- 49% of patients experienced a modest 25% dose reduction

CT, computed tomography; Tx, treatment.

1. Heist RS et al. *J Clin Oncol*. 2017;35(24):2790-2797; 2. Goldenberg DM et al. *Oncotarget*. 2015;6(26):22496–22512.

PrimO Practical Recommendations in Immuno & Molecular Oncology ADC Summit

Ongoing Studies With Sacituzumab Govitecan

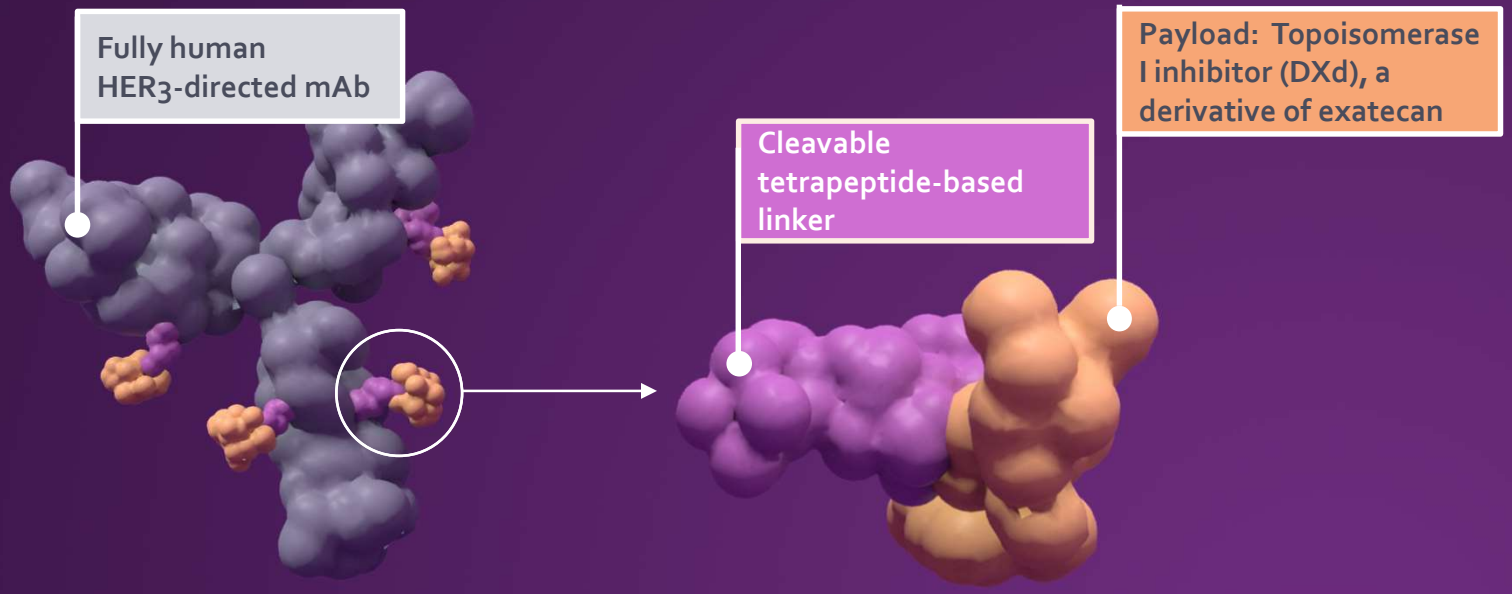
	Ph	Patients	N	Arms	1° EP	Est Study Completion
Morpheus Lung (NCT03337698)	**1/2**	• 1L cohort: pts who have not received any systemic therapy for their disease • 2L cohort consists of pts who progressed during/after Pt-containing regimen + ICI	**380**	• Randomized; multiple immunotherapy-based treatment combinations	ORR	04/2022

1L, first line.

U.S. National Library of Medicine Clinicaltrials.gov. URL: https://clinicaltrials.gov/ct2/show/NCT03337698. Accessed: November 8, 2020. Last updated: September 2, 2020.

PrimO Practical Recommendations in Immuno & Molecular Oncology ADC Summit

Patritumab Deruxtecan (U3-1402)[1,2]



57%–67% of EGFR-mutant NSCLCs show some level of HER3 expression[3,4]

Drug-to-antibody ratio: 8

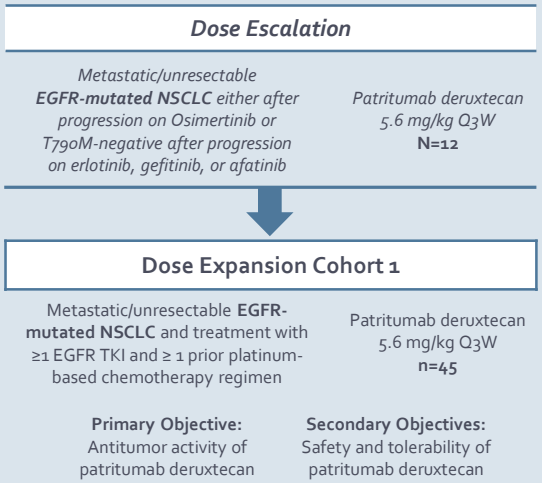
EGFR, epidermal growth factor receptor.

1. Duma N et al. *Mayo Clin Proc*. 2019;94(8):1623-1640; 2. Tan CS et al. *Mol Cancer*. 2018;17:29; 3. Yi, et al. *Mod Pathol*. 1997;10:142-148; 4. Kawano, et al. J Surg Res. 2008;146:43-48.

PrimO Practical Recommendations in Immuno & Molecular Oncology ADC Summit

Phase 1: Preliminary Phase 1 Dose Expansion Data of Patritumab Deruxtecan in Patients With EGFR-Mutated NSCLC[1-3]

STUDY DESIGN



ANTITUMOR ACTIVITY

Summary or Results	
Efficacy Measure	Total Evaluable in Cohort 1 (n=56)
Confirmed ORR (%) (95% CI %)	25% (14.4-38.4)
CR	2%
PR	23%
SD	45%
PD	16%
NE	14%
DCR (%) (95% CI)	70% (55.9-81.2)
Median DOR (95% CI) (months)	6.9 months (3.0-7.0)

SAFETY RESULTS

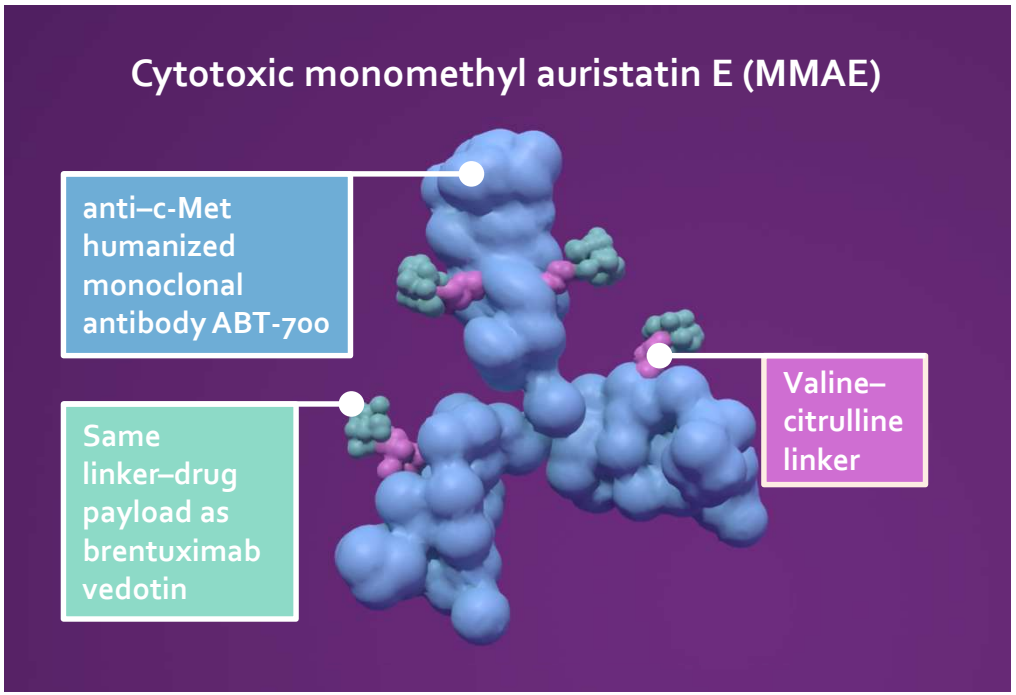
- Most common gr >3 TEAEs were thrombocytopenia and neutropenia
- TEAEs associated with treatment discontinuation (9%) include fatigue, decreased appetite, ILD, pneumonia, and URTI
  - No discontinuations due to thrombocytopenia or neutropenia
- 3 ILD events were related to treatment
- No TEAEs associated with death

Phase 1 study completion expected 12/2023

Global phase 2 study evaluating patritumab deruxtecan in similar patient population is planned

gr, grade; ILD, interstitial lung disease; URTI, upper respiratory tract infection.

1. Daiichi-Sankyo Media Press Release. URL: https://www.daiichisankyo.com/media/press_release/detail/index_4072.html. Accessed: November 8, 2020. Published: September 18, 2020; 2. Yu H et al. Efficacy and safety of patritumab deruxtecan (U3-1402), a novel HER3 directed antibody drug conjugate, in patients (pts) with EGFR-mutated (EGFRm) NSCLC. Presented at: European Society for Medical Oncology 2020 Virtual Scientific Program; September 18, 2020. Accessed November 8, 2020. https://oncologypro.esmo.org/meeting-resources/esmo-virtual-congress-2020/efficacy-and-safety-of-patritumab-deruxtecan-u3-1402-a-novel-her3-directed-antibody-drug-conjugate-in-patients-pts-with-egfr-mutated-egfrm; 3. U.S. National Library of Medicine Clnicaltrials.gov. URL: https://clinicaltrials.gov/ct2/show/NCT03260491?term=U3-1402&draw=2&rank=2. Accessed: November 8, 2020. Last updated: October 19, 2020.



- **MET amplification** is a therapeutically actionable target generally occurring in < 1% to 5% of de novo cancers. **c-Met overexpression** is more common, occurring in ≤50% of many advanced solid tumors
- MMAE binds to tubulin, thereby inhibiting mitosis and causing tumor cell death
- c-Met is a receptor tyrosine kinase expressed on the surface of epithelial and endothelial cells
- c-Met signaling dysregulation is associated with oncogenic transformation and resistance to chemotherapy and radiotherapy and correlates with poor prognosis

Telisotuzumab Vedotin (ABBV-399) is an ADC Targeting cMet Under Investigation to Treat NSCLC

Strickler JH et al. *J Clin Oncol.* 2018;26(33):3298-3306.

PrimO Practical Recommendations in Immuno & Molecular Oncology ADC Summit

Phase 1 Open-Label, Dose-Escalation Study: Telisotuzumab Vedotin + Erlotinib Demonstrated Acceptable Safety and Promising Activity in Pts With *EGFR*m c-Met+ NSCLC Who Failed Frontline EGFR TKI[1,2]

STUDY DESIGN

Patients with *EGFR*m c-Met+ NSCLC Who Failed Frontline EGFR TKI

Experimental arm A: Telisotuzumab vedotin + erlotinib

ANTITUMOR ACTIVITY

	*EGFR*m (n=29)	*EGFR* non-m+ (n=7)
ORR, % (95% CI)	34.5 (17.9, 54.3)	28.6 (3.7, 71.0)
CR, n	1	0
mDOR, mo (95% CI)	NR	NR
	(2.8, NE)	(NR, NE)
mPFS, mo (95% CI)	NR	5.9
	(2.8, NE)	(1.2, NE)
Median follow-up, mo	4	6
6-mo PFS rate (95% CI)	0.51 (0.30, 0.69)	0.43 (0.10, 0.73)

SAFETY RESULTS

- All-grade (gr; ≥20%) AEs were
  - Dermatitis acneiform (38%)
  - Diarrhea (36%)
  - Peripheral motor/sensory neuropathy (52%; 7% gr 3)
  - Dyspnea, fatigue, hypoalbuminemia (31% each)
  - Decreased appetite, nausea (24% each)
  - Asthenia, vomiting (21% each)
- Gr ≥3 (≥10%) AE: pulmonary embolism (14%)

mDOR, median duration of response; mPFS, median progression-free survival; NE, not estimable; NR, not reached.

1. Camidge DR et al. *J Clin Oncol*. 2019; 37(15):Abstract 3011; 2. U.S. National Library of Medicine Clinicaltrials.gov. URL: https://clinicaltrials.gov/ct2/show/NCT02099058. Accessed: November 8, 2020. Last updated: October 12, 2020.

PrimO Practical Recommendations in Immuno & Molecular Oncology ADC Summit

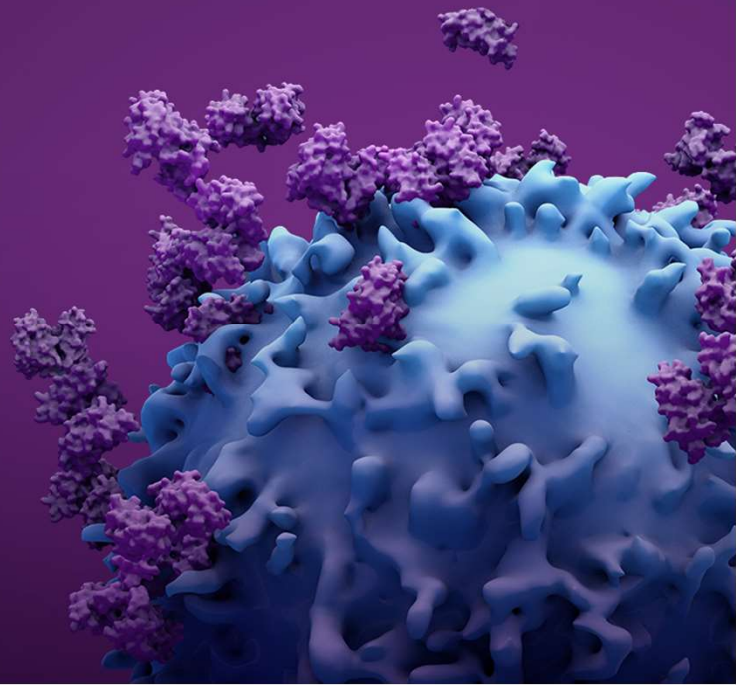
Ongoing Studies With Telisotuzumab Vedotin

	Ph	Patients	N	Arms	1° EP	Est Study Completion
NCT03539536	2	• Locally advanced/metastatic c-Met+ (via IHC) NSQ NSCLC with known EGFR status • Progressed on prior therapy (eg, ICI as monotherapy or in combination with chemo) • ≤2 lines prior chemo in the metastatic setting	310	Single arm; telisotuzumab vedotin	ORR	08/2023

U.S. National Library of Medicine Clinicaltrials.gov. URL: https://clinicaltrials.gov/ct2/show/NCT03539536. Accessed: November 8, 2020. Last updated: November 6, 2020.

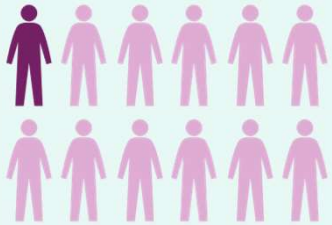
PrimO
Practical Recommendations in Immuno & Molecular Oncology
ADC Summit

Gastric Cancer



Gastric Cancer Is the Third Leading Cause of Cancer Death Worldwide[1,2]

1 in 12



783,000

DEATHS

(1 in every 12 deaths globally)[2]

Incident Cases, 2017[3]	
United States	32,239
China	561,938
Japan	106,507
EU5[a]	75,579
South Korea	24,401
Brazil	21,399
Vietnam	8,302

China accounted for nearly half of the global incident cases in 2017[3]

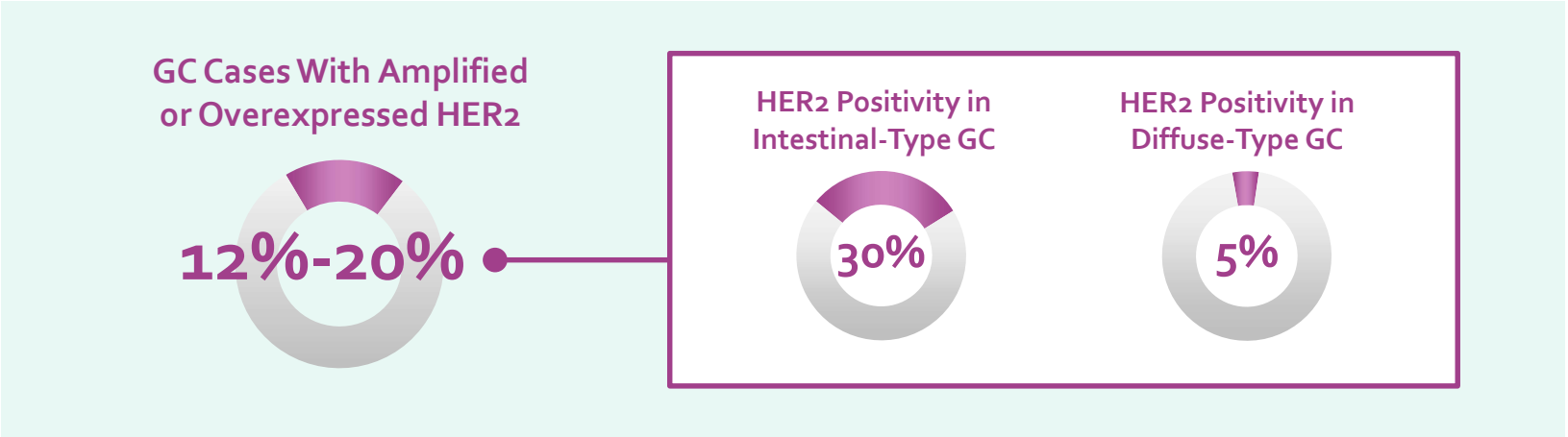
[a]EU5: France, Germany, Italy, Spain, United Kingdom.
EU, European Union.

1. Union for International Cancer Control. GLOBOCAN 2018. https://www.uicc.org/news/new-global-cancer-data-globocan-2018. Accessed November 8, 2020; 2. Bray F et al. *CA Cancer J Clin*. 2018;68:394-424;
3. GBD 2017 Stomach Cancer Collaborators. *Lancet Gastroenterol Hepatol* 2020;5:42-54.

HER2 Is an Important Biomarker and Key Driver of Tumorigenesis in Patients with GC[1,2]

HER2 Is Amplified in 12%-20% of GCs

HER2-positive expression varies by primary tumor localization[3-6]

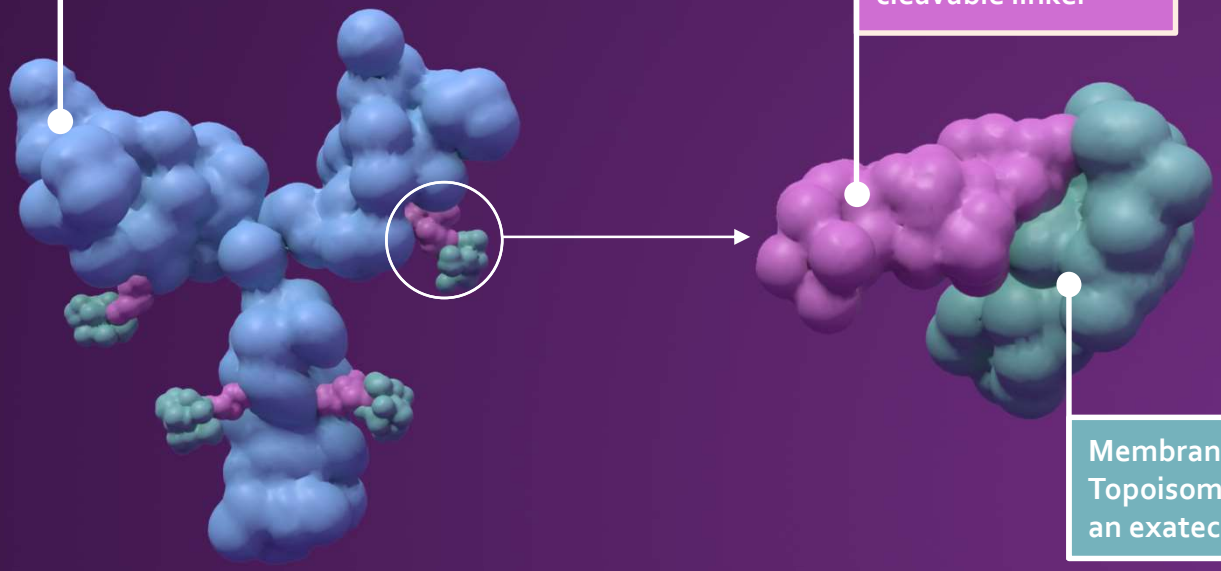


GC, gastric cancer; GEJ, gastroesophageal junction.

1. Gambardella V, et al. In: Tabernero J, Cervantes A, van Halteren H, eds. Gastrointestinal Tract Tumours: Essentials for Clinicians. Viganello-Lugano, Switzerland: ESMO Press;2016:22-27; 2. Van Cutsem E, et al. *Lancet.* 2016;388:2654-2664; 3. Tanner M, et al. *Ann Oncol.* 2005; 16: 273–278; 4. Gravalos C, et al. *Ann Oncol.* 2008;19(9):1523-29; 5. Van Cutsem E, et al. *Gastric Cancer.* 2015;18(3):476-484; 6. Janjigian YY, et al. *Ann Oncol.* 2012;23(10):2656-2662.

Trastuzumab Deruxtecan (T-DXd)

PrimO
Practical Recommendations in Immuno & Molecular Oncology
ADC Summit



Smit EF et al. Trastuzumab Deruxtecan (T-DXd; DS-8201) in patients with HER2-mutated metastatic non-small cell lung cancer: interim results of DESTINY-Lung01. Presented at: American Society for Clinical Oncology 2020 Virtual Scientific Program; May 29 – 31. Accessed November 6, 2020. https://meetinglibrary.asco.org/session/12667

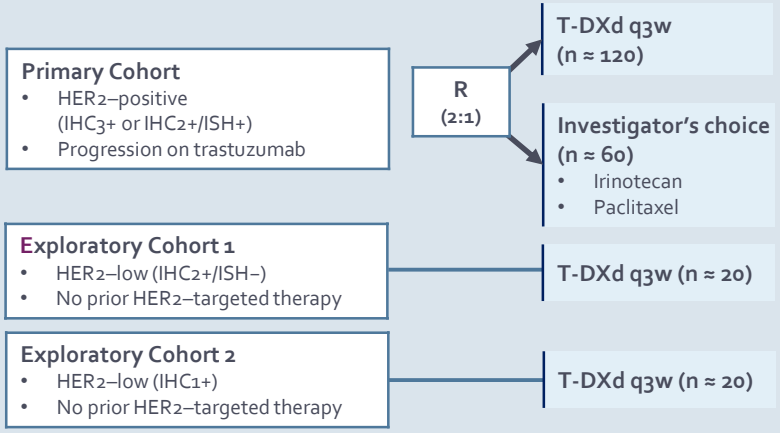
PrimO Practical Recommendations in Immuno & Molecular Oncology ADC Summit

DESTINY-Gastric01: A Phase 2, Multicenter, Open-Label Study of T-DXd In Patients With HER2-Expressing Advanced Gastric or GEJ Adenocarcinoma[1-3]

PATIENTS

Patients with HER2–expressing advanced gastric or GEJ adenocarcinoma

STUDY DESIGN



ENDPOINTS

1°

ORR

Select 2°

- OS
- PFS

1. Shitara K et al. Trastuzumab deruxtecan (T-DXd; DS-8201) in patients with HER2-positive advanced gastric or gastroesophageal junction (GEJ) adenocarcinoma: A randomized, phase II, multicenter, open-label study (DESTINY-Gastric01). Presented at: American Society for Clinical Oncology 2020 Virtual Scientific Program; May 29 – 31. Accessed November 6, 2020. URL: https://meetinglibrary.asco.org/record/185492/abstract; 2. U.S. National Library of Medicine CInicaltrials.gov. URL: https://clinicaltrials.gov/ct2/show/NCT03329690. Accessed: November 8, 2020. Last updated: September 9, 2020; 3. Shitara K et al. *N Engl J Med*. 2020;382(25):2419-2430.

PrimO Practical Recommendations in Immuno & Molecular Oncology ADC Summit

DESTINY-Gastric01: Trastuzumab Deruxtecan May Be a Safe and Effective Treatment Option for Patients With Advanced, HER2+ Gastric or GEJ Adenocarcinoma[1,2]

ANTITUMOR ACTIVITY

	Median OS (95% CI)
Trastuzumab deruxtecan	12.5 (9.6-14.3)
PC of chemo	8.4 (6.9-10.7)
HR for death, 0.59 (95% CI, 0.39 – 0.88); *P*=0.01	

	Median PFS (95% CI)
Trastuzumab deruxtecan	5.6 (4.3-6.9)
Physician's choice of chemo	3.5 (2.0-4.3)
HR for death, 0.47 (95% CI, 0.31-0.71)	

SAFETY RESULTS

- Most common gr ≥3 AEs were:
  - Decreased neutrophil count (51% in the T-DXd group vs 24% in the PC group)
  - Anemia (38% vs 23%)
  - Decreased white cell count (21% vs 11%)
  - Decreased appetite (17% vs 13%)
- 6 patients in the T-DXd group had febrile neutropenia (all events gr 3 vs 2 in the PC group (1 event each of gr 3 and 4)

HR, hazard ratio; PC, physician's choice.

1. Shitara K et al. Trastuzumab deruxtecan (T-DXd; DS-8201) in patients with HER2-positive advanced gastric or gastroesophageal junction (GEJ) adenocarcinoma: A randomized, phase II, multicenter, open-label study (DESTINY-Gastric01). Presented at: American Society for Clinical Oncology 2020 Virtual Scientific Program; May 29 – 31. Accessed November 6, 2020. URL: https://meetinglibrary.asco.org/record/185492/abstract;
2. U.S. National Library of Medicine Clnicaltrials.gov. URL: https://clinicaltrials.gov/ct2/show/NCT03329690. Accessed: November 8, 2020. Last updated: September 9, 2020; 3. Shitara K et al. *N Engl J Med*. 2020;382(25):2419-2430.

Ongoing Studies With Trastuzumab Deruxtecan in Gastric Cancer

	Ph	Patients	N	Arms	1° EP	Est Study Completion
DESTINY-Gastric02 (NCT04014075)[1]	2	Participants who have centrally confirmed HER2-psotove gastric or GEJ cancer	72	Will be treated with T-DXd by IV infusion q3w, until progression of disease or withdrawal from treatment for other reasons	ORR 2° EP: PFS, OS, DOR	08/2021
DESTINY-Gastric03 (NCT04379596)[2]	2	Patients with advanced HER2-positive gastric cancer	210	T-DXd combinations with 5-FU, capecitabine, oxaliplatin, cisplatin, durvalumab	Occurrence of AEs and SAEs and ORR	12/2022

1. U.S. National Library of Medicine Clnicaltrials.gov. URL: https://clinicaltrials.gov/ct2/show/NCT04014075. Accessed: November 8, 2020. Last updated: October 20, 2020; 2. U.S. National Library of Medicine Clnicaltrials.gov. URL: https://clinicaltrials.gov/ct2/show/NCT04379596. Accessed: November 8, 2020. Last updated: September 29, 2020.

ADCs in GI Cancer Competitive Landscape

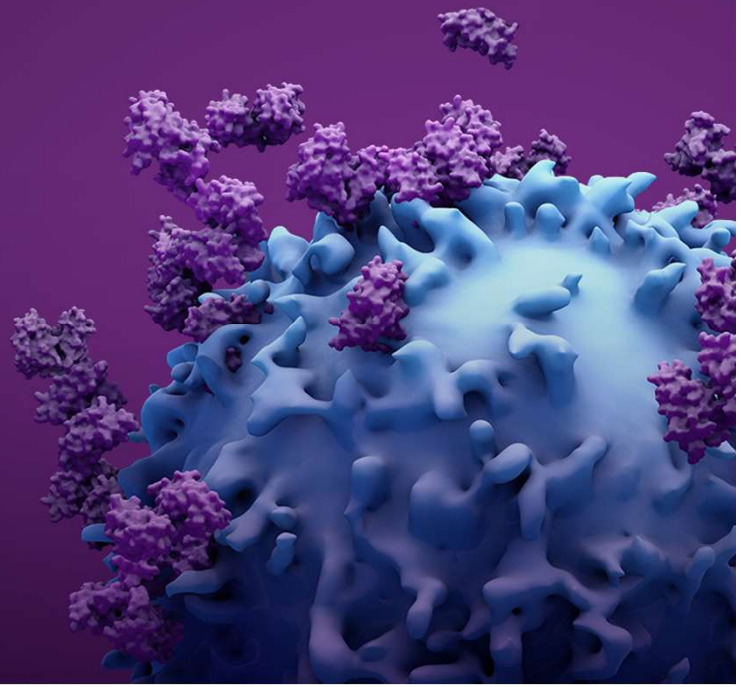
Company	Drug Name	Phase	N	Target(s)	Est Study Completion Date
AbGenomics International, Inc.	AbGn-107[1]	**1**	136	AG7 antigen	December 2020
Daiichi Sankyo Cancer Enterprise	Enhertu[2]	**BLA/ Phase 2**	72	HER2/neu or ErbB-2 topoisomerase I inhibitor	August 2021
OBI Pharma, Inc.	OBI-999[3]	**1/2**	185	antigen Globo H (Globo H, SSEA3 and SSEA4)	December 9, 2023
Daiichi Sankyo Cancer Enterprise	DS-6157[4]	**1**	100	GPR20	October 2024
Immunomedics, Inc.	Trodelvy (sacituzumab govitecan-hziy)[5]	**Preclinical**	X	Trop-2	X

Trop-2, tumor-associated calcium signal transducer 2.

1. U.S. National Library of Medicine Clnicaltrials.gov. URL: https://clinicaltrials.gov/ct2/show/NCT02908451. Accessed: November 8, 2020. Last updated: July 17, 2020; 2. U.S. National Library of Medicine Clnicaltrials.gov. URL: https://clinicaltrials.gov/ct2/show/NCT04276415. Accessed: November 8, 2020. Last updated: October 14, 2020; 3. U.S. National Library of Medicine Clnicaltrials.gov. URL: https://clinicaltrials.gov/ct2/show/NCT04084366. Accessed: November 8, 2020. Last updated: August 4, 2020; 4. U.S. National Library of Medicine Clnicaltrials.gov. URL: https://clinicaltrials.gov/ct2/show/NCT04014075. Accessed: November 8, 2020. Last updated: October 20, 2020; 5. Cardillo TM. *Bioconjug Chem.* 2015; 26(5):919-931.

PrimO
Practical Recommendations in Immuno & Molecular Oncology
ADC Summit

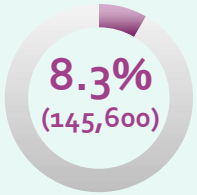
CRC



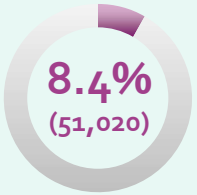
New and Effective Treatment Options for Patients With mCRC Is an Unmet Need

PrimO
Practical Recommendations in Immuno & Molecular Oncology
ADC Summit

4th MOST COMMON CANCER[1]



of all new cancer cases

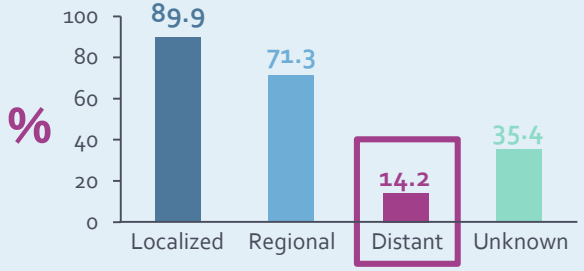


of all cancer deaths

≈50% to 60%

of patients diagnosed with early CRC will develop metastases[2]

5-YEAR SURVIVAL RATE BY STAGE[1]



14.2%

5-year survival rate for patients with mCRC

HER2 Overexpression Occurs in ~2% to 5% of all CRCs

mCRC, metastatic colorectal cancer.

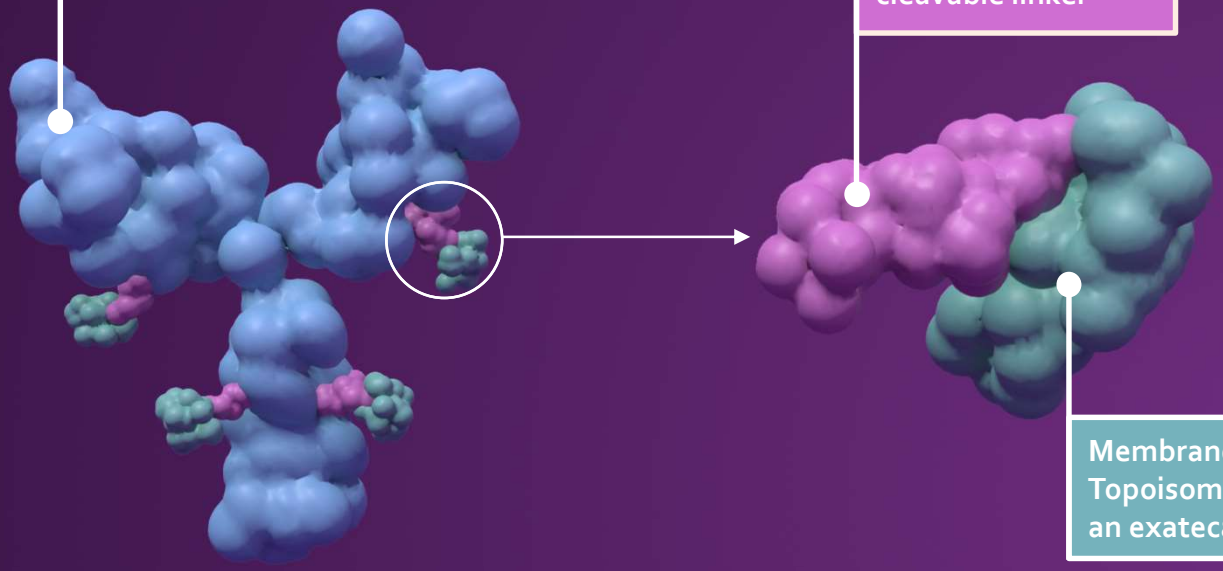
1. National Cancer Institute. SEER cancer stat facts: colorectal cancer. https://seer.cancer.gov/statfacts/html/colorect.html. Accessed March 28, 2020; 2. NCCN Clinical Practice Guidelines in Oncology: Colon Cancer Version 2.2020. National Comprehensive Cancer Network. www.nccn.org/professionals/physician_gls/pdf/colon_blocks.pdf. updated March 3, 2020. Accessed March 29, 2020.

Trastuzumab Deruxtecan (T-DXd)

PrimO
Practical Recommendations in Immuno & Molecular Oncology
ADC Summit

Humanized anti-HER2 mAb, same amino acid sequence as trastuzumab

Tetrapeptide-based cleavable linker



Deruxtecan[1,2,4]

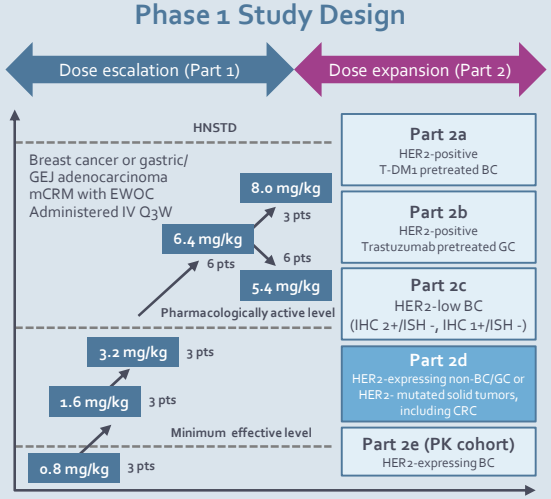
Membrane-permeable payload: Topoisomerase I inhibitor, an exatecan derivative

Smit EF et al. Trastuzumab Deruxtecan (T-DXd; DS-8201) in patients with HER2-mutated metastatic non-small cell lung cancer: interim results of DESTINY-Lung01. Presented at: American Society for Clinical Oncology 2020 Virtual Scientific Program; May 29 – 31. Accessed November 6, 2020. https://meetinglibrary.asco.org/session/12667

PrimO Practical Recommendations in Immuno & Molecular Oncology ADC Summit

J101: Phase 1, Open-Label Study Provided Preliminary Data With T-DXd for Patients With CRC

STUDY DESIGN



ANTITUMOR ACTIVITY

Efficacy measure	CRC (n=20)
Confirmed ORR, n/N (%)	3/19 (15.8)
Confirmed DCR, n/N (%)	16/19 (84.2)
OS, median (range), months	NR (1.0+, 17.9+)
PFS, median (95% CI), months	3.9 (2.1, 8.3)
Duration of follow-up, median (95% CI), months	5.6 (1.6, 12.2)

SAFETY RESULTS

- Among the 259 patients who received ≥1 dose of T-DXd, regardless of tumor type, 99.2% experienced ≥1 TEAE
  - 54.1% had a gr ≥3 TEAE, 22.8% had a serious TEAE, 4.6% had a TEAE leading to death
- Common TEAEs (≥30%):
  - Nausea, decreased appetite, vomiting, anemia, alopecia, fatigue, diarrhea, constipation
- Pts with CRC demonstrated a safety profile similar to the overall population

BC, breast cancer; EWOC, escalation with overdose control; mCRM, modified Continuous Reassessment Method; T-DM1, trastuzumab emtansine.

Yoshino T et al. A multicenter, multicohort, phase 2 study of trastuzumab deruxtecan (DS-8201a) in subjects with HER2-expressing metastatic colorectal cancer. Presented at: European Society of Medical Oncology 2018 Scientific Sessions; October 19-23, Munich, Germany.

DESTINY-CRC01: A Phase 2, Multicenter, Open-Label Study of T-DXd in Patients With HER2-Expressing Advanced CRC[1,2]

PATIENTS

- Unresectable and/or metastatic HER2-expressing CRC
- RAS/BRAF wild type
- >2 prior regimens, prior HER2 treatment allowed

STUDY DESIGN

T-DXd 6.4 mg/kg q3w

Cohort A (n=53)
HER2 Positive (IHC 3+ or IHC 2+/ISH+)

A futility monitoring was done after ≥20 patients in Cohort A had 12 weeks of follow-up to inform opening of Cohorts B and C

Cohort B (n=7)
HER2 IHC 2+/ISH−

Cohort C (n=18)
HER2 IHC 1+

ENDPOINTS

1°

- ORR in Cohort A

Select 2°

- PFS
- OS
- DOR

Anticipated Study Completion: 12/2020

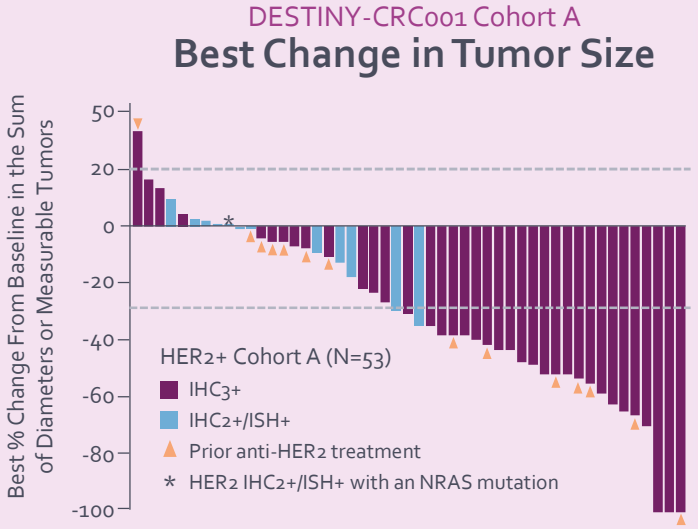
1. Siena S et al. A phase II, multicenter, open-label study of trastuzumab deruxtecan (T-DXd; DS-8201) in patients (pts) with HER2-expressing metastatic colorectal cancer (mCRC): DESTINY-CRC01. Presented at: American Society of Clinical Oncology 2020 Virtual Scientific Sessions; May 29 – 31. Accessed November 6, 2020. https://meetinglibrary.asco.org/record/185482/abstract; 2. U.S. National Library of Medicine Clinicaltrials.gov. URL: https://clinicaltrials.gov/ct2/show/NCT03384940. Accessed: November 8, 2020. Last updated: September 9, 2020.

PrimO Practical Recommendations in Immuno & Molecular Oncology ADC Summit

DESTINY-CRC01 Demonstrated Clinically Meaningful Activity With T-DXd in Patients With HER2+ Unresectable/Metastatic CRC[1,2]

ANTITUMOR ACTIVITY

	Total Evaluable in Primary Cohort (n=53)
Confirmed ORR	13 (20.3%) [12.27-31.71]
CR (%)	1.9
PR (%)	43.4
SD (%)	37.7
DCR (%) (95% CI)	83.0 (70.2-91.9)
Median DOR (months) (95% CI)	NE (4.2-NE)
Median PFS (months) (95% CI)	6.9 (4.1-NE)
Months OS (months) (95% CI)	NE (0.74-NE)



SAFETY RESULTS

Type of Adverse Event, n (%)	HER2+ Cohort A (n=53)	All Patients (n=78)
Any TEAE	53 (100)	78 (100)
Drug related	51 (96.2)	73 (93.6)
TEAE grade ≥3	32 (60.4)	48 (61.5)
Drug related	27 (50.9)	38 (48.7)
Serious TEAE	18 (34.0)	26 (33.3)
Drug related	12 (22.6)	14 (17.9)
Dose adjustments		
TEAE associated with discontinuation	5 (9.4)	7 (9.0)
Drug related	2 (3.8)	2 (2.6)
TEAE associated with dose reduction	11 (20.8)	15 (19.2)
Drug related	10 (18.9)	14 (17.9)
TEAE associated with dose interruption	20 (37.7)	27 (34.6)
Drug related	15 (28.3)	19 (24.4)
Death		
TEAE associated with death	5 (9.4)	7 (9.0)
Drug related	2 (3.8)	2 (2.6)

1. Siena S et al. A phase II, multicenter, open-label study of trastuzumab deruxtecan (T-DXd; DS-8201) in patients (pts) with HER2-expressing metastatic colorectal cancer (mCRC): DESTINY-CRC01. Presented at: American Society of Clinical Oncology 2020 Virtual Scientific Sessions; May 29 – 31. Accessed November 6, 2020. https://meetinglibrary.asco.org/record/185482/abstract; 2. AstraZeneca Media Press Release. URL: https://www.astrazeneca.com/media-centre/press-releases/2020/enhertu-achieved-a-tumour-response-rate-of-45p-in-patients-with-her2-positive-metastatic-colorectal-cancer-in-phase-ii-destiny-crc01-trial.html. Accessed: November 8, 2020. Published: May 29, 2020.

ADC in CRC Competitive Landscape

Company	Drug Name	Phase	N	Target(s)	Est Study Completion Date
AbGenomics International, Inc.	AbGn-107[1]	1	136	AG7 antigen	December 2020
Daiichi Sankyo Cancer Enterprise	Enhertu[2] (fam-trastuzumab deruxtecan-nxki)	2	90	HER2/neu or ErbB-2 Topo-I	December 2020
Takeda Pharmaceutical Co. Ltd.	TAK-164[3]	1	31	Guanylyl cyclase C	Completed

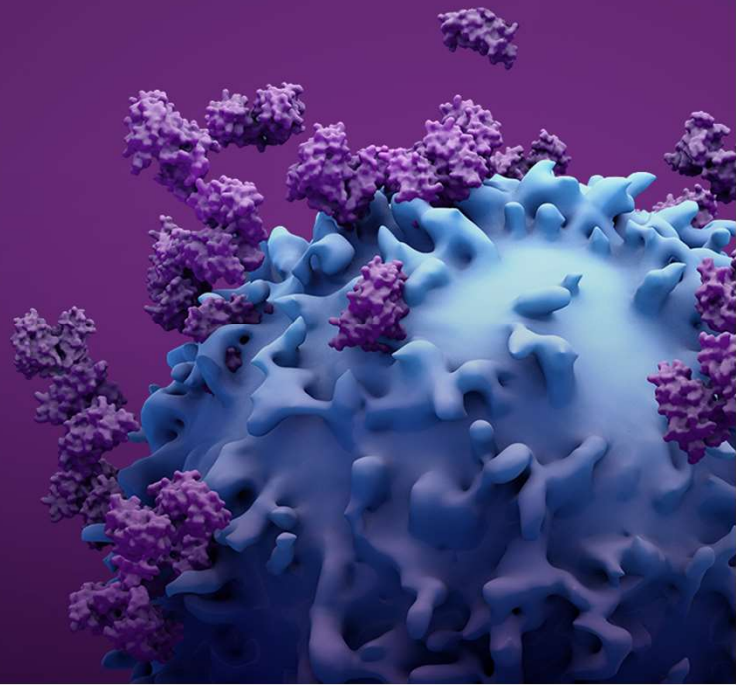
1. U.S. National Library of Medicine ClnicaltrIals.gov. URL: https://clinicaltrials.gov/ct2/show/NCT02908451. Accessed: November 8, 2020. Last updated: July 17, 2020; 2. U.S. National Library of Medicine ClnicaltrIals.gov. URL: https://clinicaltrials.gov/ct2/show/NCT03384940. Accessed: November 8, 2020. Last updated: September 9, 2020; 3. U.S. National Library of Medicine ClnicaltrIals.gov. URL: https://clinicaltrials.gov/ct2/show/NCT03449030. Accessed: November 8, 2020. Last updated: April 22, 2020.

Summary

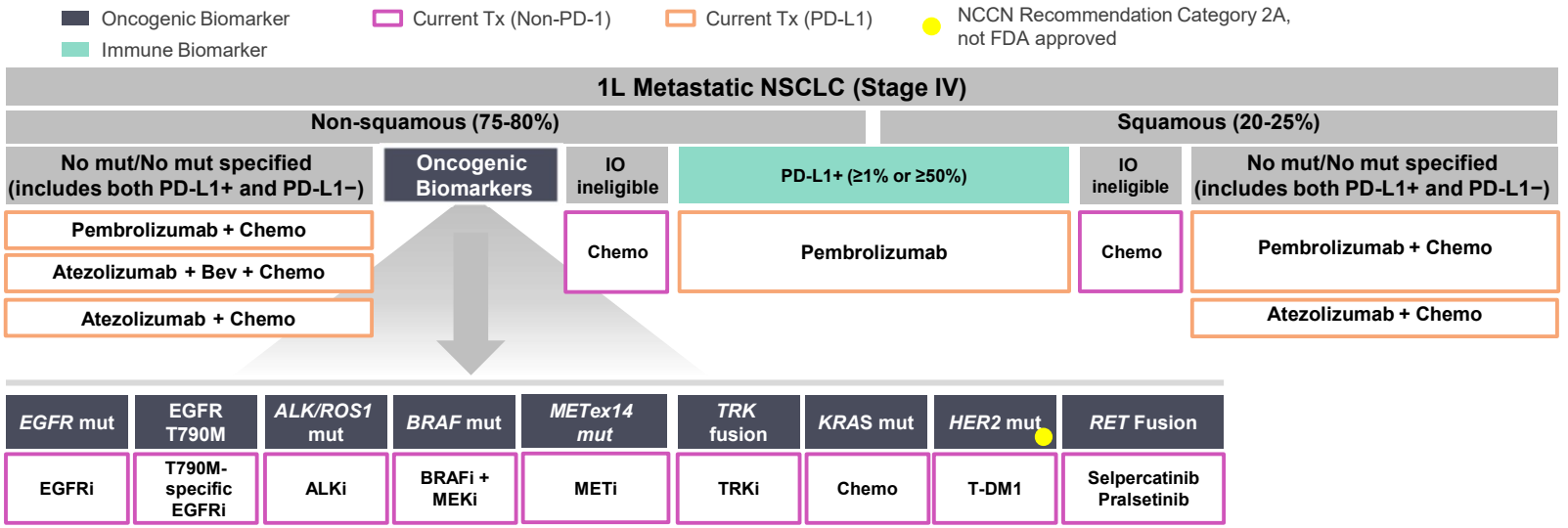
- There are currently no ADCs approved for use in patients with NSCLC, gastric cancers, and CRC
- Several ADCs, with novel mechanisms of action, are in various stages of development for NSCLC, gastric cancers, and CRCs
- These agents provide promising options for patients

PrimO
Practical Recommendations in Immuno & Molecular Oncology
ADC Summit

Clinical Applications of ADCs



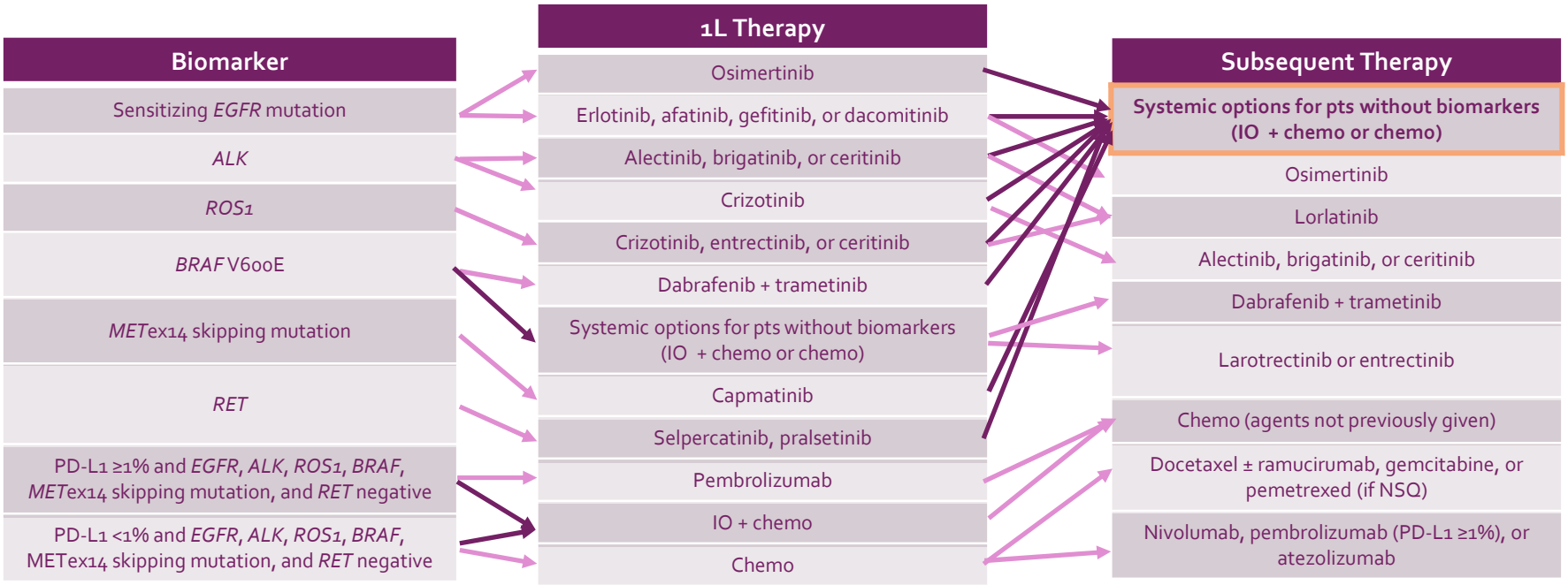
Actionable Oncogenic Drivers Changed the Treatment Paradigm for Patients With Lung Cancer



ALK, anaplastic lymphoma kinase; ALKi, anaplastic lymphoma kinase inhibitor; Bev, bevacizumab; BRAF, serine/threonine-protein kinase B-raf; chemo, chemotherapy; EGFRi, epidermal growth factor receptor inhibitor; FDA, US Food and Drug Administration; IO, immuno-oncology; KRAS, Kirsten rat sarcoma viral oncogene homolog; MEKi, MEK inhibitor; METi, MET inhibitor; mut, mutation; NCCN, National Comprehensive Cancer Network; PD-1, programmed death receptor-1; PD-L1, programmed death ligand 1; ROS1, reactive oxygen species 1; TRK, tropomyosin receptor kinase; TRKi, tropomyosin receptor kinase inhibitor.

SmartAnalyst Expertise.
Non-Small Cell Lung Cancer Clinical Practice Guidelines. NCCN. www.nccn.org/professionals/physician_gls/pdf/nscl_blocks.pdf. updated January 31, 2020. Accessed February 11, 2020.

Targeted Treatment Options Following 1L ICI Are Needed



Adapted from Non-Small Cell Lung Cancer Clinical Practice Guidelines. NCCN. www.nccn.org/professionals/physician_gls/pdf/nscl_blocks.pdf. updated January 31, 2020. Accessed February 11, 2020.

In Lung Cancer, the Impact of HER2 Alterations on Survival Is Unclear

PrimO Practical Recommendations in Immuno & Molecular Oncology ADC Summit

Author/Country	N	HER2 Alterations	Key Results
Nakamura/Japan	50	*HER2* amplification: 2%; HER2 overexpression: 26%; *HER2* gene DNA copy number ≥3: 44% NSCLC	No significant correlation between copy number increase and overexpression; **gene copy number increase, overexpression did not correlate with survival**
Suzuki/Japan	1275	*HER2* mutation: 3.6%; HER2 overexpression: 2.4%; *HER2* amplification: 19%	**HER2 overexpression, *HER2* amplification, and *HER2* mutation did not affect OS**; statistically significant associations between HER2 overexpression and amplification and between HER2 overexpression and mutation
Meert/Belgium	129	HER2 overexpression: 22.6%; *HER2* amplification: 6%	***HER2* amplification associated with shorter survival**
Kim/Korea	321	HER2 overexpression: 8.7%; *HER2* amplification: 14.3%; *HER2* mutation: 6.7% in driver oncogene-negative adenocarcinomas	**Patients with HER2 overexpression showed significantly shorter OS, DFS rates; patients with *HER2* amplification tended to have shorter OS rates**
Gow/Taiwan, China	888	HER2 mutation: 4.5%	**Patients with a HER2 mutation had better OS**
Li/China	456	HER2 overexpression: 15.4%; *HER2* mutation: 4.8%	**No correlation between *HER2* mutation and DFS or OS**
Pillai/United States	920	*HER2* mutation: 3%	**Patients with a *HER2* mutation had inferior survival**
Ninomiya/Japan	1126	HER2 overexpression: 20.1%; *HER2* amplification: 5.3%; *HER2* mutation: 2.9%	**Worse prognosis with HER2-aberrant tumors** vs *EGFR*- and *ALK*-positive tumors; HER2 IHC+ and mutation tended to be independent prognostic factors in NSCLC
Tan/United States	140	HER2 overexpression: 19%; *HER2* amplification: 5%; *HER2* mutation: 2.9%	**Patients with *HER2* gene amplification and HER2 protein IHC 3+ showed a strong tendency of shorter survival**

Zhao J and Xia Y. *JCO Precis Oncol*. 2020;4:411-425.

Efficacy of Trastuzumab in NSCLC to Date Has Been Disappointing

Agents	Study	HER2 Alterations	N	Efficacy
Trastuzumab + paclitaxel	Single-arm Ph 2	HER2 IHC 1+ to 3+; *HER2* gene number copy >1 (+ *EGFR* mut and progression on EGFR TKI monotherapy)	24 (21 with HER2 overexpression)	**ORR 46%;** DCR 63%
Trastuzumab + paclitaxel + carboplatin	Ph 2	HER2 IHC 1+ to 3+	56 (31 with HER2 overexpression)	**mPFS 3.3 mo**
Trastuzumab + cisplatin + gemcitabine	Ph 2	HER2 IHC 1+ to 3+ or a serum HER2 shed ECD concentrations ≥15 ng/mL	21 (9 with HER2 overexpression)	**ORR 38%;** DCR 81%
Trastuzumab + gemcitabine + cisplatin	Randomized Ph 2	HER2 overexpression (IHC 2+ to 3+); *HER2* amplification (FISH+); serum HER2 ECD positive	101 (5 with HER2 IHC3+; 7 with *HER2* FISH+)	**ORR 36%** (similar to control)
Trastuzumab + docetaxel or paclitaxel	Randomized Ph 2	Unselected by HER2 status	64 (20 with HER2 overexpression)	**ORR 23%** (similar to control)

ECD, extracellular domain; FISH, fluorescent in situ hybridization.
Zhao J and Xia Y. *JCO Precis Oncol*. 2020;4:411-425.

2 ADCs Currently Approved for HER2+ BC Developed With a Trastuzumab Antibody[1-3]

PrimO
Practical Recommendations in Immuno & Molecular Oncology
ADC Summit

Trastuzumab emtansine (T-DM1; Kadcyla)	Indicated, as a single agent, for the treatment of patients with HER2-positive, mBC who previously received trastuzumab and a taxane, separately or in combination. Patients should have either: • Received prior therapy for metastatic disease, or • Developed disease recurrence during or within 6 months of completing adjuvant therapy.
Trastuzumab deruxtecan (DS-8201a; T-DXd; Enhertu)	Indicated for the treatment of adult patients with unresectable or metastatic HER2-positive BC who have received 2 or more prior anti-HER2-based regimens in the metastatic setting. This indication is approved under accelerated approval based on tumor response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

mBC, metastatic breast cancer.

1. Schott AF, Hayes DF, Vora SR. UpToDate. https://www.uptodate.com/contents/systemic-treatment-for-her2-positive-metastatic-breast-cancer?topicRef=774&source=see_link. Published January 28, 2020. Accessed April 25, 2020. 2. Choi-Sledeski YM, Wermuth CG. Science Direct. 2017. https://www.sciencedirect.com/topics/neuroscience/antibody-drug-conjugate. Accessed April 21, 2020; 3. Soriot Pascal, Baselga Jose, et al. Strategic Collaboration in Oncology Trastuzumab Deruxtecan (DS-8201). Presented at: conference call for investors and analysts; March 29, 2019; Accessed May 11, 2020.

T-DM1 in NSCLC — Clinical Program Suspended[1-4]

PrimO Practical Recommendations in Immuno & Molecular Oncology ADC Summit

Treatment of Recurrences and Distant Metastases

The NCCN NSCLC Panel recommends T-DM1 for patients with *HER2* mutations based on results from a Phase 2 basket trial[2]

Phase 2 Basket Trial Results (Selected)

Patients (N=18) with advanced *HER2*-mutated lung adenocarcinomas

ORR	44% (95% CI, 22% to 69%)
PD as best response	(3) 17%
PFS (median)	5 mo (95% CI, 3 to 9 mo)
Responder PFS (median)	6 months (95% CI, 4 mo to NR)

Efficacy Not Confirmed in a Ph 2 Study of HER2 IHC+ Locally Advanced/mNSCLC:

- T-DM1 showed antitumor activity in selected patients with IHC 3+ HER2+ mNSCLC
- HER2 IHC did not predict T-DM1 activity

1. Li BT et al. J Clin Oncol. 2018;36(24):2532-2537; 2. Non-Small Cell Lung Cancer Clinical Practice Guidelines. NCCN. Version 8.2020 www.nccn.org/professionals/physician_gls/pdf/nscl_blocks.pdf. updated September 15, 2020. Accessed November 8, 2020; 3. Zhao J and Xia Y. JCO Precis Oncol. 2020;4:411-425; 4. Peters S et al. Clin Cancer Res 2019; 25(1).

T-DXd Efficacy Results in Patients With HER2-Mutated NSCLC

PrimO Practical Recommendations in Immuno & Molecular Oncology ADC Summit

Confirmed ORR	61.9% (n=26) (95% CI, 45.6% to 76.4%)
CR	2.4% (n=1)
PR	59.5 (n=25)
SD	28.6% (n=12)
PD	4.8% (n=2)
Not evaluable	4.8% (n=2)
DCR	90.5 (95% CI, 77.4% to 97.3%)
DOR, mo	NR (95% CI, 5/3 mo – NR)
PFS, median	14.0 mo (95% CI, 6.4 mo to 14.0 mo)

Enrollment in the HER2-mutated cohort was expanded with an additional 50 patients to better characterize the risk-benefit ratio of T-DXd in patients with HER2-mutated NSCLC

Anticipated study completion: 08/2021

Smit EF et al. Trastuzumab Deruxtecan (T-DXd; DS-8201) in patients with HER2-mutated metastatic non-small cell lung cancer: interim results of DESTINY-Lung01. Presented at: American Society for Clinical Oncology 2020 Virtual Scientific Program; May 29 – 31. Accessed November 6, 2020. https://meetinglibrary.asco.org/session/12667

Safety Results Consistent With What Were Previously Reported

- Low-grade GI and hematologic AEs are the most common
- Most common TEAEs associated with dose reduction were fatigue (11.9%) and nausea (9.5%)
- Most common TEAEs associated with dose interruption were decreased neutrophil count (19.0%) and lung infection (7.1%)
- Drug-related ILD events observed in this patient population were low grade, and there were no deaths
- **ILD remains an important identified risk for patients treated with T-DXd and requires careful monitoring and management**

Smit EF et al. Trastuzumab Deruxtecan (T-DXd; DS-8201) in patients with HER2-mutated metastatic non-small cell lung cancer: interim results of DESTINY-Lung01. Presented at: American Society for Clinical Oncology 2020 Virtual Scientific Program; May 29 – 31. Accessed November 6, 2020. https://meetinglibrary.asco.org/session/12667

AE of Interest With T-DXd: ILD[1-3]

- Identified across clinical development programs with T-DXd
- Protocol recommendation: monitor for symptoms. Hold T-DXd and start steroids as soon as ILD is suspected

	N	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Grade 5 n (%)	Any grade/total
Destiny-Breast01	184	5 (2.7)	15 (8.2)	1 (0.5)	0	4 (2.2)	25 (13.6)
DESTINY-CRC01	78	0	2 (2.6)	1 (1.3)	0	2 (2.6)	5 (6.4)
DESTINY-Lung01	42	0	5 (11.9)	0	0	0	5 (11.9)

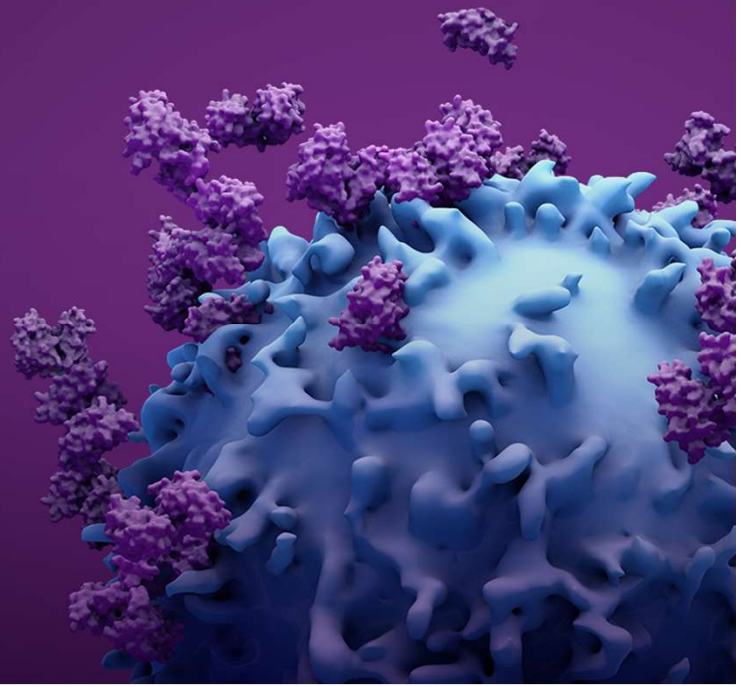
1. Modi S. Poster presented at the San Antonio Breast Cancer Symposium; December 4-7, 2018; San Antonio, TX [poster P6-17-02]; 2. Smit EF et al. Trastuzumab Deruxtecan (T-DXd; DS-8201) in patients with HER2-mutated metastatic non-small cell lung cancer: interim results of DESTINY-Lung01. Presented at: American Society for Clinical Oncology 2020 Virtual Scientific Program; May 29 – 31. Accessed November 6, 2020. https://meetinglibrary.asco.org/session/12667; 3. Siena S et al. A phase II, multicenter, open-label study of trastuzumab deruxtecan (T-DXd; DS-8201) in patients (pts) with HER2-expressing metastatic colorectal cancer (mCRC): DESTINY-CRC01. Presented at: American Society of Clinical Oncology 2020 Virtual Scientific Sessions; May 29 – 31. Accessed November 6, 2020. https://meetinglibrary.asco.org/record/185482/abstract;

Key Takeaways

- There is a need for targeted therapies in addition to, or concomitantly with, immune checkpoint inhibitors beyond the 1L setting
- Two HER2-targeted ADCs approved in BC have clinical development programs in NSCLC
  - T-DXd represents a promising treatment option for patients with HER2-mutated NSCLC; clinical development program is ongoing
  - In May 2020, T-DXd received Breakthrough Therapy Designation in the US

PrimO
Practical Recommendations in Immuno & Molecular Oncology
ADC Summit

Thank You!



Slide Breakup

- West: 1-11, 36-41 - West
- Ramalingam: 12-20, 36, 42-46
- Shroff: 21-36 (GI/CRC)