

2024 Tumor-Agnostic Approval Cheat Sheet

T-DXd (Enhertu)

FDA APPROVAL—APRIL 5, 2024

The FDA granted accelerated approval to fam-trastuzumab deruxtecan-nxki (T-DXd; Enhertu) for the treatment of adult patients with unresectable or metastatic HER2-positive (immunohistochemistry 3+) solid tumors who have received prior systemic therapy and have no satisfactory alternative treatment options.¹ This accelerated approval is based on the agent’s objective response rate and duration of response.

MECHANISM OF ACTION

T-DXd is a HER2-directed antibody-drug conjugate; the antibody is a humanized anti-HER2 IgG1, and the small molecule DXd is a topoisomerase I inhibitor attached to the antibody via a cleavable linker.²

RECOMMENDED DOSING FOR THIS INDICATION

5.4 mg/kg given as an intravenous infusion once every 3 weeks in a 21-day cycle until disease progression or unacceptable toxicity¹

PIVOTAL CLINICAL TRIALS

DESTINY-PanTumor02 (NCT04482309), DESTINY-Lung01 (NCT03505710), and DESTINY-CRC02 (NCT04744831) were phase 2 trials conducted in adults with previously treated unresectable or metastatic HER2-positive solid tumors.¹

- Patients were excluded from the trials if they had:
 - A history of interstitial lung disease (ILD)/pneumonitis requiring treatment with steroids or ILD/pneumonitis at screening and clinically significant cardiac disease
 - Active brain metastases
 - An ECOG performance status of greater than 1

BOXED WARNING

T-DXd has boxed warnings for ILD and pneumonitis, as well as embryo-fetal toxicity.

REFERENCES

1. FDA grants accelerated approval to fam-trastuzumab deruxtecan-nxki for unresectable or metastatic HER2-positive solid tumors. FDA. April 5, 2024. Accessed January 13, 2025. bit.ly/3UYSKqk
2. Enhertu. Prescribing information. Daiichi Sankyo, Inc; 2024. Accessed January 13, 2025. bit.ly/42e1m12

EFFICACY BY TUMOR TYPE IN DESTINY-PANTUMOR02, DESTINY-LUNG01, AND DESTINY-CRC02²

Tumor type	Confirmed ORR, (95% CI)
Colorectal cancer (n = 64)	46.9% (34.3%-59.8%)
Bladder cancer (n = 27)	37.0% (19.4%-57.6%)
Biliary tract cancer (n = 22)	45.5% (24.4%-67.8%)
Non-small cell lung cancer (n = 17)	52.9% (27.8%-77.0%)
Endometrial cancer (n = 16)	56.3% (29.9%-80.2%)
Ovarian cancer (n = 15)	66.7% (38.4%-88.2%)
Cervical cancer (n = 10)	70.0% (34.8%-93.3%)
Salivary gland cancer (n = 9)	66.7% (29.9%-92.5%)
Pancreatic cancer (n = 5)	0% (0%-52.2%)
Oropharyngeal neoplasm (n = 1)	PR
Vulvar cancer (n = 1)	PR
Extramammary Paget disease (n = 1)	PR
Lacrimal gland cancer (n = 1)	PR
Lip and/or oral cavity cancer (n = 1)	SD
Esophageal adenocarcinoma (n = 1)	PR
Esophageal squamous cell carcinoma (n = 1)	PD

ORR, objective response rate; PD, progressive disease; PR, partial response; SD, stable disease.

MOST COMMON AEs WITH T-DXd IN DESTINY-BREAST01 (NCT03248492), DESTINY-PANTUMOR02, DESTINY-LUNG01, AND DESTINY-CRC02²

AEs	T-DXd 5.4 mg/kg (n = 347)	
	All grade	Grade 3/4
Nausea	69.0%	7.0%
Fatigue	59.0%	10.0%
Vomiting	35.0%	3.5%
Decreased appetite	34.0%	2.6%
Alopecia	34.0%	0.3%
Diarrhea	31.0%	4.3%
Constipation	28.0%	0.6%
Stomatitis	20.0%	0.9%
Upper respiratory tract infection	20.0%	0.0%

AEs, adverse effects; T-DXd, trastuzumab deruxtecan.

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Repotrectinib (Augtyro)

FDA APPROVAL—JUNE 13, 2024

The FDA granted accelerated approval to repotrectinib (Augtyro) for the treatment of patients 12 years or older with locally advanced or metastatic solid tumors harboring an *NTRK* gene fusion or where surgical resection is likely to result in severe morbidity and who have progressed after treatment or have no satisfactory alternative therapy.¹

MECHANISM OF ACTION

Repotrectinib is a ROS1 inhibitor.²

RECOMMENDED DOSING FOR THIS INDICATION

160 mg given orally once daily for 14 days, then increased to twice daily until disease progression or unacceptable toxicity¹

PIVOTAL CLINICAL TRIAL

TRIDENT-1 (NCT03093116) was a multicenter, single-arm, open-label, phase 1/2 trial conducted in adults with locally advanced or metastatic *NTRK* gene fusion-positive solid tumors.¹

EFFICACY BY TUMOR TYPE WITH REPOTRECTINIB IN TKI-NAIVE PATIENTS²

Tumor type	Confirmed ORR, (95% CI)
Non-small cell lung cancer (n = 21)	62% (38%-82%)
Thyroid cancer (n = 5)	100% (48%-100%)
Salivary gland cancer (n = 3)	100% (29%-100%)
Soft tissue sarcoma (n = 3)	33% (0.8%-91%)
Breast cancer (n = 2)	PD and PD
Other cancer (n = 2)	SD and SD
Glioblastoma (n = 1)	SD
Cholangiocarcinoma (n = 1)	PD
Colorectal cancer (n = 1)	SD
Peripheral nerve sheath tumor (n = 1)	PR

ORR, objective response rate; PD, progressive disease; PR, partial response; SD, stable disease; TKI, tyrosine kinase inhibitor.

EFFICACY BY TUMOR TYPE WITH REPOTRECTINIB IN TKI-PRETREATED PATIENTS²

Tumor type	Confirmed ORR, (95% CI)
Non-small cell lung cancer (n = 14)	43% (18%-71%)
Salivary gland cancer (n = 8)	88% (47%-100%)
Soft tissue sarcoma (n = 6)	17% (0.4%-64%)
Thyroid cancer (n = 4)	50% (7%-93%)
Glioblastoma (n = 3)	33.3% (0.8%-91%)
Cholangiocarcinoma (n = 2)	PR and PD
Colorectal cancer (n = 2)	PR and SD
Peripheral nerve sheath tumor (n = 2)	PR and PR
Neuroendocrine tumor (n = 2)	PR and PR
Pancreatic cancer (n = 2)	PD and PD
Other (n = 2)	SD and PD
Breast cancer (n = 1)	PR

ORR, objective response rate; PD, progressive disease; PR, partial response; SD, stable disease; TKI, tyrosine kinase inhibitor.

MOST COMMON AEs WITH REPOTRECTINIB IN ROS1-POSITIVE NSCLC/*NTRK*-POSITIVE SOLID TUMORS IN TRIDENT-1²

AEs	Repotrectinib (n = 426)	
	All grade	Grade 3/4
Dizziness	65.0%	2.8%
Dysgeusia	54.0%	0.0%
Peripheral neuropathy	49.0%	1.4%
Constipation	38.0%	0.2%
Dyspnea	30.0%	6.0%
Fatigue	30.0%	1.2%
Ataxia	28.0%	0.5%
Cognitive impairment	25.0%	0.9%
Nausea	20.0%	0.7%
Muscular weakness	20.0%	2.0%

AEs, adverse effects; NSCLC, non-small cell lung cancer.

REFERENCES

1. FDA grants accelerated approval to repotrectinib for adult and pediatric patients with *NTRK* gene fusion-positive solid tumors. FDA. June 13, 2024. Accessed January 13, 2025. bit.ly/4eGQtr4
2. Augtyro. Prescribing information. Bristol Myers Squibb; 2024. Accessed January 13, 2025. bit.ly/4aebjjo