COR2ED

THE HEART OF MEDICAL EDUCATION

DEVELOPED BY PRECISION ONCOLOGY CONNECT

This programme is developed by PRECISION ONCOLOGY CONNECT, an international group of experts in the field of detection and treatment of targetable genetic/genomic alterations in various cancers, and brought to you alongside OBSTETRICS & GYNECOLOGY CONNECT, an international group of experts in the field of obstetrics and gynecology.

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PRECISION ONCOLOGY CONNECT ANIMATED VIDEO

UNDERSTANDING HER2 TESTING IN GYNECOLOGICAL CANCERS: BEST PRACTICES AND TREATMENT IMPLICATIONS

Prof. Fernando A. Soares
University of São Paulo, Brazil

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EDUCATIONAL OBJECTIVES

Provide Expert Opinion on HER2 immunohistochemistry in ovarian, cervical and endometrial cancers, focusing on best practices, which guidelines exist and scoring criteria to follow:

1. Understand **best practices in HER2 immunohistochemistry**
2. Be able to implement **optimal immunohistochemistry testing and scoring of staining** for HER2 expression
3. Recognise the **appropriate placement of therapies** targeting HER2 alterations (including ADCs) across the patient journey

HER2, human epidermal growth factor receptor 2

CLINICAL TAKEAWAYS

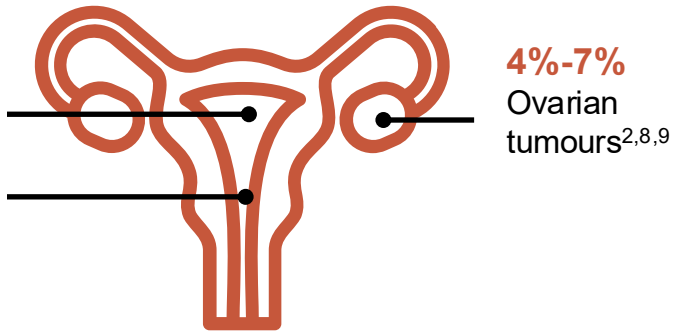
- **HER2 IHC testing** is recommended in **p53-aberrant endometrial cancer (EC)**, **advanced or recurrent cervical cancer**, and **recurrent ovarian cancer**, as **HER2 status guides treatment selection**. HER2 assessment and reporting should follow the **CAP gynecologic reporting template**.
- In EC, patients with **HER2+ uterine serous carcinoma are eligible for 1st-line carboplatin–paclitaxel + trastuzumab**. In this setting, HER2 positivity is defined as **IHC 3+** (strong complete or basolateral/lateral membranous staining in >30% of tumour cells [TC]) or **IHC 2+** (strong staining in ≤30% of TC, or weak-to-moderate staining in ≥10% of TC) **with ISH+**.
- In the **recurrent or metastatic setting** across endometrial, cervical, and ovarian cancers, patients with **HER2-positive disease** are eligible for **≥2nd-line treatment with T-DXd** in certain circumstances. Here, HER2 positivity is defined as **IHC 3+** (strong complete or basolateral/lateral staining in ≥10% of TC) or **IHC 2+** (weak-to-moderate complete or basolateral/lateral staining in ≥10% of TC).
- **Standardisation across pre-analytic, analytic, and post-analytic phases** is essential for reliable HER2 interpretation. In the absence of gynecological-specific guidance, **established ASCO/CAP breast cancer standards** can be applied.

CAP, College of American Pathologists; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; ISH, in situ hybridisation; NCCN, National Comprehensive Cancer Network; T-DXd, trastuzumab deruxtecan.

HER2 EXPRESSION AND TREATMENT IMPLICATIONS

HER2 IHC TESTING CAN INFORM CLINICAL DECISIONS FOR CERTAIN PATIENTS WITH GYNECOLOGIC CANCERS

HER2-Positivity Prevalence Varies Across Gynecologic Tumour Types



NCCN Guidelines: Who to Test?

	Tumour type	The role of HER2 IHC testing according to NCCN Guidelines
✓	Endometrial[10]	Recommended for all patients with p53 aberrant carcinomas, regardless of histology
✓	Cervical[11]	Recommended for all patients with advanced metastatic, or recurrent cervical carcinomas
✓	Ovarian[12]	Recommended for all patients with recurrent ovarian cancer

HER2-Positivity Treatment Implications in Metastatic Settings

	Line of therapy	Endometrial Cancer	Cervical Cancer	Ovarian Cancer
HER2-Targeted Treatment Options	1L[13]	Carboplatin-paclitaxel + **trastuzumab**[c] for patients with HER2+ (IHC 3+ or 2+/ISH+) uterine serous carcinoma or carcinosarcoma[13]	N/A	N/A
	2L+[14]	**T-DXd** in patient with IHC 3+/2+[14]	**T-DXd** in patient with IHC 3+/2+[14]	**T-DXd** in patient with IHC 3+/2+[14]

[a] Varies according to histological subtype; [b] Expression rate of 44.1% with IHC alone vs 5.0% according to traditional method (combined ISH/FISH)[6]; [c] Patients who have not received prior trastuzumab

1/2L, first/second line; FISH, fluorescent in-situ hybridisation; IHC, immunohistochemistry; N/A, not applicable; NCCN, National Comprehensive Cancer Network; T-DXd, trastuzumab deruxtecan

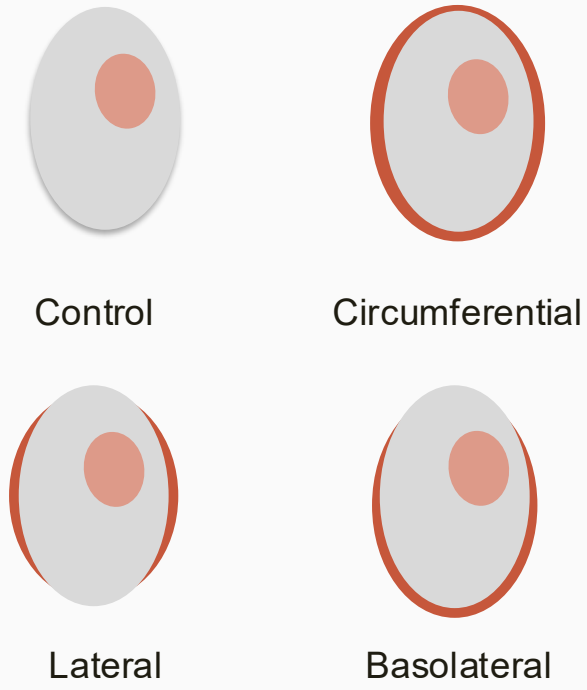
1. Vermij L, et al. Cancers. 2021;13(1):44; 2. Uzunparmak B, et al. Ann Oncol. 2023;34:1035-46; 3. Buza N, et al. Mod Pathol. 2013;26:1605-12; 4. Halle MK, et al. Br J Cancer. 2018;118:378-87; 5. Itkin B, et al. PLoS One. 2021;16(9):e0257976; 6. Xu Q, et al. Oncol Lett. 2025;29(5):217; 7. Shi H, et al. Pathol Clin Res. 2021;7:86-95; 8. Chung YW, et al. J Gynecol Oncol. 2019;30:e75; 9. Tuefferd M, et al. PLoS One. 2007;2:e1138; 10. NCCN Guidelines: Uterine Neoplasms. Version 2.2026; Available here (accessed Jan 20, 2026); 11. NCCN Guidelines: Cervical Cancer. Version 2.2026. Available here (accessed Jan 20, 2026); 14. NCCN Guidelines: Ovarian Cancer Including Fallopian Tube Cancer and Primary Peritoneal Cancer. Version 3.2025. Available here (accessed Jan 20, 2026); 13. Fader AN, et al. Clin Cancer Res. 2020;26(15):3928-35 (including full protocol); 14. Meric-Bernstam F, et al. J Clin Oncol. 2024;42(1):47-58

HER2 IHC SCORING

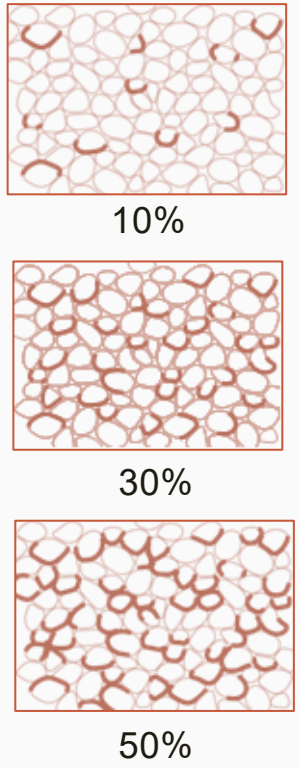
IHC, immunohistochemistry

DIFFERENCES TO CONSIDER IN HER2 IHC SCORING CRITERIA

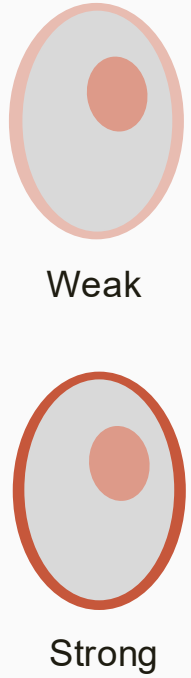
1. Staining patterns[1-3]



2. Percentage of cells stained[4-6]



3. Intensity of staining[4-5]



CAP, College of American Pathologists; IHC, immunohistochemistry

1. Abrahao-Machado LF and Scapulatempo-Neto C. World J Gastroenterol. 2016;22(19):4619-25; 2. Wolff AC, et al. Arch Pathol Lab Med. 2023;147(9):993-1000; 3. Bartley AN, et al. J Clin Oncol. 2017;35(4):446-64; 4. Hagemann IS, et al. Arch Pathol Lab Med. 2023;147(10):1148-57. 5. CAP. Template for Reporting Results of Biomarker Testing of Specimens From Patients With Carcinoma of Gynecologic Origin. Version 1.3.0.0. Available here (accessed Jan 20, 2024); 6. Valtorta E, et al. Mod Pathol. 2015;28:1481-91.

GYNECOLOGIC CANCERS CAP REPORTING TEMPLATE:

HER2 STATUS FOR TRASTUZUMAB USE

- Based on the enrolment criteria for trastuzumab in the randomised phase 2 clinical trial NCT01367002 **for endometrial carcinoma**

IHC Score	HER2 test interpretation	HER2 status
0	No staining in tumour cells	Negative
1+	*Faint and incomplete membrane staining, or weak complete staining in <10% of tumour cells*	Negative
2+	Strong complete or basolateral/lateral staining in ≤30%, or weak–moderate staining in ≥10% of tumour cells	ISH amplification? (No / Yes)
3+	*Strong complete or basolateral/lateral membrane staining in >30% of tumour cells*	Positive

Reporting ISH (FISH) results

Result	Criteria (dual-probe assay)
Negative	• FISH HER2/CEP17 ratio less than 2.0, ***and*** • Average HER2 copy number less than 6 per nucleus
Positive	• FISH HER2/CEP17 ratio greater or equal to 2.0, **or** • FISH HER2/CEP17 ratio less than 2.0 with average *HER2,* copy number equal to or greater than 6 per nucleus

CAP, College of American Pathologists; CEP17, chromosome enumeration probe 17; IHC, immunohistochemistry

1. CAP. Template for Reporting Results of Biomarker Testing of Specimens From Patients With Carcinoma of Gynecologic Origin. Version 1.3.0.0. Available here (accessed Jan 20, 2024)

GYNECOLOGIC CANCERS CAP REPORTING TEMPLATE:

HER2 STATUS FOR T-DXd USE

- Based on the enrolment criteria for T-DXd in the DESTINY-PanTumor02 phase 2 clinical trial (NCT04482309) **for endometrial, cervical or ovarian carcinoma**

IHC Score	HER2 test interpretation	HER2 status
0	**Biopsy:** No tumour cell staining **Surgical specimen:** No staining or membrane staining in <10% of tumour cells	Negative
1+	**Biopsy:** ≥5 tumour cells with faint/barely perceptible membrane staining (any %) **Surgical specimen:** Faint, incomplete membrane staining in ≥10% of tumour cells	Negative
2+	**Biopsy:** ≥5 tumour cells with weak–moderate complete or basolateral/lateral staining (any %) **Surgical specimen:** Weak–moderate complete or basolateral/lateral staining in ≥10% of tumour cells	Equivocal
3+	**Biopsy:** ≥5 tumour cells with strong complete or basolateral/lateral staining (any %) **Surgical specimen:** Strong complete or basolateral/lateral staining in ≥10% of tumour cells	Positive

IHC, immunohistochemistry; T-DXd, trastuzumab deruxtecan

1. CAP. Template for Reporting Results of Biomarker Testing of Specimens From Patients With Carcinoma of Gynecologic Origin. Version 1.3.0.0. Available here (accessed Jan 20, 2024)

HER2 TESTING:
PROCESS AND CONSIDERATIONS

EVOLUTION OF HER2 SCORING GUIDELINES

2007
ASCO-CAP
Breast Criteria
First guidelines for HER2 testing by a joint ASCO-CAP committee[1,2]

2015
HERACLES Trial
CRC Criteria
Developed to enrol patients for the H**ERACLES** trial[3]

2016
ASCO-ASCP-CAP
Gastric Criteria
HER2 testing guidelines by the ASCO-CAP joint committee[4]

2018
Fader Trial
ESC Criteria
Modified version of ASCO-CAP breast criteria developed to enrol patients with **endometrial serous** cancer for the **Fader trial**[5,6]

2023
ASCO-CAP
Breast Criteria
Following updates in 2013 and 2018, the latest **breast** ASCO-CAP guideline update was in 2023[7]

There are only ASCO-CAP guidelines for two tumour types,[8] but many other types require HER2 testing[9]

ASCO, American Society of Clinical Oncology; ASCP, American Society for Clinical Pathology; CAP, College of American Pathologists; CRC, colorectal cancer; ESC, endometrial serous carcinoma

1. Wolff AC, et al. J Clin Oncol. 2007;25(1):118-45; 2. Wolff AC, et al. J Clin Oncol. 2023;41:3867-72; 3. Valtorta E, et al. Mod Pathol. 2015;28:1481-91; 4. Bartley AN, et al. J Clin Oncol. 2017;35(4):446-64; 5. Fader AN, et al. J Clin Oncol. 2018;36(20):2044-51; 6. Buza N, et al. Mod Pathol. 2021;34:1194-202; 7. Wolff AC, et al. Arch Pathol Lab Med. 2023;147(9):993-1000; 8. Lee EK, et al. Gynecol Oncol. 2025;195:152-64; 9. Ismail A, et al. Oncologist. 2025;30:oyaf258

BEST PRACTICE IN HER2 TESTING AND INTERPRETATION

HER2 TESTING MUST BE STANDARDISED ACROSS PRE-ANALYTIC, ANALYTIC, AND POST-ANALYTIC PHASES TO ENSURE RELIABLE INTERPRETATION*

Pre-analytic

Tissue processing

Analytic

Staining and quality assessment of control/ test tissue sample

Post-analytic

Interpretation scoring and reporting

- Cold ischemia as short as possible (<1 h)
- Prompt tissue fixation in 10 % neutral buffered formalin in a 10:1 vol ratio
- Fixation time h from 6 to 72 h
- Slicing specimens at 5–10 mm interval to ensure adequate tissue fixation
- Use of formalin-fixed paraffin-embedded cell blocks for cytology samples
- Use of freshly cut paraffin sections for analysis (preferrable within 1-2 days or less than 4 weeks)
- Fixing bone specimen for at least 1 h in 10% neutral buffered formalin before decalcification using EDTA
- Communicate with the surgeons or radiologists

***In the absence of gynecological-specific guidance, established ASCO/CAP breast cancer standards can be applied**

EDTA, ethylenediaminetetraacetic acid.

1.Marabi M & Tse G.M, et al. Hum Pathol. 2025 Aug:162:105818.

BEST PRACTICE IN HER2 TESTING AND INTERPRETATION.

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Pre-analytic

Tissue processing

Analytic

Staining and quality assessment of control/ test tissue sample

Post-analytic

Interpretation scoring and reporting

- Standardised operating procedures must be in place and updated as necessary
- Assay procedure standardization
- Choice of antibody clone and being aware of its performance (VENTANA PATHWAY B45 vs DAKO HercepTest (mab) vs DAKO HercepTest (pAb)
- Considerations on antigen retrieval method, enzymatic activity, reaction time, temperature and substrate concentration
- Strict adherence to kit assay protocols
- Use of appropriate batch and/or on-slide controls for every run
- Use of validated controls with wide range of HER2 expressions (score 0, 1+, 2+ and 3+)
- Check and audit controls regularly
- Test runs by trained personnel
- Consider reference laboratory service depending on circumstance

***In the absence of gynecological-specific guidance, established ASCO/CAP breast cancer standards can be applied**

HER2, human epidermal growth factor receptor 2.

1.Marabi M & Tse G.M, et al. Hum Pathol. 2025 Aug:162:105818.

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Pre-analytic

Tissue processing

Analytic

Staining and quality assessment of control/ test tissue sample

Post-analytic

Interpretation scoring and reporting

- Only interpret membrane staining and in invasive tumour
- Avoid crushed or marked edge artefacts
- Use the magnification and “I–C-E” method when reading the slides
- Get a second pathologist's review on cases near cut-off points, preferably from the same lab
- Re-test using the same sample or a different sample as necessary
- Correlate histological tumour types with the expected IHC results
- Consider use of digital or computerized methods or clinically validated artificial intelligence algorithm assistance
- Participating in focused educations and training programs on HER2 scoring interpretation
- Communicate with the treating clinicians
- Give the IHC interpretation (negative vs positive), specifying the staining pattern and % estimation

***In the absence of gynecological-specific guidance, established ASCO/CAP breast cancer standards can be applied**

HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry.

1.Marabi M & Tse G.M, et al. Hum Pathol. 2025 Aug:162:105818

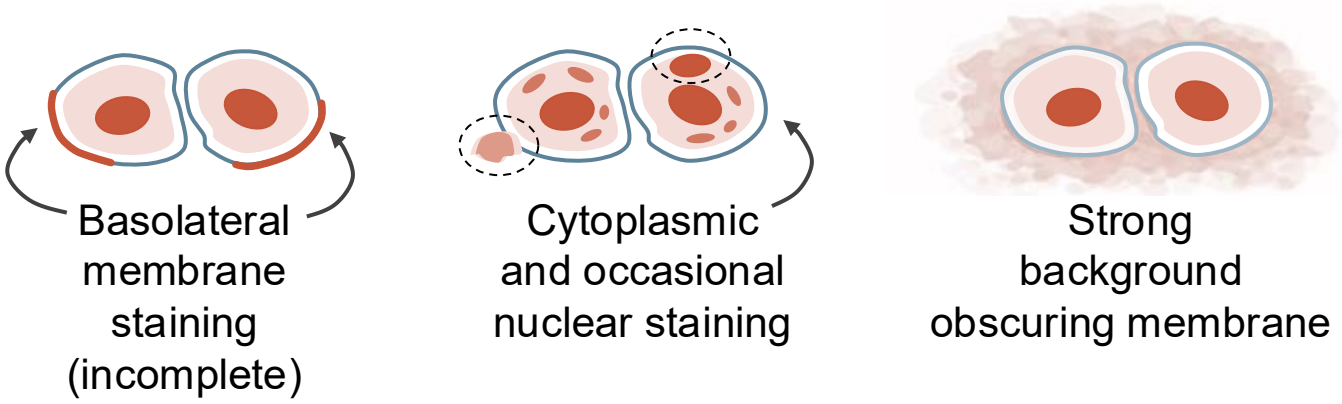
HER2 TESTING: CONSIDERATIONS FOR ACCURATE ASSESSMENT

1. Repeat testing on newly obtained tumour tissue is recommended **in metastatic disease**[1]

2. Areas with **the following features should not be selected** for HER2 IHC assessment[2]:

Feature	Low-power clue	High-power clue
Haemorrhage	Red, amorphous areas	Sheets of RBCs
Necrosis	Pale, acellular zones	Ghost cells, debris
Autolysis	Diffuse poor morphology	Smudged nuclei
Fibrosis	Hypocellular stroma	Dense collagen

3. Potential artefacts that may affect HER2 IHC interpretation include[2]:



IHC, immunohistochemistry; RBC, red blood cell

1. Wolff A.C, et al. J Clin Oncol. 2023;41(22):3867-3872;
2. Recommendations informed by the clinical and diagnostic pathology experience of Dr Fernando Soares

MAKING THE REPORT ACCESSIBLE FOR CLINICIANS

SUGGESTIONS THAT MAY REDUCE THE COMMUNICATION BARRIER

Communication barriers between the pathologist's report and the clinician's interpretation may negatively impact patient care and should be addressed early. Below are several proposed strategies:

1. **Use active communication to clarify different aspects of the report**
   - Opportunities to do this may include tumour boards, clinical rounds, via phone communication, or in one-on-one slide reviews[1]
   - This can help avoid confusion, for example if clinicians are not aware when ordering that ISH and NGS cannot be used to detect protein expression[2]
2. **Use the comments section in the report, where the pathologic diagnosis alone does not convey all relevant information**[1]
3. **Standardise grammatical structure**[1]
4. **Explain any diagnostic limitations**[1]

ISH, in situ hybridisation; NGS, next-generation sequencing

1. Mirham L, et al. Am J Clin Pathol. 2021;156:521-8; 2. Recommendations informed by the clinical and diagnostic pathology experience of Dr Fernando Soares

T-DXd IN HER2+ SOLID TUMOURS: DESTINY-PanTumor02 TRIAL

T-DXd, trastuzumab deruxtecan

DESTINY-PanTumor02: A PHASE 2 STUDY OF T-DXd FOR HER2-EXPRESSING SOLID TUMOURS[1,2]

AN OPEN-LABEL, MULTICENTRE STUDY (NCT04482309)

Key eligibility criteria

- Advanced solid tumours not eligible for curative therapy
- 2L+ patient population
- HER2 expression (IHC 3+ or 2+)
  - Local test or central test by HercepTest if local test not feasible (ASCO/CAP gastric cancer scoring)[a]
- Prior HER2-targeting therapy allowed
- ECOG/WHO PS 0-1

T-DXd
5.4 mg/kg Q3W

40 per cohort[b]

- Endometrial cancer
- Cervical cancer
- Ovarian cancer
- Bladder cancer
- Other tumours[c]
- Biliary tract cancer
- Pancreatic cancer

Primary endpoint

- Confirmed ORR (investigator)

Secondary endpoints

- DoR, DCR, PFS, OS
- Safety

Exploratory analysis

- Subgroup analyses by HER2 status

Primary analysis data cut-off: 8 June 2023
Median follow up: 12.75 mo

Baseline characteristics

- 267 patients received treatment; 202 (75.7%) based on local HER2 testing
  - 111 (41.6%) patients were IHC 3+ based on HER2 test (local or central) at enrolment, primary efficacy analysis (all patients)
  - **75 (28.1%) patients were IHC 3+ on central testing,** sensitivity analysis on efficacy endpoints (subgroup analyses)
- Median age was 62 years (23-85) and **109 (40.8%) patients had received ≥3 lines of therapy**

[a] Patients were eligible for either test. All patients were centrally confirmed; [b] Planned recruitment, cohorts with no objective responses in the first 15 patients were to be closed; [c] Patients with tumours that express HER2, excluding tumours in the tumour-specific cohorts, and breast cancer, non-small cell lung cancer, gastric cancer, and colorectal cancer

2L, second-line; ASCO, American Society of Clinical Oncology; CAP, College of American Pathologists; DCR, disease control rate; DoR, duration of response; ECOG, Eastern Cooperative Oncology Group; IHC, immunohistochemistry; mo, months; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PS, performance status; Q3W, every 3 weeks; T-DXd, trastuzumab deruxtecan; WHO, World Health Organization

1.Meric-Bernstam F, et al. Ann Oncol. 2023;34(Suppl):S1273-S1274. Oral presentation (LBA34) presented at ESMO 2023: 2.Meric-Bernstam F, et al. J Clin Oncol. 2024;42(1):47-58

PATIENT DISPOSITION

	Cervical	Endometrial	Ovarian	BTC	Pancreatic	Bladder	Other[a]	All patients
Patients treated, n	40	40	40	41	25	41	40	267
Ongoing treatment at DCO, n (%)	**10 (25.0)**	**14 (35.0)**	**6 (15.0)**	**3 (7.3)**	**1 (4.0)**	**5 (12.2)**	**5 (12.5)**	**44 (16.5)**
Discontinued treatment, n (%)	30 (75.0)	26 (65.0)	34 (85.0)	38 (92.7)	24 (96.0)	36 (87.8)	35 (87.5)	223 (83.5)
Disease progression	21 (52.5)	18 (45.0)	29 (72.5)	22 (53.7)	17 (68.0)	26 (63.4)	23 (57.5)	156 (58.4)
Adverse event	4 (10.0)	2 (5.0)	3 (7.5)	8 (19.5)	3 (12.0)	4 (9.8)	6 (15.0)	30 (11.2)
Other[b]	5 (12.5)	6 (15.0)	2 (5.0)	8 (19.5)	4 (16.0)	6 (14.6)	6 (15.0)	37 (13.9)
Median follow up at DCO (range), months	7.2 (0.9-23.0)	14.6 (0.8-24.2)	12.7 (0.7-23.7)	6.0 (0.7-20.0)	4.9 (1.1-19.8)	12.0 (0.4-21.2)	12.0 (0.7-23.9)	9.7 (0.4-24.2)
Median duration of treatment at DCO (range), months	5.5 (0.7-19.8)	9.0 (0.7-24.4)	5.9 (0.7-23.0)	3.5 (0.7-20.1)	2.1 (0.7-11.0)	6.2 (0.4-18.0)	6.9 (0.7-19.9)	5.5 (0.4-24.4)

[a] Includes salivary gland cancer (n=19), malignant neoplasm of unknown primary site (n=5), extramammary Paget's disease (n=3), melanoma (n=2), oropharyngeal neoplasm (n=2), adenoid cystic carcinoma, adenocarcinoid tumour of the appendix, head and neck, intestinal adenocarcinoma, lip and/or cavity, oesophageal adenocarcinoma, oesophageal squamous cell carcinoma, testis and vulva (all n=1); [b] Includes patients who were lost to follow-up (n=1) and patients who discontinued for unknown reasons (n=3), patient decision (n=10), investigator decision (n=5), and other reasons (n=22; n=16 of which died while on treatment)

BTC, biliary tract cancer; DCO, data cut-off (Nov 16, 2022)

1.Meric-Bernstam F, et al. J Clin Oncol. 2023;41(Suppl):LBA3000. Oral presentation (LBA3000) presented at ASCO Annual Meeting 2023

BASELINE CHARACTERISTICS

Characteristic	All patients (N=267)
Median age (range), years	62 (23-85)
Female, n (%)	178 (66.7)
Race, n (%) White Asian Other Not reported	 163 (61.0) 87 (32.6) 6 (2.25) 5 (1.9)
Median prior lines of therapy (range) 0, n (%) 1, n (%) 2, n (%) ≥3, n (%)	2 (0-13) 3 (1.1) 71 (26.6) 84 (31.5) 107 (40.1)
Prior HER2 therapy, n (%) Monoclonal antibody Tyrosine kinase inhibitor	 33 (12.4) 1 (0.4)

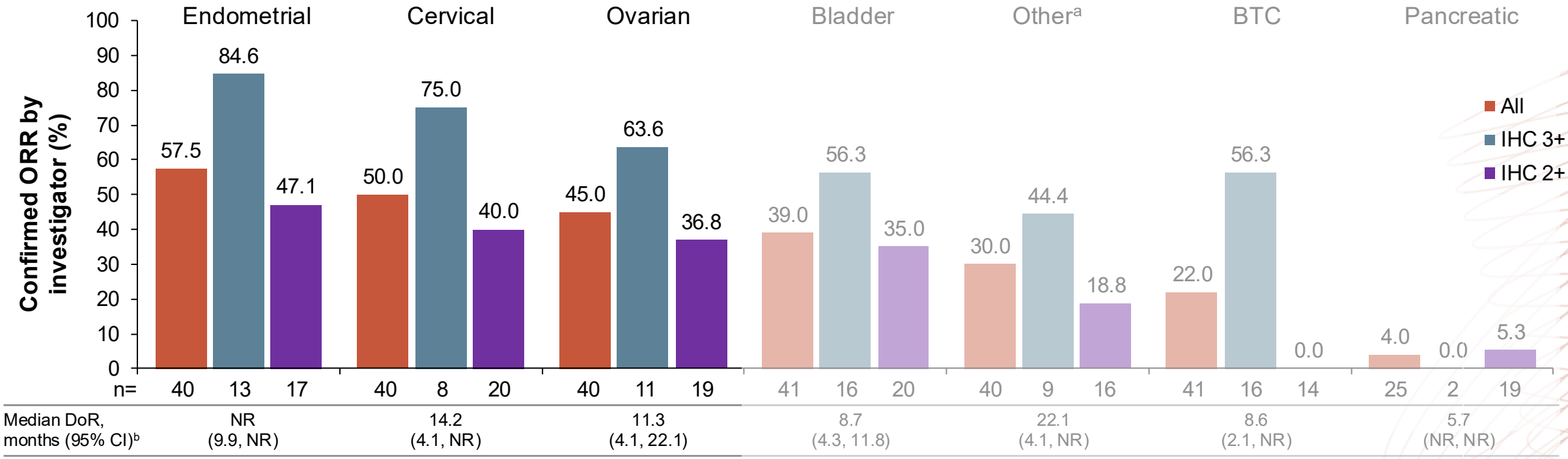
Characteristic	All patients (N=267)
ECOG PS, n (%) 0 1 2	 126 (47.2) 140 (52.4) 1 (0.4)
HER2 testing for eligibility, n (%)[a] Local Central	 202 (75.7) 61 (22.8)
HER2-expression for eligibility, n (%)[a] IHC 3+ IHC 2+ IHC 1+[b]	 111 (41.6) 151 (56.6) 5 (1.9)
Centrally confirmed HER2 status for efficacy evaluation, n (%) IHC 3+ IHC 2+ IHC 1+ IHC 0 Unknown[c]	 75 (28.1) 125 (46.8) 25 (9.4) 30 (11.2) 12 (4.5)

[a] HER2 expression for eligibility was based on local assessment, based on any HER2 test, where available; [b] In the cervical cohort, five patients with IHC 1+ status were included per protocol; [c] Includes patients whose samples were not evaluable and may have included patients who did not provide a sample for central testing

ECOG PS, Eastern Cooperative Oncology Group performance status; IHC, immunohistochemistry

1 Meric-Bernstam F, et al. J Clin Oncol. 2024;42(1):47-58

OBJECTIVE RESPONSE AND DURATION OF RESPONSE[1,2]



	All patients (N=267	IHC 3+ (n=75)	IHC 2+ (n=125)
ORR, % (95% CI)	37.1 (31.3, 43.2)	61.3 (49.4, 72.4)	27.2 (19.6, 35.9)
Median DoR, months (95% CI)[b]	11.3 (9.6, 17.8)	22.1 (9.6, NR)	9.8 (4.3, 12.6)

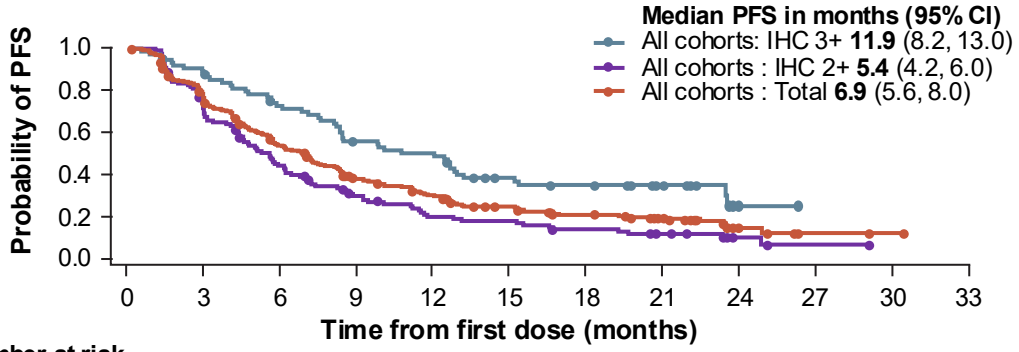
Analysis of ORR by investigator was performed in patients who received ≥1 dose of T-DXd; all patients (n=267; including 67 patients with IHC 1+ [n=25], IHC 0 [n=30], or unknown IHC status [n=12] by central testing) and patients with centrally confirmed HER2 IHC 3+ (n=75) or IHC 2+ (n=125) status. Analysis of DoR was performed in patients with objective response who received ≥1 dose of T-DXd; all patients (n=99; including 19 patients with IHC 1+ [n=6], IHC 0 [n=9], or unknown IHC status [n=4] by central testing) and patients with centrally confirmed HER2 IHC 3+ (n=46) or IHC 2+ (n=34) status. [a] Responses in extramammary Paget's disease, head and neck cancer, oropharyngeal neoplasm, and salivary gland cancer; [b] Includes patients with a confirmed objective response only

BTC, biliary tract cancer; CI, confidence interval; DoR, duration of response; IHC, immunohistochemistry; NR, not reached; ORR, objective response rate; T-DXd, trastuzumab deruxtecan

1.Meric-Bernstam F, et al. Ann Oncol. 2023;34(Suppl):S1273-S1274. Oral presentation (LBA34) presented at ESMO 2023; 2.Meric-Bernstam F, et al. J Clin Oncol. 2024;42(1):47-58

EFFICACY ENDPOINT: PFS BY HER2 STATUS PER COHORT[1,2]

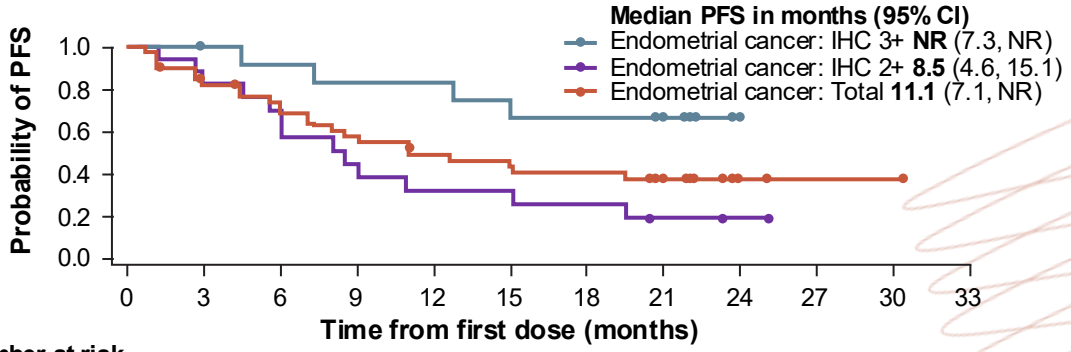
ALL COHORTS



Number at risk

IHC 3+	75	63	51	39	34	23	19	12	1	0		
IHC 2+	125	78	50	31	20	18	13	9	3	1	0	
Total	267	185	132	89	68	51	39	25	6	2	1	0

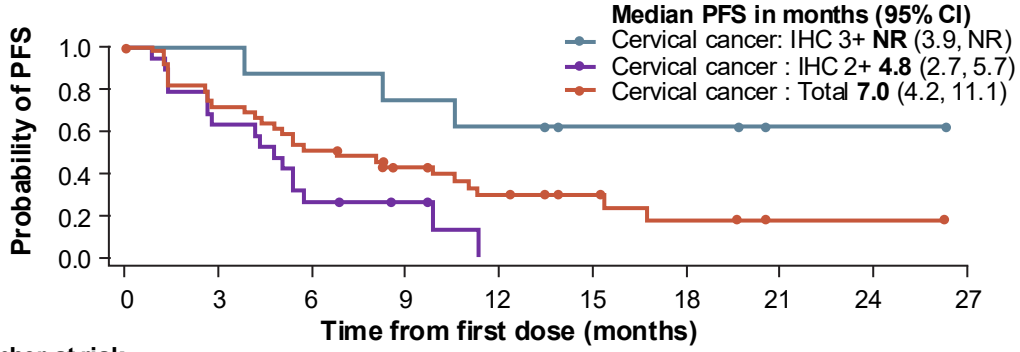
ENDOMETRIAL CANCER



Number at risk

IHC 3+	13	12	11	10	10	9	8	5	0			
IHC 2+	17	14	11	7	5	5	4	2	1	0		
Total	40	31	27	21	17	16	14	8	2	1	1	0

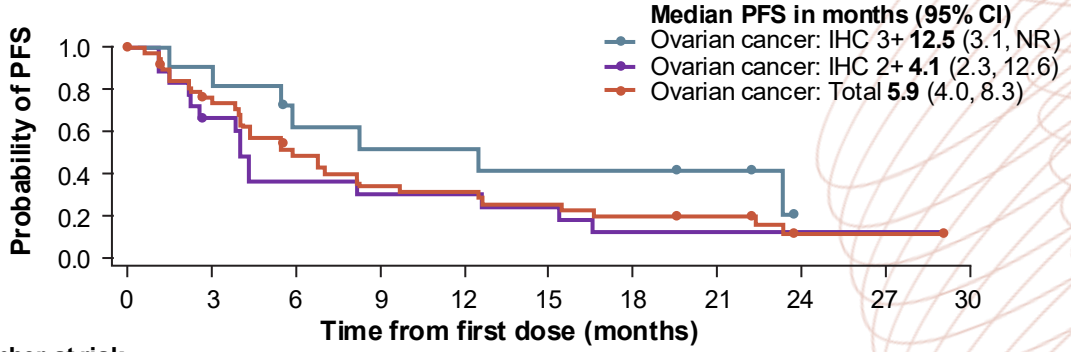
CERVICAL CANCER



Number at risk

IHC 3+	8	8	7	6	5	3	3	1	1	0
IHC 2+	20	12	5	3	0					
Total	40	28	20	14	9	6	3	1	1	0

OVARIAN CANCER



Number at risk

IHC 3+	11	10	6	5	5	4	4	3	0		
IHC 2+	19	11	6	5	5	4	2	2	1	1	0
Total	40	28	17	12	11	9	7	6	1	1	0

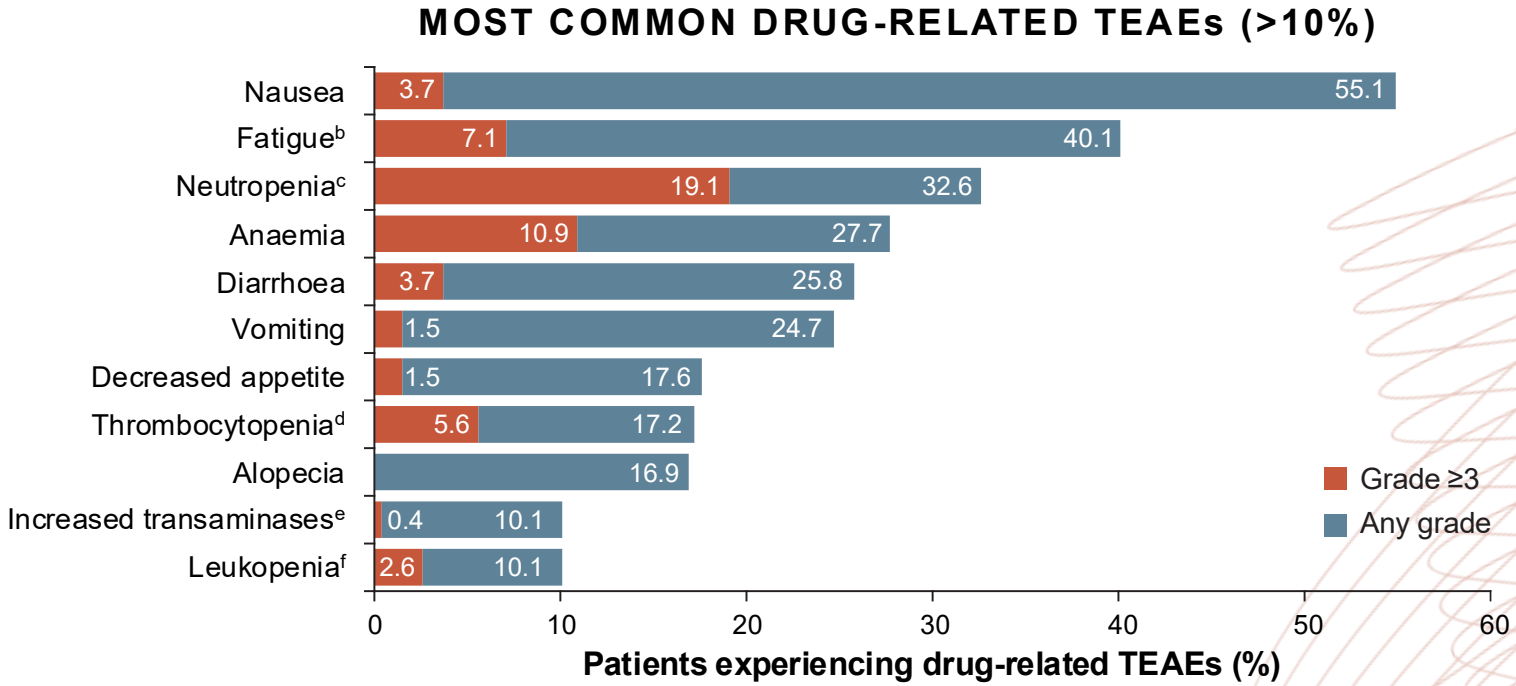
Circle indicates a censored observation

CI, confidence interval; IHC, immunohistochemistry; NR, not reached; PFS, progression-free survival 1.

1.Meric-Bernstam F, et al. Ann Oncol. 2023;34(Suppl):S1273-S1274. Oral presentation (LBA34) presented at ESMO 2023; 2.Meric-Bernstam F, et al. J Clin Oncol. 2024;42(1):47-58

SAFETY SUMMARY[1,2]

N (%)	All patients (N=267)
Any drug-related TEAEs	226 (84.6)
Drug-related TEAEs Grade ≥3	109 (40.8)
Serious drug-related TEAEs	36 (13.5)
Drug-related TEAEs associated with dose discontinuations	23 (8.6)
Drug-related TEAEs associated with dose interruptions	54 (20.2)
Drug-related TEAEs associated with dose reductions	54 (20.2)
Drug-related TEAEs associated with deaths	4 (1.5)[a]



ILD/pneumonitis adjudicated as T-DXd related, n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Any grade
All patients (N=267)	7 (2.6)	17 (6.4)	1 (0.4)	0	3 (1.1)	28 (10.5)

Analyses were performed in patients who received ≥1 dose of T-DXd (N=267); median total treatment duration 5.6 months (range 0.4-31.1)

[a] Included pneumonia (n=1), organising pneumonia (n=1), pneumonitis (n=1), and neutropenic sepsis (n=1); [b] Category includes the preferred terms fatigue, asthenia, and malaise; [c] Category includes the preferred terms neutrophil count decreased and neutropenia; [d] Category includes the preferred terms platelet count decreased and thrombocytopenia; [e] Category includes the preferred terms aspartate aminotransferase increased, alanine aminotransferase increased, gamma-glutamyltransferase increased, hypertransaminasemia; [f] Category includes the preferred terms white blood cell count decreased and leukopenia

ILD, interstitial lung disease; T-DXd, trastuzumab deruxtecan; TEAE, treatment-emergent adverse event

1.Meric-Bernstam F, et al. Ann Oncol. 2023;34(Suppl):S1273-S1274. Oral presentation (LBA34) presented at ESMO 2023; 2.Meric-Bernstam F, et al. J Clin Oncol. 2024;42(1):47-58

DESTINY-PanTumor02: CONCLUSIONS[1,2]

DP-02 TRIAL SUPPORTS THE POTENTIAL ROLE OF T-DXd AS A TUMOUR-AGNOSTIC THERAPY FOR PATIENTS WITH HER2-EXPRESSING SOLID TUMOURS

- **T-DXd demonstrated clinically meaningful activity** across a broad range of **HER2-expressing solid tumours**:
  - **ORR:** 37.1% in all patients and 61.3% in patients with IHC 3+
  - **Durable responses:** median DoR 11.3 months in all patients and 22.1 months in patients with IHC 3+
- **Durable responses led to clinically meaningful progression-free and overall survival outcomes:**
  - **PFS:** 6.9 months in all patients and 11.9 months in patients with IHC 3+
  - **OS:** 13.4 months in all patients and 21.1 months in patients with IHC 3+
- **The safety of T-DXd was consistent with the known profile**

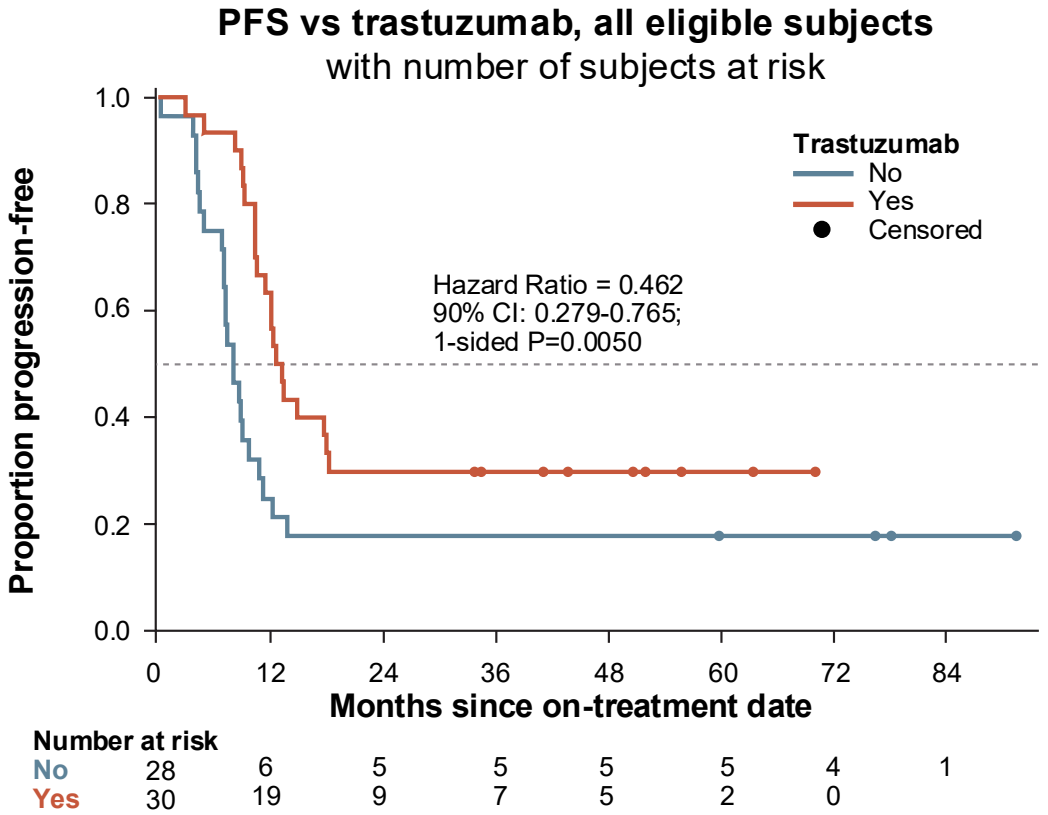
The FDA granted accelerated approval to T-DXd for adult patients with unresectable or metastatic HER2+ solid tumours who have received prior systemic treatment and have no satisfactory alternative treatment options[3]

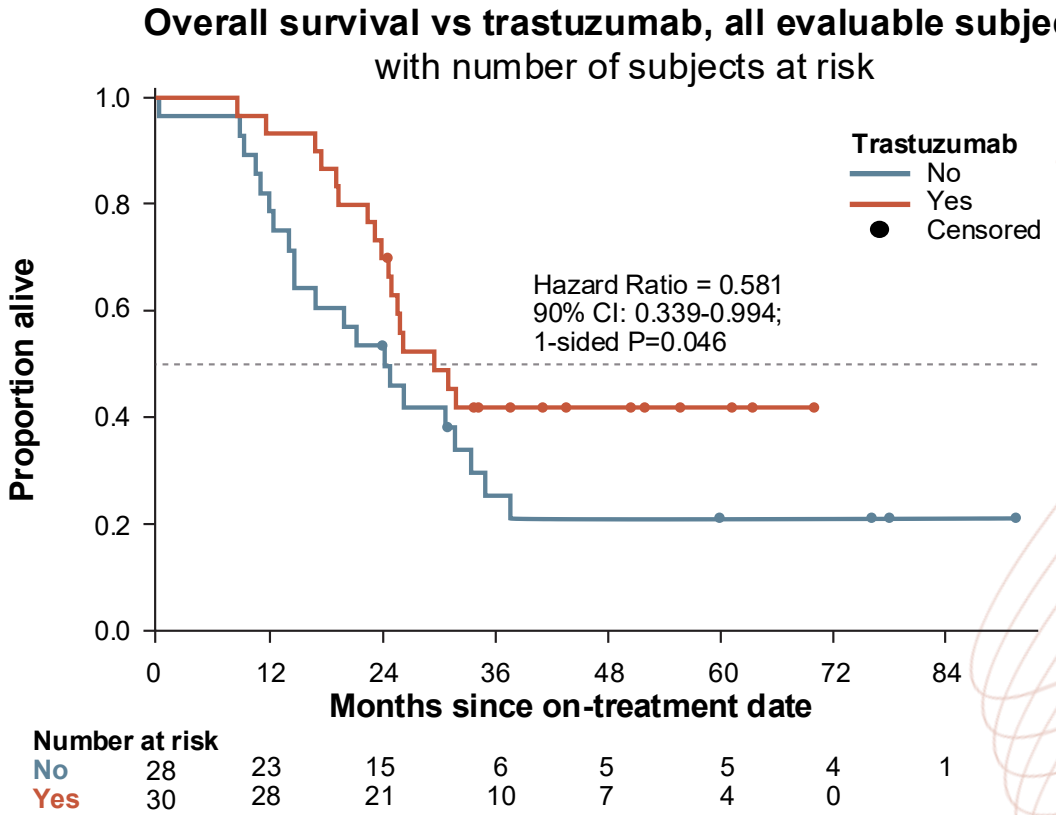
DoR, duration of response; FDA, Food and Drug Administration; IHC, immunohistochemistry; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; T-DXd, trastuzumab deruxtecan

1. Meric-Bernstam F, et al. Ann Oncol. 2023;34(Suppl):S1273-S1274. Oral presentation (LBA34) presented at ESMO 2023; 2. Meric-Bernstam F, et al. J Clin Oncol. 2024;42(1):47-58; 3. FDA grants accelerated approval to fam-trastuzumabderuxtecan-nxki for unresectable or metastatic HER2-positive solid tumors. Available here (accessed Jan 20, 2026)

CARBOPLATIN-PACLITAXEL + TRASTUZUMAB IN HER2+ ENDOMETRIAL CANCER: NCT01367002 TRIAL

ADDITION OF TRASTUZUMAB TO CP IMPROVES mPFS AND OS IN ADVANCED/RECURRENT HER2+ UTERINE SEROUS CARCINOMA





mPFS was 8.0 months in patients who received CP and 12.9 months in patients who received CP+T

OS was 24.4 months in patients who received (CP) and 29.6 months in patients who received CP+T

CI, confidence interval; CP, carboplatin-paclitaxel; mPFS, median progression-free survival; OS, overall survival; PFS, progression-free survival; T, trastuzumab

1. Fader AN, et al. Clin Cancer Res. 2020;26(15):3928-35

CONCLUSIONS

CONCLUSIONS

- **HER2 is now a clinically actionable biomarker in gynecological cancers**, with treatment implications that vary by tumour type and line of therapy.
- **Accurate and standardised HER2 testing is essential** to ensure appropriate access to both first-line and later-line HER2-targeted treatments.
- Clear, **structured pathology reporting aligned with CAP standards is critical** to support correct interpretation and multidisciplinary treatment decisions.
- **Close collaboration between pathologists and oncologists** is increasingly important as HER2-directed strategies expand across gynecological malignancies

CAP, College of American Pathologists; HER2, human epidermal growth factor receptor 2.

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