2024 ESMO IMMUNO-ONCOLOGY
Annual Congress

TRASTUZUMAB DERUXTECAN AND PEMBROLIZUMAB IN IMMUNO-ONCOLOGY-NAIVE HER2-EXPRESSING OR *HER2*-MUTANT NON–SMALL CELL LUNG CANCER: INTERIM ANALYSIS OF A PHASE 1B STUDY

Presentation 118MO

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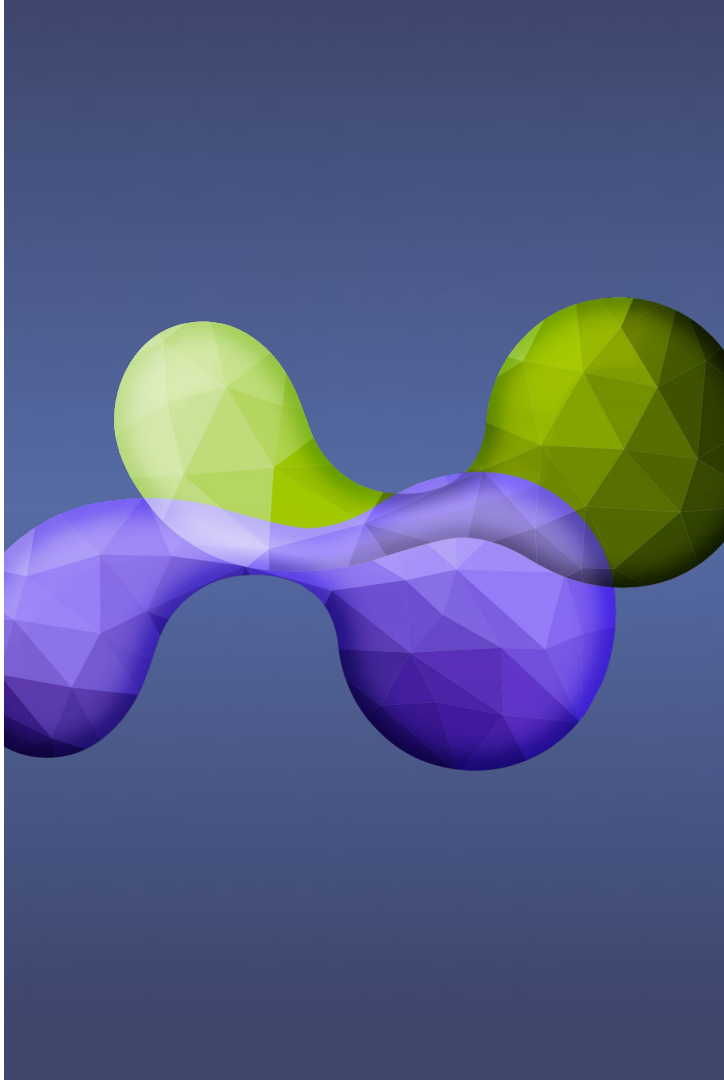
ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE



DECLARATION OF INTERESTS

Antoine Italiano

Grants or contracts from any entity: AstraZeneca, Bayer, Daiichi Sankyo, GSK, MSD, Parthenon

Payment or honoraria for lectures, presentations, speakers' bureaus, manuscript writing, or educational events: AstraZeneca, Bayer, Daiichi Sankyo, GSK, MSD, Parthenon

Participation on a drug safety monitoring board or advisory board: AstraZeneca, Bayer, Daiichi Sankyo, GSK, MSD, Parthenon

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BACKGROUND

- T-DXd is approved in many countries for the treatment of patients with *HER2*m unresectable or metastatic NSCLC who have previously received a systemic therapy and, in the United States, for the treatment of patients with HER2-positive (IHC 3+) solid tumors who have previously received systemic treatment and have no satisfactory alternative treatment options[1]
- Pembrolizumab is a PD-1–blocking antibody, approved as a single agent for first-line treatment of patients who have NSCLC expressing PD-L1[2]
- Results of preclinical studies showed that the HER2-directed ADC T-DXd enhanced antitumor immunity and combination therapy with T-DXd and an anti–PD-1 antibody was more effective than either treatment alone[3]
  - T-DXd has a potential additive effect with immune checkpoint inhibitors that target the PD-1/PD-L1 pathway to enhance tumor immunogenicity alongside tumor cell death[4]

The objective in this interim analysis was to evaluate the preliminary clinical efficacy and safety of T-DXd + pembrolizumab in patients with IO-naive HER2-expressing or *HER2*m (1L+) NSCLC from the U106 study (NCT04042701)

1L+, first-line plus; ADC, antibody-drug conjugate; HER2, human epidermal growth factor receptor 2; *HER2*m, *HER2* mutant; IHC, immunohistochemistry; IO, immuno-oncology; NSCLC, non–small cell lung cancer; PD-1, programmed death 1; PD-L1, programmed death ligand 1; T-DXd, trastuzumab deruxtecan.

1. Enhertu. Package insert. Daiichi Sankyo; 2024. 2. Keytruda. Package insert. Merck Sharp & Dohme LLC, Rahway, NJ, USA; 2024. Merck & Co., Inc. 3. Iwata TN et al. *Mol Cancer Ther*. 2018;17:1494-1503. 4. Vanneman M et al. *Nat Rev Cancer*. 2014;12(4):237-251.

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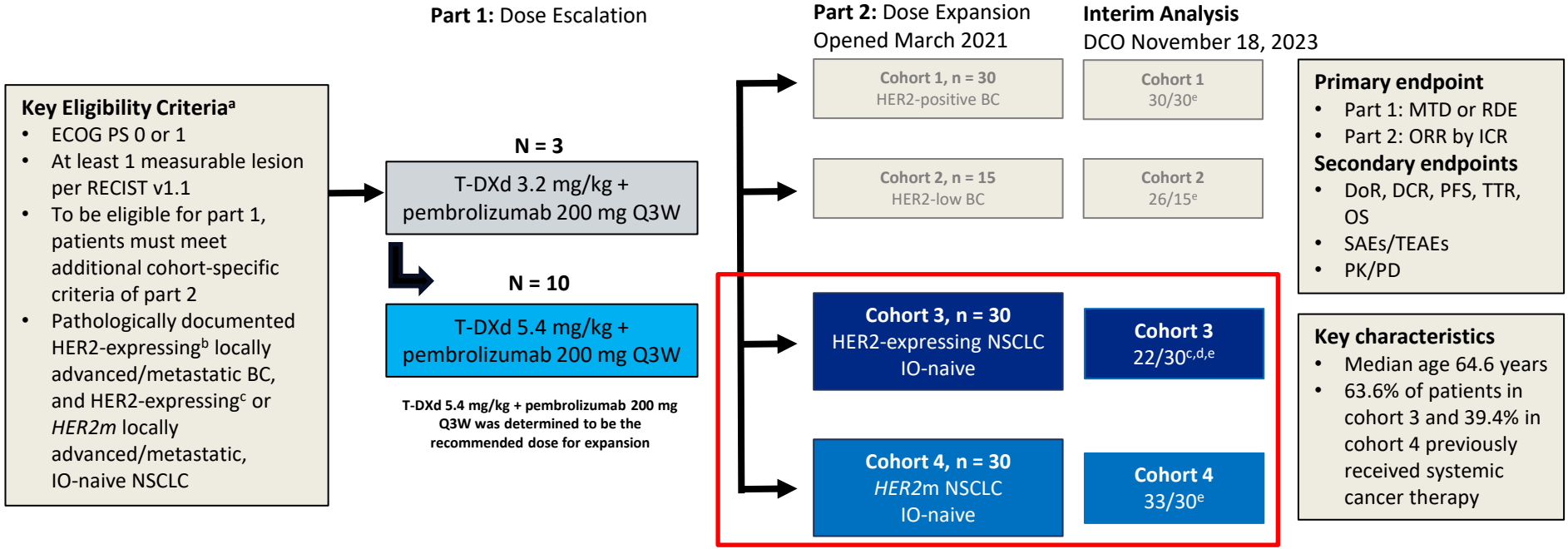
DS8201-A-U106: OPEN-LABEL, PHASE 1B STUDY (NCT04042701)



BC, breast cancer; CNS, central nervous system; DCR, disease control rate; DCO, data cutoff; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; HER2, human epidermal growth factor receptor 2; *HER2*m, HER2 mutant; ICR, independent central review; IHC, immunohistochemistry; IO, immuno-oncology; MTD, maximum tolerated dose; NSCLC, non–small cell lung cancer; ORR, objective response rate; OS, overall survival; PD, pharmacodynamics; PK, pharmacokinetics; PFS, progression-free survival; Q3W, every 3 weeks; RDE, recommended dose for expansion; RECIST, Response Evaluation Criteria in Solid Tumours; SAE, serious adverse event; T-DXd, trastuzumab deruxtecan; TEAE, treatment-emergent adverse event; TTR, time to response.

[a]Patients with clinically active CNS metastases (defined as untreated and/or needing anticonvulsants to control symptoms) were ineligible for inclusion. However, patients with clinically inactive brain metastases or with brain metastases that were no longer symptomatic and did not require treatment with corticosteroids or anticonvulsants within 2 months of enrollment could be included. [b]Assessed by central testing. [c]Local or central HER2 IHC 1+ (n = 6, 27.3%), 2+ (n = 8, 36.4%), or 3+ (n = 8, 36.4%). [d]Included 3 patients with *HER2*m NSCLC. [e]Actual/planned enrollment.

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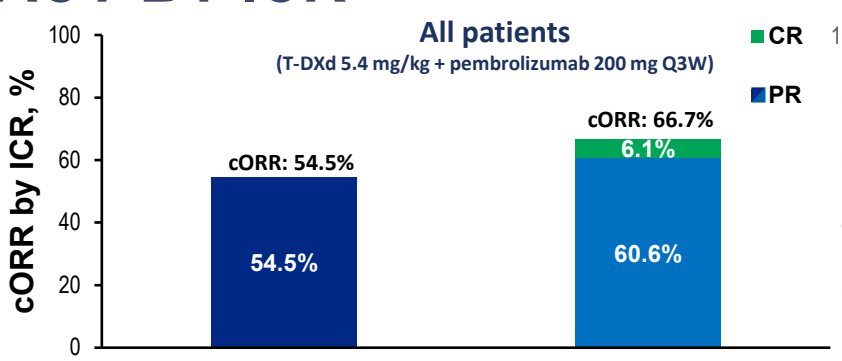
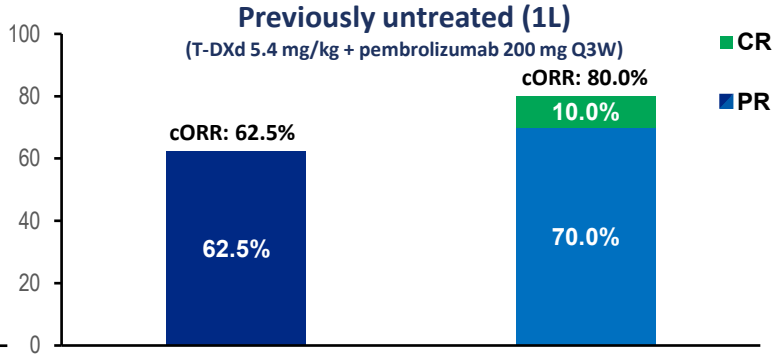
EFFICACY BY ICR





	Cohort 3 HER2-expressing NSCLC n = 22	Cohort 4 *HER2*m NSCLC[a] n = 33	Cohort 3 HER2-expressing NSCLC n = 8	Cohort 4 *HER2*m NSCLC[a] n = 20
cORR by ICR, n (%) [95% CI]	**12 (54.5) [32.2-75.6]**	**22 (66.7) [48.2-82.0]**	**5 (62.5) [24.5-91.5]**	**16 (80.0) [56.3-94.3]**
CR, n (%)	0	2 (6.1)	0	2 (10.0)
PR, n (%)	12 (54.5)[b]	20 (60.6)	5 (62.5)	14 (70.0)
SD, n (%)	7 (31.8)	8 (24.2)	2 (25.0)	3 (15.0)
PD, n (%)	0	0	0	0
NE, n (%)	3 (13.6)	3 (9.1)	1 (12.5)	1 (5.0)
DCR, n (%) [95% CI]	19 (86.4) [65.1-97.1]	30 (90.9) [75.5-98.1]	7 (87.5) [47.3-99.7]	19 (95.0) [75.1-99.9]
DoR of CR or PR, median (95% CI), months	20.2 (4.2-NE)	15.1 (8.1-22.1)	20.2 (6.9-NE)	19.9 (4.6-NE)
PFS, median (95% CI), months[c]	15.1 (5.6-NE)	11.3 (5.8-21.3)	23.5 (0.8-NE)	21.3 (5.8-NE)

1L, first line; cORR, confirmed objective response rate; CR, complete response; DCR, disease control rate; DoR, duration of response; HER2, human epidermal growth factor receptor 2; *HER2*m, *HER2* mutant; ICR, independent central review; IHC, immunohistochemistry; NE, not evaluable; NSCLC, non–small cell lung cancer; PD, progressive disease; PFS, progression-free survival; PR, partial response; SD, stable disease; T-DXd, trastuzumab deruxtecan.
[a]Includes 3 patients (1 previously untreated) who received T-DXd 5.4 mg/kg during part 1. [b]HER2 status: 7 IHC 3+, 3 IHC 2+, and 2 IHC 1+. [c]Median PFS is from Kaplan-Meier analysis and CI for median was computed using the Brookmeyer-Crowley method.

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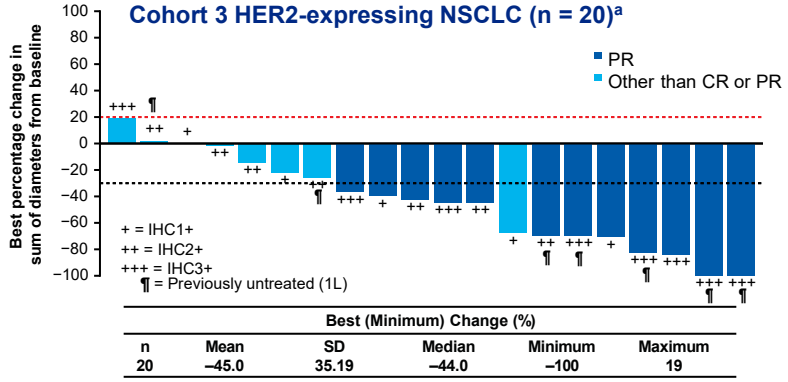
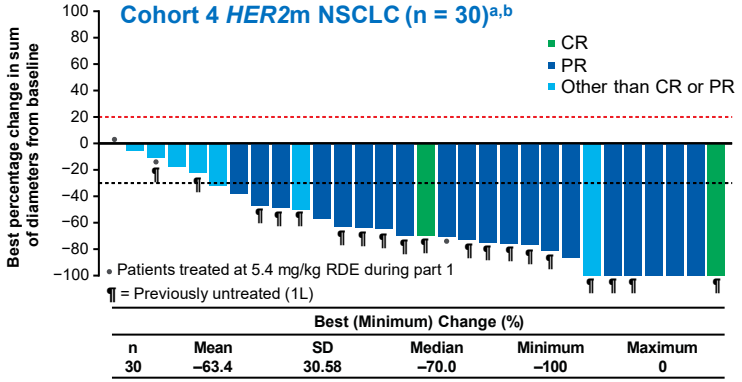
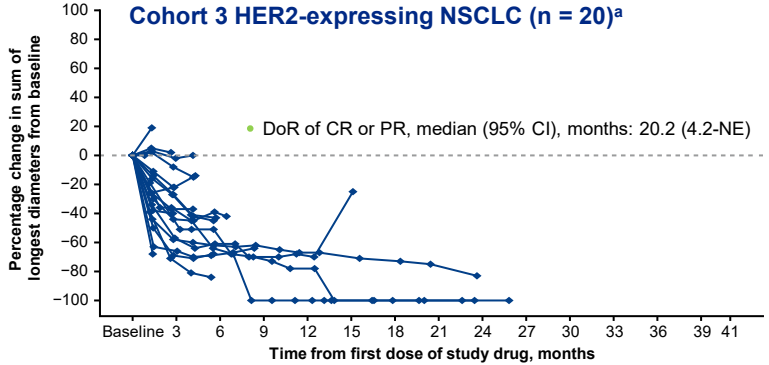
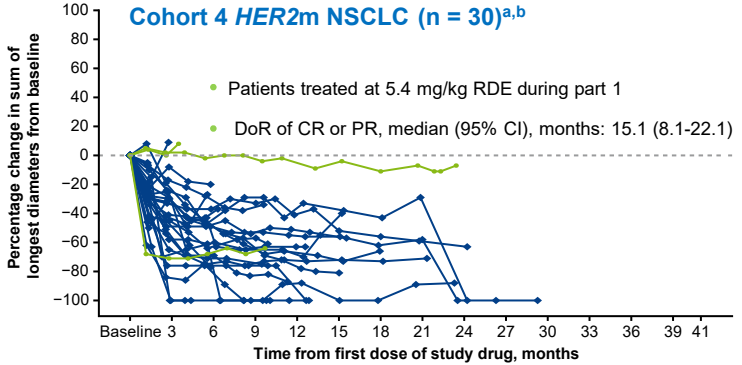
CHANGE FROM BASELINE IN SUM OF DIAMETERS









CI, confidence interval; CR, complete response; DoR, duration of response; HER2, human epidermal growth factor receptor 2; *HER2*m, *HER2* mutant; IHC, immunohistochemistry; NE, not evaluable; NSCLC, non–small cell lung cancer; PR, partial response; RDE, recommended dose for expansion; T-DXd, trastuzumab deruxtecan. [a]2 patients in cohort 3 and 3 patients in cohort 4 were not included because they did not have postbaseline scans. [b]Includes 3 patients with *HER2*m NSCLC treated with T-DXd 5.4 mg/kg during part 1.

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SAFETY

	Cohort 3 HER2-expressing NSCLC n = 22	Cohort 4 *HER2*m NSCLC[a] n = 33	All NSCLC patients N = 55	Overall BC + NSCLC patients N = 111
Duration of follow-up, median (range), months	5.9 (0.3-26)	15.2 (0.5-35)	12.9 (0.3-35)	14.7 (0.3-35.0)
Treatment duration, median (range), months T-DXd | pembrolizumab	5.2 (1-26) | 5.2 (1-26)	9.7 (1-33) | 9.7 (1-27)	6.9 (1-33) | 6.9 (1-27)	6.9 (1-33) | 6.9 (1-27)
Grade ≥3 drug-related TEAEs,[b] n (%)	5 (22.7)	16 (48.5)	21 (38.2)	40 (36.0)
Serious drug-related TEAEs,[b] n (%)	3 (13.6)	11 (33.3)	14 (25.5)	22 (19.8)
Drug-related TEAEs associated with death,[b] n (%)	0	1 (3.0)[c]	1 (1.8)	1 (0.9)

- In the HER2-expressing NSCLC cohort (n = 22), 2 patients[d] (9.1%) had adjudicated drug-related ILD/pneumonitis (1 grade 2; 1 grade 3)
  - Median time to onset of first ILD/pneumonitis event was 212 days (range, 210-214 days)
- In the *HER2*m NSCLC cohort (n = 33[a]), 9 patients (27.3%) had adjudicated drug-related ILD/pneumonitis (8 grade 2; 1 grade 5)
  - Median time to onset of first ILD/pneumonitis event was 70 days (range, 6-548 days)

BC, breast cancer; HER2, human epidermal growth factor receptor 2; *HER2*m, *HER2* mutant; ILD, interstitial lung disease; NSCLC, non–small cell lung cancer; T-DXd, trastuzumab deruxtecan; TEAE, treatment-emergent adverse effect. [a]Includes 3 patients (1 previously untreated) who received T-DXd 5.4 mg/kg during part 1. [b]Drug-related TEAEs may be associated with T-DXd and/or pembrolizumab. [c]Adjudicated as drug-related pneumonitis. [d]Both patients were treatment-naïve, and no *HER2* mutation was reported.

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CONCLUSIONS

- Combination therapy with T-DXd plus pembrolizumab showed preliminary antitumor activity in patients with IO-naive (1L+) HER2-expressing and *HER2*m NSCLC
  - In HER2-expressing NSCLC (n = 22), the cORR by ICR was 54.5%, median DoR was 20.2 months, and median PFS was 15.1 months
    - In the previously untreated (1L) NSCLC subgroup (n = 8), the cORR by ICR was 62.5%, median DoR was 20.2 months, and median PFS was 23.5 months
  - In *HER2*m NSCLC (n = 33), the cORR by ICR was 66.7%, median DoR was 15.1 months, and median PFS was 11.3 months
    - In previously untreated (1L) NSCLC subgroup (n = 20), the cORR by ICR was 80.0%, median DoR was 19.9 months, and median PFS was 21.3 months
- The preliminary safety profile was generally consistent with the known safety of the individual drugs and was generally manageable; ILD remains an important risk associated with T-DXd treatment and patients should be monitored for signs and symptoms
- Further research in a larger data set is necessary in this patient population

1L+, first-line plus; cORR, confirmed objective response rate; DoR, duration of response; HER2, human epidermal growth factor receptor 2; *HER2*m, *HER2* mutant; ICR, independent central review; IO, immuno-oncology; NSCLC, non–small cell lung cancer; PFS, progression-free survival; T-DXd, trastuzumab deruxtecan.

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We thank

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for their participation

&

The study site staff
for their contributions

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Andre Wang, PharmD, and Sara Duggan, PhD (ApotheCom), and was funded by Daiichi Sankyo, Inc.

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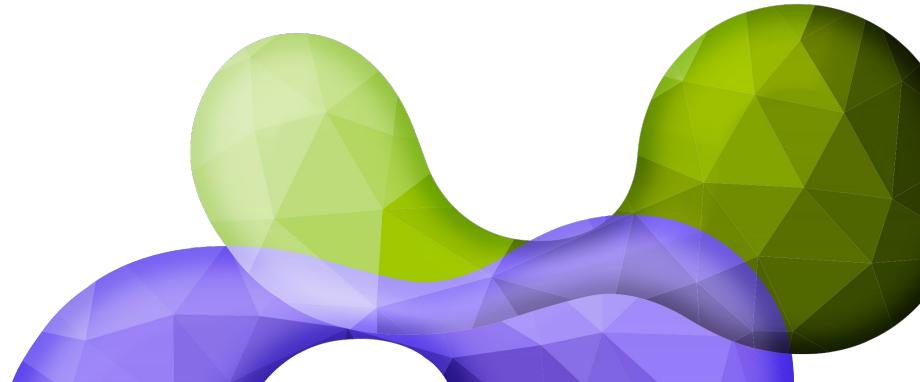
SUPPLEMENTARY CONTENT



PLAIN LANGUAGE SUMMARY

Why did we perform this research?

- Trastuzumab deruxtecan (T-DXd) is an anticancer therapy that targets a protein called human epidermal growth factor receptor 2 (HER2).[1,2] There is evidence to suggest that combining therapies that target HER2 with other agents that help to control immune system responses (immunotherapy [IO]), such as pembrolizumab, could result in enhanced anticancer activity.[3] Given that T-DXd monotherapy is approved for use in patients with previously treated metastatic non–small cell lung cancer (NCSLC) whose tumors have activating *HER2* mutations,[4] researchers are interested in assessing potential additive effects when combining T-DXd with IO in patients with HER2-expressing or *HER2* mutant (*HER2*m) NSCLC.

How did we perform this research?

- Patients with IO-naive (first-line and beyond) HER2-expressing or *HER2*m NSCLC were eligible for this study. This was a 2-part study in which in part 1 the recommended dose of T-DXd plus pembrolizumab was determined, and then, in part 2, patients were assigned to cohort 3 (HER2-expressing NSCLC; immunohistochemistry score of 1+/2+/3+) or to cohort 4 (*HER2*m NSCLC). The primary endpoint was confirmed objective response rate (cORR) by independent central review, which is the proportion of patients who had either a partial or complete response to treatment according to assessment of tumor shrinkage. At the time of this interim data cutoff date (November 18, 2023), 22 patients in cohort 3 and 33 patients in cohort 4 had received T-DXd 5.4 mg/kg plus pembrolizumab 200 mg intravenously every 3 weeks.

What were the findings of this research?

- The findings from this interim analysis demonstrated that T-DXd in combination with pembrolizumab showed initial antitumor activity, and the preliminary safety profile was consistent with the known safety profiles of the individual drugs and was generally manageable in patients with IO-naive (first-line and beyond) HER2-expressing and *HER2*m NSCLC. The cORR by independent central review was 54.5% in patients with HER2-expressing NSCLC and 66.7% in patients with *HER2*m NSCLC.

What are the implications of this research?

- These findings regarding the combination of T-DXd and IO support further research in patients with HER2-expressing and *HER2*m NSCLC in a larger data set.

Where can I access more information?

- To learn more about the DS8201-A-U106 study, you can visit https://clinicaltrials.gov/study/NCT04042701

1. Nakada T et al. *Chem Pharm Bull.* 2019;67(3):173-185. 2. Ogitani Y et al. *Clin Cancer Res.* 2016;22(20):5097-5108. 3. Vanneman M et al. *Nat Rev Cancer.* 2014;12:237-251. 4. Enhertu. Package insert. Daiichi Sankyo; 2024.

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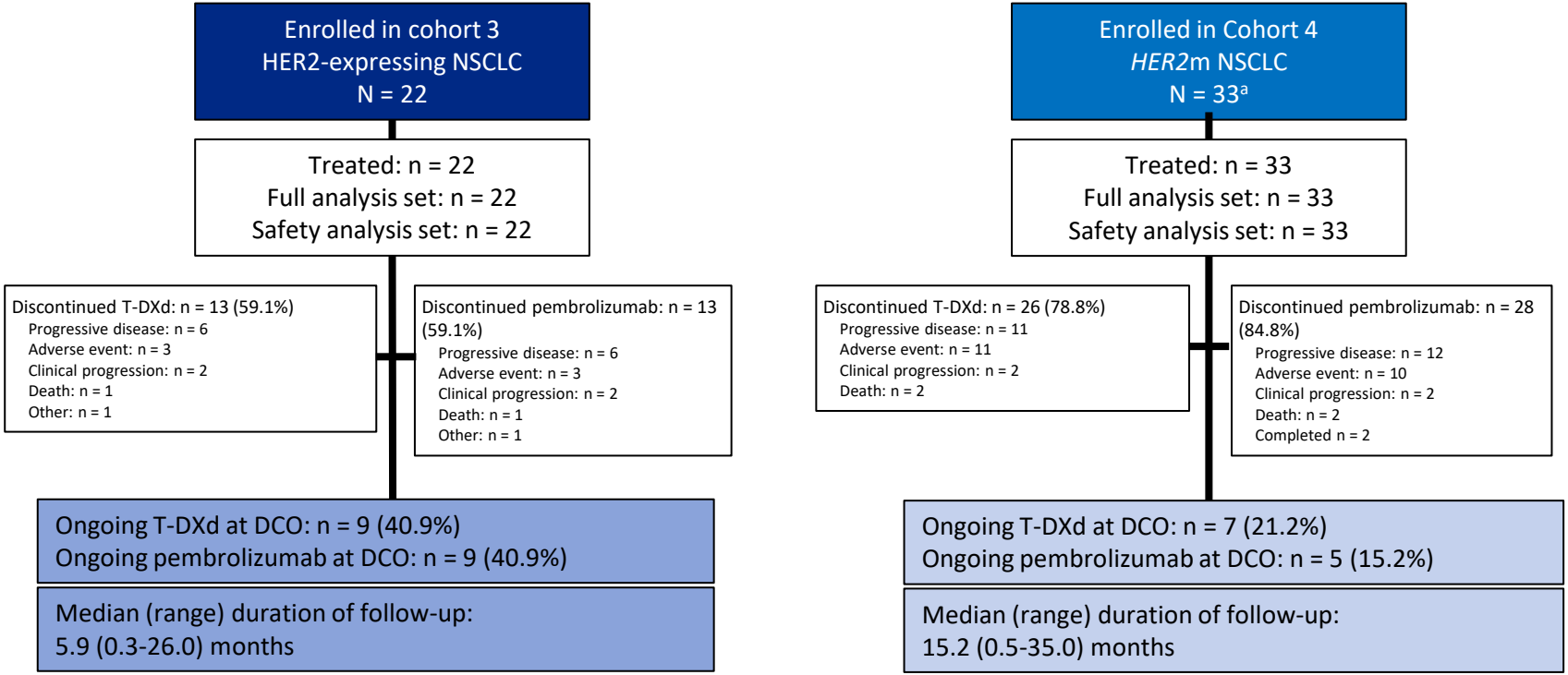
PATIENT DISPOSITION



DCO, data cutoff; HER2, human epidermal growth factor receptor 2; *HER2*m, *HER2* mutant; NSCLC, non–small cell lung cancer; RDE, recommended dose for expansion; T-DXd, trastuzumab deruxtecan.
[a]Includes 3 patients (1 previously untreated) who received the RDE of T-DXd 5.4 mg/kg during part 1.

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BASELINE CHARACTERISTICS AND PRIOR THERAPY

	Cohort 3 HER2-expressing NSCLC n = 22	Cohort 4 *HER2*m NSCLC[a] n = 33	All NSCLC patients N = 55
Age, median (range), years	64.2 (39.9-80.5)	66.0 (38.3-85.6)	64.6 (38.3-85.6)
Sex, n (%), Male | Female	12 (54.5) | 10 (45.5)	13 (39.4) | 20 (60.6)	25 (45.5) | 30 (54.5)
Region of enrollment, n (%), United States | Europe	0 | 22 (100)	2 (6.1) | 31 (93.9)	2 (3.6) | 53 (96.4)
Smoking history, n (%), Never | Former | Current	3 (13.6) | 13 (59.1) | 6 (27.3)	24 (72.7) | 9 (27.3) | 0	27 (49.1) | 22 (40.0) | 6 (10.9)
ECOG PS, n (%), 0 | 1 | 2	8 (36.4) | 13 (59.1) | 1 (4.5)	7 (21.2) | 26 (78.8) | 0	15 (27.3) | 39 (70.9) | 1 (1.8)
History of brain metastasis, n (%)	8 (36.4)	8 (24.2)	16 (29.1)
HER2 IHC[b] for enrollment, n (%), IHC 1+ | IHC 2+ | IHC 3+	6 (27.3) | 8 (36.4) | 8 (36.4)	- | - | -	- | - | -
***EGFR* mutation, n (%),** Positive | Negative | Not tested/missing	10 (45.5) | 10 (45.5) | 2 (9.1)	0 | 32 (97.0) | 1 (3.0)	10 (18.2) | 42 (76.4) | 3 (5.5)
Any previous systemic cancer therapy, n (%), Yes | No	14 (63.6) | 8 (36.4)[c]	13 (39.4) | 20 (60.6)	27 (49.1) | 28 (50.9)
Unique regimens in metastatic/locally advanced setting, n (%)			
0	8 (36.4)	22 (66.7)	30 (54.5)
1	8 (36.4)	7 (21.2)	15 (27.3)
2	0	2 (6.1)	2 (3.6)
3	5 (22.7)	2 (6.1)	7 (12.7)
≥4	1 (4.5)	0	1 (1.8)
Unique regimens in the metastatic/locally advanced setting, median (range), n	1.0 (0-5)	0 (0-3)	0 (0-5)

ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; HER2, human epidermal growth factor receptor 2; *HER2*m, *HER2* mutant; IHC, immunohistochemistry; NSCLC, non–small cell lung cancer; T-DXd, trastuzumab deruxtecan.

[a]Includes 3 patients (1 previously untreated) who received T-DXd 5.4 mg/kg during part 1.

[b]Local or central. [c]One patient had a *BRAF* mutation (not *BRAF V600*) and had not received previous treatment.

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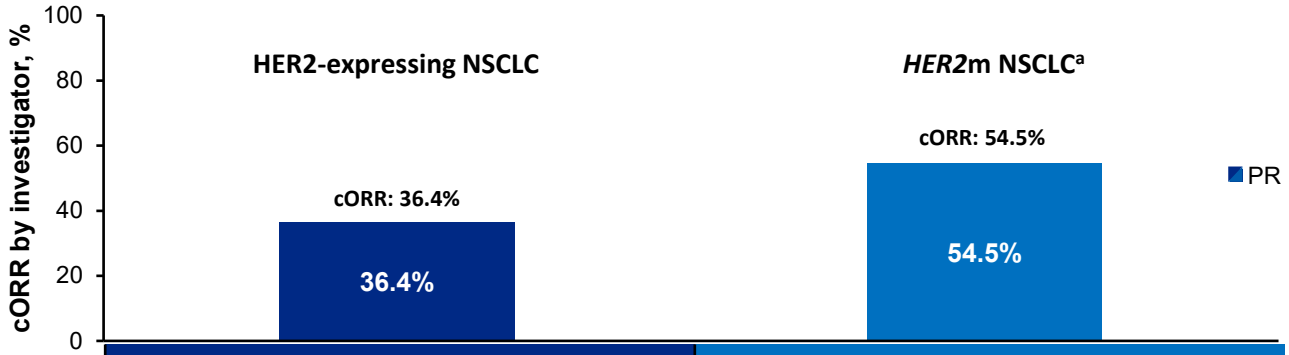
EFFICACY BY INVESTIGATOR ASSESSMENT



	Cohort 3 HER2-expressing NSCLC n = 22	Cohort 4 *HER2*m NSCLC n = 33
cORR, n (%) [95% CI]	**8 (36.4) [17.2-59.3]**	**18 (54.5) [36.4-71.9]**
CR, n (%)	0	0
PR, n (%)	8 (36.4)	18 (54.5)
SD, n (%)	10 (45.5)	11 (33.3)
PD, n (%)	2 (9.1)	1 (3.0)
NE, n (%)	2 (9.1)	3 (9.1)
DCR, n (%) [95% CI]	18 (81.8) [59.7-94.8]	29 (87.9) [71.8-96.6]
DoR of CR or PR, median (95% CI), months	13.8 (2.9-NE)	26.6 (9.3-NE)

cORR, confirmed objective response rate; CR, complete response; DCR, disease control rate; DoR, duration of response; HER2, human epidermal growth factor receptor 2; *HER2*m, *HER2* mutant; NE, not evaluable; NSCLC, non–small cell lung cancer; PD, progressive disease; PR, partial response; SD, stable disease.

[a]Includes 3 patients (1 previously untreated) who received T-DXd 5.4 mg/kg during part 1.

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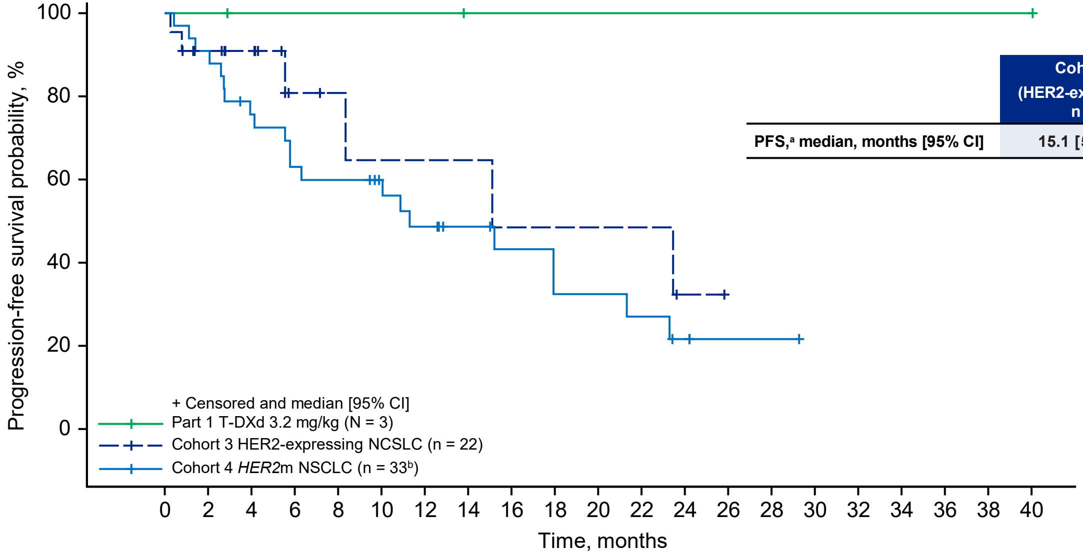
PROBABILITY OF PFS



	Cohort 3 (HER2-expressing) n = 22	Cohort 4 (*HER2*m) n = 33[b]
PFS,[a] median, months [95% CI]	**15.1 [5.6-NE]**	**11.3 [5.3-21.3]**

No. of patients still at risk

Part 1: 3 3 3 2 2 2 2 2 2 2 2 2 2 2 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
Cohort 3: 22 19 17 14 14 10 6 6 5 4 4 4 4 4 4 4 3 3 3 3 3 3 3 3 1 1 0
Cohort 4: 33 32 30 26 24 23 20 19 19 19 16 14 13 10 10 10 8 8 6 6 6 6 5 5 3 1 1 1 1 1 0

HER2, human epidermal growth factor receptor 2; *HER2*m, *HER2* mutant; NE, not evaluable; NSCLC, non–small cell lung cancer; PFS, progression-free survival; T-DXd, trastuzumab deruxtecan.
[a]Median PFS is from Kaplan-Meier analysis, and CI for median was computed using the Brookmeyer-Crowley method. [b]Includes 3 patients with *HER2m* NSCLC treated with T-DXd 5.4 mg/kg during part 1.

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ADDITIONAL SAFETY (DRUG-RELATED TEAES)[a]

	Cohort 3 (HER2-expressing NSCLC) n = 22	Cohort 4 (*HER2*m NSCLC)[a] n = 33	All NSCLC patients N = 55	Overall BC + NSCLC patients N = 111
Duration of follow-up, median (range), months	5.9 (0.3-26)	15.2 (0.5-35)	12.9 (0.3-35)	–
Treatment duration, median (range), months				
T-DXd	5.2 (1-26)	9.7 (1-33)	6.9 (1-33)	6.9 (1-33)
Pembrolizumab	5.2 (1-26)	9.7 (1-27)	6.9 (1-27)	6.9 (1-27)
Any drug-related TEAEs,[b] n (%)	21 (95.5)	31 (93.9)	52 (94.5)	107 (96.4)
Drug-related TEAEs associated with discontinuation,[b] n (%)	3 (13.6)	10 (30.3)	13 (23.6)	24 (21.6)
Drug-related TEAEs associated with interruption,[b] n (%)	3 (13.6)	15 (45.5)	18 (32.7)	35 (31.5)
Drug-related TEAEs associated with T-DXd dose reduction,[c] n (%)	2 (9.1)	5 (15.2)	7 (12.7)	19 (17.1)

BC, breast cancer; HER2, human epidermal growth factor receptor 2; *HER2*m, *HER2* mutant; NSCLC, non–small cell lung cancer; TEAE, treatment-emergent adverse effect; T-DXd, trastuzumab deruxtecan.
[a]Includes 3 patients (1 previously untreated) who received T-DXd 5.4 mg/kg during part 1. [b]Drug-related TEAEs may be associated with T-DXd and/or pembrolizumab. [c]All events were related to T-DXd.

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MOST FREQUENT TEAES BY PREFERRED TERM (≥20% OF OVERALL BC + NSCLC)

Preferred term, n (%)	Cohort 3 (HER2-expressing NSCLC) n = 22	Cohort 4 (*HER2*m NSCLC) n = 33	All NSCLC patients N = 55	Overall BC + NSCLC patients N = 111
Nausea	18 (81.8)	27 (81.8)	45 (81.8)	87 (78.4)
Diarrhea	9 (40.9)	17 (51.5)	26 (47.3)	52 (46.8)
Asthenia	17 (77.3)	16 (48.5)	33 (60.0)	50 (45.0)
Constipation	10 (45.5)	12 (36.4)	22 (40.0)	47 (42.3)
Decreased appetite	11 (50.0)	13 (39.4)	24 (43.6)	42 (37.8)
Vomiting	6 (27.3)	14 (42.4)	20 (36.4)	42 (37.8)
Fatigue	1 (4.5)	7 (21.2)	8 (14.5)	41 (36.9)
Anemia	6 (27.3)	13 (39.4)	19 (34.5)	40 (36.0)
Alopecia	3 (13.6)	14 (42.4)	17 (30.9)	37 (33.3)
Headache	5 (22.7)	11 (33.3)	16 (29.1)	37 (33.3)
Dyspnea	6 (27.3)	14 (42.4)	20 (36.4)	34 (30.6)
Pyrexia	8 (36.4)	9 (27.3)	17 (30.9)	34 (30.6)
Cough	5 (22.7)	13 (39.4)	18 (32.7)	34 (30.6)
Aspartate aminotransferase increased	0	17 (51.5)	17 (30.9)	29 (26.1)
Alanine aminotransferase increased	1 (4.5)	13 (39.4)	14 (25.5)	25 (22.5)
COVID-19	4 (18.2)	10 (30.3)	14 (25.5)	23 (20.7)

BC, breast cancer; HER2, human epidermal growth factor receptor 2; *HER2*m, *HER2* mutant; NSCLC, non–small cell lung cancer; RDE, recommended dose for expansion; TEAEs, treatment-emergent adverse effects.
Includes patients from parts 1 and 2 treated with RDE.

Antoine Italiano, MD, PhD

MOST FREQUENT GRADE ≥3 TEAES BY PREFERRED TERM (≥2% OF OVERALL BC + NSCLC)

Preferred term, n (%)	Cohort 3 (HER2-expressing NSCLC) n = 22	Cohort 4 (*HER2*m NSCLC) n = 33	All NSCLC patients N = 55	Overall BC + NSCLC patients N = 111
Asthenia	2 (9.1)	4 (12.1)	6 (10.9)	9 (8.1)
Nausea	1 (4.5)	2 (6.1)	3 (5.5)	8 (7.2)
Vomiting	1 (4.5)	3 (9.1)	4 (7.3)	8 (7.2)
Anemia	1 (4.5)	1 (3.0)	2 (3.6)	7 (6.3)
Neutropenia	0	1 (3.0)	1 (1.8)	7 (6.3)
Alanine aminotransferase increased	0	3 (9.1)	3 (5.5)	5 (4.5)
Fatigue	0	0	0	5 (4.5)
Aspartate aminotransferase increased	0	2 (6.1)	2 (3.6)	4 (3.6)
Dyspnea	2 (9.1)	1 (3.0)	3 (5.5)	4 (3.6)
General physical health deterioration	0	1 (3.0)	1 (1.8)	4 (3.6)
Hypokalemia	1 (4.5)	2 (6.1)	3 (5.5)	4 (3.6)
Thrombocytopenia	1 (4.5)	1 (3.0)	2 (3.6)	4 (3.6)
Acute kidney injury	0	1 (3.0)	1 (1.8)	3 (2.7)
Lipase increased	0	1 (3.0)	1 (1.8)	3 (2.7)
Lymphocyte count decreased	0	3 (9.1)	3 (5.5)	3 (2.7)
Pleural effusion	0	2 (6.1)	2 (3.6)	3 (2.7)
Pneumonitis	0	2 (6.1)	2 (3.6)	3 (2.7)
Pulmonary embolism	1 (4.5)	2 (6.1)	3 (5.5)	3 (2.7)

BC, breast cancer; HER2, human epidermal growth factor receptor 2; *HER2*m, *HER2* mutant; NSCLC, non-small cell lung cancer; RDE, recommended dose for expansion; TEAE, treatment-emergent adverse effect.
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