Passion for Innovation.
Compassion for Patients.™

Daiichi-Sankyo

R&D Day 2021

DAIICHI SANKYO CO., LTD.

Dec 14/15, 2021

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Speakers

Sunao Manabe
President and CEO

Ken Takeshita
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Head of Research Function

Gilles Gallant
Head of Global Oncology Development

Agenda

1. **Introduction**
2. R&D strategy
3. Q&A session

5-Year Business Plan (FY2021-FY2025) for Sustainable Growth

We will achieve our 2025 Goal, **Global Pharma Innovator with Competitive Advantage in Oncology**, and will shift to further growth towards our 2030 Vision

As of FY2020

- Oncology business launched
- Edoxaban growing
- Regional value being enhanced
- AZ strategic alliance
- Increased RD investment

2030 Vision

Innovative Global Healthcare Company Contributing to the Sustainable Development of Society

- Global top 10 in Oncology
- Additional growth pillars being source of revenue and profit
- New products being source of profit in each business unit
- Contributing to sustainable development of society through our business

Strategic Pillars for the 5-Year Business Plan (FY2021-FY2025)

Achieve FY2025 Goal and Shift to Further Growth

Maximize 3ADCs

- Maximize Enhertu® and Dato-DXd through strategic alliance with AstraZeneca
- Maximize HER3-DXd without a partner
- Expand work force and supply capacity flexibly depending on changes around product potential

Profit growth for current business and products

- Maximize Lixiana® profit
- Grow Tarlige®, Nilemdo®, etc. quickly
- Transform to profit structure focused on patented drugs
- Profit growth for American Regent and Daiichi Sankyo Healthcare

Identify and build pillars for further growth

- Identify new growth drivers following 3ADCs
- Select and advance promising post DXd-ADC modalities

Create shared value with stakeholders

- Patients: Contributing to patients through "Patient Centric Mindset"
- Shareholders: Balanced investment for growth and shareholder returns
- Society: Environment load reduction across the value chain, and actions against pandemic risks
- Employees: Create one DS culture through fostering our core behaviors

- Data-driven management through DX, and company-wide transformation through advanced digital technology
- Agile decision making through new global management structure

*3ADCs: 1) Enhertu, Trastuzumab deruxtecan (T-DXd, DS-8201), 2) Datopotamab deruxtecan (Dato-DXd, DS-1062) and 3) Patritumab deruxtecan (HER3-DXd, U3-1402)

Progress after R&D Day 2020

Maximize 3ADCs

- Strong market penetration and approval of new indication for Enhertu®
- Steady progress in development of 3ADCs

DB-03 results will serve as a tail wind. Multiple pivotal studies for Dato-DXd and HER3-DXd, in addition to Enhertu®, have started

Identify new growth drivers following 3ADCs

- Clinical data for the fourth DXd-ADC, DS-7300, presented for the first time at ESMO 2021

Growing expectation for DS-7300 in SCLC, ESCC, CRPC, etc.

Select and advance promising post DXd-ADC modalities

- Good progress in development of DS-5670, the LNP-mRNA vaccine
- Approval of Delytact® and Yescarta®

Establishment of technologies have advanced, development experiences and know-how for various modalities have been accumulated

3ADCs are **on track**, and post-3ADC growth drivers are being **identified**.
In addition, **viable options are increasing** for post DXd-ADC modalities
We are off to a **good start** towards achieving our 5-year business plan, and realizing our 2030 Vision

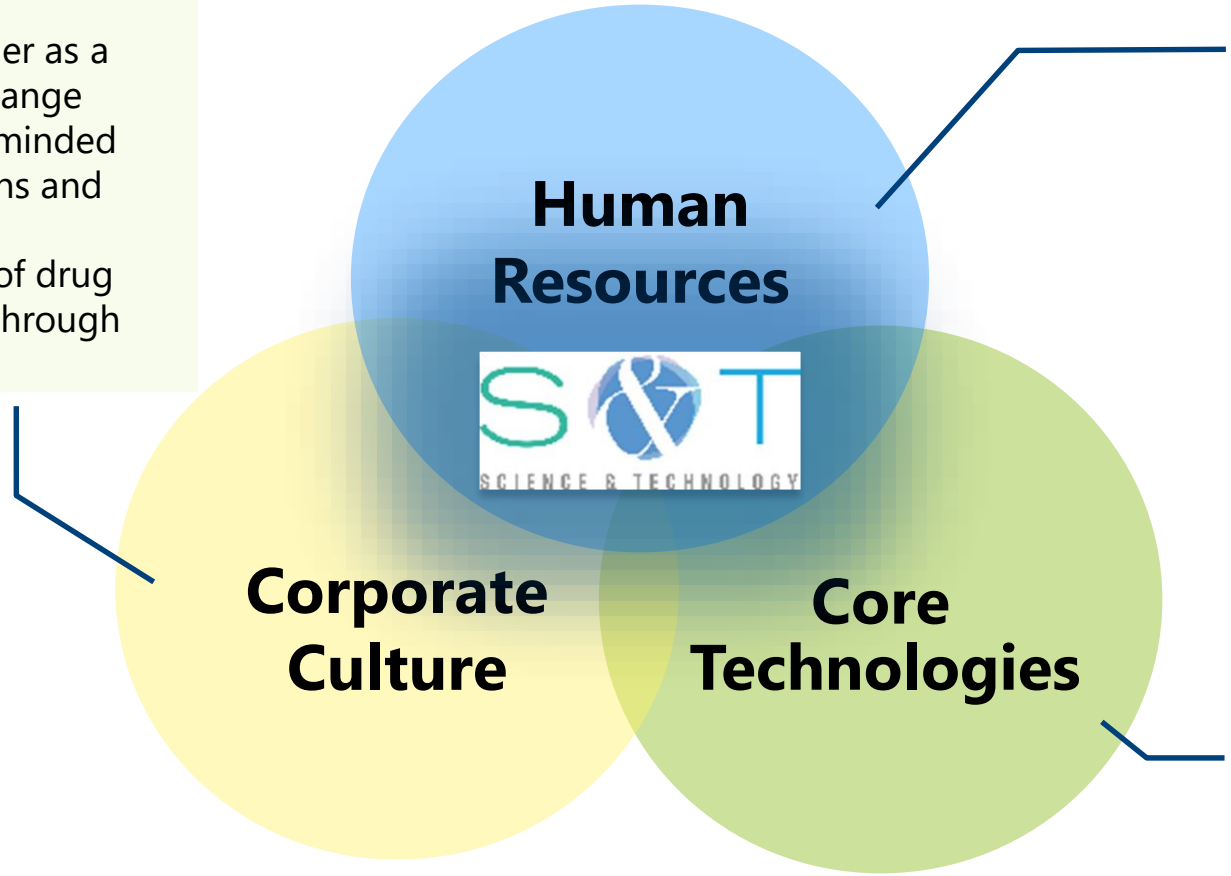
SCLC: small cell lung cancer, ESCC: esophageal squamous cell carcinoma, CRPC: castration resistant prostate cancer

Towards Sustainable Growth

Further enhancement of our strength "Science & Technology" is essential for sustainable growth

Our Strength

- Our corporate culture: Researchers respect each other as a specialist in science and exchange opinions in a free and open-minded manner regardless of positions and tenure
- Techniques and experiences of drug development handed down through our history



- Pursue cutting-edge science
- Scientific assessment capabilities
- Technologies originated from craftspersonship
- A high level of engagement
- Eagerness for innovation

- Our proprietary ADC technology platform
- Medicinal chemistry, protein engineering, drug evaluation, computational science and translational research

Agenda

1. Introduction
2. **R&D strategy**
3. Q&A session

Introduction

DXd-ADCs

Next Pillars - Clinical

Next Pillars - Research

Transformation of R&D

Daiichi Sankyo's Purpose and R&D Vision

Purpose	**Contribute to the enrichment of quality of life around the world**
R&D Vision	**Source of innovation for improving patient's lives**

Serve Patients Globally

by delivering our strength,

Science & Technology

worldwide

DS Strategy to Enrich Our Delivery to Patients

3 and Alpha strategy is evolving

3ADCs

- ENHERTU®
- Dato-DXd
- HER3-DXd

&

Alpha

- Oncology
- Specialty Medicine
- Vaccine

3ADCs Value Maximization

Rising stars

Next Pillars

Our Imperatives: How to Achieve Our Strategy

DXd-ADCs

- **Expand** the programs of 3ADCs to maximize their values
- **Accelerate** Rising Star ADCs
  - **DS-7300**
  - **DS-6000**

Next Pillars

- **Validate** new FIC/BIC Alpha assets
- **Identify** promising New Modalities
  - 2nd generation ADC: DS-9606, etc.
  - New concept ADC
  - LNP-mRNA, Gene therapy, etc.

Transformation of R&D

- **Create** ONE Global R&D team: Streamlined, Scalable, Sustainable
- **Enhance** Our Capabilities: Strategic expertise, Talent development

Introduction

DXd-ADCs

Next Pillars - Clinical

Next Pillars - Research

Transformation of R&D

World ADC Awards – Most Promising Clinical Candidate

- **HER3-DXd** received the World ADC Awards as the **"Most Promising Clinical Candidate"** at the World ADC San Diego 2021 meeting in October

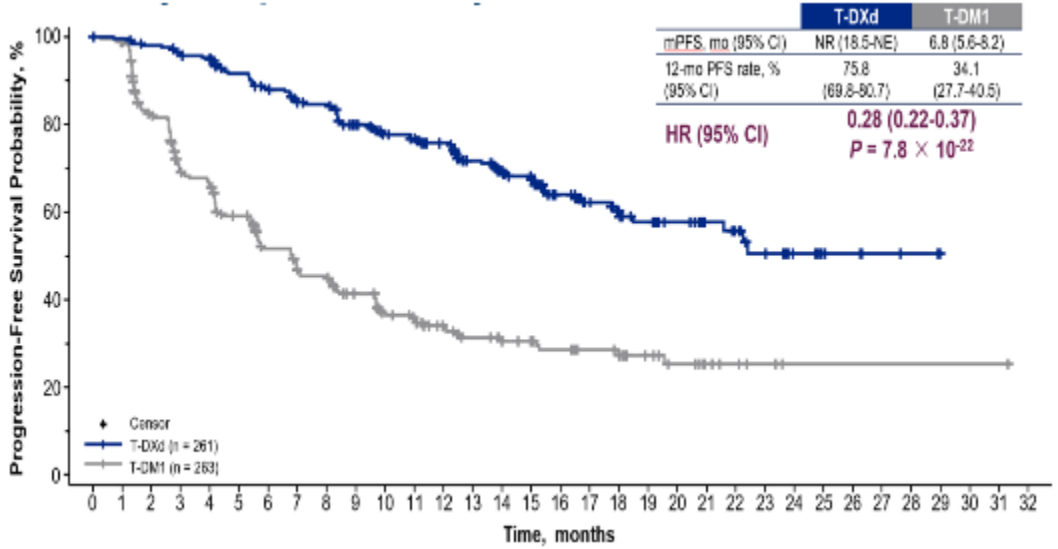
- Our **3ADCs** won the award **3 years** in a row
  - ENHERTU® (2019)
    Dato-DXd (2020)
    HER3-DXd (2021)

Reaffirmed that our DXd-ADC technology has been recognized throughout the world

ENHERTU® - DESTINY-Breast03 data

- DESTINY-Breast03 data **deepened the confidence** in our DXd-ADC technology
- Filing planned in FY2021 Q3
- ENHERTU® was included in ESMO Clinical Practice Guideline in Oct and NCCN breast cancer guidelines as 2L treatment with category 1 recommendation in Nov

DESTINY-Breast03 Efficacy
Primary end point: PFS by BICR



Median PFS follow-up for T-DXd was 15.5 months (range, 15.1-16.6) and for T-DM1 was 13.9 months (range, 11.8-15.1)
HR, hazard ratio; INV, investigator; mo, month; NE, not estimable; NR, not reached; PFS, progression free survival

DXd-ADC Franchise

3ADCs

Rising Stars

	Project (Target)	Target indications	Discovery	Pre-Clinical	Ph1	Ph2	Ph3	Filed	Launched
1	ENHERTU® (HER2)	Breast, Gastric, NSCLC, CRC, etc.							
2	Dato-DXd (TROP2)	NSCLC, Breast, etc.							
3	HER3-DXd (HER3)	NSCLC, Breast							
4	DS-7300 (B7-H3)	ESCC, CRPC, SCLC, etc.							
5	DS-6000 (CDH6)	Renal, Ovarian							
6	DS-3939 (TA-MUC1)	Solid tumors							
7	DS-XXXX (Undisclosed)	Undisclosed							

Timeline indicates the most advanced stage of each project

CRC: colorectal cancer, CRPC: castration-resistant prostate cancer, ESCC: esophageal squamous cell carcinoma, GIST: gastrointestinal stromal tumor, NSCLC: non small cell lung cancer,. SCLC: small cell lung cancer

ENHERTU® Vision

Transform treatment and outcomes for patients with HER2-targetable tumors and become the #1 Agent of Choice

③
- Establish ENHERTU® in GC, NSCLC, & CRC
- Explore tumor-agnostic opportunities

Expand leadership across other HER2-targetable tumors

②
- Reshape the BC treatment paradigm to embed ENHERTU® as the SOC in HER2 Low

Redefine Breast Cancer treatment paradigm and create HER2 Low

①
- Establish ENHERTU® as the clear SOC in 3L and 2L HER2+ mBC
- Expand into HER2+ 1L mBC and eBC

Transform treatment outcomes for HER2+ breast cancer patients

ENHERTU®: Clinical Development Program Highlights

Opportunities across breast cancer, HER2-low and other tumors

	NEOADJUVANT / ADJUVANT		1L METASTATIC	2L METASTATIC	3L METASTATIC
HER2-low BREAST CANCER	HR+[1]: chemotherapy ± endocrine therapy		endocrine ± CDK4/6i[2]	DESTINY-Breast04 DESTINY-Breast06 **Post CDK4/6i**	
	HR-[3]: chemotherapy		Replace/displace chemotherapy		
HER2-positive BREAST CANCER	DESTINY-Breast11 Neoadjuvant replace chemotherapy	DESTINY-Breast05 Post neoadjuvant replace trastuzumab emtansine (T-DM1)	DESTINY-Breast09 **REPLACE** chemotherapy + trastuzumab + pertuzumab	DESTINY-Breast03 **REPLACE** trastuzumab emtansine (T-DM1)	DESTINY-Breast01 DESTINY-Breast02 **POST** trastuzumab emtansine (T-DM1) ✓ US, JP, EU, UK, Canada, Israel, Brazil, Australia, CH, Singapore approvals
	Chemotherapy + trastuzumab + pertuzumab				
BEYOND BREAST CANCER	• Expand into other cancer types: gastric, NSCLC, CRC[4] and others • Conducting multiple combination trials to push the boundaries of patient outcomes				✓ HER2+ mGC US, JP, Israel, Singapore approvals

1. Hormone receptor positive 2. Cyclin-dependent kinase 4/6 inhibitor 3. Hormone receptor negative 4. Colorectal cancer

Trastuzumab Deruxtecan (T-DXd) Versus Trastuzumab Emtansine (T-DM1) in Patients With HER2+ Metastatic Breast Cancer: Subgroup Analyses From the Randomized Phase 3 Study DESTINY-Breast03

Sara A. Hurvitz, MD[a], Sung-Bae Kim, Wei-Pang Chung,
Seock-Ah Im, Yeon Hee Park, Roberto Hegg, Min-Hwan Kim, Ling-Ming Tseng, Vanessa Petry, Chi-Feng Chung,
Hiroji Iwata, Erika Hamilton, Giuseppe Curigliano, Binghe Xu, Caleb Lee,
Yali Liu, Jillian Cathcart, Emarjola Bako, Sunil Verma, Javier Cortes

On behalf of the DESTINY-Breast03 investigators

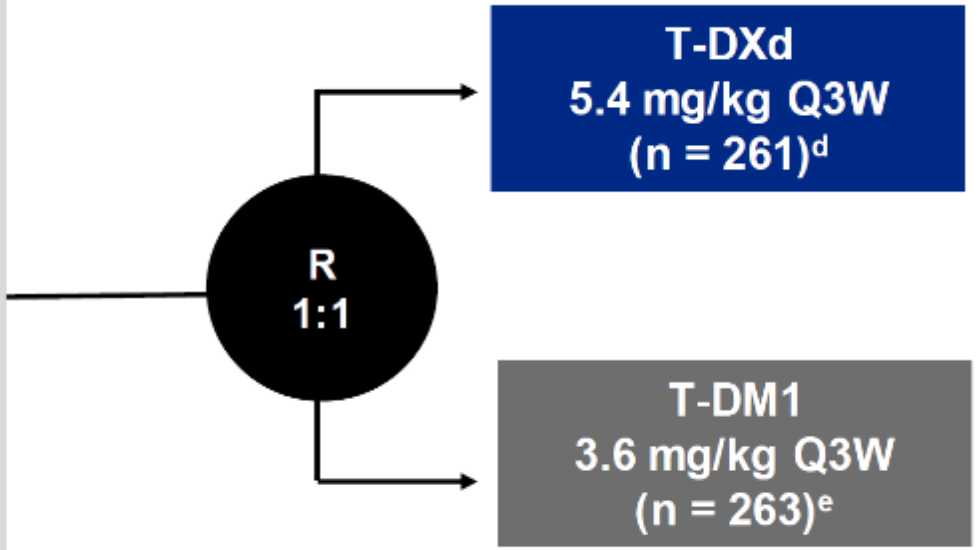
[a]Department of Medicine, David Geffen School of Medicine, University of California, Los Angeles, Jonsson Comprehensive Cancer Center, Los Angeles, CA USA

DESTINY-Breast03: First Randomized Phase 3 Study of T-DXd

An open-label, multicenter study (NCT03529110)

Patients (N = 524)
- Unresectable or metastatic HER2-positive[a] breast cancer that has been previously treated with trastuzumab and a taxane[b]
- Could have clinically stable, treated brain metastases[c]
  - ≥2 weeks between end of whole brain radiotherapy and study enrollment

Stratification factors
- Hormone receptor status
- Prior treatment with pertuzumab
- History of visceral disease



Primary endpoint
- PFS (BICR)

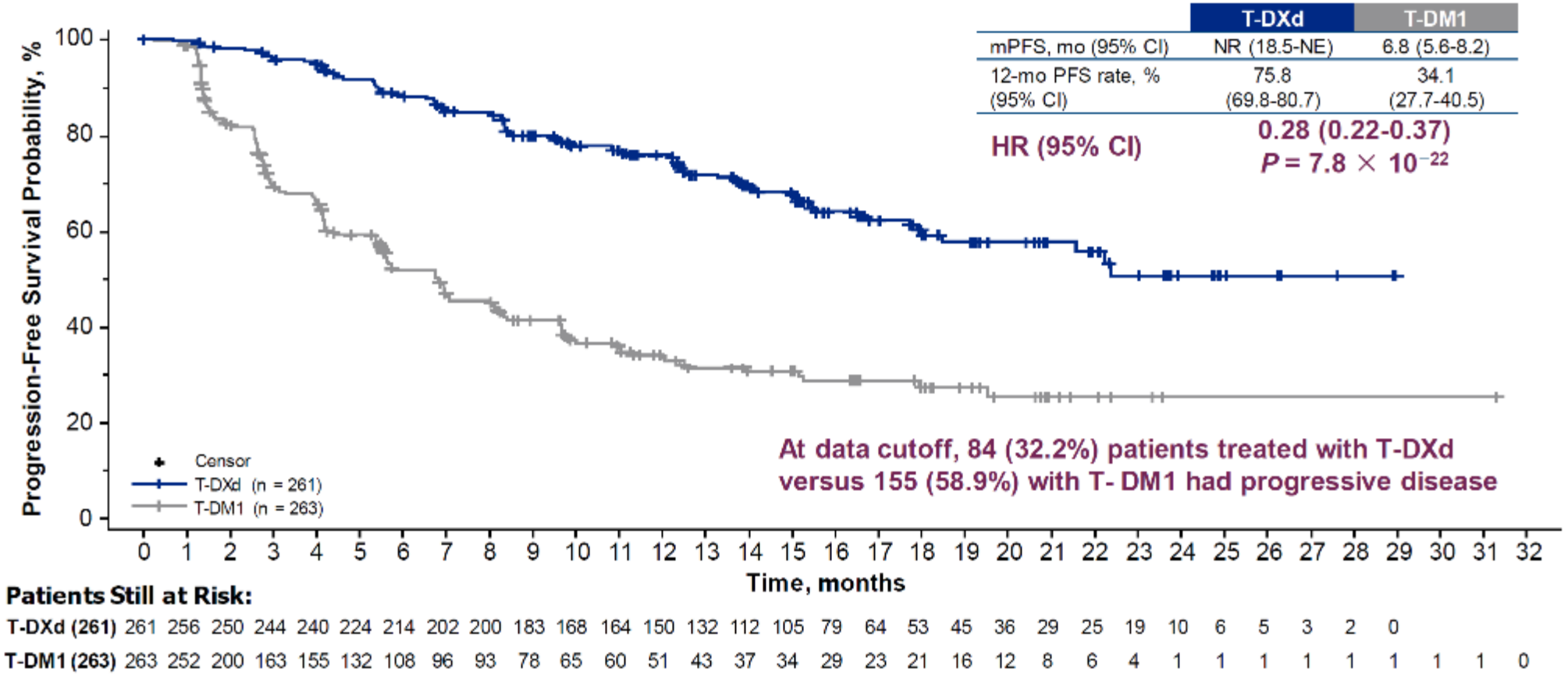
Key secondary endpoint
- OS

Secondary endpoints
- ORR (BICR and investigator)
- DOR (BICR)
- PFS (investigator)
- Safety

- At the time of data cutoff (May 21, 2021), 125 (48.6%) T-DXd patients and 214 (82.0%) T-DM1 patients had discontinued treatment
- Median follow up was 15.9 months
- BMs were measured at baseline by CT or MRI and lesions were monitored throughout the study

BICR, blinded independent central review; BM, brain metastasis; CT, computed tomography; DOR, duration of response; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; ISH, in situ hybridization; MRI, magnetic resonance imagining; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; Q3W, every 3 weeks; R, randomization; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan.
[a]HER2 IHC3+ or IHC2+/ISH+ based on central confirmation. [b]Progression during or <6 months after completing adjuvant therapy involving trastuzumab and a taxane. [c]Prior to protocol amendment, patients with stable, untreated BM were eligible. [d]4patients were randomly assigned but not treated. [e]2patients were randomly assigned but not treated.

Primary Endpoint: PFS by BICR



	T-DXd	T-DM1
mPFS, mo (95% CI)	NR (18.5-NE)	6.8 (5.6-8.2)
12-mo PFS rate, % (95% CI)	75.8 (69.8-80.7)	34.1 (27.7-40.5)
HR (95% CI)	0.28 (0.22-0.37)	
	$P = 7.8 \times 10^{-22}$	

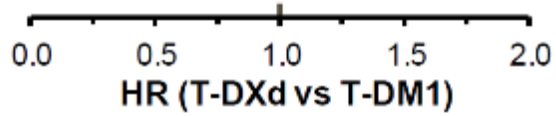
BICR, blinded independent central review; HR, hazard ratio; mPFS, median progression-free survival; NE, not estimable; NR, not reached; PFS, progression-free survival; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan.

Median PFS follow-up for T-DXd was 15.5 months (range, 15.1-16.6) and was 13.9 months (range, 11.8-15.1) for T-DM1.

Cortés et al. *Ann Oncol*. 2021; 32(suppl_5):S1283-S1346. 10.1016/annonc/annonc741

PFS in Key Subgroups

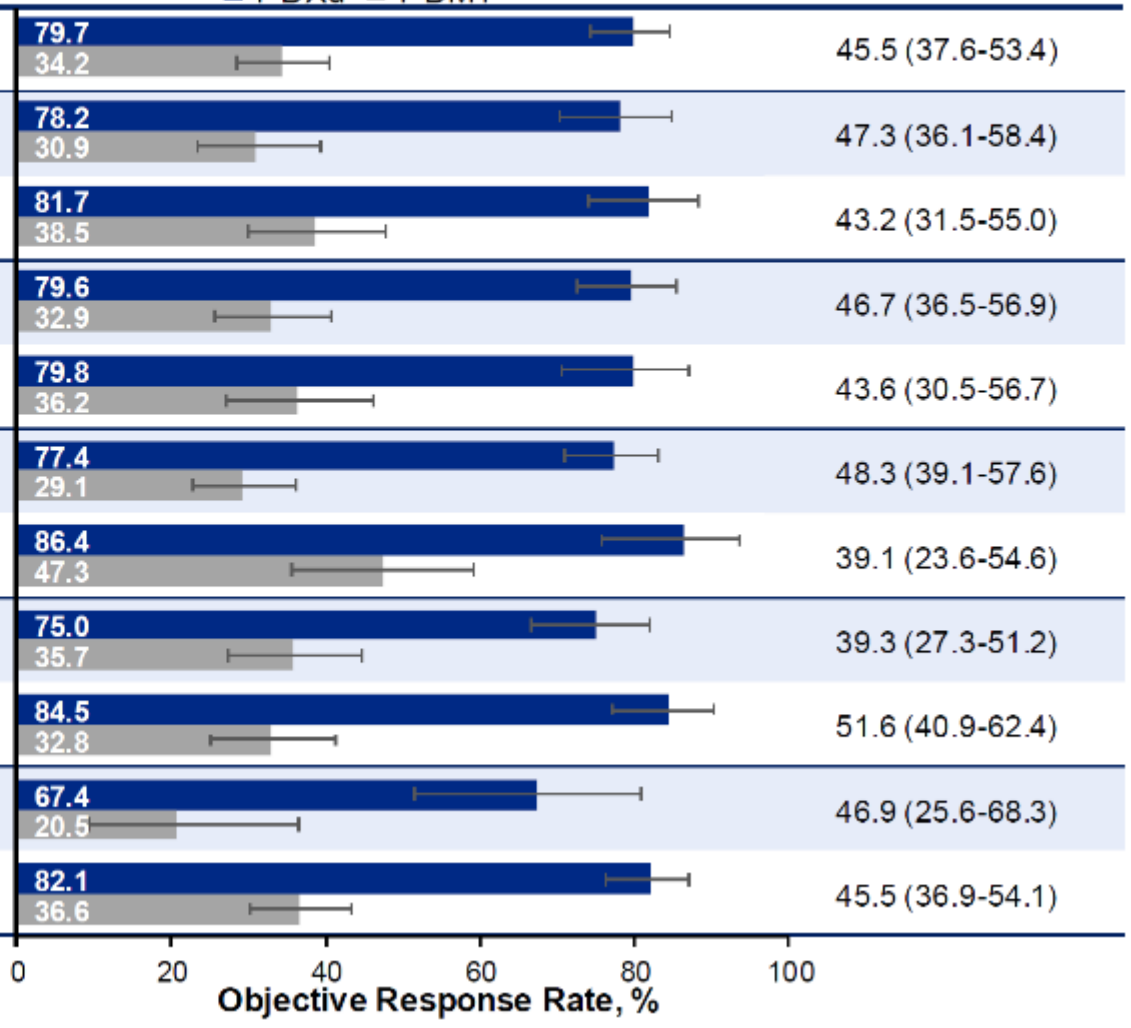
		Number of Events		Median PFS, mo (95% CI)		HR (95% CI)
		T-DXd	T-DM1	T-DXd	T-DM1	
All patients		87/261	158/263	NE (18.5-NE)	6.8 (5.6-8.2)	0.2840 (0.2165-0.3727)
Hormone receptor status	Positive (n = 272)	46/133	84/139	22.4 (17.7-NE)	6.9 (4.2-9.8)	0.3191 (0.2217-0.4594)
	Negative (n = 248)	41/126	73/122	NE (18.0-NE)	6.8 (5.4-8.3)	0.2965 (0.2008-0.4378)
Prior pertuzumab treatment	Yes (n = 320)	57/162	98/158	NE (18.5-NE)	6.8 (5.4-8.3)	0.3050 (0.2185-0.4257)
	No (n = 204)	30/99	60/105	NE (16.5-NE)	7.0 (4.2-9.7)	0.2999 (0.1924-0.4675)
Visceral disease	Yes (n = 384)	72/195	123/189	22.2 (16.5-NE)	5.7 (4.2-7.0)	0.2806 (0.2083-0.3779)
	No (n = 140)	15/66	35/74	NE (NE-NE)	11.3 (6.8-NE)	0.3157 (0.1718-0.5804)
Prior lines of therapy[a]	0-1 (n = 258)	46/132	75/126	22.4 (17.9-NE)	8.0 (5.7-9.7)	0.3302 (0.2275-0.4794)
	≥2 (n = 266)	41/129	83/137	NE (16.8-NE)	5.6 (4.2-7.1)	0.2828 (0.1933-0.4136)
Patients with BM	Yes (n = 82)	22/43	27/39	15.0 (12.5-22.2)	3.0 (2.8-5.8)	0.2465 (0.1341-0.4529)
	No (n = 442)	65/218	131/224	NE (22.4-NE)	7.1 (5.6-9.7)	0.2971 (0.2199-0.4014)



BM, brain metastasis; HR, hazard ratio; NE, not estimable; PFS, progression-free survival; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan.
[a]Patients with rapid progression on (neo)adjuvant therapy were included. Line of therapy does not include endocrine therapy.

Confirmed ORR Across Patient Subgroups

		T-DXd (n = 261) No. of Patients With Confirmed CR/PR	T-DM1 (n = 263) No. of Patients With Confirmed CR/PR	Difference of T-DXd vs T-DM1, % (95% CI)
All patients		208/261	90/263	45.5 (37.6-53.4)
Hormone receptor status	Positive (n = 272)	104/133	43/139	47.3 (36.1-58.4)
	Negative (n = 248)	103/126	47/122	43.2 (31.5-55.0)
Prior pertuzumab treatment	Yes (n = 320)	129/162	52/158	46.7 (36.5-56.9)
	No (n = 204)	79/99	38/105	43.6 (30.5-56.7)
Visceral disease	Yes (n = 384)	151/195	55/189	48.3 (39.1-57.6)
	No (n = 140)	57/66	35/74	39.1 (23.6-54.6)
Prior lines of therapy[a]	0-1 (n = 258)	99/132	45/126	39.3 (27.3-51.2)
	≥2 (n = 266)	109/129	45/137	51.6 (40.9-62.4)
Patients with BM	Yes (n = 82)	29/43	8/39	46.9 (25.6-68.3)
	No (n = 442)	179/218	82/224	45.5 (36.9-54.1)



BM, brain metastasis; CR, complete response; ORR, objective response rate; PR, partial response; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan.

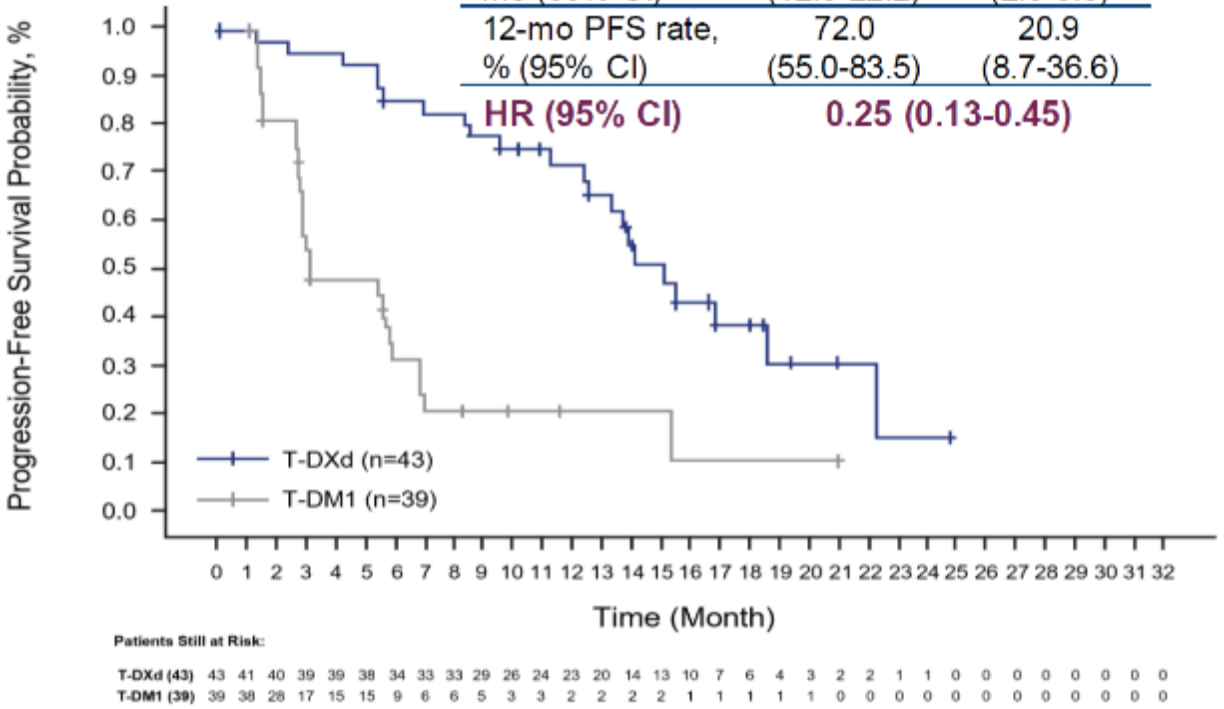
[a]Patients with rapid progression on (neo)adjuvant therapy were included. Line of therapy does not include endocrine therapy.

PFS KM Curves for Patients With and Without BM

Limited to stable BM

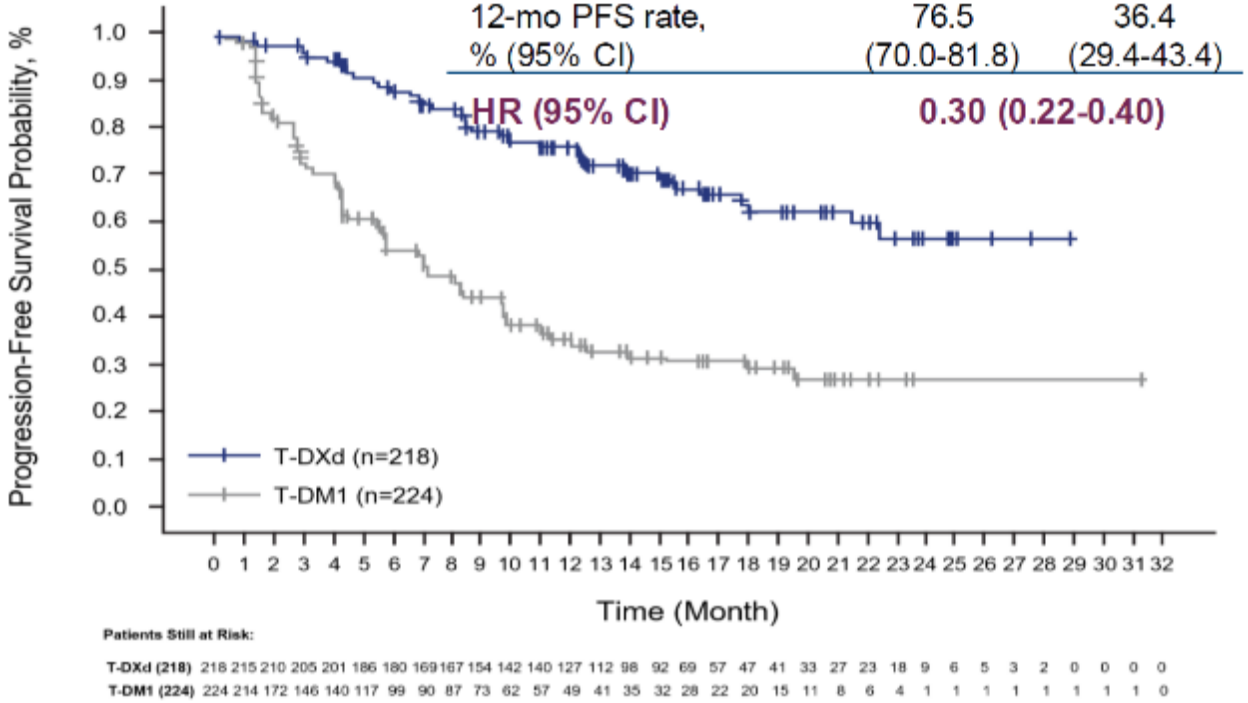
Brain Metastases at Baseline

	T-DXd	T-DM1
mPFS, mo (95% CI)	15.0 (12.5-22.2)	3.0 (2.8-5.8)
12-mo PFS rate, % (95% CI)	72.0 (55.0-83.5)	20.9 (8.7-36.6)
HR (95% CI)	0.25 (0.13-0.45)	



No Brain Metastases at Baseline

	T-DXd	T-DM1
mPFS, mo (95% CI)	NE (22.2-NE)	7.1 (5.6-9.7)
12-mo PFS rate, % (95% CI)	76.5 (70.0-81.8)	36.4 (29.4-43.4)
HR (95% CI)	0.30 (0.22-0.40)	



At data cutoff, in patients with BM at baseline, PD was observed:

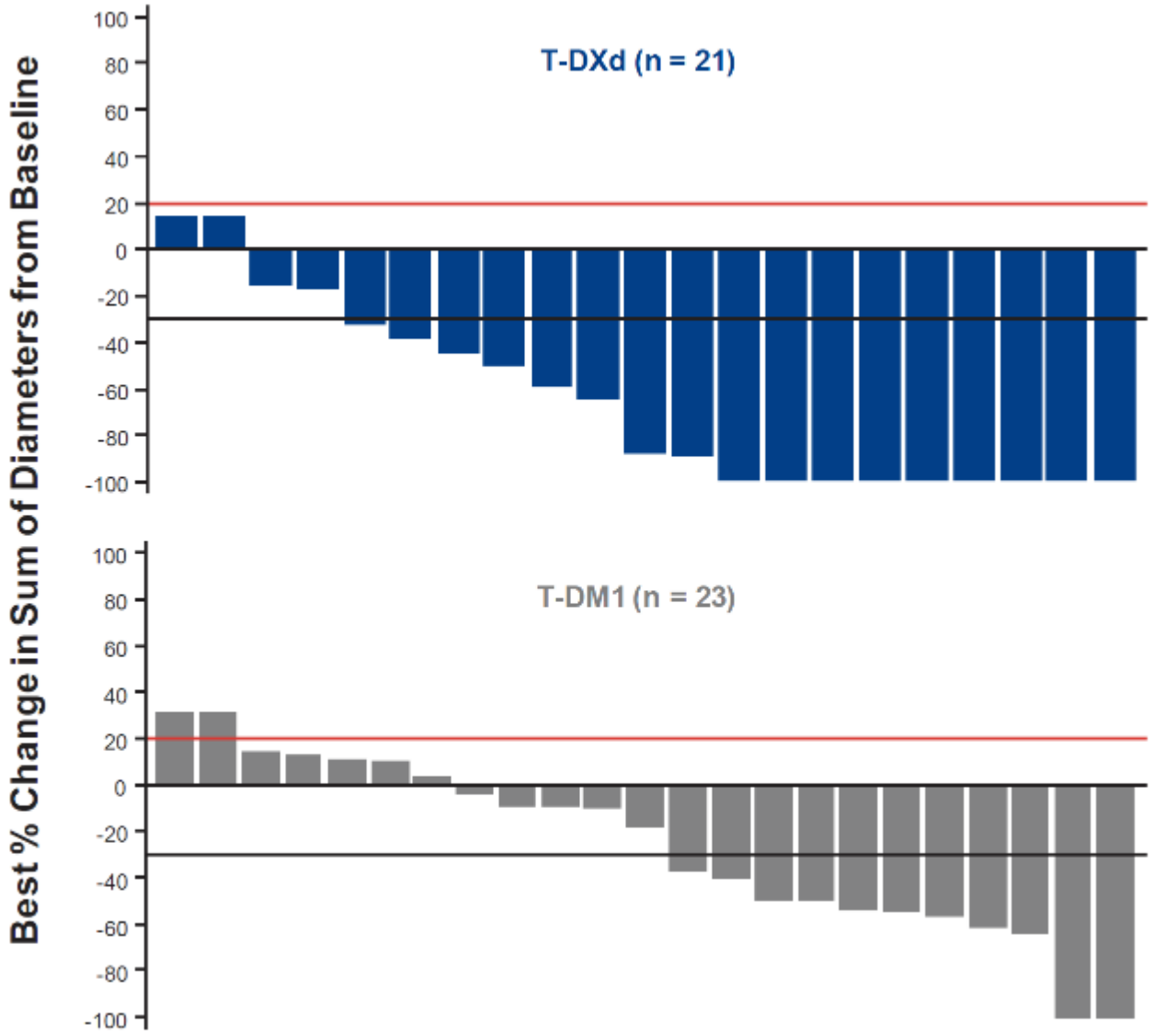
- In 21/43 treated with T-DXd versus 27/39 with T-DM1
  - In the brain in 9/21 treated with T-DXd versus 11/27 with T-DM1

At data cutoff, in patients without BM at baseline, PD was observed:

- In 63/218 treated with T-DXd versus 128/224 with T-DM1
  - In the brain in 4/63 treated with T-DXd versus 1/128 with T-DM1

mPFS, median progression-free survival; PD, progressive disease; PFS, progression-free survival; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan

Intracranial Response per BICR using RECIST 1.1



	T-DXd (n = 36)	T-DM1 (n = 36)
Best Overall Response, n (%)[a]		
CR	10 (27.8)	1 (2.8)
PR	13 (36.1)	11 (30.6)
Non-CR/Non-PD	6 (16.7)	7 (19.4)
SD	4 (11.1)	7 (19.4)
PD	1 (2.8)	8 (22.2)
Not Evaluable	0	1 (2.8)
Missing	2 (5.6)	1 (2.8)
Subjects with Objective Response of CR or PR, n	23	12

CR, complete response; DCR, disease control rate; mDOR, median duration of response; PD, progressive disease; PR, partial response; SD, stable disease; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan.
Table includes target and non-target lesions. Only patients with target lesion assessments are eligible for inclusion in waterfall.
Red line at 20% indicates progressive disease; black line at -30% indicates partial response.
[a]Denominator for percentages is the number of subjects in the full analysis set with brain metastases tumor assessment

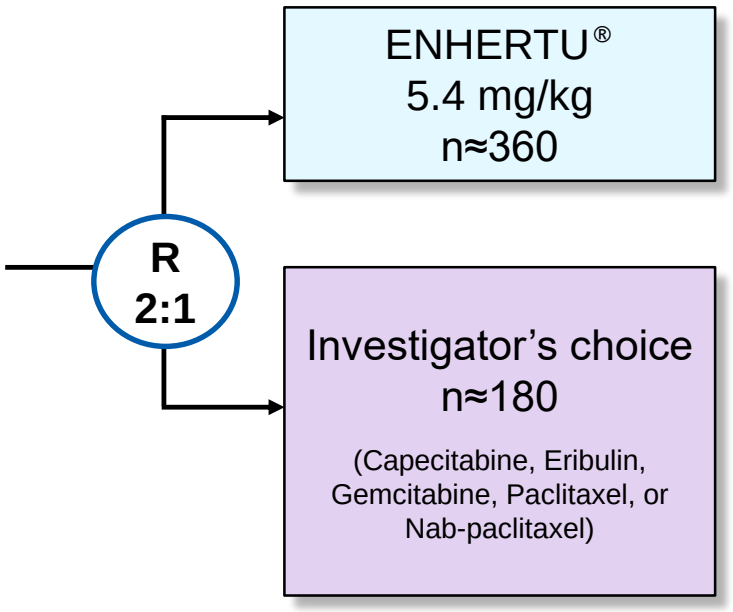
HER2 low BC development is gated by DB-04 outcome

DESTINY-Breast04

Ph3 study of ENHERTU® compared to existing 2L & 3L HER2-negative monotherapies for HER2 low breast cancer

Key Eligibility Criteria

- HER2-low (IHC 1+ or IHC 2+/ISH-)
- Unresectable or metastatic breast cancer
- Previously treated with 1 or 2 lines of chemotherapy in the metastatic setting
- If HR-positive, must be refractory to endocrine therapy, no restriction on prior targeted therapy



Primary endpoint
- PFS (BICR) in HR+

Key Secondary endpoints
- PFS (BICR) HR+ & HR-
- OS in HR+
- OS in OS in HR+ & HR-

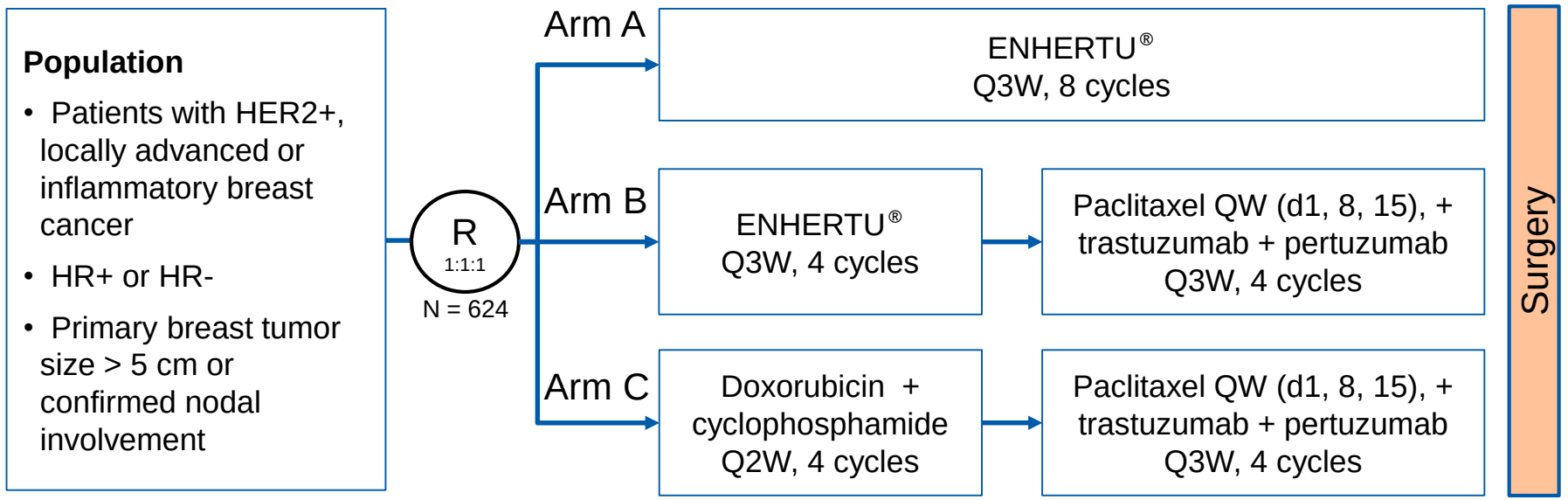
Secondary endpoints
- PFS (INV) in HR+
- ORR in HR+
- DoR (BICR) in HR+

The data readout timing of DB-04 expected in Q4 FY2021 as scheduled.

Newly started study

DESTINY-Breast11

Phase 3 study of neoadjuvant ENHERTU® monotherapy or ENHERTU® followed by THP compared to ddAC-THP in patients with high-risk HER2+ early stage breast cancer



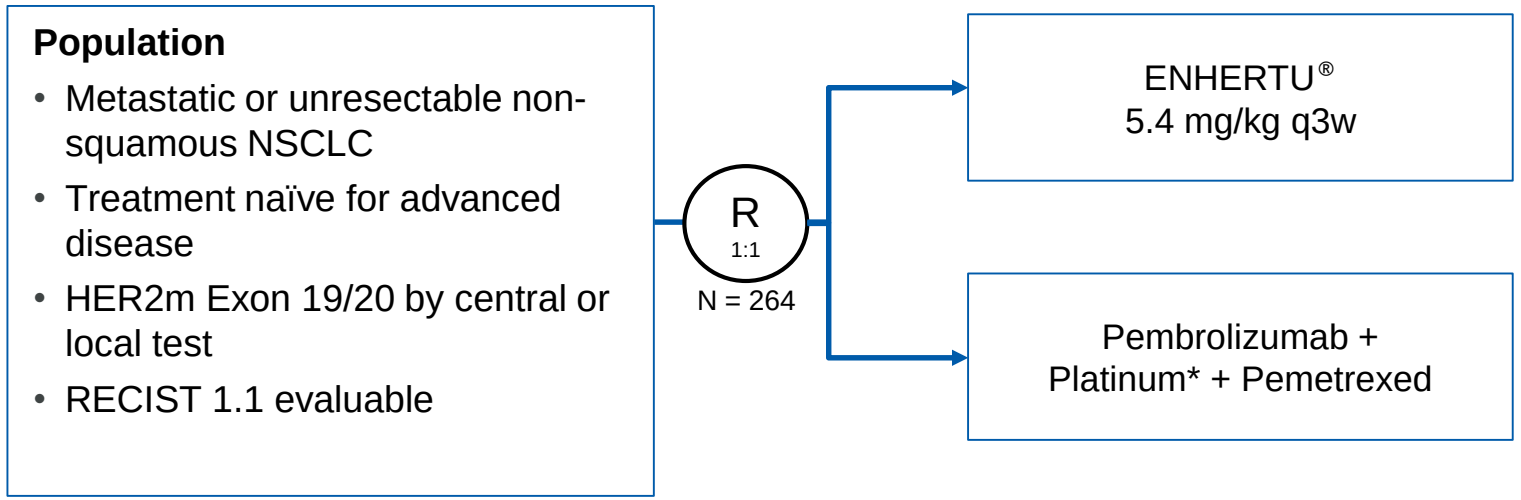
Primary Endpoint:
- Pathologic complete response (ypT0/Tis ypN0)

ddAC: dose dense adriamycin + cyclophosphamide, THP: taxane + herceptin + pertuzumab

New study planned

DESTINY-Lung04

Ph3 study of T-DXd as 1L treatment of NSCLC harboring HER2 exon 19 or 20 mutations



Primary Endpoint:
- PFS (BICR)

Prespecified subgroups include: HER2 co-amplification; PD-L1 status (≥1%)
* Investigator choice of cisplatin or carboplatin

ENHERTU®: Clinical Development Plan | Breast cancer

As of Dec 2021			FY2020	FY2021	FY2022	Planning
HER2 Positive		Metastatic 3L+	DESTINY-Breast01 completed			
			DESTINY-Breast02 monotherapy vs PC			
		Metastatic 2L	DESTINY-Breast03 monotherapy vs T-DM1			
			DESTINY-Breast07 combination (2L/1L) Ph1b/2			
		Metastatic 1L				
			DESTINY-Breast09 T-DXd ± pertuzumab vs THP			
		Post-neoadjuvant	DESTINY-Breast05 monotherapy vs T-DM1			
		Neoadjuvant	DESTINY-Breast11 T-DXd vs T-DXd / THP vs AC / THP			
		Adjuvant				Phase 3
HER2 Low	HR+ HR-	Metastatic Post Chemo	DESTINY-Breast04 monotherapy vs PC			
			DESTINY-Breast08 combination			
		Post-neoadjuvant				Phase 3
	HR+	Metastatic Chemo Naive	DESTINY-Breast06 monotherapy vs PC			
	HR-	Metastatic 1L	BEGONIA durvalumab combination Ph1b/2 (Arm 6)			
		Neoadjuvant				Phase 3

Ph 1 ongoing | Ph 2 ongoing | Ph 3 ongoing | New | Completed

Study initiation & end points are all shown as either beginning of 1H or 2H

AC: adriamycin + cyclophosphamide, THP: taxane + Herceptin + pertuzumab, PC: physician's choice

ENHERTU®: Clinical Development Plan | GC & NSCLC

As of Dec 2021			FY2020	FY2021	FY2022	Planning
Gastric	HER2 Positive	Metastatic 3L+	DESTINY-Gastric01	DESTINY-Gastric06 monotherapy China Ph2		
		Metastatic 2L	DESTINY-Gastric02 monotherapy - West			
				DESTINY-Gastric04 mono vs ramucirumab+paclitaxel		
			DESTINY-Gastric03 combination (2L/1L) Ph1b/2			
		Metastatic 1L				Phase 3
NSCLC	HER2 Expressing	Metastatic 2L+	DESTINY-Lung01 monotherapy			
			HUDSON durvalumab combination			
		Metastatic 2L				Phase 3
		Metastatic 1L		DESTINY-Lung03 combination		
						Phase 3
	HER2 Mutated	Metastatic 2L+	DESTINY-Lung01 monotherapy			
				DESTINY-Lung02 monotherapy		
		Metastatic 1L			DESTINY-Lung04 mono vs SOC	

Ph 1 ongoing | Ph 2 ongoing | Ph 3 ongoing | New | Completed

Study initiation & end points are all shown as either beginning of 1H or 2H

GC: gastric cancer, NSCLC: non-small cell lung cancer, SOC: standard of care

ENHERTU®: Clinical Development Plan | CRC & other tumors

As of Dec 2021			FY2020	FY2021	FY2022	Planning
CRC	HER2 Expressing	Metastatic 3L	DESTINY-CRC01 monotherapy	DESTINY-CRC02 monotherapy		
Other Tumors/ multiple tumors	HER2 Expressing	Metastatic 2L	Nivolumab combination (breast, bladder)			
			Pembrolizumab combination (breast, NSCLC)			
			DESTINY-PanTumor02			
	HER2 Mutated	Metastatic 2L	DESTINY-PanTumor01			

Ph 1 ongoing | Ph 2 ongoing | Ph 3 ongoing | New | Completed

Study initiation & end points are all shown as either beginning of 1H or 2H

CRC: colorectal cancer, NSCLC: non small cell lung cancer

Dato-DXd Vision

Transform treatment and outcomes for patients with a broad range of solid tumors

③
- Enabled by DXd innovations, Deliver Dato-DXd to Multiple Cancer Indications

Transform treatment outcomes well beyond NSCLC and Breast cancer

②
- Establish Dato-DXd (and DXd platform) as TROP2 ADC of choice across Breast Cancer

Take TROP2-directed ADC therapy to an unprecedented level of efficacy in Breast cancer

①
- Establish Dato-DXd as the First and Best-in-Class TROP2 ADC for NSCLC

Introduce Dato-DXd as a key monotherapy for patients with relapsed/refractory disease, followed by combination with immunotherapy for first-line metastatic disease

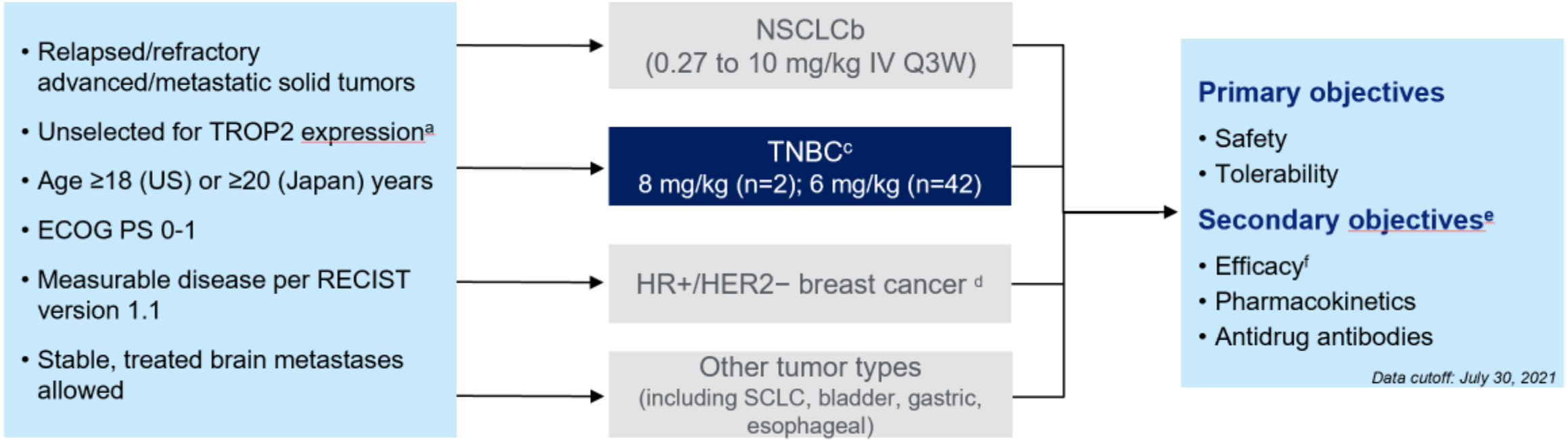
Datopotamab Deruxtecan (Dato-DXd) in Advanced/Metastatic HER2 Negative Breast Cancer: Triple Negative Breast Cancer Results from the Phase 1 TROPION-PanTumor01 Study

Ian Krop,[1] Dejan Juric,[2] Toshio Shimizu,[3] Anthony Tolcher,[4] Alexander Spira,[5] Toru Mukohara,[6] Aaron E. Lisberg,[7] Takahiro Kogawa,[8] Kyriakos P. Papadopoulos,[9] Erika Hamilton,[10] Senthil Damodaran,[11] Jonathan Greenberg,[12] Wen Gu,[12] Fumiaki Kobayashi,[13] Takahiro Jikoh,[13] Yui Kawasaki,[13] Funda Meric-Bernstam,[11] Aditya Bardia[2]

[1]Dana-Farber Cancer Institute, Boston, MA; [2]Department of Hematology/Oncology, Massachusetts General Hospital Cancer Center, Harvard Medical School, Boston, MA; [3]National Cancer Center Hospital, Tokyo, Japan; [4]NEXT Oncology, San Antonio, TX; [5]Virginia Cancer Specialists, Fairfax, VA; [6]Department of Medical Oncology, National Cancer Center Hospital East, Kashiwa, Japan; [7]UCLA Jonsson Comprehensive Cancer Center, Santa Monica, CA; [8]Advanced Medical Development Center, The Cancer Institute Hospital of JFCR, Tokyo, Japan; [9]START Center for Cancer Care San Antonio, San Antonio, TX; [10]Sarah Cannon Research Institute/Tennessee Oncology, Nashville, TN; [11]The University of Texas MD Anderson Cancer Center, Houston, TX; [12]Daiichi Sankyo Inc., Basking Ridge, NJ; [13]Daiichi Sankyo Co, Ltd, Tokyo, Japan

TROPION-PanTumor01 (NCT03401385)

Phase 1 Study in Relapsed/Refractory Metastatic Solid Tumors



ECOG PS, Eastern Cooperative Oncology Group performance status; Q3W, every 3 weeks; RECIST, Response Evaluation Criteria in Solid Tumors.
[a] Pretreatment tumor tissue was required for retrospective analysis of TROP2 expression. [b] Results from the NSCLC cohort have been previously reported.[1,2] [c] Includes patients treated in the dose-escalation and dose-expansion portions. [d] Enrollment in the HR+/HER2− cohort is now complete and data will be forthcoming. [e] Exploratory objectives include analyses of biomarkers associated with response. [f] Response assessments are based on RECIST 1.1.

1.Garon E, et al. WCLC 2021. Abstract 156; 2 Meric-Bernstam F, et al. ASCO 2021.

Baseline Characteristics

Patient characteristics	TNBC n=44
Age, median (range), years	53 (32-82)
Country, n (%)	
US	31 (70)
Japan	13 (30)
ECOG PS, n (%)	
0	18 (41)
1	26 (59)
De novo metastatic disease, n (%)	
Yes	14 (32)
No	30 (68)

Patient characteristics (cont)	TNBC n=44
Brain metastases, n (%)	5 (11)
Prior therapies in metastatic setting, median (range), n	3 (1-10)
≥2 prior lines of therapy, n (%)[a]	30 (68)
Previous systemic treatment, n (%)	
Taxanes	40 (91)
Platinum-based chemotherapy	23 (52)
Immunotherapy	19 (43)
PARPi	7 (16)
Topo I inhibitor-based ADC[b]	13 (30)

Data cutoff: July 30, 2021

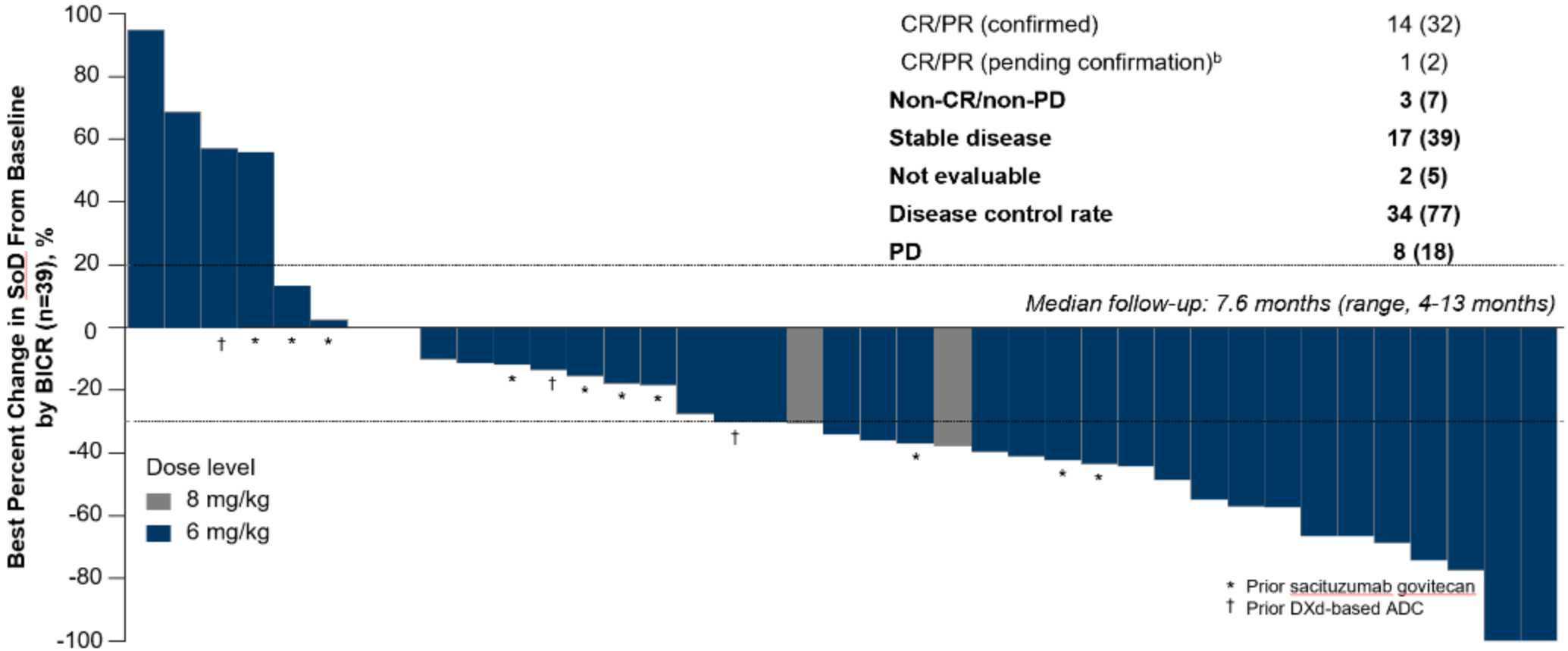
PARPi, poly(ADP-ribose) polymerase inhibitor; Topo I, topoisomerase I.

[a] Includes prior lines of therapy in the metastatic setting. [b] Sacituzumab govitecan, n=10; trastuzumab deruxtecan, n=2; patritumab deruxtecan, n=1.

Antitumor Responses by BICR

All patients with TNBC

Patients, n (%)[a]	All Patients (n=44)
ORR	**15 (34)**
CR/PR (confirmed)	14 (32)
CR/PR (pending confirmation)[b]	1 (2)
Non-CR/non-PD	**3 (7)**
Stable disease	**17 (39)**
Not evaluable	**2 (5)**
Disease control rate	**34 (77)**
PD	**8 (18)**



Data cutoff: July 30, 2021

BICR, blinded independent central review; CR, complete response; ORR, objective response rate; PD, progressive disease; PR, partial response; SoD, sum of diameters.

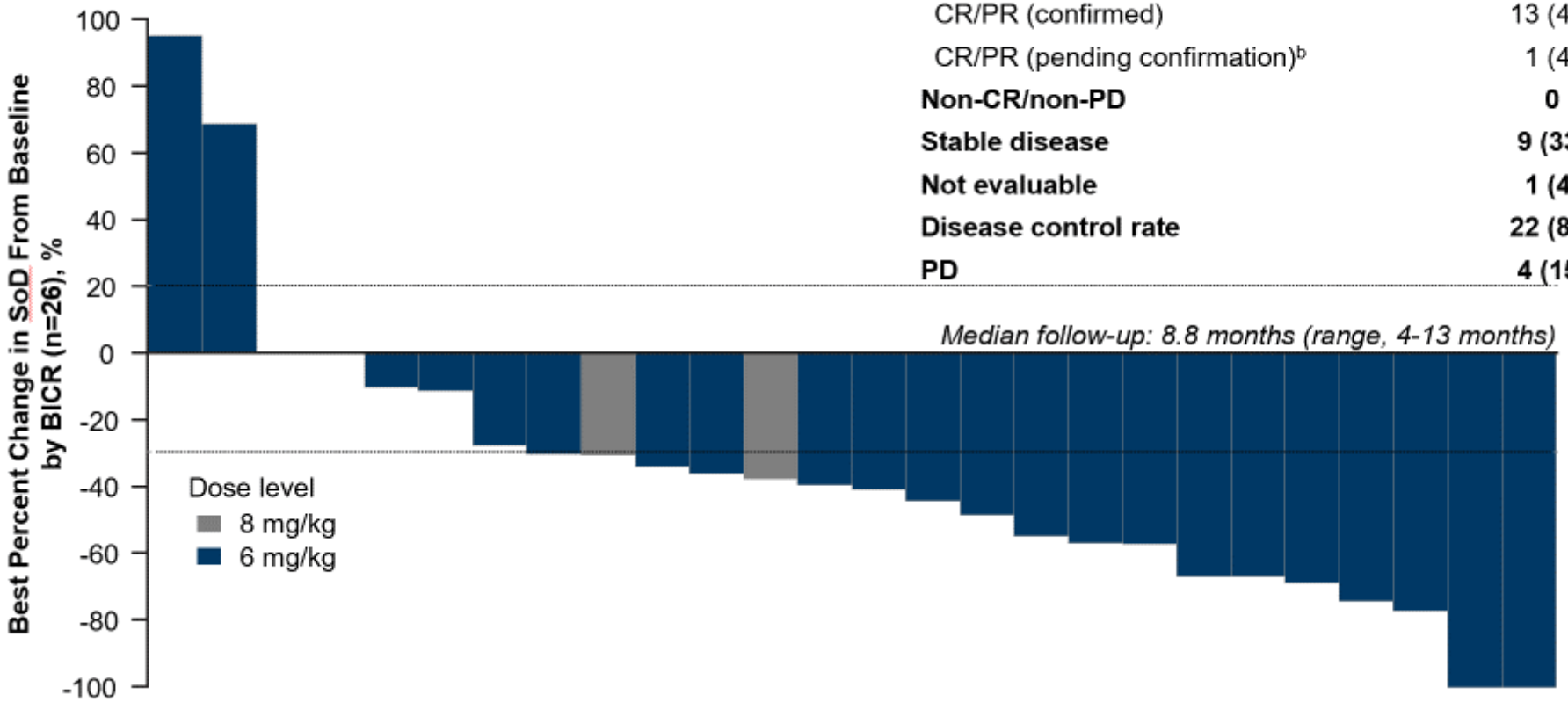
[a] Includes response evaluable patients who had ≥1 postbaseline tumor assessment or discontinued treatment. Postbaseline tumor assessments were not yet available for 2 patients at the data cutoff. Three patients were not confirmed to have a target lesion per BICR and therefore had a best overall response of non-CR/non-PD.

[b] Includes patients with an unconfirmed response but are ongoing treatment.

Antitumor Responses by BICR

Patients with TNBC without prior Topo I inhibitor-based ADC

Patients, n (%)[a]	SG/DXd Naïve Patients with Measurable Disease at BL (n=27)
ORR	**14 (52)**
CR/PR (confirmed)	13 (48)
CR/PR (pending confirmation)[b]	1 (4)
Non-CR/non-PD	**0**
Stable disease	**9 (33)**
Not evaluable	**1 (4)**
Disease control rate	**22 (81)**
PD	**4 (15)**

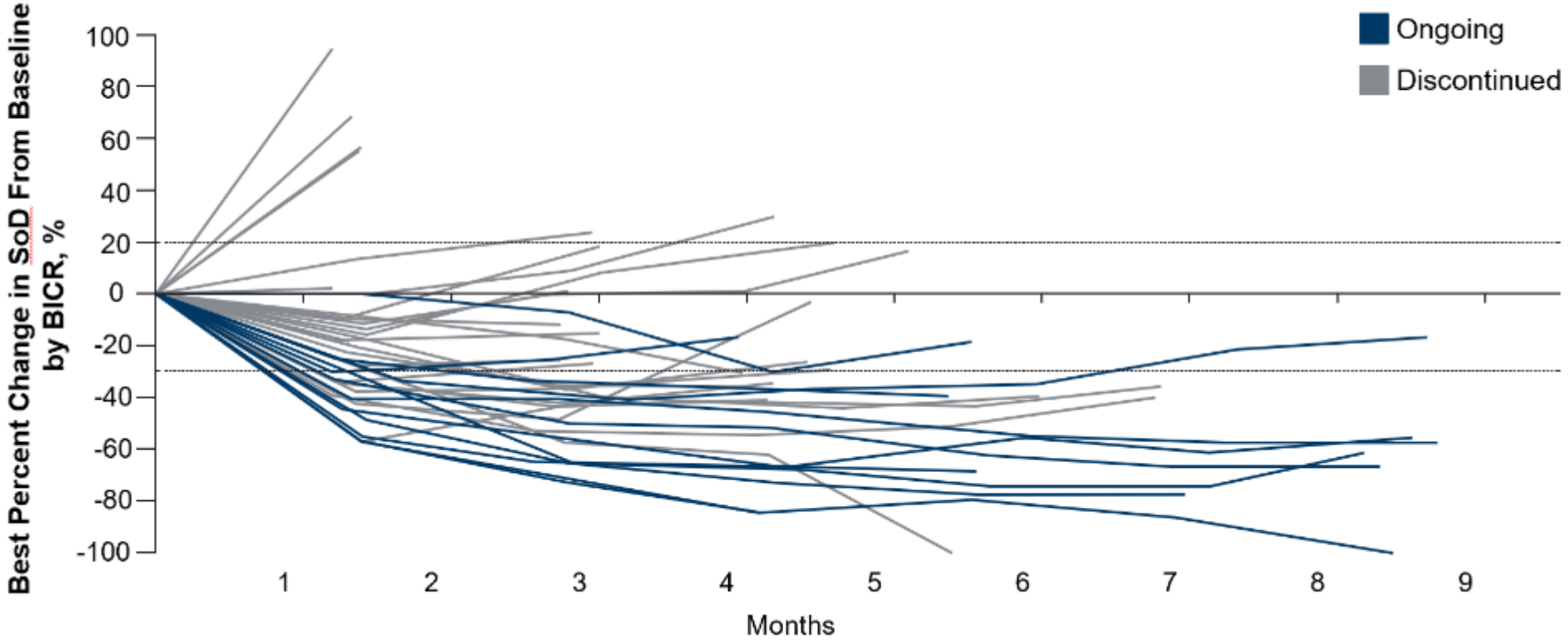


Data cutoff: July 30, 2021

BL, baseline; SG; sacituzumab govitecan..

[a] Includes response evaluable patients who had ≥1 postbaseline tumor assessment or discontinued treatment. Postbaseline tumor assessments were not yet available for 1 patient at the data cutoff. [b] Includes patients with an unconfirmed response but are ongoing treatment.

Duration of Disease Control in Patients with TNBC



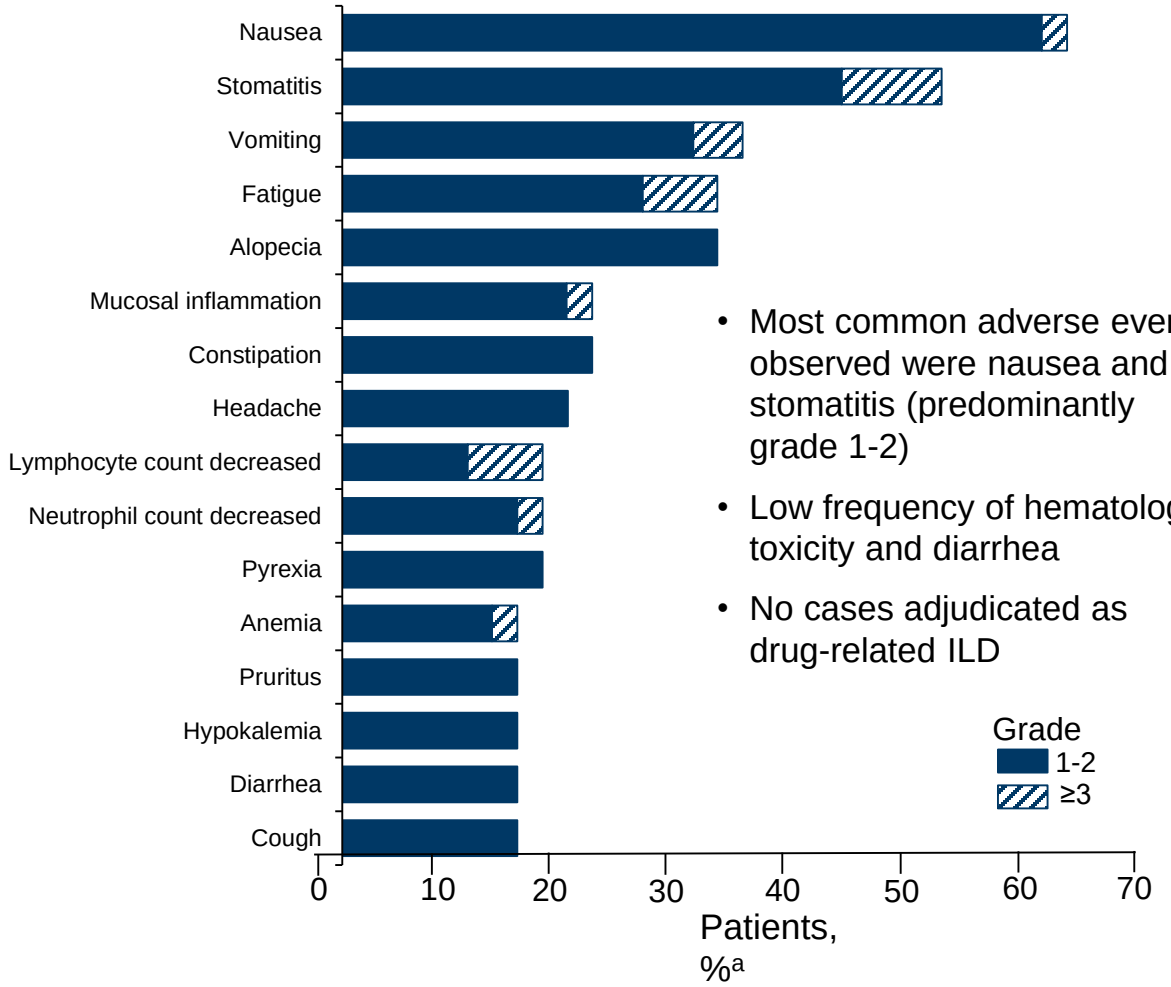
Data cutoff: July 30, 2021

- The median duration of response was not reached (range, 2.7-7.4+ months), with the majority of responses ongoing at the data cutoff

Safety Summary

Patients, n (%)	TNBC n=44
All-grade TEAEs	43 (98)
Grade ≥3	20 (45)
All-grade treatment-related TEAEs	43 (98)
Grade ≥3	**10 (23)**
Dose adjustments	
Dose reduction due to AEs	8 (18)
Treatment interruption due to AEs	6 (14)
Treatment discontinuation due to AEs	1 (2)
Serious TEAEs	8 (18)
Treatment related	2 (5)
Fatal TEAEs	0
Treatment related	0

TEAES in ≥15% of Patients



- Most common adverse events observed were nausea and stomatitis (predominantly grade 1-2)
- Low frequency of hematologic toxicity and diarrhea
- No cases adjudicated as drug-related ILD

Data cutoff: July 30, 2021

AE, adverse event; TEAE, treatment-emergent adverse event.

Newly started study

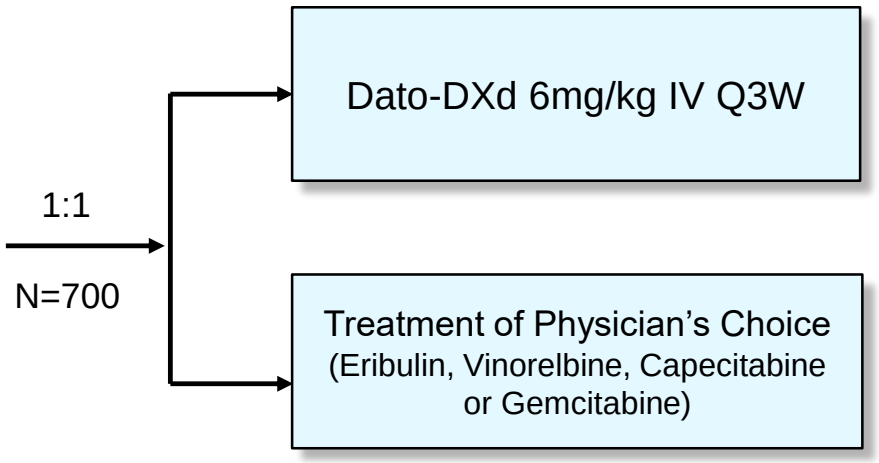
TROPION-Breast01

Ph3 Study of Dato-DXd vs treatment of physician's choice in 2nd/3rd Line HR+ HER2- mBC

Key Eligibility Criteria:

- HR+ HER2- BC patients previously treated with one or two^ lines of chemotherapy in advanced/metastatic setting:
  - Progressed or not suitable for endocrine therapy
  - Progressed following most recent antineoplastic therapy
- Targeted agents (such as mTOR inhibitors, PD-1/PD-L1 inhibitors), endocrine therapies and CDK4/6 inhibitors on their own do not contribute to the count of prior lines of chemotherapy, although regimens with such agents in combination with chemotherapy would still count as one line of chemotherapy*.

^3L population capped at 50%
*Prior PARP inhibitors will be regarded as a line of chemotherapy



Stratification factors:

- 1 vs 2 lines of chemo in adv./met. setting
- Geographic location
- Previous CDK 4/6 inhibitor

Dual primary endpoint
PFS (BICR) and OS

Secondary endpoints
PFS (inv), ORR, DoR, TTR, DCR, PRO, TEAE, PK, immunogenicity

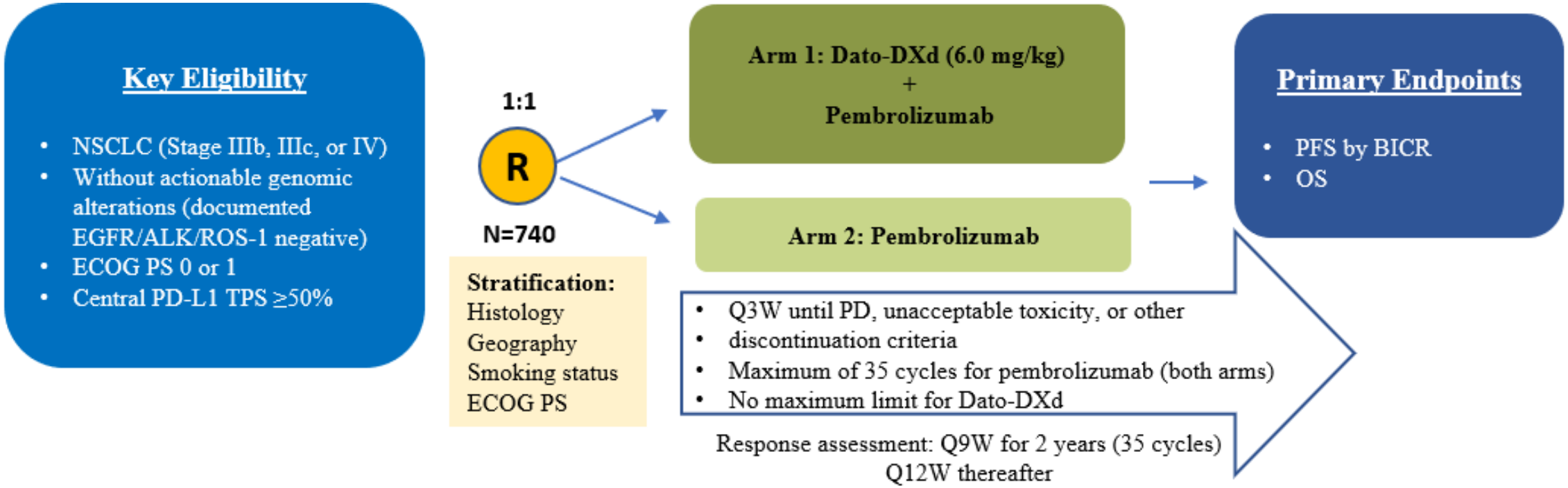
Exploratory endpoints
PFS-2, Trop2 IHC expression, other biomarkers, exposure/efficacy relationship, additional PRO

Response assessment: Scan q6w (based on 6 mo. mPFS in control arm)

New study planned

TROPION-Lung08

Ph3 study to evaluate add-on strategy to pembro monotherapy in 1L NSCLC without actionable genomic alternations



Dato-DXd: Clinical Development Plan | NSCLC

As of Dec 2021			FY2020	FY2021	FY2022	Planning
NSCLC	Without actionable mutations	Metastatic 2L/3L	TROPION-PanTumor01	TROPION-Lung01		
	ICI combination Without actionable mutations	Metastatic 1L/2L		TROPION-Lung02 (+pembrolizumab)		
				TROPION-Lung04 (+durvalumab)		
		Metastatic 1L		TROPION-Lung08 (+pembrolizumab) In PD-L1 ≥50%		Additional studies in 1L NSCLC*
	With actionable mutations	Metastatic 2L+	TROPION-PanTumor01	TROPION-Lung05		

*Includes PD-L1 <50%, where SOC is often PD-1/PD-L1 inhibitor + chemotherapy.

Ph 1 ongoing | Ph 2 ongoing | Ph 3 ongoing | New | Completed

Study initiation & end points are all shown as either beginning of 1H or 2H

ICI: immune checkpoint inhibitor, NSCLC: non small cell lung cancer

Dato-DXd: Clinical Development Plan | Breast & other tumors

As of Dec 2021			FY2020	FY2021	FY2022	Planning
Breast	HR+HER2-	Metastatic 2L+		TROPION-Breast01		
				TROPION-PanTumor01		
	TNBC	Metastatic 2L+				Phase 3
		Metastatic 1L		BEGONIA durvalumab combination Ph1b/2 (Arm 7)		
Other Tumors*				TROPION-PanTumor01		

*Other tumors are gastric, esophageal, urothelial, and SCLC. Inclusion of these tumors is based upon TROP2 expression as well as preclinical and other evidence that Dato-DXd may be effective.

Ph 1 ongoing | Ph 2 ongoing | Ph 3 ongoing | New | Completed

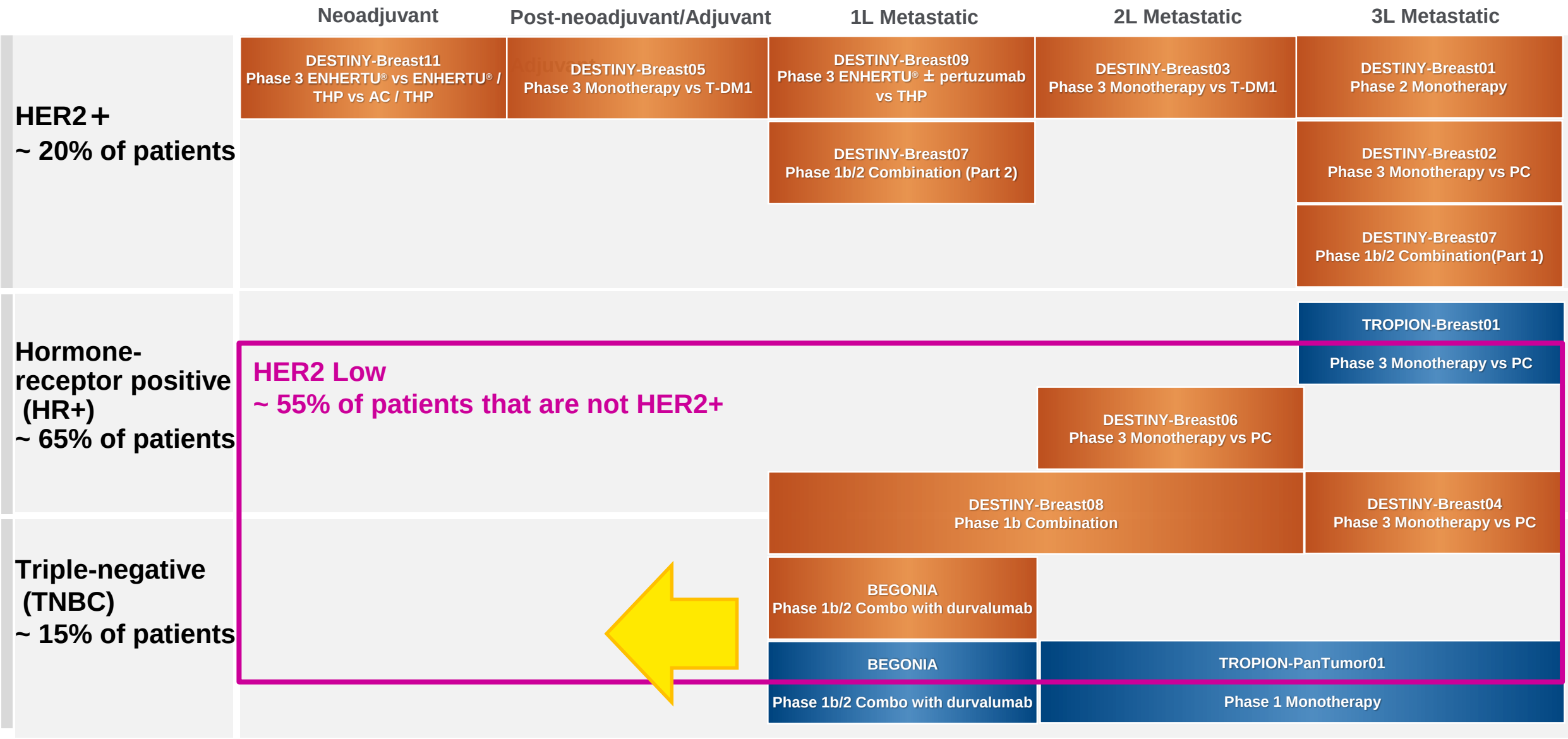
Study initiation & end points are all shown as either beginning of 1H or 2H

SCLC: small cell lung cancer, TNBC: triple negative breast cancer

ENHERTU® & Dato-DXd: Breast Cancer Clinical Development Highlights

ENHERTU®
Dato-DXd

Daiichi-Sankyo



HER3-DXd Vision

Transform treatment and outcomes for patients with HER3-expressing tumors with First-in-Class HER3 directed ADC

③
- Expand in NSCLC beyond EGFRm
- Explore opportunities across HER3-expressing tumors

Expand in NSCLC and across other HER3-expressing tumors

②
- Introduce HER3-DXd as monotherapy or in combination in the treatment paradigm of HER3-expressing Breast Cancers

Establish HER3-DXd as a treatment option for Breast Cancer Patients

①
- Establish HER3-DXd as the monotherapy SOC in EGFRm NSCLC post EGFR TKI
- Expand HER3-DXd in combination with EGFR TKIs into earlier lines of therapy

Transform treatment outcomes for EGFRm NSCLC patients

NSCLC: non small cell lung cancer, SOC: standard of care, TKI: tyrosine kinase inhibitor

HER3-DXd: Clinical Development Plan | NSCLC & other tumors

As of Dec 2021			FY2020	FY2021	FY2022	Planning
NSCLC	EGFR mutated	Advanced/ Metastatic 3L~	Ph1 dose expansion			
				HERTHENA-Lung01 monotherapy		
		Advanced/ Metastatic 2L				
				Osimertinib combination Ph1b		
		Advanced/ Metastatic 1L				
CRC	All comers	Metastatic 3L~	Monotherapy Ph2 (Terminated)			
Breast	HER3 expressing	Metastatic BC	Monotherapy Ph1/2			

Ph 1 ongoing | Ph 2 ongoing | Ph 3 ongoing | New | Completed

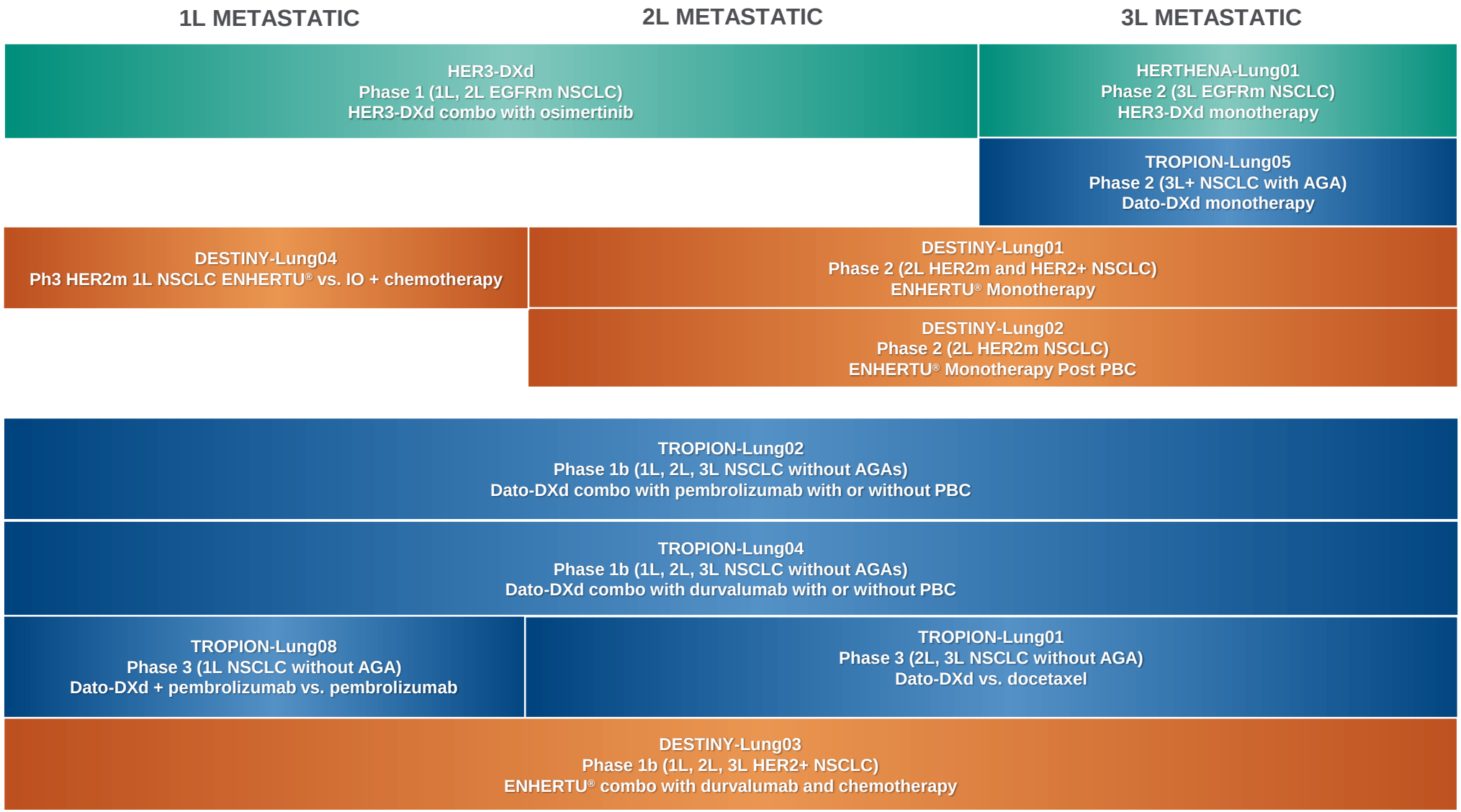
Study initiation & end points are all shown as either beginning of 1H or 2H

BC: breast cancer, CRC: colorectal cancer, NSCLC: non small cell lung cancer

ENHERTU®, Dato-DXd & HER3-DXd: Lung Cancer Clinical Development Highlights

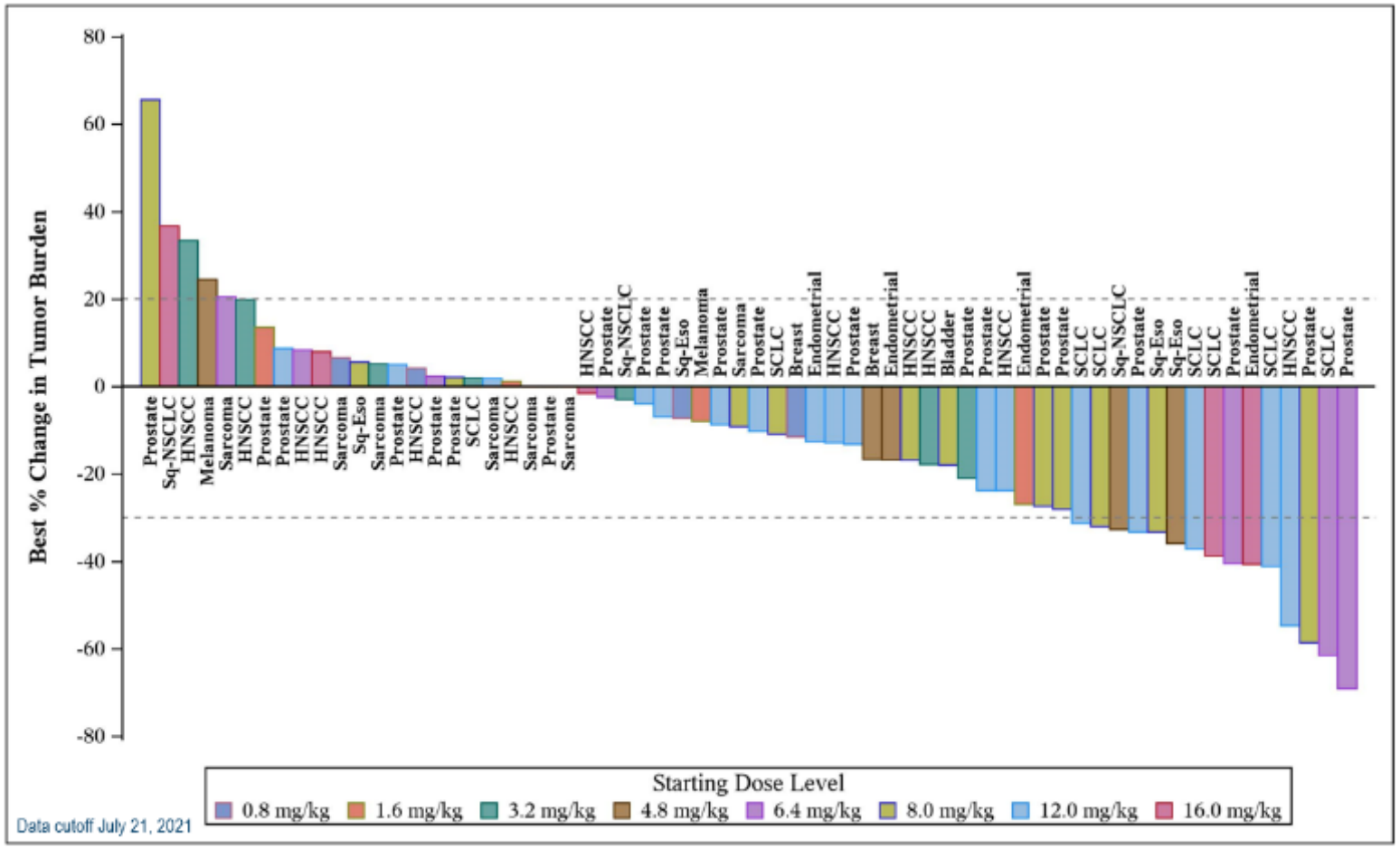
ENHERTU®
Dato-DXd
HER3-DXd

Daiichi-Sankyo



DS-7300: Highlight at ESMO 2021

DS-7300 Ph1/2 study in solid tumors
Dose escalation interim analysis



- **DS-7300**, 4th DXd-ADC, is a B7-H3 directed ADC; no B7-H3 directed therapies are currently approved for treatment of any cancer.
- DS-7300 showed **promising early clinical activity** in heavily pre-treated patients with several types of advanced solid tumors as well as tolerable safety with no DLTs observed.
- This provides preliminary evidence that targeting B7-H3 with DS-7300 may become a new treatment strategy across several types of cancer where current therapeutic options are limited.

DS-7300: High-level Directions

Current expansion cohorts in Ph1/2

- ESCC
- CRPC
- SCLC

Further clinical development

- Fast to market as **Monotherapy**
- **Combination** with SOC(s) to pursue earlier line(s)
- **Explore** other tumor(s) known to express B7-H3

Waiting for data for other tumors

Updates from ongoing Ph1/2 will be disclosed at major oncology upcoming conferences

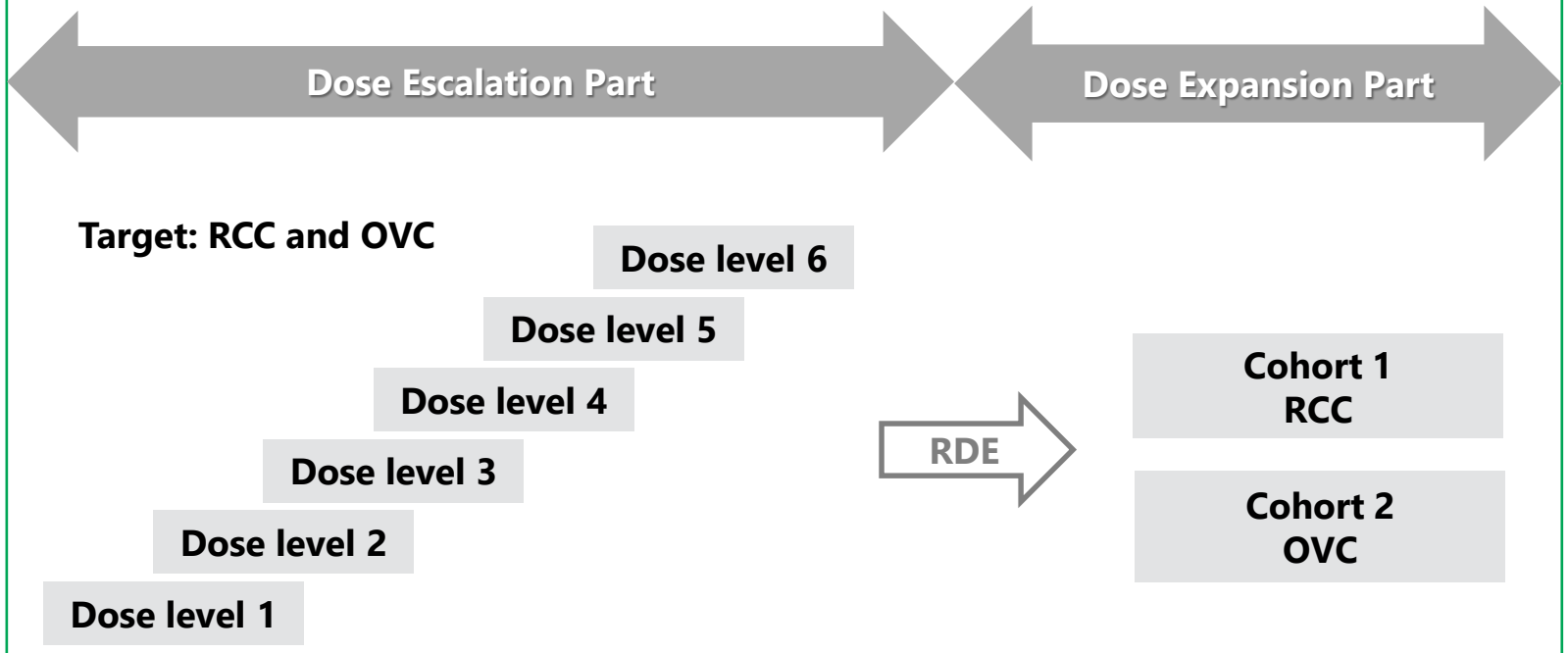
CRPC: castration-resistant prostate cancer, ESCC: esophageal squamous cell carcinoma, SCLC: small cell lung cancer

DS-6000: Ph1 Study Plan

CDH6 (cadherin 6)

- Member of CDH family. The function of CDH6 is still to be fully elucidated. It is said to be related to cell-cell adhesion, epithelial to mesenchymal transition (EMT) and metastasis
- In developmental stage, CDH6 is expressed in kidney, endometrium, placenta and CNS, and **minimal expression in adult normal tissues**
- Highly expressed in **renal cell carcinoma (RCC)** and **ovarian cancer (OVC)**

Ph1 study



- Assess CDH6 levels in all patients retrospectively

- Ph1 study started in Jan 2021, and dose escalation part is currently ongoing

Early efficacy signal in both RCC and OVC are starting to be observed

Introduction

DXd-ADCs

Next Pillars - Clinical

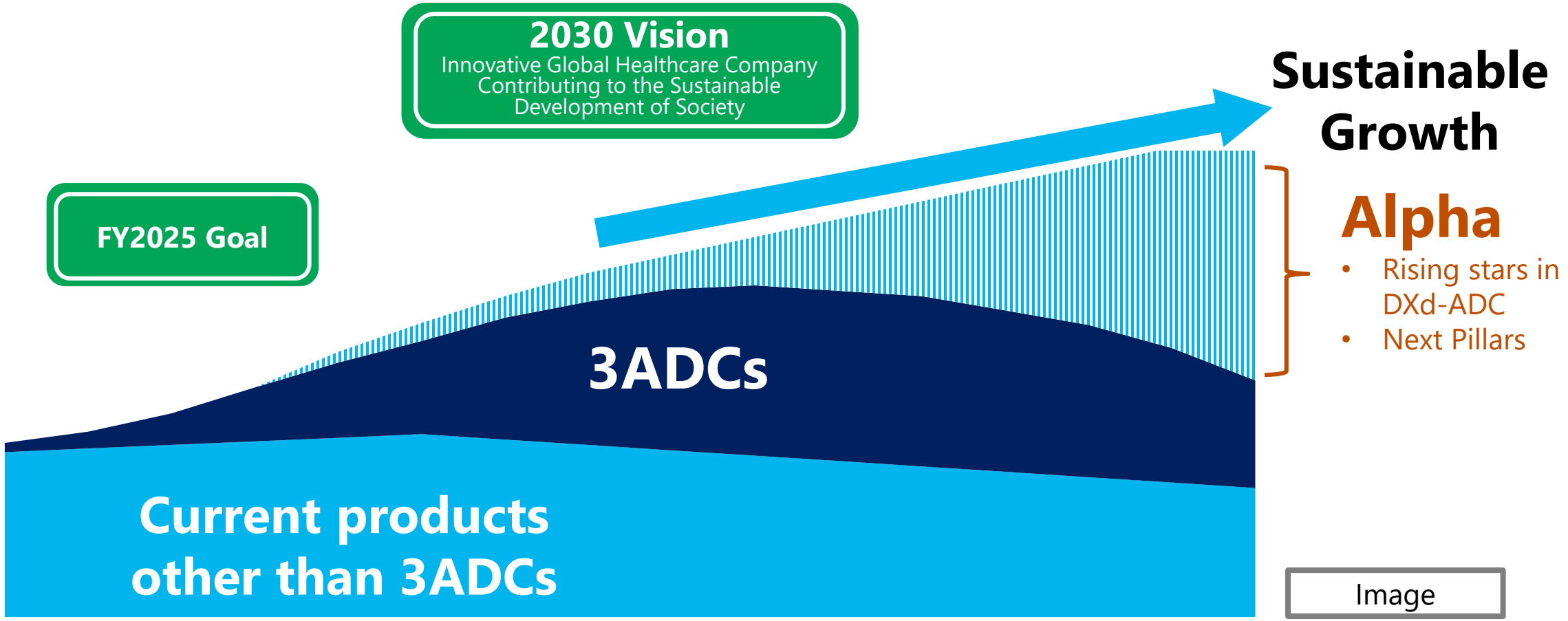
Next Pillars - Research

Transformation of R&D

Identify and Build Pillars for Further Growth Beyond 3ADCs

Continuously develop products and modalities as pillars for our sustainable growth

- Identify new growth drivers following 3ADCs
- Select and advance promising post DXd-ADC modalities



Assumption: revenue for the current products other than 3ADCs will decrease at a constant rate after FY2026

Highlights of Alpha clinical pipeline and recent launch

Phase 1	Phase 2	Phase 3	Launched
DS-7300 (JP/US) B7-H3-directed ADC ESCC, CRPC, SCLC, etc. Rising Stars	**DS-3201** (JP) EZH1/2 inhibitor ATL/L TLR	**Quizartinib** (JP/US/EU/Asia) FLT3 inhibitor 1L AML TLR	**Teserpaturev (DELYTACT/G47Δ)** (JP) Oncolytic virus Malignant glioma
DS-6000 (US) CDH6-directed ADC Renal cell carcinoma, ovarian cancer	**DS-3201** (JP/US/EU/Asia) EZH1/2 inhibitor PTCL		
DS-1055 (JP/US) Anti-GARP antibody Solid tumors	**DS-3201** (EU) EZH1/2 inhibitor BCL		
DS-1211 (US) TNAP inhibitor Pseudoxanthoma elasticum	**DS-5670** (JP) mRNA vaccine COVID-19		
DS-6016 (JP) Anti-ALK2 antibody Fibrodysplasia Ossificans Progressiva			
DS-7011 (US) Anti-TLR7 antibody Systemic lupus erythematosus NEW			

Oncology
Specialty medicine
Vaccine

AML: acute myeloid leukemia, ATL/L: adult T-cell leukemia/lymphoma, BCL: B cell lymphoma, CRPC: castration-resistant prostate cancer, ESCC: esophageal squamous cell carcinoma, SCLC: small cell lung cancer, PTCL: peripheral T-cell lymphoma

We're looking for innovative ways to address unmet medical needs, taking advantage of our unique strengths

Valemetostat (DS-3201): Why we are studying and the status

Why Valemetostat is innovative

- Dual EZH1 and EZH2, overcomes weakness of EZH2 only inhibitor
- Activity in both T and B cell lymphomas
- Joins a growing list of epigenetic agents active in certain cancers

Status

Adult T-cell Leukemia/Lymphoma (ATL)

- Ph2 study results selected for oral presentation at ASH 2021
- **NDA filing in Japan for R/R ATL planned in Dec 2021**
- Orphan drug designation for ATL granted in Japan Nov 2021

Peripheral T-cell Lymphoma (PTCL)

- Registrational Ph2 study for R/R PTCL; FSD Jun 2021
- SAKIGAKE designation in Japan
- Orphan drug designation for PTCL granted in US Dec 2021

B-cell Lymphoma (BCL)

- Study for R/R BCL in collaboration with LYSA (EU); FSD Jun 2021
  - ✓ Signal validation study in monotherapy
  - ✓ 6 cohorts of patients including 2 biology-driven cohorts (EZH2)

LYSA: The Lymphoma Study Association, R/R: relapsed/refractory

DS-7011: Anti-TLR7 antibody

First-in-class compound

Coming soon in Clinical

- **Target indication: Systemic lupus erythematosus (SLE)**
  - Chronic autoimmune disease characterized by autoantibody production, inflammation, and tissue damage in multiple organs
  - Important cause of morbidity and mortality and unmet medical need
- It is estimated that 5 million people worldwide live with lupus
- Supported by AMED (Japan Agency for Medical Research and Development) CiCLE program since April 2020

Mechanism of Action

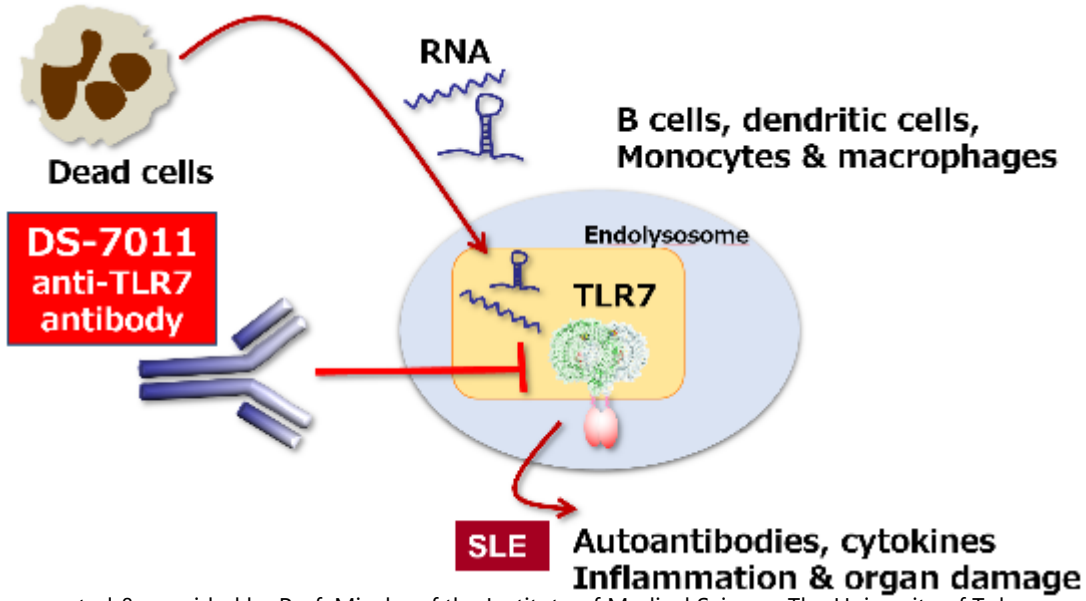


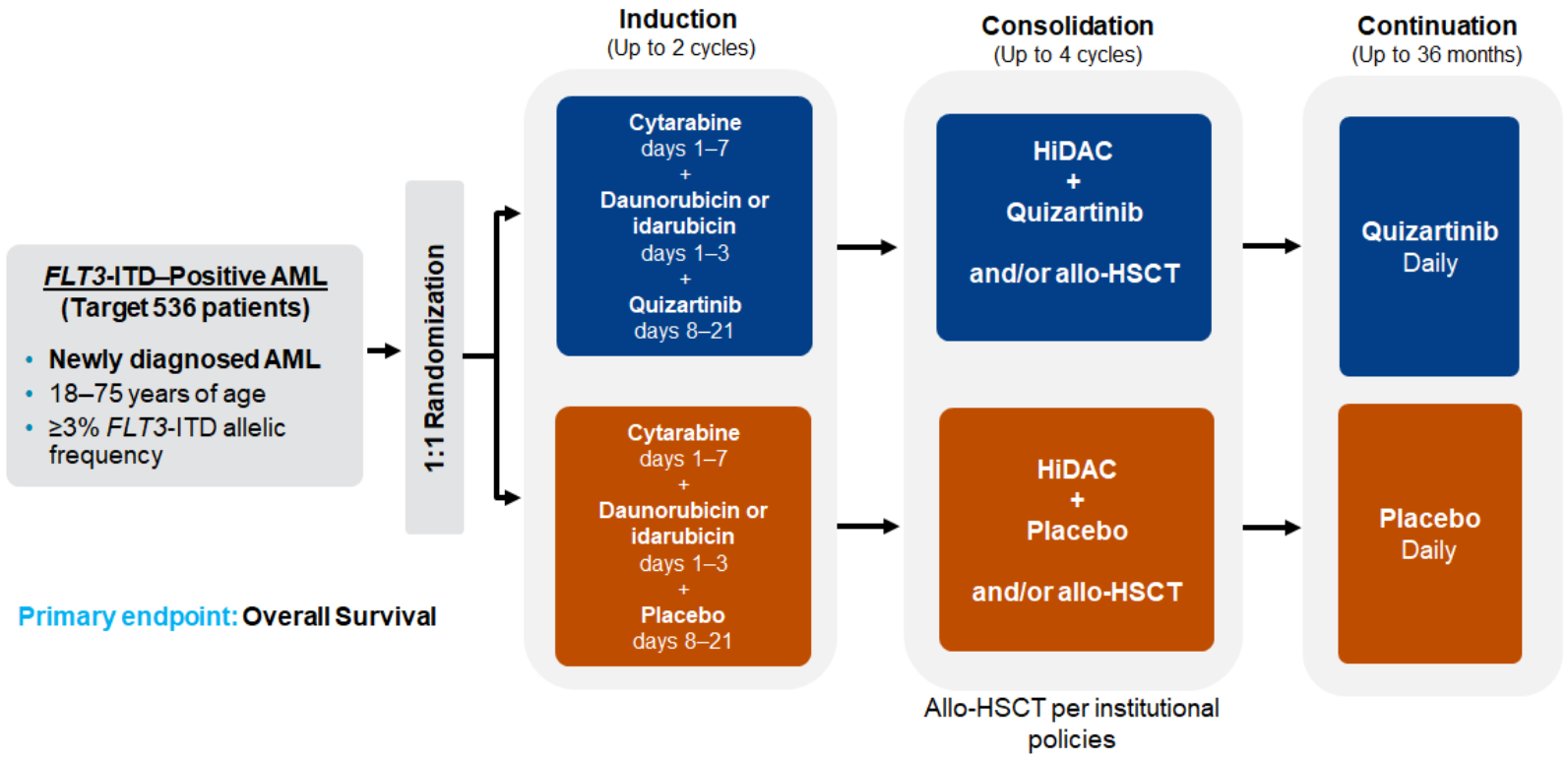
Diagram created & provided by Prof. Miyake of the Institute of Medical Science, The University of Tokyo

Phase 1 Studies

- **IND filed on Nov 17, 2021**
- **Phase 1a**
  - Double-blinded, placebo-controlled, randomized
  - Single ascending intravenous and subcutaneous doses
  - Sequential cohorts of healthy subjects in three stages
    - ✓ Stage 3 will investigate subjects of Japanese ethnicity
  - Objectives: Safety, pharmacokinetics, pharmacodynamics, and immunogenicity
  - Planned start date: January 2022
- **Phase 1b**
  - Double-blinded, placebo-controlled, randomized
  - Multiple intravenous doses (3 doses, one every 4 weeks)
  - Two parallel arms of SLE patients
  - Objectives: Safety, pharmacokinetics, pharmacodynamics, immunogenicity, and preliminary efficacy

Quizartinib:

QuANTUM-First study met primary endpoint of Overall Survival



- High unmet medical need for patients with FLT3-ITD positive AML
- Global submission and launch plans underway
- Data to be presented next year

AML: acute myeloid leukemia, HSCT: hematopoietic stem cell transplantation

ClinicalTrials.gov identifier: NCT02668653

Introduction

DXd-ADCs

Next Pillars - Clinical

Next Pillars - Research

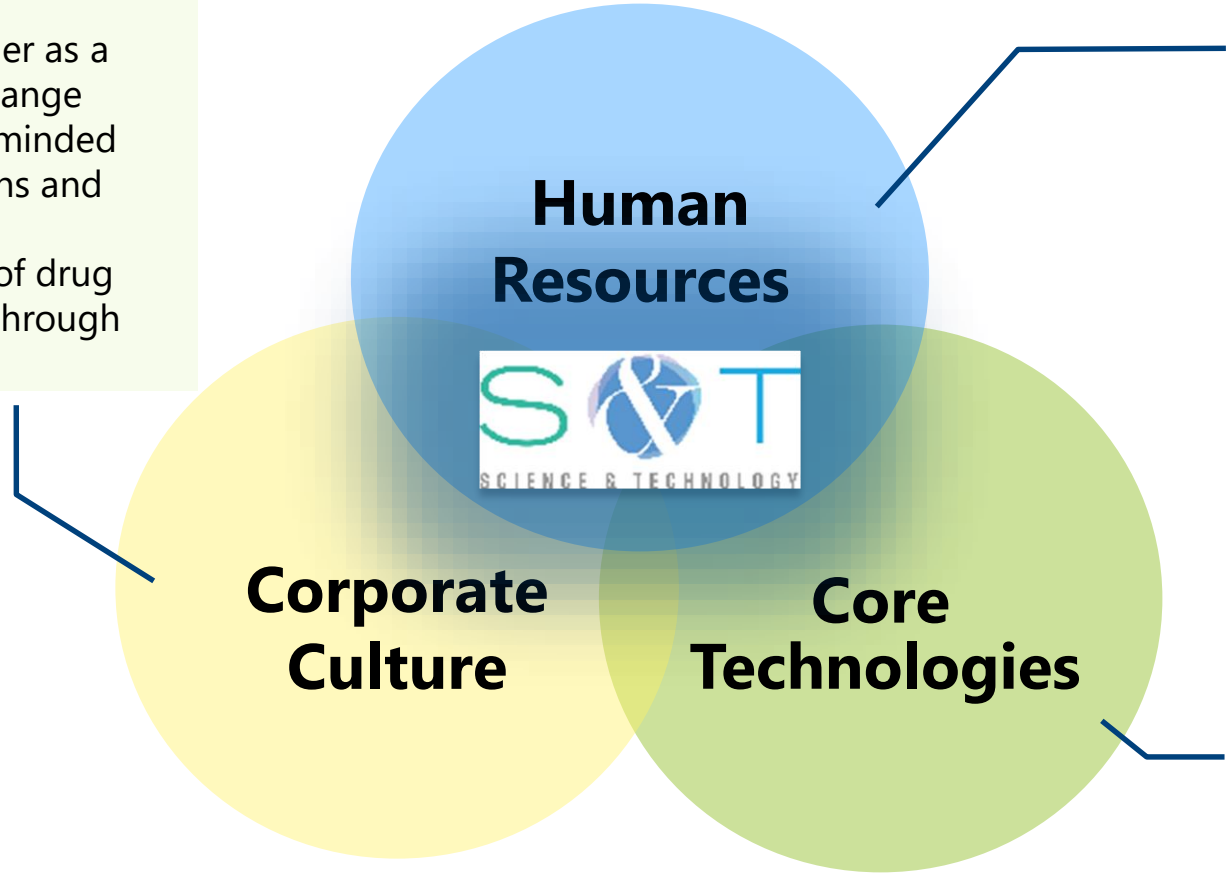
Transformation of R&D

Towards Sustainable Growth

Further enhancement of our strength "Science & Technology" is essential for sustainable growth

Our Strength

- Our corporate culture:
  Researchers respect each other as a specialist in science and exchange opinions in a free and open-minded manner regardless of positions and tenure
- Techniques and experiences of drug development handed down through our history



- Pursue cutting-edge science
- Scientific assessment capabilities
- Technologies originated from craftspersonship
- A high level of engagement
- Eagerness for innovation

- Our proprietary ADC technology platform
- Medicinal chemistry, protein engineering, drug evaluation, computational science and translational research

Research Strategy

Goal: Bring our innovations to meet unmet medical needs

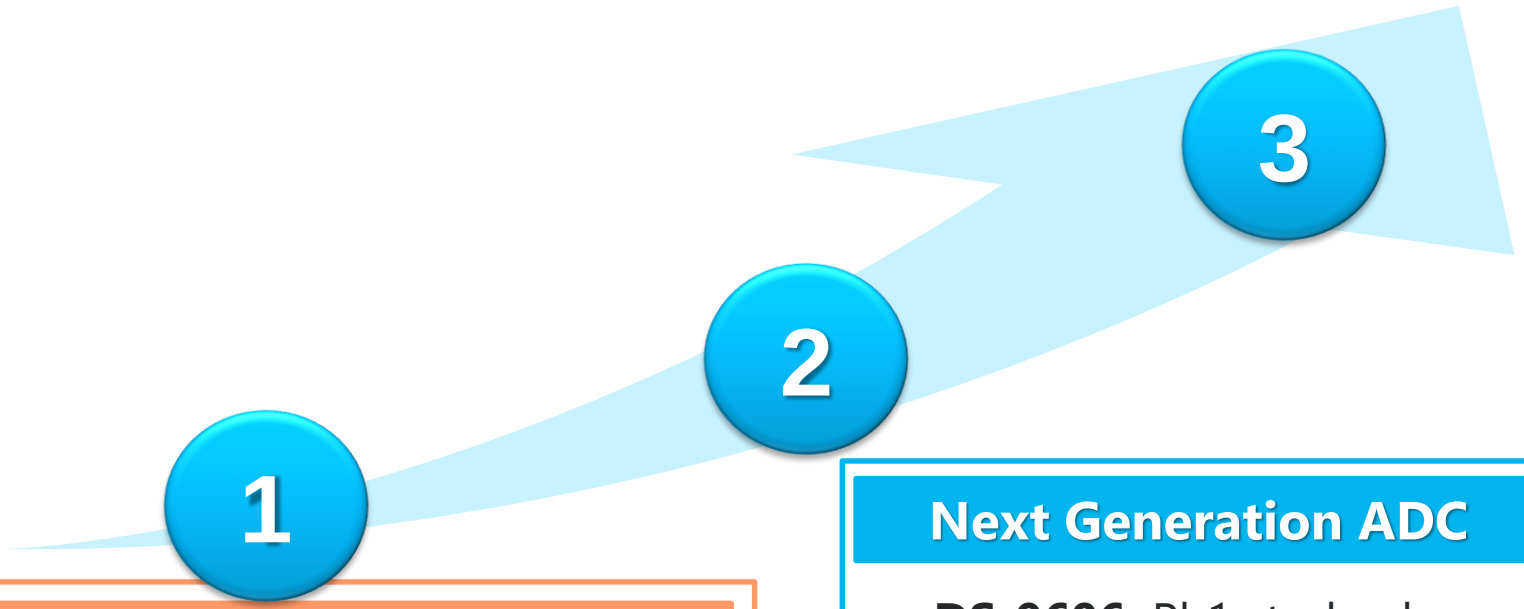
Research focus to maintain competitiveness in global pharma arena

- Comprehensive and continuous review ongoing in Oncology and Specialty Medicine research programs
- External input

Build on areas of scientific strengths

- ADC technology
- Modalities and technologies
- Scientific freedom at discovery stage with close access to clinical expertise to understand unmet medical needs

Sustainable ADC Development



DXd-ADC

- **ENHERTU®:** Launched in multiple indications
- **Dato-DXd:** Ph3 in NSCLC/HR+ BC
- **HER3-DXd:** Pivotal Ph2 in EGFR mut NSCLC
- **DS-7300:** Promising efficacy at Ph1
- **DS-6000:** Ph1 ongoing
- **DS-3939:** Ph1 study planned
- **DS-XXXX:** Preclinical studies ongoing

Next Generation ADC

- **DS-9606:** Ph1 study planned
- **Project XX**
  - ▪
  - ▪

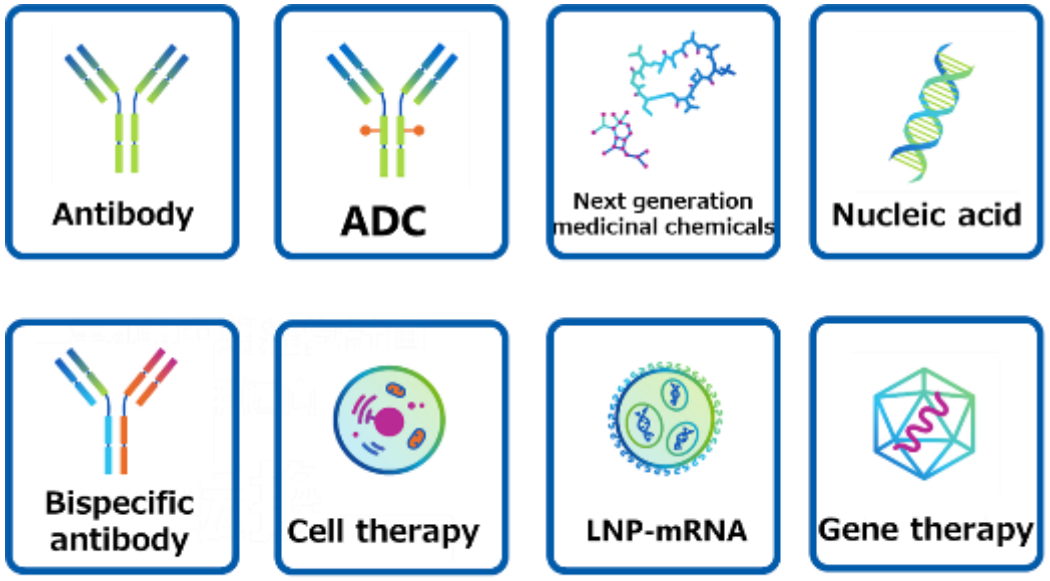
New Concept ADC

- **Project XX**
  - ▪
  - ▪

BC: breast cancer, HR: hormone receptor, NSCLC: non small cell lung cancer

Daiichi Sankyo's Multi-modality Strategy

Optimized modality

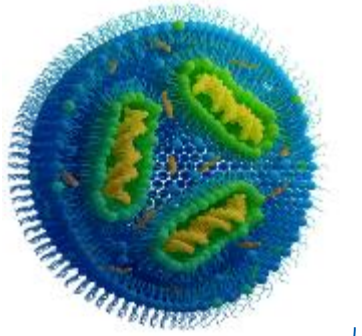


High Unmet Medical Need

- **Select and develop** the most suitable modality for a target disease/etiology from optimized or newly established modalities
- **Appropriate assessment/judgement** of our next growth drivers is the key for sustainable growth
  - Ensure continuous flow of high potential drug candidates by appropriate assessment and prioritization
  - Ensure acceleration of drug development once promising drug candidates are identified

LNP-mRNA vaccine

Characteristics of DS-5670



Lipid nanoparticle(LNP)-mRNA

- **DS original cationic lipid** is applied
- **Receptor Binding Domain (RBD)** is applied as antigen

  but not entire spike protein

◆**Top priority:** Develop domestic COVID-19 vaccine

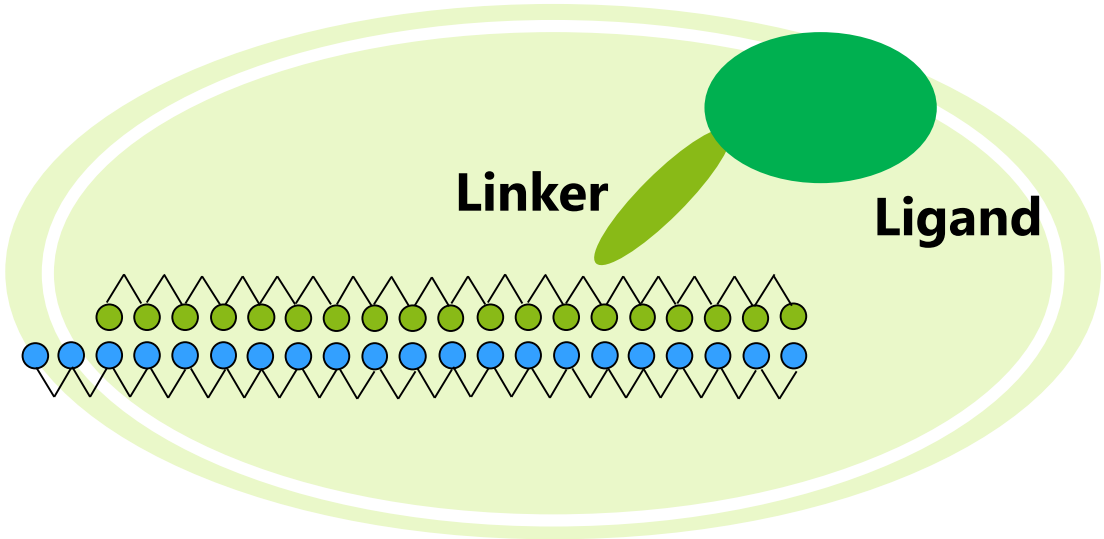
◆**Next step:** Build a platform that streamlines development and manufacturing of vaccines for future emerging/re-emerging infectious diseases.

- ➢ Several research themes using LNP-mRNA technology are ongoing

Participating in AMED's vaccine development support program "Development of mRNA vaccine for COVID-19"

Next Generation siRNA Platform

iMED-siRNA



iMED-siRNA: Further improvement with modified nucleotides and ligand-linkers from MED-siRNA (alternately combined 2'-O-methyl RNA and DNA)

Main features of *iMED-siRNA*

- Knock-down of disease-related gene effectively
- Long duration of action
- ex-Hepatic delivery
- Multiple research themes are ongoing

Gene Therapy

Gene therapy offers novel treatments that cannot be achieved with small molecule or antibody drugs

Patient number

Non-Rare Disease

Starting with Rare Disease
- ✓ High probability of success
- ✓ DS products: 2 INDs in 2024-2025
- ✓ Collaboration with Ultragenyx

Expand to Non-Rare Disease
- ✓ Establishment of technology platform
  - GOI of new Mode of Action
- ✓ Discovery research toward "Change SOC"
  - CNS, Cardio-Renal, Retinal diseases, etc.

Monogenic Rare Disease

2020 2021 2022 2023 2024 2025 2026 2027 2028 2029 2030 2031 2032 2033 2034 2035

Timing of INDs (preliminary)

Rare diseases ★★★★▪▪▪▪

Non-Rare diseases ☆▪▪▪▪

Collaborations with AAV Players to enrich Pipelines and gain Technology

2020～
ViGeneron

2021～
LogicBio Therapeutics

CNS: central nervous system, GOI: gene of interest

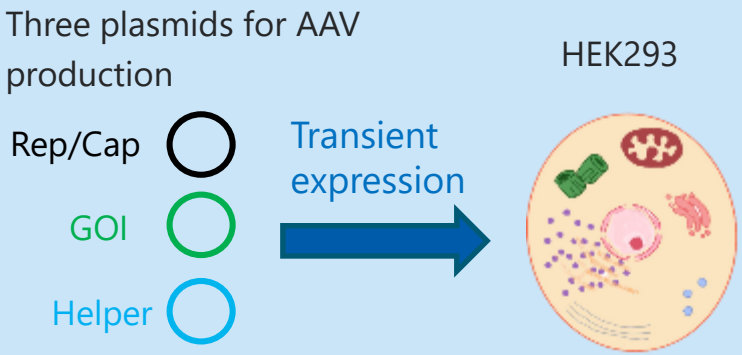
Strategic Partnership with Ultragenyx

Achieved initial target of Technology transfer,
on track to start manufacturing investigational gene therapy drug by the mid-2020s

- Entered into a strategic partnership with Ultragenyx Pharmaceutical Inc. for non-exclusive use of Adeno-associated virus (AAV) vector production system (Mar. 2020)
- **Achieved initial target of technology transfer (Nov 2021)**
- On track to establish AAV vector manufacturing technologies

AAV production systems

PCL cell system	HEK293 cell system
Recombinant cells harboring genes for AAV production	Three plasmids for AAV production



PCL: producer cell line

Introduction

DXd-ADCs

Next Pillars - Clinical

Next Pillars - Research

Transformation of R&D

Create ONE Global R&D team

Now that DXd-ADC technology platform is proving to be promising and various modalities have potentials to become the new growth drivers following the 3ADCs, optimization of R&D organization is crucial to enable efficient global development of rich pipeline.

BEFORE

- Collaboration of regional teams (**East and West**)
- Multiple layers for decision making

Inefficiency

Redundancy

To Be

- **Unified global organization**
- Simplified governance with more empowerment

Streamlined

Scalable

Sustainable

Enhance Our Capabilities

Become Competitive at Global Level

Daiichi Sankyo unique model to build development capabilities for global oncology company

- **Research**
  - Oncology Research pipeline is solid
  - Our ADC technology is first-class and will continue to be very productive in generating next generation ADCs for oncology and non-oncology applications
  - Many other specialized, unique scientific strengths in both Oncology and Specialty Medicine, including applications of therapeutic modalities beyond traditional small molecules and biologics
- **Precision Medicine***
  - Key technologies and platforms for Precision Medicine can maximize project value through drug discovery and development phases
- **Development**
  - Global Project Teams, the cross-functional teams and center of our R&D, are enabled and empowered
  - Further enhance global drug development capabilities regardless of geographic location

*A form of medicine that uses information about a person's own genes or proteins to prevent, diagnose, or treat disease.

Agenda

1. Introduction

2. R&D strategy

3. **Q&A session**

Appendix

- FY2021 News Flow
- Major R&D Milestones in FY2021
- Major R&D Pipeline
- SABCS ENHERTU® presentation
  - DB-03 subanalysis data
- SABCS Dato-DXd presentation
  - TNBC data from Ph1 study
- ASH DS-3201 presentation
  - ATL Ph2 data

FY2021 News Flow

As of Dec 2021

Planned data disclosures

ASCO Genitourinary Cancers Symposium (Feb 17-19)	
DS-7300	Solid tumor Ph1/2 • CRPC subanalysis data

Regulatory decisions

Efient®	Ischemic stroke • Japan: FY2021 Q3

Planned regulatory submissions

Enhertu®	DESTINY-Breast03: HER2 positive BC, 2L, Ph3 • FY2021 Q3
Valemetostat (DS-3201)	Registrational Ph2: ATL/L • Japan: FY2021 Q3

Key data readouts

Enhertu®	DESTINY-Breast04: HER2 low BC, post chemo, Ph3 • FY2021 Q4

Planned pivotal study initiation

Enhertu®	DESTINY-Lung04: HER2 mutated NSCLC, 1L, Ph3 • FY2021 Q3
Dato-DXd	TROPION-Lung08: NSCLC w/o AGAs, 1L, pembrolizumab combo Ph3 • FY2021 Q4
DS-5670	Ph3: COVID-19 mRNA vaccine • FY2021 Q4

Underlined: New or updated from FY2021 Q2

AGA: actionable genomic alterations, AML: acute myeloid leukemia, ATL/L: adult T-cell leukemia/lymphoma, BC: breast cancer, CRPC: castric resistant prostate cancer, GC: gastric cancer, NSCLC: non small cell lung cancer

Major R&D Milestones in FY2021 (3ADCs)

As of Dec 2021

Project		Target Indications [phase, study name]	FY2021 Q1	Q2	Q3	Q4
ENHERTU®	BC	HER2+, 2L [P3, DESTINY-Breast03]		TLR obtained	Filing anticipated	
		HER2 low, post chemo [P3, DESTINY-Breast04]				TLR anticipated
		HER2+, 1L [P3, DESTINY-Breast09]	Study started			
		HER2+, neoadjuvant [P3, DESTINY-Breast11]			**Study started**	
	GC	HER2+, 2L [P2, DESTINY-Gastric02]	TLR obtained		**Filed (Europe)**	
		HER2+, 2L [P3, DESTINY-Gastric04]	Study started			
		HER2+, 3L [P2, DESTINY-Gastric06]		Study started		
	NSCLC	HER2+/mutated [P2, DESTINY-Lung01]	TLR obtained			
		HER2+, combination [P1b, DESTINY-Lung03]			**Study started**	
		HER2 mutated, 1L [P3, DESTINY-Lung04]			Study start planned	
Dato-DXd		TNBC, durvalumab combo [P1b/2, BEGONIA]	Study started			
		HR+ BC, 2/3L [P3, TROPION-Breast01]			**Study started**	
		NSCLC w/o AGAs, 1L, pembrolizumab combo [P3, TROPION-Lung08]				Study start planned
HER3-DXd		EGFR mutated NSCLC, osimertinib combo [P1]	Study started			

Red underlined: new or updated from FY2021 Q2

AGA: actionable genomic alterations, BC: breast cancer, GC: gastric cancer, NSCLC: non-small cell lung cancer, TLR: Top Line Results, TNBC: triple negative breast cancer

Major R&D Milestones in FY2021 (Alpha)

As of Dec 2021

Project	Target Indications [phase, study name, region]	FY2021 Q1	Q2	Q3	Q4
Quizartinib	AML, 1L [P3, JP/US/EU/Asia]			**TLR obtained**	
Pexidartinib	Tenosynovial giant cell tumor [P2, JP]	Study started			
Teserpaturev/G47Δ	Malignant glioma [IIS, JP]	Approved			
Valemetostat (DS-3201)	ATL/lymphoma [P2 registration, JP]		TLR obtained	**Filing anticipated (JP)**	
	PTCL [P2 registration, JP/US/EU/Asia]	Study started			
DS-1594	AML, ALL [P1/2, US]	Study started			
Lixiana®	AF in the very elderly [P3, ELDERCARE-AF, JP]		Approved		
Efient®	Ischemic stroke [P3, PRASTRO III, JP]			Approval anticipated	
Tarlige®	Central neuropathic pain [P3, JP]	Filed			
DS-6016	Fibrodysplasia Ossificans Progressiva [P1, JP]	Study started			
VN-0200	RS virus vaccine [P1, JP]	Study started			
DS-5670	COVID-19 mRNA vaccine [P2, JP]			**Study started**	
	COVID-19 mRNA vaccine [P3, TBD]				Study start planned

Red underlined: new or updated from FY2021 Q2

AF: atrial fibrillation, ALL: acute lymphoblastic leukemia, AML: acute myeloid leukemia, ATL: adult T-cell leukemia, IIS: investigator-initiated study, PTCL: peripheral T-cell lymphoma, TBD: to be determined, TLR: Top Line Results

Major R&D Pipeline: 3ADCs

As of Dec 2021

Phase 1		Phase 2	Phase 3	Submitted
(JP/US) NSCLC, TNBC, HR+ BC TROPION-PanTumor01	(US/EU/Asia) HER2+ BC 2L~/1L DESTINY-Breast07	(US/EU/Asia) TNBC (durvalumab combo) BEGONIA	(JP/US/EU/Asia)HER2+ BC 3L DESTINY-Breast02	(JP/US/EU/Asia) HER2+ BC 2L DESTINY-Breast03
(JP/US/EU/Asia) NSCLC (w/o actionable mutation, pembrolizumab combo) TROPION-Lung02	(US/EU/Asia) HER2 low BC chemo naïve/ post chemo DESTINY-Breast08	(China) HER2+ GC 3L DESTINY-Gastric06	(JP/US/EU/Asia) HER2 low BC post chemo DESTINY-Breast04	(US/EU) HER2+ GC 2L DESTINY-Gastric02
(JP/US/EU/Asia) NSCLC (w/o actionable mutation, durvalumab combo) TROPION-Lung04	(US/EU/Asia) HER2+ GC combo, 2L~/1L DESTINY-Gastric03	(JP/US/EU)HER2+/mutated NSCLC 2L~ DESTINY-Lung01	(JP/US/EU/Asia) HER2+ BC post neoadjuvant DESTINY-Breast05	
(US/EU/Asia) TNBC (durvalumab combo) BEGONIA	(EU/Asia)HER2+ NSCLC (durvalumab combo) 1L DESTINY-Lung03	(JP/US/EU/Asia) HER2 mutated NSCLC 2L~ DESTINY-Lung02	(JP/US/EU/Asia) HER2 low BC chemo naive DESTINY-Breast06	
(JP/US/EU/Asia) NSCLC	(US/EU) BC, bladder (nivolumab combo)	(US/EU/Asia) NSCLC (durvalumab combo) 2L~ HUDSON	(US)HER2+ BC 1L DESTINY-Breast09	
(JP/US)EGFR mutated NSCLC (osimertinib combo)	(US/EU) BC, NSCLC (pembrolizumab combo)	(JP/US/EU) HER2+ CRC 3L DESTINY-CRC01	(JP/US/EU/Asia) HER2+ BC neoadjuvant DESTINY-Breast11	
(JP/US) BC		(JP/US/EU/Asia) HER2+ CRC 3L DESTINY-CRC02	(JP/EU/Asia) HER2+ GC 2L DESTINY-Gastric04	
		(US/EU/Asia) HER2 mutated tumor DESTINY-PanTumor01	(US/EU/Asia) NSCLC 1L (w/ exon 19 or exon 20 mutation) DESTINY-Lung04	
		(US/EU/Asia) HER2 expressing tumor DESTINY-PanTumor02	(JP/US/EU/Asia) NSCLC (w/o actionable mutation) TROPION-Lung01	
		(JP/US/EU/Asia) NSCLC (w/ actionable mutation) TROPION-Lung05	(JP/US/EU/Asia) HR+ BC 2/3L TROPION-Breast01	
		(JP/US/EU/Asia) EGFR mutated NSCLC HERTHENA-Lung01		

ENHERTU®

Dato-DXd

HER3-DXd

BC: breast cancer, CRC: colorectal cancer, GC: gastric cancer, NSCLC: non-small cell lung cancer, TNBC: triple negative breast cancer

□: project in oncology that is planned to be submitted for approval based on the results of phase 2 trials

: Breakthrough Designation (US)

Major R&D Pipeline: Alpha

As of Dec 2021

Phase 1		Phase 2	Phase 3	Submitted
DS-7300 (JP/US) B7-H3-directed ADC ESCC, CRPC, SCLC, etc.	**PLX2853** (US) BET inhibitor AML	**Valemetostat (DS-3201)** (JP) EZH1/2 inhibitor ATL/L	**Quizartinib** (JP/US/EU/Asia) FLT3 inhibitor 1L AML	**Tarlige** (JP) $\alpha_2\delta$ Ligands Central neuropathic pain
DS-6000 (US) CDH6-directed ADC Renal cell carcinoma, ovarian cancer	**PLX2853** (US) BET inhibitor Solid tumor	**Valemetostat (DS-3201)** (JP/US/EU/Asia) EZH1/2 inhibitor PTCL	**Pexidartinib** (JP/Asia) CSF-1/KIT/FLT3 inhibitor Tenosynovial giant cell tumor	**Efient** (JP) ADP receptor inhibitor Ischemic stroke
DS-1055 (JP/US) Anti-GARP antibody Solid tumors	**PLX2853** (US) BET inhibitor Gynecologic neoplasms, ovarian cancer	**DS-1001** (JP) Mutant IDH1 inhibitor Glioma	**Minnebro** (JP) MR blocker Diabetic nephropathy	**VN-0107/MEDI3250** (JP) Live attenuated influenza vaccine nasal spray
DS-1211 (US) TNAP inhibitor Pseudoxanthoma elasticum	**PLX2853** (US) BET inhibitor Prostate cancer	**DS-5141** (JP) ENA oligonucleotide DMD	**VN-0102/JVC-001** (JP) Measles mumps rubella combined vaccine	
DS-6016 (JP) Anti-ALK2 antibody Fibrodysplasia Ossificans Progressiva	**DS-1594** (US) Menin-MLL binding inhibitor AML, ALL	**DS-5670** (JP) mRNA vaccine COVID-19		
DS-7011 (US) Anti-TLR7 antibody Systemic lupus erythematosus	**VN-0200** (JP) RS virus vaccine RS virus			

Oncology
Specialty medicine
Vaccine

AF: atrial fibrillation, ALL: acute lymphoblastic leukemia, AML: acute myeloid leukemia, ATL/L: adult T-cell leukemia/lymphoma, CRPC: castration-resistant prostate cancer, DMD: Duchenne muscular dystrophy, ESCC: esophageal squamous cell carcinoma, GIST: gastrointestinal stromal tumor, SCLC: small cell lung cancer, PTCL: peripheral T-cell lymphoma

□: project in oncology that is planned to be submitted for approval based on the results of phase 2 trials : SAKIGAKE Designation (JP) Orphan drug designation (JP/US/Europe)

Trastuzumab Deruxtecan (T-DXd) Versus Trastuzumab Emtansine (T-DM1) in Patients With HER2+ Metastatic Breast Cancer: Subgroup Analyses From the Randomized Phase 3 Study DESTINY-Breast03

Sara A. Hurvitz, MD[a], Sung-Bae Kim, Wei-Pang Chung,
Seock-Ah Im, Yeon Hee Park, Roberto Hegg, Min-Hwan Kim, Ling-Ming Tseng, Vanessa Petry, Chi-Feng Chung,
Hiroji Iwata, Erika Hamilton, Giuseppe Curigliano, Binghe Xu, Caleb Lee,
Yali Liu, Jillian Cathcart, Emarjola Bako, Sunil Verma, Javier Cortes

On behalf of the DESTINY-Breast03 investigators

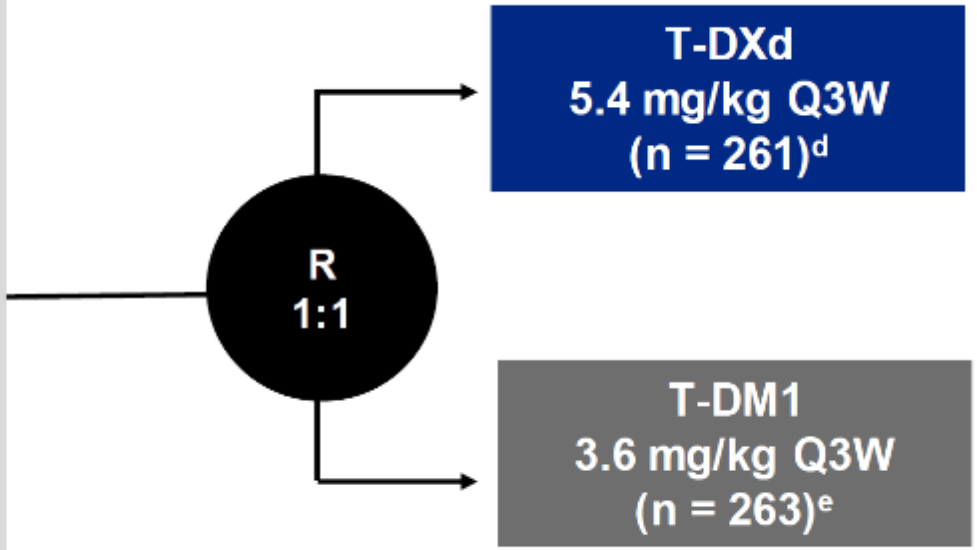
[a]Department of Medicine, David Geffen School of Medicine, University of California, Los Angeles, Jonsson Comprehensive Cancer Center, Los Angeles, CA USA

DESTINY-Breast03: First Randomized Phase 3 Study of T-DXd

An open-label, multicenter study (NCT03529110)

Patients (N = 524)
- Unresectable or metastatic HER2-positive[a] breast cancer that has been previously treated with trastuzumab and a taxane[b]
- Could have clinically stable, treated brain metastases[c]
  - ≥2 weeks between end of whole brain radiotherapy and study enrollment

Stratification factors
- Hormone receptor status
- Prior treatment with pertuzumab
- History of visceral disease



Primary endpoint
- PFS (BICR)

Key secondary endpoint
- OS

Secondary endpoints
- ORR (BICR and investigator)
- DOR (BICR)
- PFS (investigator)
- Safety

- At the time of data cutoff (May 21, 2021), 125 (48.6%) T-DXd patients and 214 (82.0%) T-DM1 patients had discontinued treatment
- Median follow up was 15.9 months
- BMs were measured at baseline by CT or MRI and lesions were monitored throughout the study

BICR, blinded independent central review; BM, brain metastasis; CT, computed tomography; DOR, duration of response; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; ISH, in situ hybridization; MRI, magnetic resonance imagining; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; Q3W, every 3 weeks; R, randomization; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan.
[a]HER2 IHC3+ or IHC2+/ISH+ based on central confirmation. [b]Progression during or <6 months after completing adjuvant therapy involving trastuzumab and a taxane. [c]Prior to protocol amendment, patients with stable, untreated BM were eligible. [d]4patients were randomly assigned but not treated. [e]2patients were randomly assigned but not treated.

Baseline Characteristics and Prior Therapies

	T-DXd n = 261	T-DM1 n = 263
Age, median (range), years	54.3 (27.9-83.1)	54.2 (20.2-83.0)
Female, n (%)	260 (99.6)	262 (99.6)
Region, n (%)		
Europe	54 (20.7)	50 (19.0)
Asia	149 (57.1)	160 (60.8)
North America	17 (6.5)	17 (6.5)
Rest of world	41 (15.7)	36 (13.7)
HER2 status (IHC[a]), n (%)		
3+	234 (89.7)	232 (88.2)
2+ (ISH amplified)	25 (9.6)	30 (11.4)
1+ | Not evaluable	1 (0.4) | 1 (0.4)	0 | 1 (0.4)
ECOG PS, n (%)		
0 | 1	154 (59.0) | 106 (40.6)	175 (66.5) | 87 (33.1)
Hormone receptor, n (%)		
Positive | Negative	131 (50.2) | 130 (49.8)	134 (51.0) | 129 (49.0)
History of BM, n (%)		
Yes | No	62 (23.8) | 199 (76.2)	52 (19.8) | 211 (80.2)
BM at baseline,[b] n (%)		
Yes | No	43 (16.5) | 218 (83.5)	39 (14.8) | 224 (85.2)
Visceral disease, n (%)		
Yes | No	184 (70.5) | 77 (29.5)	185 (70.3) | 78 (29.7)
Prior treatment for mBC, n (%)	240 (92.0)	234 (89.0)
Prior lines of therapy in the metastatic setting,[c] n (%)		
0-1 | ≥2	132 (50.6) | 129 (49.4)	126 (47.9) | 137 (52.1)
Prior cancer therapy,[d] n (%)		
Trastuzumab	260 (99.6)	262 (99.6)
Pertuzumab	162 (62.1)	158 (60.1)

BM, brain metastasis; ECOG PS, Eastern Cooperative Oncology Group performance status; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; ISH, in situ hybridization; BC, metastatic breast cancer; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan.

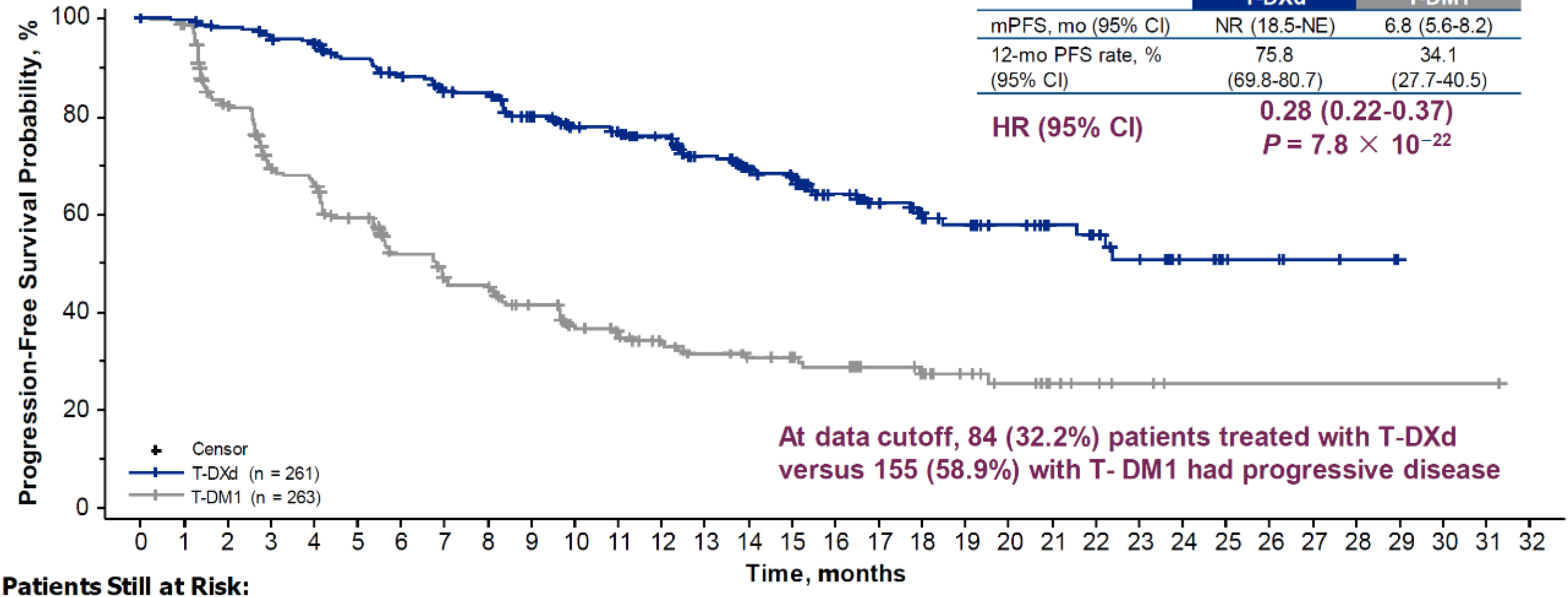
[a]HER2-status as evaluated by central laboratory. [b]Patients with BM at baseline compose the patient population described in all subsequent slides. [c]includes patients with rapid progression as 1 line of treatment**.** Rapid progression defined as progression within 6 months of (neo)adjuvant therapy or 12 months if regimen contained pertuzumab. Line of therapy does not include endocrine therapy. [d]All patients received at least 1 prior cancer therapy. One patient who underwent prior T-DM1 treatment was enrolled in error in the T-DXd arm.

Primary Endpoint: PFS by BICR

	T-DXd	T-DM1
mPFS, mo (95% CI)	NR (18.5-NE)	6.8 (5.6-8.2)
12-mo PFS rate, % (95% CI)	75.8 (69.8-80.7)	34.1 (27.7-40.5)

HR (95% CI) 0.28 (0.22-0.37)

$P = 7.8 \times 10^{-22}$



At data cutoff, 84 (32.2%) patients treated with T-DXd versus 155 (58.9%) with T- DM1 had progressive disease

Patients Still at Risk:

T-DXd (261)	261	256	250	244	240	224	214	202	200	183	168	164	150	132	112	105	79	64	53	45	36	29	25	19	10	6	5	3	2	0		
T-DM1 (263)	263	252	200	163	155	132	108	96	93	78	65	60	51	43	37	34	29	23	21	16	12	8	6	4	1	1	1	1	1	1	1	1	0

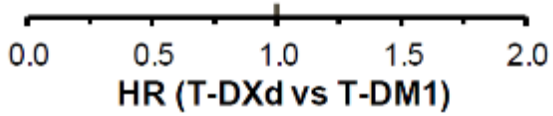
BICR, blinded independent central review; HR, hazard ratio; mPFS, median progression-free survival; NE, not estimable; NR, not reached; PFS, progression-free survival; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan.

Median PFS follow-up for T-DXd was 15.5 months (range, 15.1-16.6) and was 13.9 months (range, 11.8-15.1) for T-DM1.

Cortés et al. *Ann Oncol*. 2021; 32(suppl_5):S1283-S1346. 10.1016/annonc/annonc741

PFS in Key Subgroups

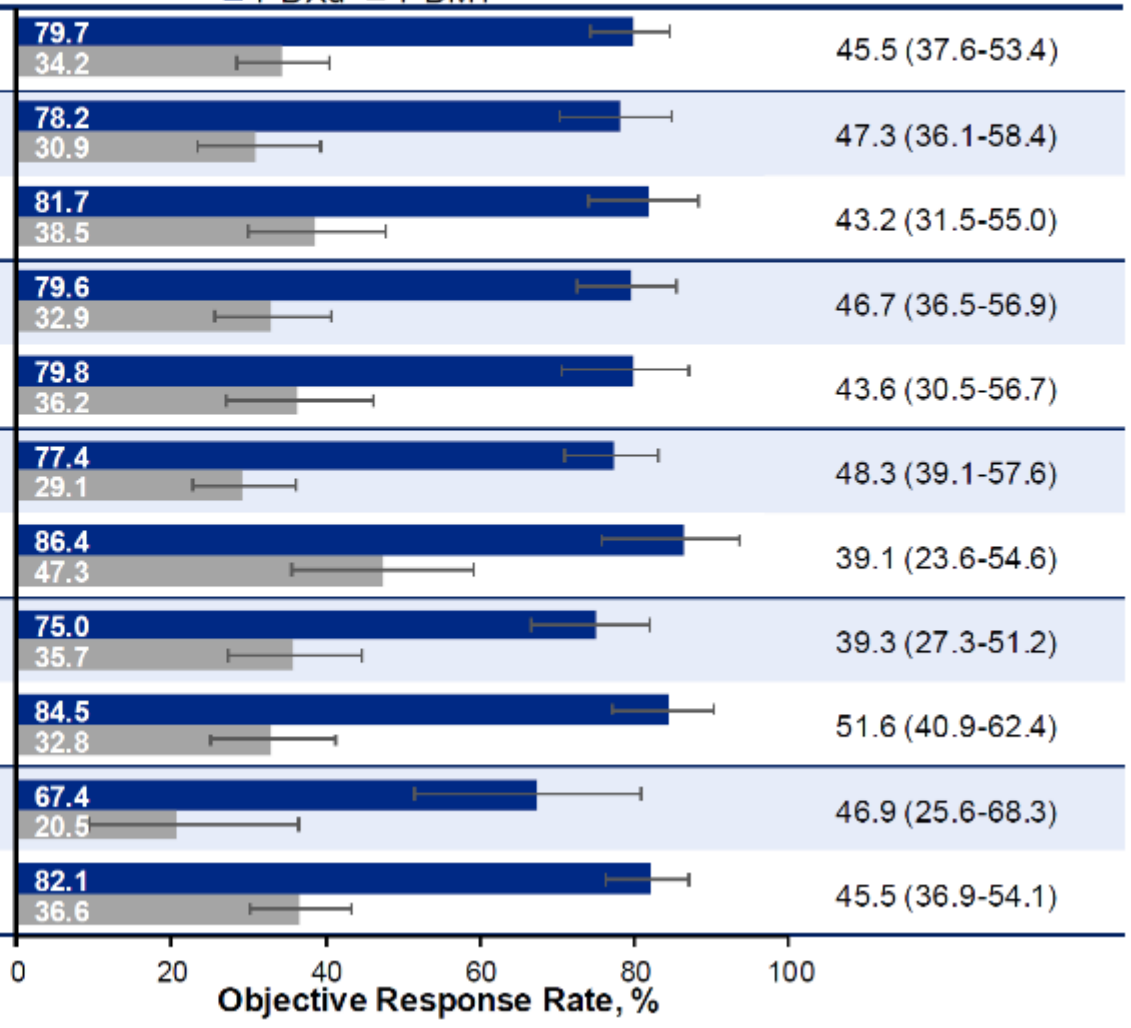
		Number of Events		Median PFS, mo (95% CI)		HR (95% CI)
		T-DXd	T-DM1	T-DXd	T-DM1	
All patients		87/261	158/263	NE (18.5-NE)	6.8 (5.6-8.2)	0.2840 (0.2165-0.3727)
Hormone receptor status	Positive (n = 272)	46/133	84/139	22.4 (17.7-NE)	6.9 (4.2-9.8)	0.3191 (0.2217-0.4594)
	Negative (n = 248)	41/126	73/122	NE (18.0-NE)	6.8 (5.4-8.3)	0.2965 (0.2008-0.4378)
Prior pertuzumab treatment	Yes (n = 320)	57/162	98/158	NE (18.5-NE)	6.8 (5.4-8.3)	0.3050 (0.2185-0.4257)
	No (n = 204)	30/99	60/105	NE (16.5-NE)	7.0 (4.2-9.7)	0.2999 (0.1924-0.4675)
Visceral disease	Yes (n = 384)	72/195	123/189	22.2 (16.5-NE)	5.7 (4.2-7.0)	0.2806 (0.2083-0.3779)
	No (n = 140)	15/66	35/74	NE (NE-NE)	11.3 (6.8-NE)	0.3157 (0.1718-0.5804)
Prior lines of therapy[a]	0-1 (n = 258)	46/132	75/126	22.4 (17.9-NE)	8.0 (5.7-9.7)	0.3302 (0.2275-0.4794)
	≥2 (n = 266)	41/129	83/137	NE (16.8-NE)	5.6 (4.2-7.1)	0.2828 (0.1933-0.4136)
Patients with BM	Yes (n = 82)	22/43	27/39	15.0 (12.5-22.2)	3.0 (2.8-5.8)	0.2465 (0.1341-0.4529)
	No (n = 442)	65/218	131/224	NE (22.4-NE)	7.1 (5.6-9.7)	0.2971 (0.2199-0.4014)



BM, brain metastasis; HR, hazard ratio; NE, not estimable; PFS, progression-free survival; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan.
[a]Patients with rapid progression on (neo)adjuvant therapy were included. Line of therapy does not include endocrine therapy.

Confirmed ORR Across Patient Subgroups

		T-DXd (n = 261) No. of Patients With Confirmed CR/PR	T-DM1 (n = 263) No. of Patients With Confirmed CR/PR	Difference of T-DXd vs T-DM1, % (95% CI)
All patients		208/261	90/263	45.5 (37.6-53.4)
Hormone receptor status	Positive (n = 272)	104/133	43/139	47.3 (36.1-58.4)
	Negative (n = 248)	103/126	47/122	43.2 (31.5-55.0)
Prior pertuzumab treatment	Yes (n = 320)	129/162	52/158	46.7 (36.5-56.9)
	No (n = 204)	79/99	38/105	43.6 (30.5-56.7)
Visceral disease	Yes (n = 384)	151/195	55/189	48.3 (39.1-57.6)
	No (n = 140)	57/66	35/74	39.1 (23.6-54.6)
Prior lines of therapy[a]	0-1 (n = 258)	99/132	45/126	39.3 (27.3-51.2)
	≥2 (n = 266)	109/129	45/137	51.6 (40.9-62.4)
Patients with BM	Yes (n = 82)	29/43	8/39	46.9 (25.6-68.3)
	No (n = 442)	179/218	82/224	45.5 (36.9-54.1)



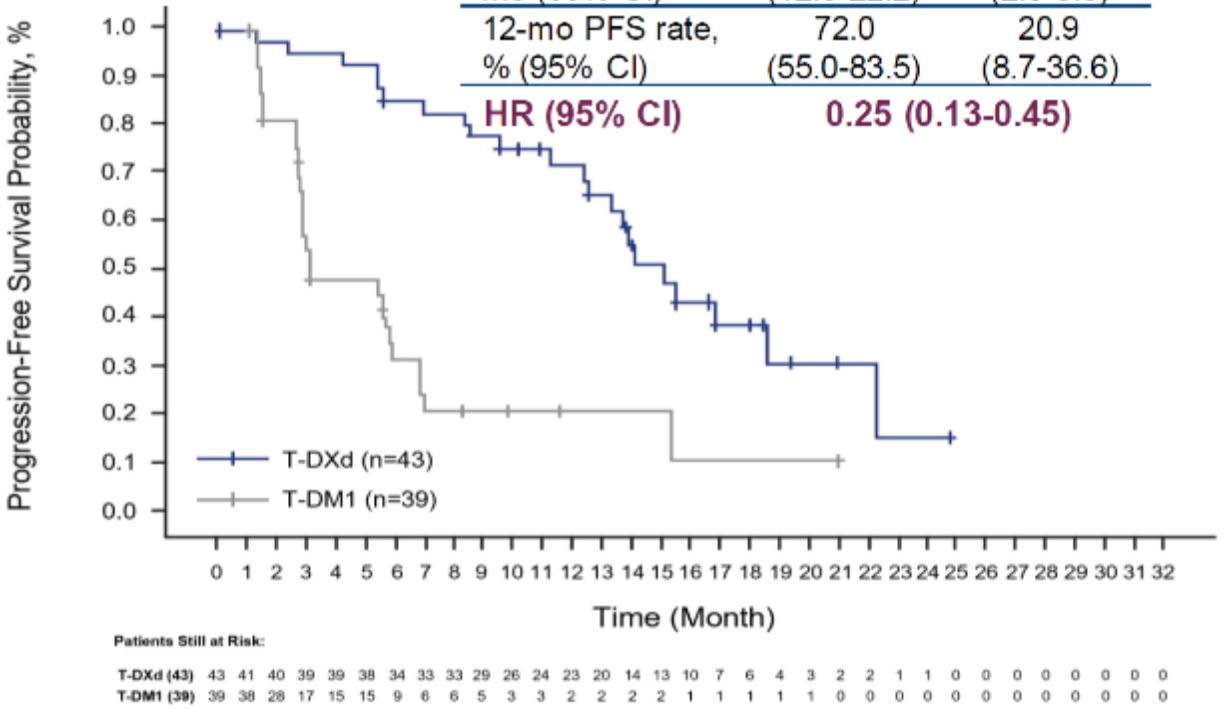
BM, brain metastasis; CR, complete response; ORR, objective response rate; PR, partial response; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan.

[a]Patients with rapid progression on (neo)adjuvant therapy were included. Line of therapy does not include endocrine therapy.

PFS KM Curves for Patients With and Without BM

Brain Metastases at Baseline

	T-DXd	T-DM1
mPFS, mo (95% CI)	15.0 (12.5-22.2)	3.0 (2.8-5.8)
12-mo PFS rate, % (95% CI)	72.0 (55.0-83.5)	20.9 (8.7-36.6)
HR (95% CI)	0.25 (0.13-0.45)	

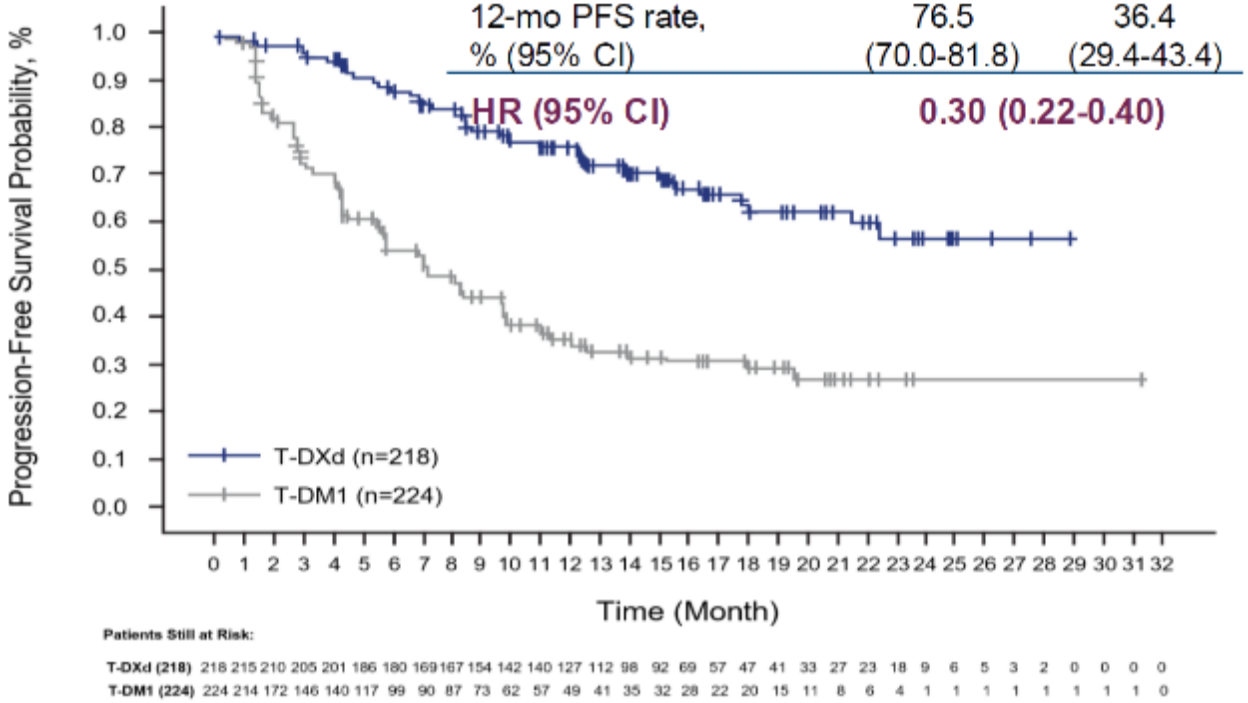


At data cutoff, in patients with BM at baseline, PD was observed:

- In 21/43 treated with T-DXd versus 27/39 with T-DM1
  - In the brain in 9/21 treated with T-DXd versus 11/27 with T-DM1

No Brain Metastases at Baseline

	T-DXd	T-DM1
mPFS, mo (95% CI)	NE (22.2-NE)	7.1 (5.6-9.7)
12-mo PFS rate, % (95% CI)	76.5 (70.0-81.8)	36.4 (29.4-43.4)
HR (95% CI)	0.30 (0.22-0.40)	



At data cutoff, in patients without BM at baseline, PD was observed:

- In 63/218 treated with T-DXd versus 128/224 with T-DM1
  - In the brain in 4/63 treated with T-DXd versus 1/128 with T-DM1

mPFS, median progression-free survival; PD, progressive disease; PFS, progression-free survival; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan

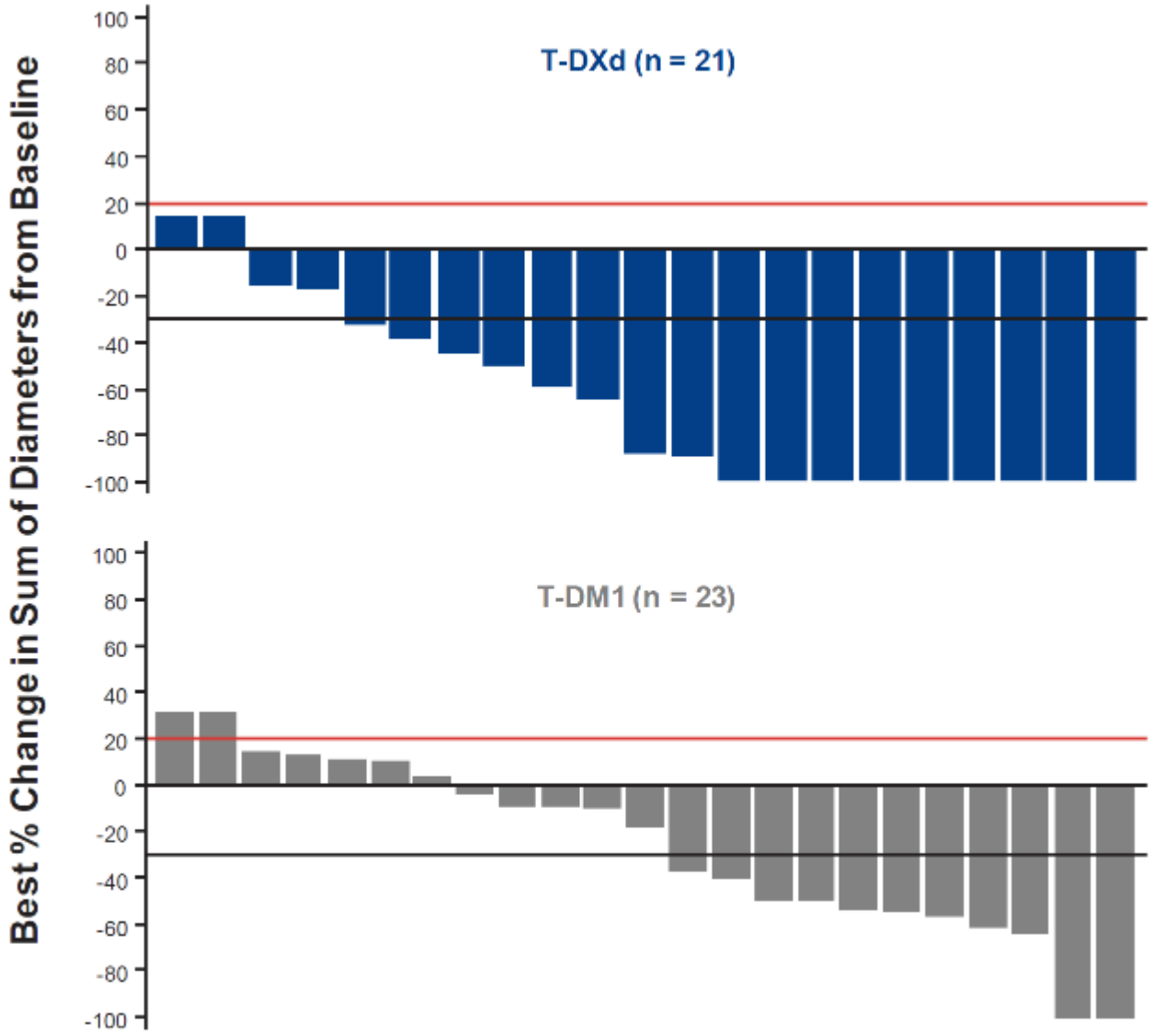
Confirmed ORR and Best Overall Response

	T-DXd			T-DM1		
	Overall Population (n = 261)[a]	Patients with BMs (n = 43)	Patients without BMs (n = 218)	Overall Population (n = 263)[a]	Patients with BMs (n = 39)	Patients without BMs (n = 224)
Confirmed ORR						
n (%)[b]	208 (79.7)	29 (67.4)	179 (82.1)	90 (34.2)	8 (20.5)	82 (36.6)
[95% CI]	[74.3-84.4]	[51.5-80.9]	[76.4-87.0]	[28.5-40.3]	[9.3-36.5]	[30.3-43.3]
CR	42 (16.1)	2 (4.7)	40 (18.3)	23 (8.7)	0	23 (10.3)
PR	166 (63.6)	27 (62.8)	139 (63.8)	67 (25.5)	8 (20.5)	59 (26.3)
SD	44 (16.9)	11 (25.6)	33 (15.1)	112 (42.6)	22 (56.4)	90 (40.2)
PD	3 (1.1)	1 (2.3)	2 (0.9)	46 (17.5)	7 (17.9)	39 (17.4)
Not evaluable	6 (2.3)	2 (4.7)	4 (1.8)	15 (5.7)	2 (5.1)	13 (5.8)
CR + PR + SD (DCR)	252 (96.6)	40 (93.0)	212 (97.2)	202 (76.8)	30 (76.9)	172 (76.8)
mDOR, mo	NE	12.9	NE	NE	7.2	NE
[95% CI]	[20.3-NE]	[8.5-NE]	[20.3-NE]	[12.6-NE]	[2.8-NE]	[12.6-NE]

BM, brain metastasis; CR, complete response; DCR, disease control rate; mDOR, median duration of response; NE, not estimable; ORR, objective response rate; PD, progressive disease; PR, partial response; SD, stable disease; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan.

[a]Only subjects with measurable disease at baseline and at least one postbaseline target lesion assessment are included. [b]Based on BICR.

Intracranial Response per BICR using RECIST 1.1



	T-DXd (n = 36)	T-DM1 (n = 36)
Best Overall Response, n (%)[a]		
CR	10 (27.8)	1 (2.8)
PR	13 (36.1)	11 (30.6)
Non-CR/Non-PD	6 (16.7)	7 (19.4)
SD	4 (11.1)	7 (19.4)
PD	1 (2.8)	8 (22.2)
Not Evaluable	0	1 (2.8)
Missing	2 (5.6)	1 (2.8)
Subjects with Objective Response of CR or PR, n	23	12

CR, complete response; DCR, disease control rate; mDOR, median duration of response; PD, progressive disease; PR, partial response; SD, stable disease; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan.
Table includes target and non-target lesions. Only patients with target lesion assessments are eligible for inclusion in waterfall.
Red line at 20% indicates progressive disease; black line at -30% indicates partial response.
[a]Denominator for percentages is the number of subjects in the full analysis set with brain metastases tumor assessment

Overall and Exposure-Adjusted Safety Summary

Type of Adverse Events	T-DXd n = 257	T-DM1 n = 261
Any TEAE		
n (%)	256 (99.6)	249 (95.4)
Exposure-adjusted incidence per patient-year[a]	0.87	1.43
TEAE of grade ≥3		
n (%)	134 (52.1)	126 (48.3)
Exposure-adjusted incidence per patient-year[a]	0.46	0.72
Serious TEAE		
n (%)	49 (19.1)	47 (18.0)
Exposure-adjusted incidence per patient-year[a]	0.17	0.27
TEAE associated with discontinuation		
n (%)	35 (13.6)	19 (7.3)
Exposure-adjusted incidence per patient-year[a]	0.12	0.11
TEAE associated with dose reduction		
n (%)	55 (21.4)	33 (12.6)
Exposure-adjusted incidence per patient-year[a]	0.19	0.19
TEAE associated with an outcome of death		
n (%)	5 (1.9)	5 (1.9)
Exposure-adjusted incidence per patient-year[a]	0.02	0.03

- **Median treatment duration was 14.3 months (range, 0.7-29.8) for T-DXd and 6.9 months (range, 0.7-25.1) for T-DM1**
- **Although rates of any TEAEs and TEAEs of grade ≥3 were generally similar between arms, EAIRs were lower with T-DXd versus T-DM1**
- **Although rates of TEAEs associated with discontinuation were greater with T-DXd versus T-DM1, EAIRs were generally similar**

EAIR, exposure-adjusted incidence rate; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan; TEAE, treatment-emergent adverse event.
Relationship to study drug was determined by the treating investigator.
[a]Total patient-years of exposure were 292.86 years for T-DXd and 174.48 years for T-DM1. Patient-years of exposure are the treatment duration with year as unit.

TEAEs in ≥20% of Patients

System Organ Class Preferred Term, n (%)	T-DXd (n = 257)		T-DM1 (n = 261)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Blood and lymphatic system disorders				
Neutropenia[a]	110 (42.8)	49 (19.1)	31 (11.9)	8 (3.1)
Anemia[b]	84 (32.7)	15 (5.8)	45 (17.2)	11 (4.2)
Leukopenia[c]	78 (30.4)	17 (6.6)	22 (8.4)	1 (0.4)
Thrombocytopenia[d]	66 (25.7)	18 (7.0)	139 (53.3)	65 (24.9)
Gastrointestinal disorders				
Nausea	195 (75.9)	17 (6.6)	79 (30.3)	1 (0.4)
Vomiting	126 (49.0)	4 (1.6)	26 (10.0)	1 (0.4)
Diarrhea	75 (29.2)	1 (0.4)	18 (6.9)	1 (0.4)
Constipation	88 (34.2)	0	51 (19.5)	0
General disorders				
Fatigue[e]	126 (49.0)	13 (5.1)	90 (34.5)	2 (0.8)
Headache	56 (21.8)	0	42 (16.1)	0
Investigations				
AST increased	66 (25.7)	2 (0.8)	105 (40.2)	13 (5.0)
ALT increased	56 (21.8)	4 (1.6)	77 (29.5)	12 (4.6)
Metabolism and nutrition disorders				
Decreased appetite	75 (29.2)	3 (1.2)	44 (16.9)	0
Skin and subcutaneous tissue disorders				
Alopecia	95 (37.0)	1 (0.4)[f]	8 (3.1)	0

ALT, alanine aminotransferase; AST, aspartate aminotransferase; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan; TEAE, treatment-emergent adverse event.
Adverse events were managed according to the protocol.
[a]This category includes the preferred terms neutrophil count decreased and neutropenia. [b]This category includes the preferred terms hemoglobin decreased, red blood cell count decreased, anemia, and hematocrit decreased. [c]This category includes the preferred terms white blood cell count decreased and leukopenia. [d]This category includes platelet count decreased and thrombocytopenia. [e]This category includes the preferred terms fatigue, asthenia, and malaise. [f]Cases of alopecia reported during the study were graded based on the clinical judgement of the investigator. One case of alopecia was categorized as grade 3 by investigator despite grade 3 alopecia not being recognized by the NCI Common Terminology criteria. The events outcome is reported as recovered by investigator.

Interstitial Lung Disease/Pneumonitis in Different Regions

Adjudicated as Drug-Related ILD/Pneumonitis,[a] n (%)							
		Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Any Grade
Overall	T-DXd (n = 257)	7 (2.7)	18 (7.0)	2 (0.8)	0	0	27 (10.5)
	T-DM1 (n = 261)	4 (1.5)	1 (0.4)	0	0	0	5 (1.9)
Asia subgroup	T-DXd (n = 147)	5 (3.4)	10 (6.8)	1 (0.7)	0	0	16 (10.9)
	T-DM1 (n = 159)	3 (1.9)	1 (0.6)	0	0	0	4 (2.5)
Non-Asia subgroup	T-DXd (n = 110)	2 (1.8)	8 (7.3)	1 (0.9)	0	0	11 (10.0)
	T-DM1 (n = 102)	1 (1.0)	0	0	0	0	1 (1.0)

- No grade 4 or 5 adjudicated drug-related ILD/pneumonitis events observed with T-DXd
- ILD/pneumonitis rates were similar between the overall population and the Asia subgroup and between the Asia and the non-Asia subgroups

ILD, interstitial lung disease; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan.
Asia subgroup defined as patients enrolled in China, Hong Kong, Japan, Republic of Korea, and Taiwan.
[a]Patients with history of ILD/pneumonitis necessitating steroids were excluded.

Conclusions

T-DXd treatment demonstrated consistent efficacy benefit (PFS and ORR) over T-DM1 across patient subgroups

- PFS by BICR HR of 0.28 ($P = 7.8 \times 10^{-22}$) overall
- Confirmed ORR for T-DXd of 79.7% versus 34.2% for T-DM1 (CR, 16.1% vs 8.7%)

In patients with and without BMs, T-DXd treatment resulted in greater efficacy compared to T-DM1

- Patients with BMs: mPFS of 15.0 mo with T-DXd versus 3.0 mo with T-DM1; confirmed ORR of 67.4% for T-DXd versus 20.5% for T-DM1
- Lower rates of PD with T-DXd (32.2%) versus T-DM1 (58.9%); for patients with BMs, 48.8% with T-DXd versus 69.2% with T-DM1

T-DXd treatment is associated with substantial intracranial response and reduction in CNS disease

- 27.8% intracranial CR for T-DXd versus 2.8% for T-DM1
- 2.8% intracranial PD for T-DXd versus 22.2% for T-DM1

T-DXd demonstrated a manageable and tolerable safety profile

- No difference between Asia (10.9%) and non-Asia (10.0%) regions in ILD/pneumonitis rates, with no grade 4 or 5 ILD/pneumonitis events

These data support T-DXd becoming the standard of care for second-line HER2+ mBC

BICR, blinded independent central review; BM, brain metastasis; CR, complete response; HR, hazard ratio; ILD, interstitial lung disease; mBC, metastatic breast cancer; mPFS, median progression-free survival; ORR, objective response rate; PD, progressive disease; PFS, progression-free survival; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan.

Datopotamab Deruxtecan (Dato-DXd) in Advanced/Metastatic HER2 Negative Breast Cancer: Triple Negative Breast Cancer Results from the Phase 1 TROPION-PanTumor01 Study

Ian Krop,[1] Dejan Juric,[2] Toshio Shimizu,[3] Anthony Tolcher,[4] Alexander Spira,[5] Toru Mukohara,[6] Aaron E. Lisberg,[7] Takahiro Kogawa,[8] Kyriakos P. Papadopoulos,[9] Erika Hamilton,[10] Senthil Damodaran,[11] Jonathan Greenberg,[12] Wen Gu,[12] Fumiaki Kobayashi,[13] Takahiro Jikoh,[13] Yui Kawasaki,[13] Funda Meric-Bernstam,[11] Aditya Bardia[2]

[1]Dana-Farber Cancer Institute, Boston, MA; [2]Department of Hematology/Oncology, Massachusetts General Hospital Cancer Center, Harvard Medical School, Boston, MA; [3]National Cancer Center Hospital, Tokyo, Japan; [4]NEXT Oncology, San Antonio, TX; [5]Virginia Cancer Specialists, Fairfax, VA; [6]Department of Medical Oncology, National Cancer Center Hospital East, Kashiwa, Japan; [7]UCLA Jonsson Comprehensive Cancer Center, Santa Monica, CA; [8]Advanced Medical Development Center, The Cancer Institute Hospital of JFCR, Tokyo, Japan; [9]START Center for Cancer Care San Antonio, San Antonio, TX; [10]Sarah Cannon Research Institute/Tennessee Oncology, Nashville, TN; [11]The University of Texas MD Anderson Cancer Center, Houston, TX; [12]Daiichi Sankyo Inc., Basking Ridge, NJ; [13]Daiichi Sankyo Co, Ltd, Tokyo, Japan

Introduction

- Effective treatment options for patients with advanced/metastatic TNBC that has relapsed or is refractory to standard treatments are limited
- TROP2 is highly expressed in various human malignancies including breast cancer[1,2]
- The ongoing TROPION-PanTumor01 study (NCT03401385) is evaluating the safety and efficacy of the TROP2-directed ADC datopotamab deruxtecan (Dato-DXd) in advanced/metastatic breast cancer, NSCLC and other tumor types[3-5]
  - Based on clinical results and exposure-response analyses for safety and efficacy, 6 mg/kg was selected for expansion across other tumors and the phase 3 TROPION-Lung01 and TROPION-Breast01 trials[3,6-8]
- Here we present updated results for the TNBC cohort (data cutoff July 30, 2021)

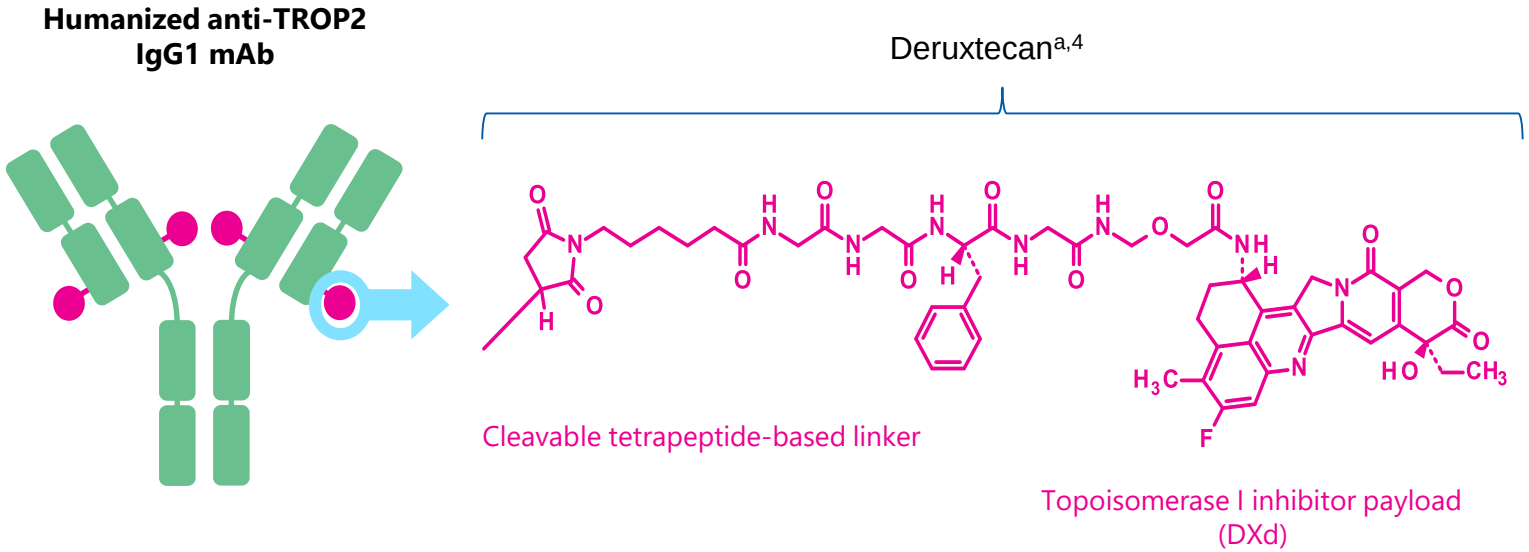
ADC, antibody-drug conjugate; HR, hormone receptor; NSCLC, non-small cell lung cancer; TNBC, triple negative breast cancer; TROP2, trophoblast cell-surface antigen 2.

1. Zeng P, et al. *Sci Rep*. 2016;20:33658; 2. Ambrogi F, et al. *PLoS One*. 2014;9(5):e96993; 3. Garon E, et al. WCLC 2021. Abstract 156; 4. Bardia A, et al. ESMO Breast Cancer 2021. [Abstract LBA4].
5. ClinicalTrials.gov. Accessed November 4, 2021 https://clinicaltrials.gov/ct2/show/NCT03401385. 6. Meric-Bernstam F, et al. ASCO 2021. Abstract 9058;
7. Spira A, et al. WCLC 2020. Abstract 3407; 8. ClinicalTrials.gov Accessed November 4, 2021. https://clinicaltrials.gov/ct2/show/NCT05104866.

Datopotamab Deruxtecan (Dato-DXd) Was Designed With 7 Key Attributes

Dato-DXd is an ADC with 3 components[1,2]:

- A humanized anti-TROP2 IgG1[3] monoclonal antibody attached to:
- A topoisomerase I inhibitor payload, an exatecan derivative, via
- A tetrapeptide-based cleavable linker



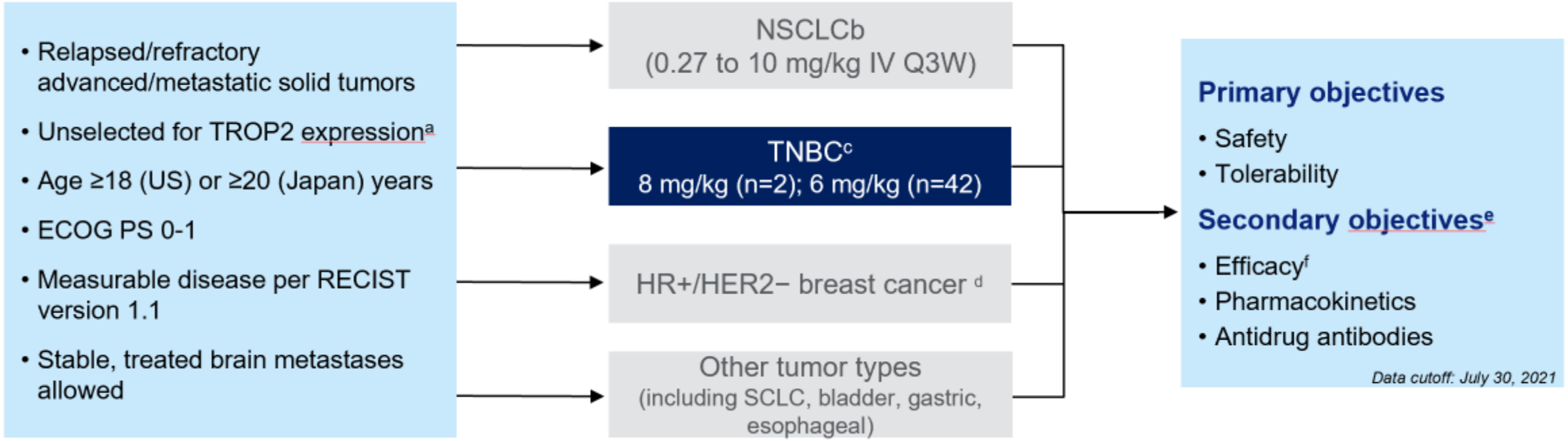
Payload mechanism of action: topoisomerase I inhibitor [b,1]
High potency of payload [b,2]
Optimized drug to antibody ratio ≈4 [b,c,1]
Payload with short systemic half-life [b,c,2]
Stable linker-payload [b,2]
Tumor-selective cleavable linker [b,2]
Bystander antitumor effect [b,2,5]

[a] Image is for illustrative purposes only; actual drug positions may vary. [b] The clinical relevance of these features is under investigation. [c] Based on animal data.

1. Okajima D, et al. AACR-NCI-EORTC 2019; [abstract C026]; 2. Nakada T, et al. *Chem Pharm Bull*. 2019;67(3):173-185; 3. Daiichi Sankyo Co. Ltd. DS-1062. Daiichi Sankyo.com. Accessed October 6, 2020. https://www.daiichisankyo.com/media_investors/investor_relations/ir_calendar/files/005438/DS-1062%20Seminar%20Slides_EN.pdf; 4. Krop I, et al. SABCS 2019; [abstract GS1-03]; 5. Ogitani Y, et al. *Cancer Sci*. 2016;107(7):1039-1046.

TROPION-PanTumor01 (NCT03401385)

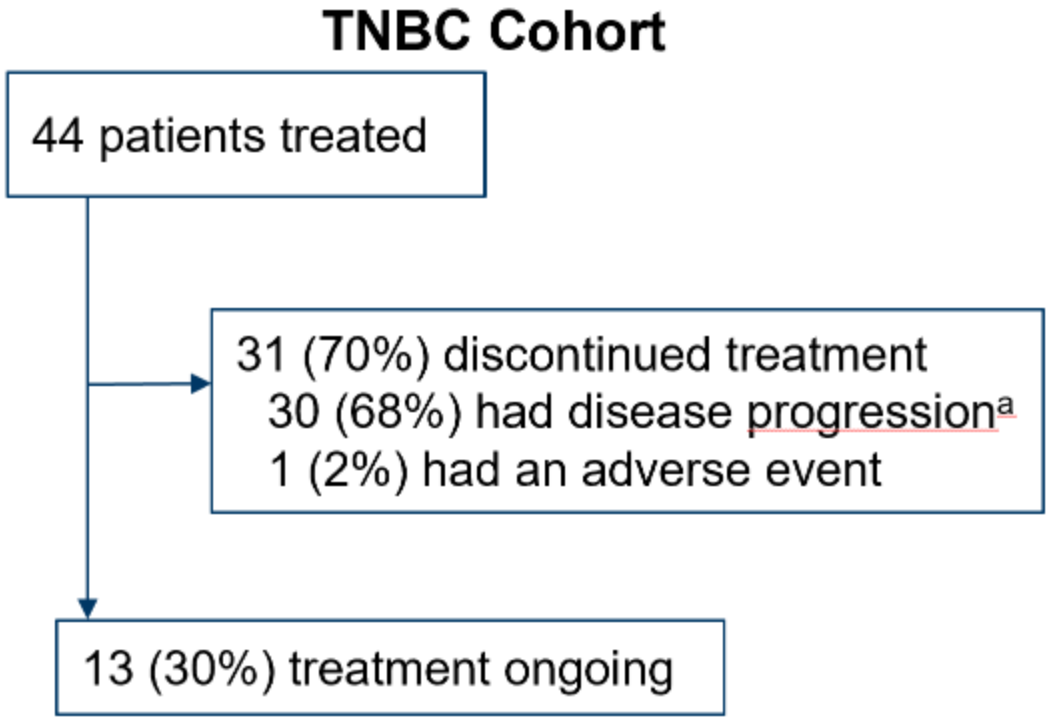
Phase 1 Study in Relapsed/Refractory Metastatic Solid Tumors



ECOG PS, Eastern Cooperative Oncology Group performance status; Q3W, every 3 weeks; RECIST, Response Evaluation Criteria in Solid Tumors.
[a] Pretreatment tumor tissue was required for retrospective analysis of TROP2 expression. [b] Results from the NSCLC cohort have been previously reported.[1,2] [c] Includes patients treated in the dose-escalation and dose-expansion portions. [d] Enrollment in the HR+/HER2− cohort is now complete and data will be forthcoming. [e] Exploratory objectives include analyses of biomarkers associated with response. [f] Response assessments are based on RECIST 1.1.

1.Garon E, et al. WCLC 2021. Abstract 156; 2 Meric-Bernstam F, et al. ASCO 2021.

Patient Disposition



Last patient enrolled April 2021; median follow-up: 7.6 months (range, 4-13 months)

Data cutoff: July 30, 2021

[a] Progression includes progressive disease per RECIST 1.1 and clinical progression.

Baseline Characteristics

Patient characteristics	TNBC n=44
Age, median (range), years	53 (32-82)
Country, n (%)	
US	31 (70)
Japan	13 (30)
ECOG PS, n (%)	
0	18 (41)
1	26 (59)
De novo metastatic disease, n (%)	
Yes	14 (32)
No	30 (68)

Patient characteristics (cont)	TNBC n=44
Brain metastases, n (%)	5 (11)
Prior therapies in metastatic setting, median (range), n	3 (1-10)
≥2 prior lines of therapy, n (%)[a]	30 (68)
Previous systemic treatment, n (%)	
Taxanes	40 (91)
Platinum-based chemotherapy	23 (52)
Immunotherapy	19 (43)
PARPi	7 (16)
Topo I inhibitor-based ADC[b]	13 (30)

Data cutoff: July 30, 2021

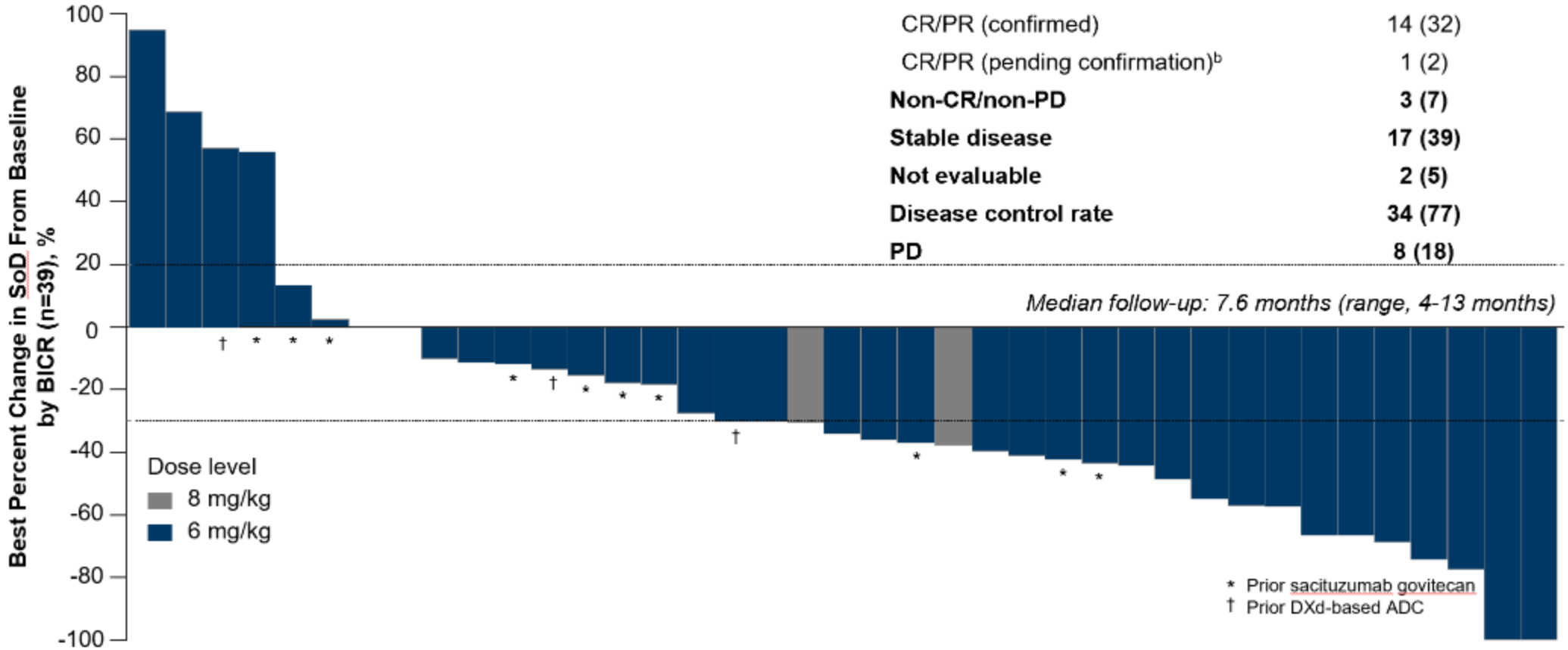
PARPi, poly(ADP-ribose) polymerase inhibitor; Topo I, topoisomerase I.

[a] Includes prior lines of therapy in the metastatic setting. [b] Sacituzumab govitecan, n=10; trastuzumab deruxtecan, n=2; patritumab deruxtecan, n=1.

Antitumor Responses by BICR

All patients with TNBC

Patients, n (%)[a]	All Patients (n=44)
ORR	**15 (34)**
CR/PR (confirmed)	14 (32)
CR/PR (pending confirmation)[b]	1 (2)
Non-CR/non-PD	**3 (7)**
Stable disease	**17 (39)**
Not evaluable	**2 (5)**
Disease control rate	**34 (77)**
PD	**8 (18)**



Data cutoff: July 30, 2021

BICR, blinded independent central review; CR, complete response; ORR, objective response rate; PD, progressive disease; PR, partial response; SoD, sum of diameters.

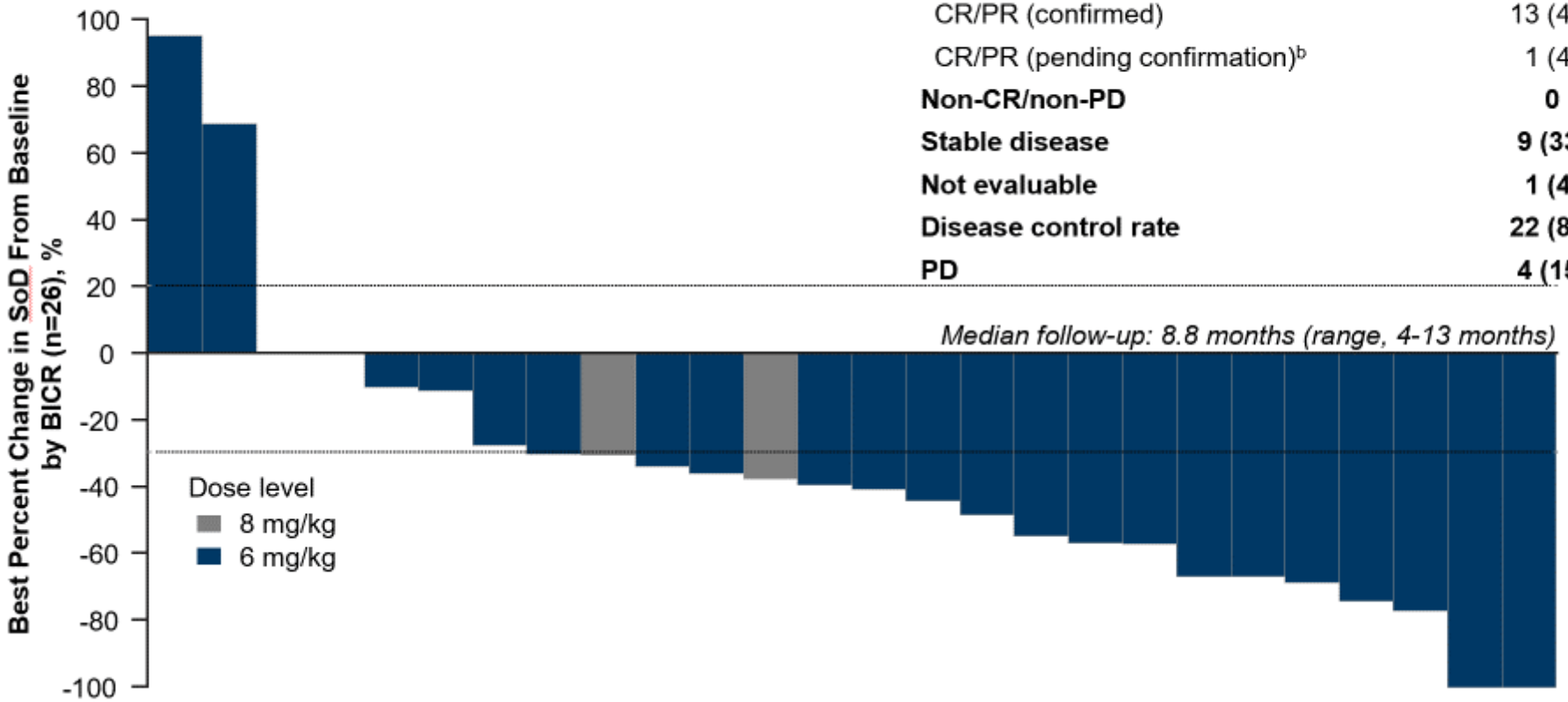
[a] Includes response evaluable patients who had ≥1 postbaseline tumor assessment or discontinued treatment. Postbaseline tumor assessments were not yet available for 2 patients at the data cutoff. Three patients were not confirmed to have a target lesion per BICR and therefore had a best overall response of non-CR/non-PD.

[b] Includes patients with an unconfirmed response but are ongoing treatment.

Antitumor Responses by BICR

Patients with TNBC without prior Topo I inhibitor-based ADC

Patients, n (%)[a]	SG/DXd Naïve Patients with Measurable Disease at BL (n=27)
ORR	**14 (52)**
CR/PR (confirmed)	13 (48)
CR/PR (pending confirmation)[b]	1 (4)
Non-CR/non-PD	**0**
Stable disease	**9 (33)**
Not evaluable	**1 (4)**
Disease control rate	**22 (81)**
PD	**4 (15)**

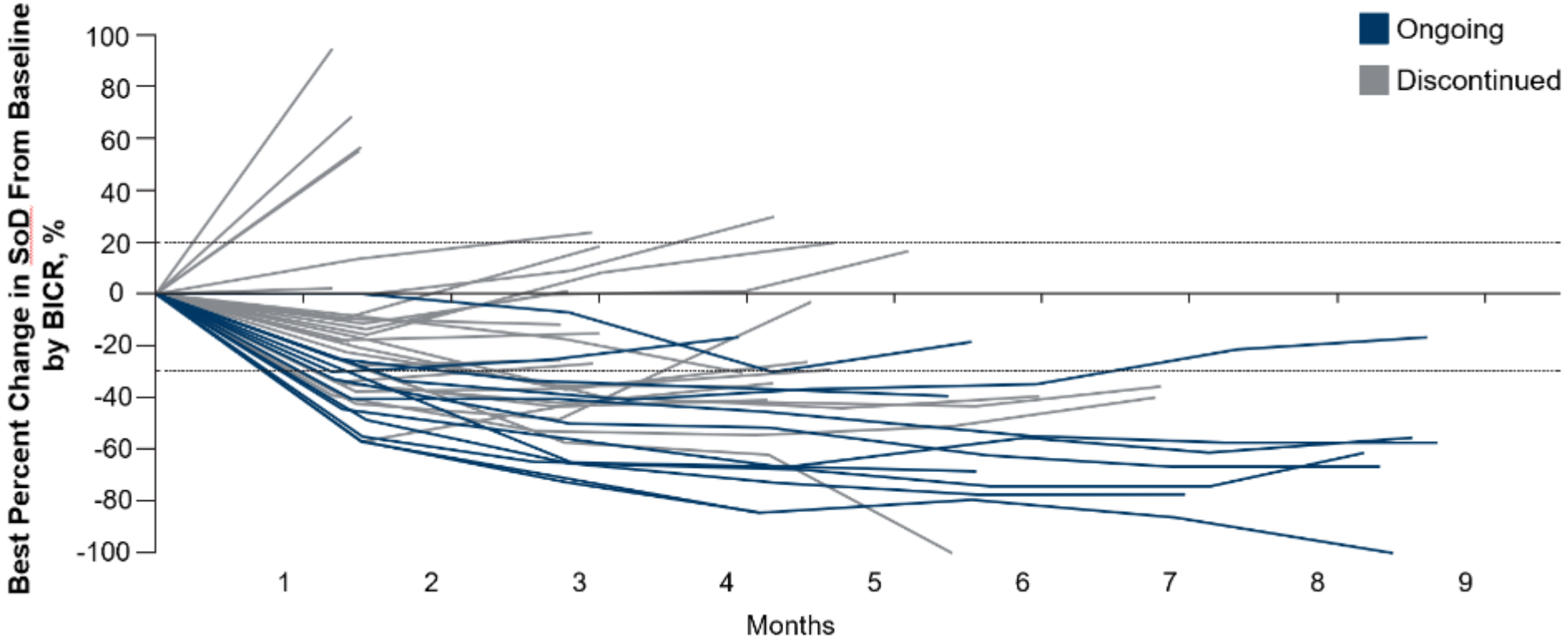


Data cutoff: July 30, 2021

BL, baseline; SG; sacituzumab govitecan..

[a] Includes response evaluable patients who had ≥1 postbaseline tumor assessment or discontinued treatment. Postbaseline tumor assessments were not yet available for 1 patient at the data cutoff. [b] Includes patients with an unconfirmed response but are ongoing treatment.

Duration of Disease Control in Patients with TNBC



Data cutoff: July 30, 2021

- The median duration of response was not reached (range, 2.7-7.4+ months), with the majority of responses ongoing at the data cutoff

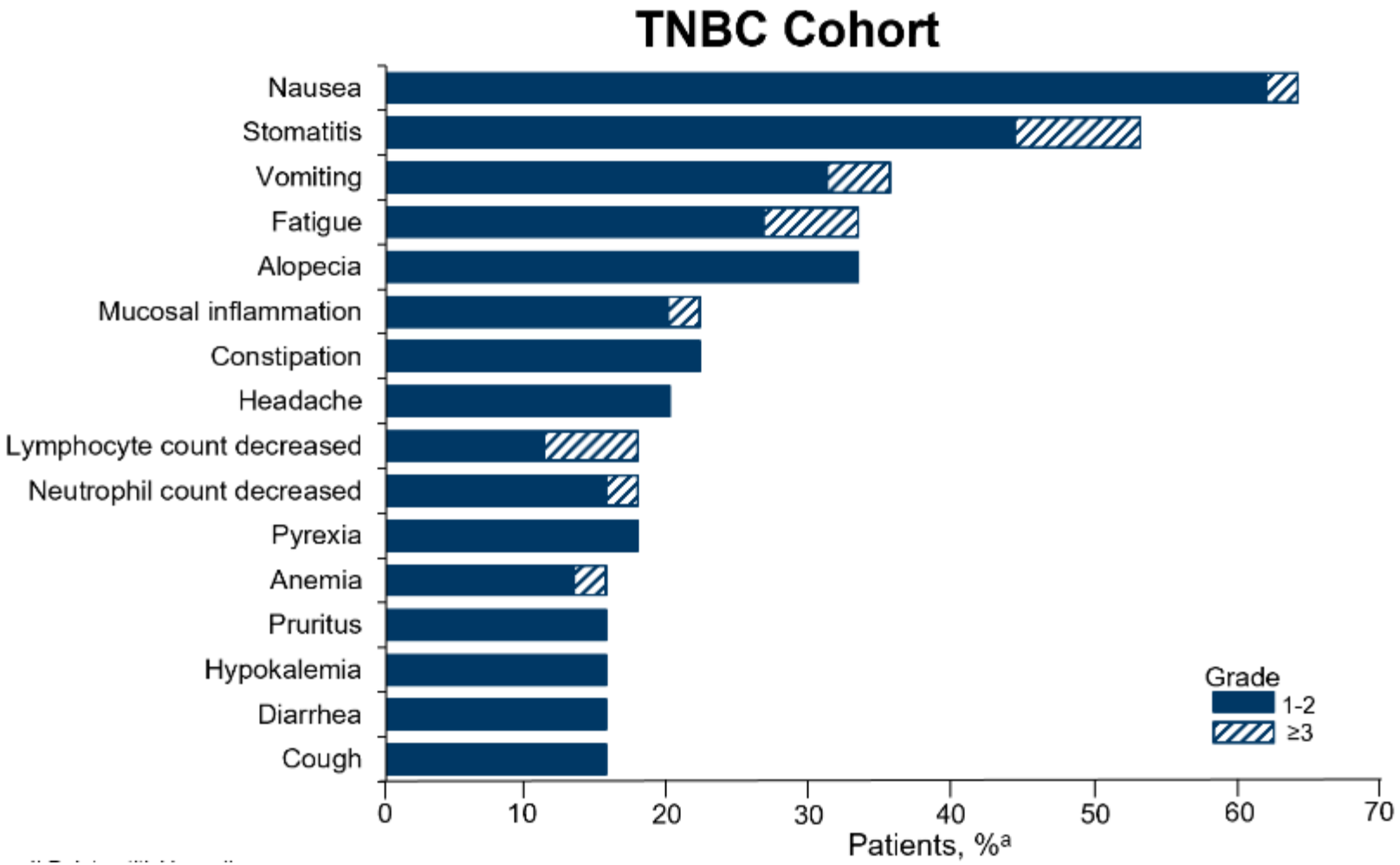
Overall Safety Summary

Patients, n (%)	TNBC n=44
All-grade TEAEs	43 (98)
Grade ≥3	20 (45)
All-grade treatment-related TEAEs	43 (98)
Grade ≥3	10 (23)
Dose adjustments	
Dose reduction due to AEs	8 (18)
Treatment interruption due to AEs	6 (14)
Treatment discontinuation due to AEs	1 (2)
Serious TEAEs	8 (18)
Treatment related	2 (5)
Fatal TEAEs	0
Treatment related	0

Data cutoff: July 30, 2021

AE, adverse event; TEAE, treatment-emergent adverse event.

Treatment-Emergent Adverse Events in ≥ 15% of Patients



- Most common adverse events observed were nausea and stomatitis (predominantly grade 1-2)
- Low frequency of hematologic toxicity and diarrhea
- No cases adjudicated as drug-related ILD

Data cutoff: July 30, 2021

ILD, interstitial lung disease.
[a] n=44 patients.

Conclusions

- In heavily pretreated patients with TNBC, Dato-DXd showed highly encouraging and durable efficacy
  - ORR by BICR was 34% in all patients with TNBC
  - ORR by BICR was 52% in patients with measurable disease at baseline who are treatment naïve to Topo I inhibitor-based ADC therapies
- In patients, Dato-DXd demonstrated a manageable safety profile with no new safety signals
  - Low grade nausea and stomatitis were most frequent
  - Neutropenia and diarrhea were uncommon
- The HR+/HER2- cohort is now fully enrolled and data are forthcoming
- Further studies of Dato-DXd in breast cancer are warranted
  - BEGONIA is an ongoing trial in TNBC to evaluate efficacy and safety of Dato-DXd plus durvalumab
  - TROPION-Breast01, a phase 3 trial in HR+/HER2- BC, has been initiated (NCT05104866)
  - Phase 3 trial in TNBC is planned

Pivotal Phase 2 Study of the EZH1 and EZH2 Inhibitor Valemetostat (DS-3201b) in Patients With Relapsed or Refractory Adult T-Cell Leukemia/Lymphoma (ATL)

Makoto Yoshimitsu, MD, PhD[1], Koji Izutsu, MD, PhD[2], Shinichi Makita, MD, PhD, FACP[2], Kisato Nosaka, MD, PhD[3], Atae Utsunomiya, MD, PhD[4], Shigeru Kusumoto, MD[5], Satoko Morishima, MD, PhD[6], Kunihiro Tsuaksaki, MD, PhD[7], Toyotaka Kawatama, MD, PhD[8], Takaaki Ono, MD, PhD[9], Shinya Rai, MD, PhD[10], Hiroo Katsuya, MD[11], Jun Ishikawa, MD, PhD[12], Hironori Yamada, MSc[13], Kazunobu Kato, MD, PhD[14], Masaya Tachibana, PhD[13], Yasuyuki Kakurai, PhD[13], Nobuaki Adachi, PhD[13], Kensei Tobinai, MD[2], Kentaro Yonekura, MD, PhD[4], and Kenji Ishitsuka, MD, PhD[1]

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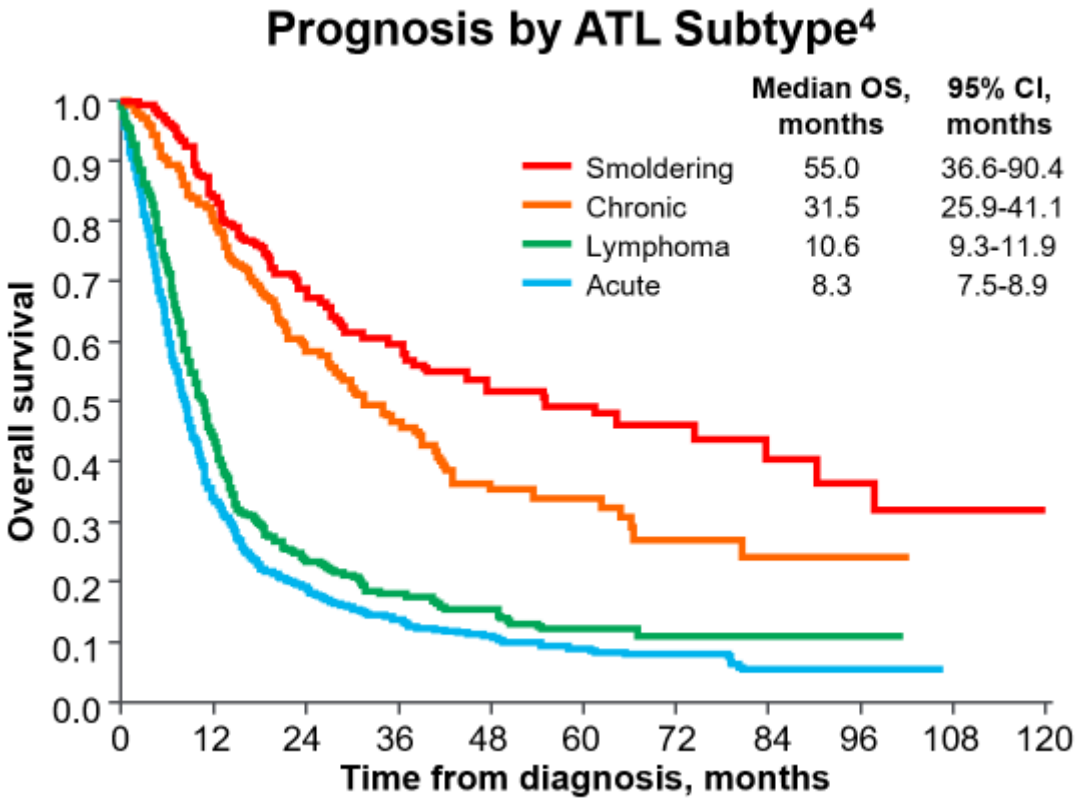
Prognosis of patients with relapsed/refractory ATL is poor

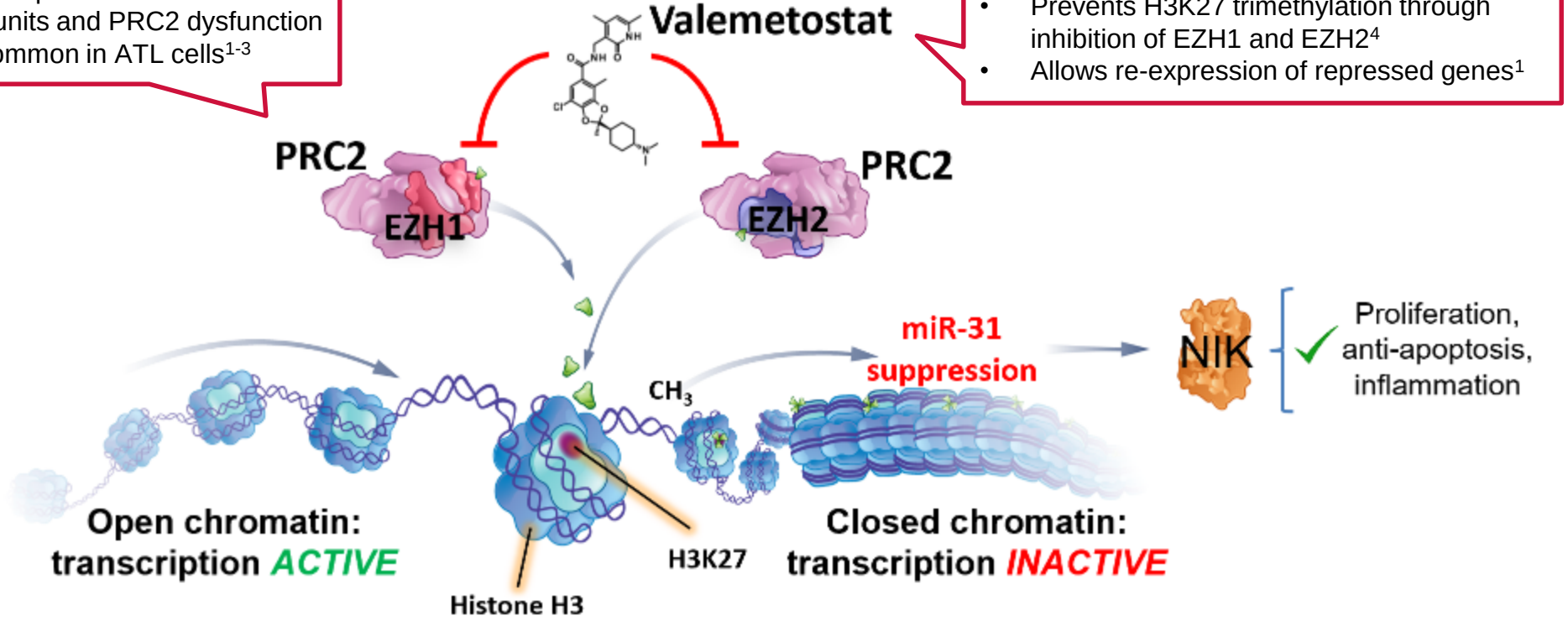
- Of the ATL subtypes, acute and lymphoma are the most aggressive and have a poor prognosis
  - ≈90% of patients experience relapse within months of completing intensive treatment[1]
- Few effective therapeutic options exist for R/R ATL
  - Mogamulizumab: ORR = 50%[2]
  - Lenalidomide: ORR = 42%[3]
- **Novel drug targets and molecular therapies are essential to the treatment of patients with R/R ATL**



1. Mehta-Shah N, et al. *Oncol Pract.* 2017;13:487-493.
2. Ishida T, et al. *J Clin Oncol*. 2012;8:837-842.
3. Ishida T, et al. *J Clin Oncol*. 2016;34;4086-4093.
4. Katsuya H, et al. *Blood*. 2015;126:2570-2577.

Valemetostat is a novel, potent, and selective dual inhibitor of EZH1 and EZH2

- Overexpression of PRC2 subunits and PRC2 dysfunction is common in ATL cells[1-3]



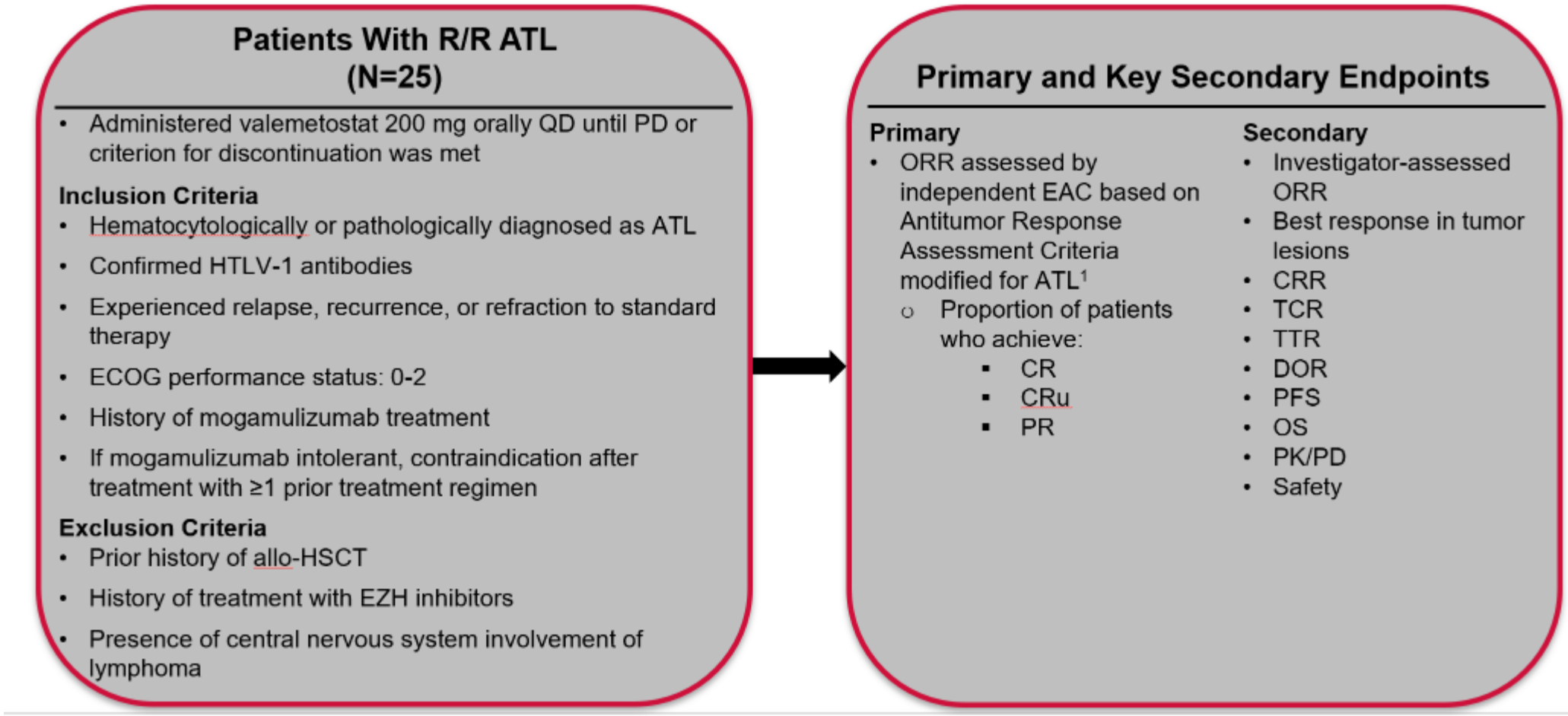
- Prevents H3K27 trimethylation through inhibition of EZH1 and EZH2[4]
- Allows re-expression of repressed genes[1]

Valemetostat inhibition of EZH1 and EZH2 drives re-expression of miR-31 and promotes blockade of NIK/NFκb-dependent tumorigenesis[1]

1. Yamagishi M, et al. *Cell Rep.* 2019;29(8):2321-2337.e7.
2. Sasaki D, et al. *Haematologica*. 2011;96(5):712-719.
3. Yamagishi M, et al. *Cancer Cell*. 2012;21(1):121-135.
4. Honma D, et al. *Cancer Sci*. 2017;108(10):2069-2078.

Valemetostat (DS-3201b) phase 2 single-arm study in R/R ATL

NCT04102150



CR, complete remission; CRR, complete remission rate; CRu, unconfirmed complete remission; DOR, duration of response; EAC, Efficacy Assessment Committee; ECOG, European Cooperative Oncology Group; HSCT, hematopoietic stem cell transplantation; ORR, overall response rate; OS, overall survival; PD, pharmacodynamics; PFS, progression-free survival; PK, pharmacokinetics; PR, partial response; TCR, tumor control rate; TTR, time to response 1. Tsukasaki K, et al. *J Clin Oncol*. 2009; 27(3):453-459.

Baseline patient and disease characteristics

Patient characteristics	Patients (N=25)
Age, median (range), years	69.0 (59-84)
Female sex, n (%)	13 (52.0)
ECOG performance status, n (%)	
0	13 (52.0)
1	10 (40.0)
2[a]	2 (8.0)
Prior lines of therapy, median (range)	3 (1-8)
Prior mogamulizumab therapy, n (%)	
Yes	24 (96.0)
No	1 (4.0)
Prior HSCT, n (%)	
No	25 (100.0)

Disease characteristics	Patients (N=25)
ATL subtype, n (%)	
Acute	16 (64.0)
Lymphoma	6 (24.0)
Unfavorable chronic	3 (12.0)
Disease status, n (%)	
Relapsed	8 (32.0)
Recurrent	6 (24.0)
Refractory	11 (44.0)

- Patients were heavily pretreated with a median of 3 prior lines of therapy (range, 1-8)
- 24 of 25 patients received prior mogamulizumab treatment

[a] One patient had ECOG performance status of 2 at initial screening but had advanced to 3 on cycle 1 day 1.

Responses of R/R ATL patients treated with valemetostat 200 mg once daily

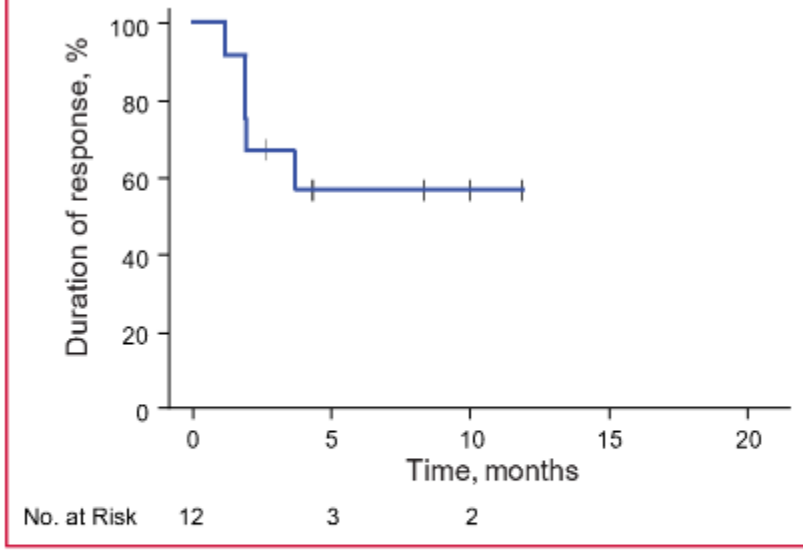
Population	N	ORR, n (%)	CR, n (%)	CRu, n (%)	PR, n (%)	SD, n (%)	RD/PD, n (%)
All patients	25	12 (48.0)	5 (20.0)	0	7 (28.0)	10 (40.0)	3 (12.0)
ATL subtype							
Acute	16	10 (62.5)	5 (31.3)	0	5 (31.3)	4 (25.0)	2 (12.5)
Lymphoma	6	1 (16.7)	0	0	1 (16.7)	5 (83.3)	0
Unfavorable chronic	3	1 (33.3)	0	0	1 (33.3)	1 (33.3)	1 (33.3)
Disease site							
Nodal or extranodal lesions	20	10 (50.0)	6 (30.0)	2 (10.0)	2 (10.0)	7 (35.0)	3 (15.0)
Skin lesions[a]	7	3 (42.9)	1 (14.3)	NE	2 (28.6)	3 (42.9)	1 (14.3)
Peripheral blood	9	8 (88.9)	2 (22.2)	NE	6 (66.7)	1 (11.1)	0
Disease status							
Relapsed	8	3 (37.5)	1 (12.5)	0	2 (25.0)	4 (50.0)	1 (12.5)
Recurrent	6	4 (66.7)	1 (16.7)	0	3 (50.0)	2 (33.3)	0
Refractory[b]	11	5 (45.5)	3 (27.3)	0	2 (18.2)	4 (36.4)	2 (18.2)

- The centrally reviewed ORR was 48% (90% CI, 30.5-65.9%)
- The null hypothesis (H0: ORR ≤5%) was rejected under a 1-sided binomial test with a significance level of 5% (*P*<.0001)

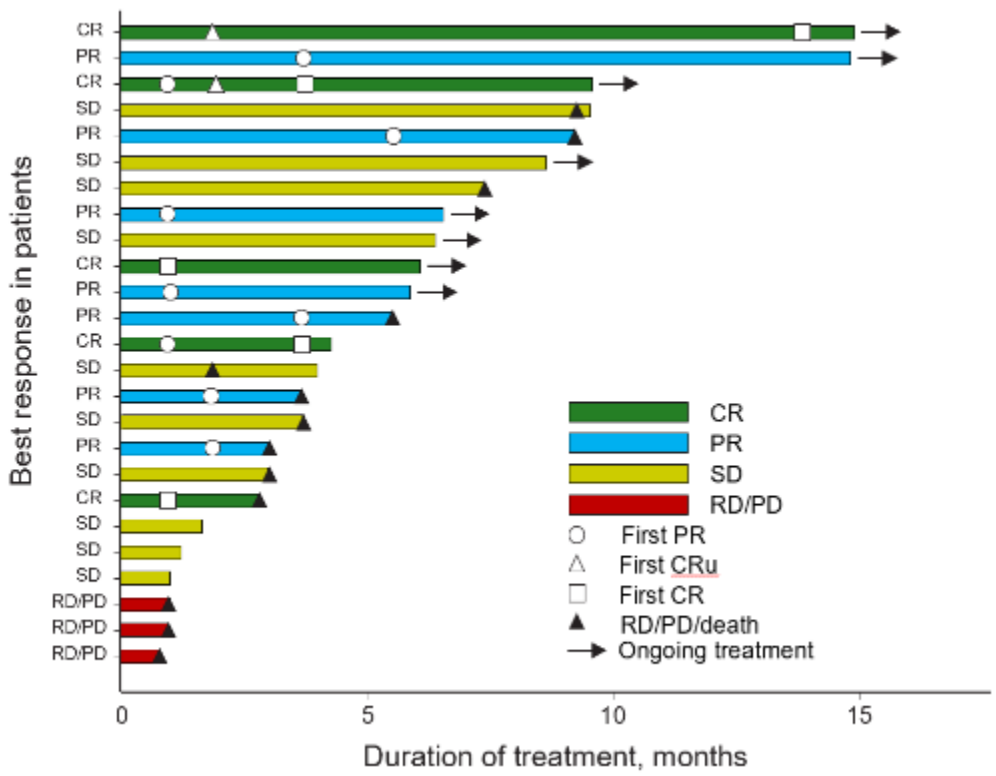
[a] One patient was not evaluated for skin lesions after baseline assessment. [b] Refractory: received ≥1 prior chemotherapy, achieved SD and required a treatment switch, or received ≥1 prior chemotherapy and experienced PD.

Duration of response and best responses in R/R ATL patients treated with valemetostat 200 mg once daily

Duration of Response



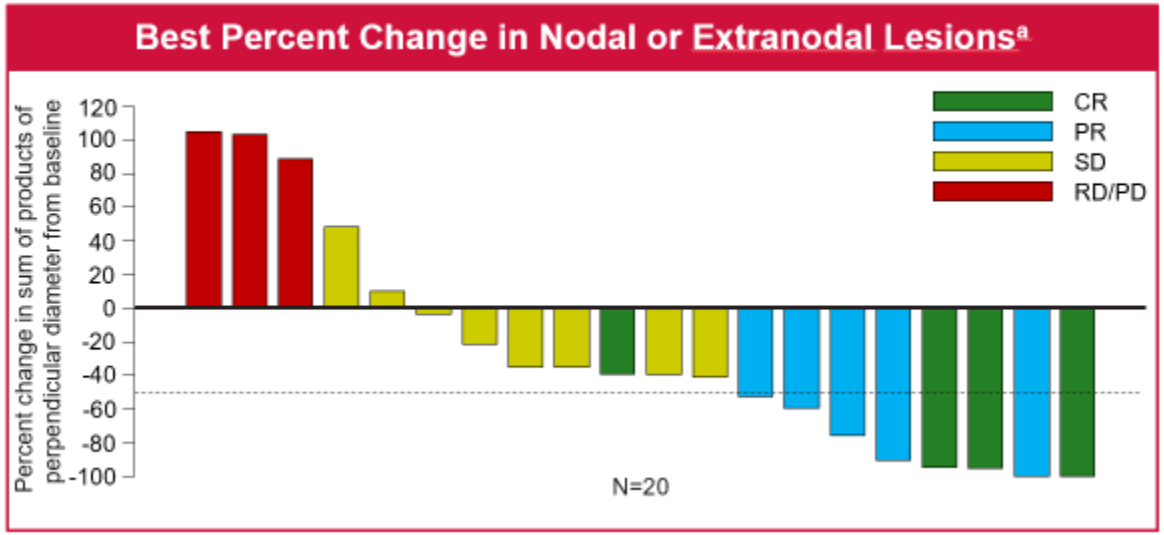
Patient Best Responses Over Time

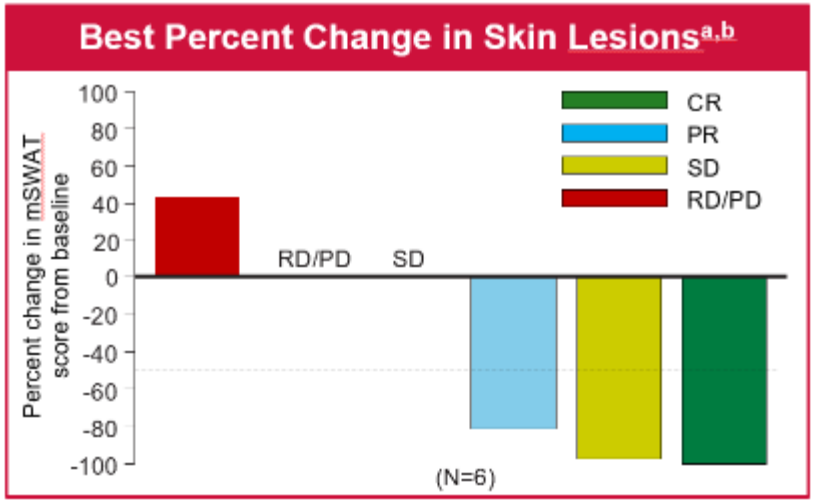


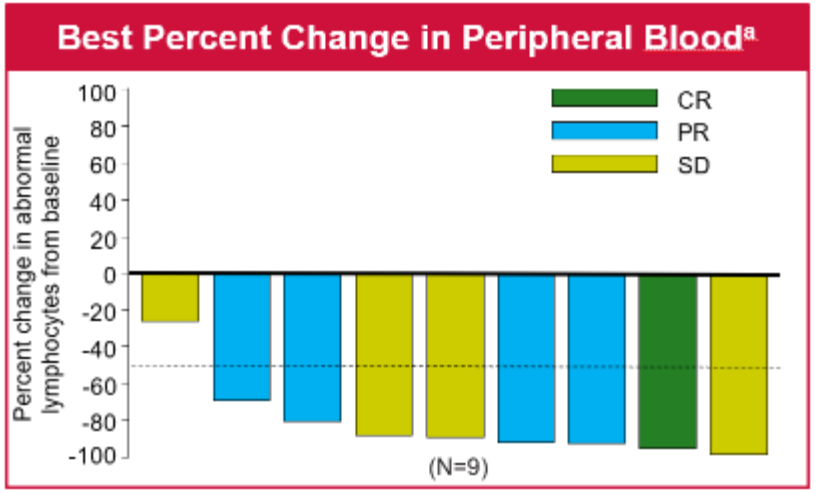
- At data cutoff (April 24, 2021), 8 patients were undergoing treatment
- The median duration of response was not reached (95% CI, 1.87 months-NR)
- The median time to first response was 1.43 months (range, 1.0-5.6 months)

NR, not reached

Change in lesions of patients with R/R ATL treated with valemetostat 200 mg once daily







- We observed a trend toward a decrease in measurable lesions across all disease sites assessed
- A ≥50% reduction from baseline in nodal or extranodal lesions, skin lesions, and peripheral blood was observed in 8/20, 3/6, and 8/9 patients, respectively

[a] Assessed by the Efficacy Assessment Committee. [b] One subject did not undergo assessment after baseline measurement.

Overall Safety

Patients, n (%)	(N=25)
TEAEs	25 (100.0)
TRAEs	24 (96.0)
Serious TEAEs	8 (32.0)
Serious TRAEs	7 (28.0)
Grade ≥3 TEAEs	15 (60.0)
Grade ≥3 TRAEs	14 (56.0)
TEAEs leading to discontinuation	2 (8.0)
TRAEs leading to discontinuation	2 (8.0)

- Dose interruption or reductions due to adverse events occurred in 5 (20.0%) and 2 (8.0%) patients treated with valemetostat, respectively
- No new safety signals emerged in the present study
- No treatment-related deaths occurred

TEAEs, n (%)	(N=25)	
Hematologic	**All grades (≥20%)**	**Grade ≥3**
Platelet count decreased[a]	20 (80.0)	8 (32.0)
Anemia	12 (48.0)	8 (32.0)
Neutrophil count decreased[b]	7 (28.0)	3 (12.0)
Lymphocyte count decreased	6 (24.0)	4 (16.0)
White blood cell count decreased	5 (20.0)	3 (12.0)
Nonhematologic	**All grades (≥20%)**	**Grade ≥3**
Alopecia	10 (40.0)	0
Dysgeusia	9 (36.0)	0
Decreased appetite	5 (20.0)	2 (8.0)
Pyrexia	5 (20.0)	0

[a] For platelet count decreased, there were 5 (20.0%) grade 3 and 3 (12.0%) grade 4 events. [b] For neutrophil count decreased, there were 2 (8.0%) grade 3 and 1 (4.0%) grade 4 events.

Conclusions

- Valemetostat shows therapeutic efficacy in patients with a history of mogamulizumab therapy for R/R ATL
  - The primary endpoint was met with an ORR of 48.0% as assessed by an independent EAC
  - The mDOR had not been reached with a median follow-up of 6.5 months
- The safety profile of valemetostat was acceptable and consistent with phase 1 results[1]
  - The majority of TEAEs were hematologic and were manageable with interventional care
  - 2 (8.0%) TEAEs led to discontinuation, 5 (20.0%) required dose interruption, and 2 (8.0%) required dose reduction
- Collectively, our findings in this pivotal phase 2 single-arm study indicate that valemetostat demonstrates promising efficacy and an acceptable safety profile for patients with R/R ATL

1. Kusumoto S, et al. EHA 2021. Abstract S218.

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