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AZ2019

Meet AZN management: ASCO 2019
Breakout 4: trastuzumab deruxtecan

José Baselga, Executive Vice President, Oncology R&D

3 June 2019

Forward-looking statements

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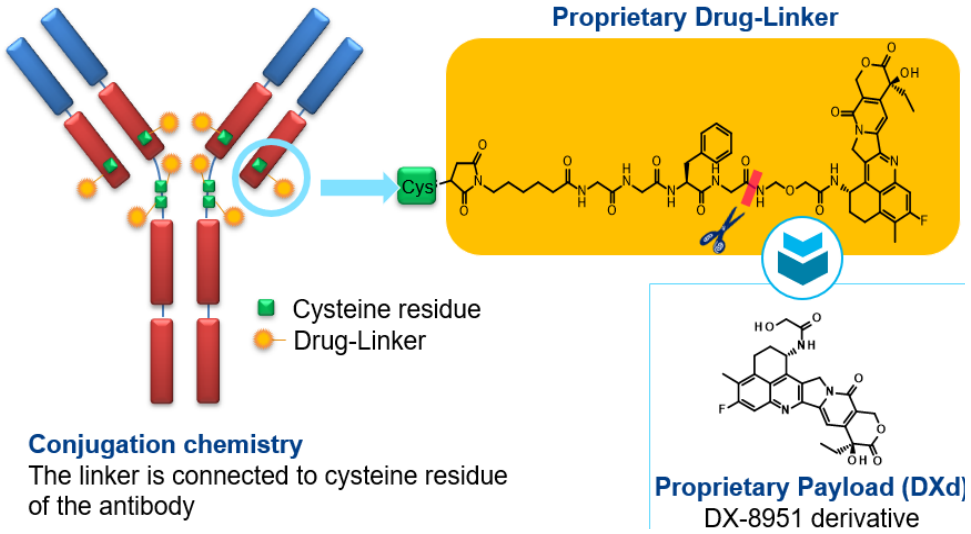
Trastuzumab deruxtecan

A state-of-the-art HER2[1]-targeted, second-generation ADC[2]

Differentiated ADC



Potential best-in-class ADC for HER2-positive breast cancer

- Higher-intensity chemotherapy (more payload on each antibody)
- Membrane permeability (potential HER2-low applicability)
- Selective protease-cleavable linker
- Short half-life of free payload reduces systemic toxicities

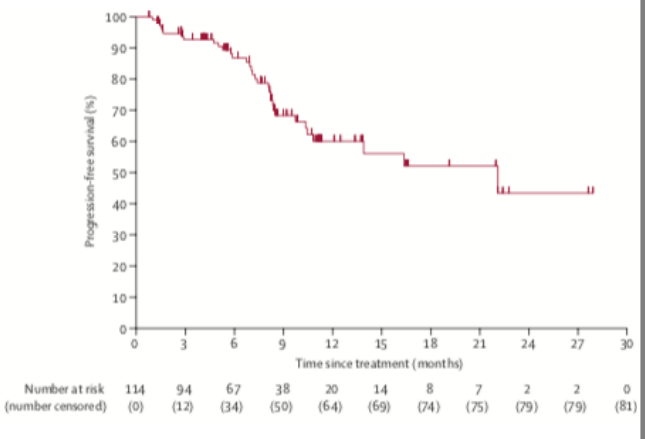
Potential first-in-class ADC for HER2-low cancers

1. Human epidermal growth factor receptor 2.
2. Antibody drug conjugate.

Sources: Daiichi Sankyo R&D event, December 2018, US label for trastuzumab emtansine and Ogitani et al, 2016.

Trastuzumab deruxtecan
Unprecedented Phase I/II data

Differentiated ADC



Progression-free survival in HER2-positive breast cancer

59.5%
confirmed objective response rate

93.7%
confirmed disease control rate[1]

20.7 months
median duration of response[2]

Unprecedented data in advanced HER2-posistive breast cancer

Phase II primary endpoint met

News Release
Regulatory News Service

AstraZeneca

8 May 2019 07:00 BST

Trastuzumab deruxtecan demonstrated clinically-meaningful response in patients with refractory HER2-positive metastatic breast cancer, a population with high unmet need

Pivotal Phase II DESTINY-Breast01 trial met primary endpoint, supporting global regulatory submission plan to start in H2 2019

AstraZeneca and Daiichi Sankyo Company, Limited (Daiichi Sankyo) today announced positive top-line results for the pivotal Phase II DESTINY-Breast01 trial of trastuzumab deruxtecan (DS-8201). The HER2-targeting antibody drug conjugate (ADC) and potential new medicine was evaluated in patients with HER2-positive, unresectable and/or metastatic breast cancer previously treated with trastuzumab emtansine.

The response rate in DESTINY-Breast01, as assessed by an independent review committee, confirms in a heavily-pretreated, global patient population the unprecedented clinical activity in the recently-published Phase I trial. The safety and tolerability profile of trastuzumab deruxtecan was also consistent with previous experience. These results are expected to support planned global regulatory submissions, including a Biologics License Application with the US Food and Drug Administration (FDA) anticipated in the second half of 2019.

DESTINY-Breast01 is a pivotal Phase II, open-label, global, multicentre, two-part trial of trastuzumab deruxtecan. The optimal dose of 5.4mg/kg was previously identified in part one of the trial. Today's results from part two evaluated the efficacy and safety of that dose in patients who have failed or discontinued previous treatment with trastuzumab emtansine.

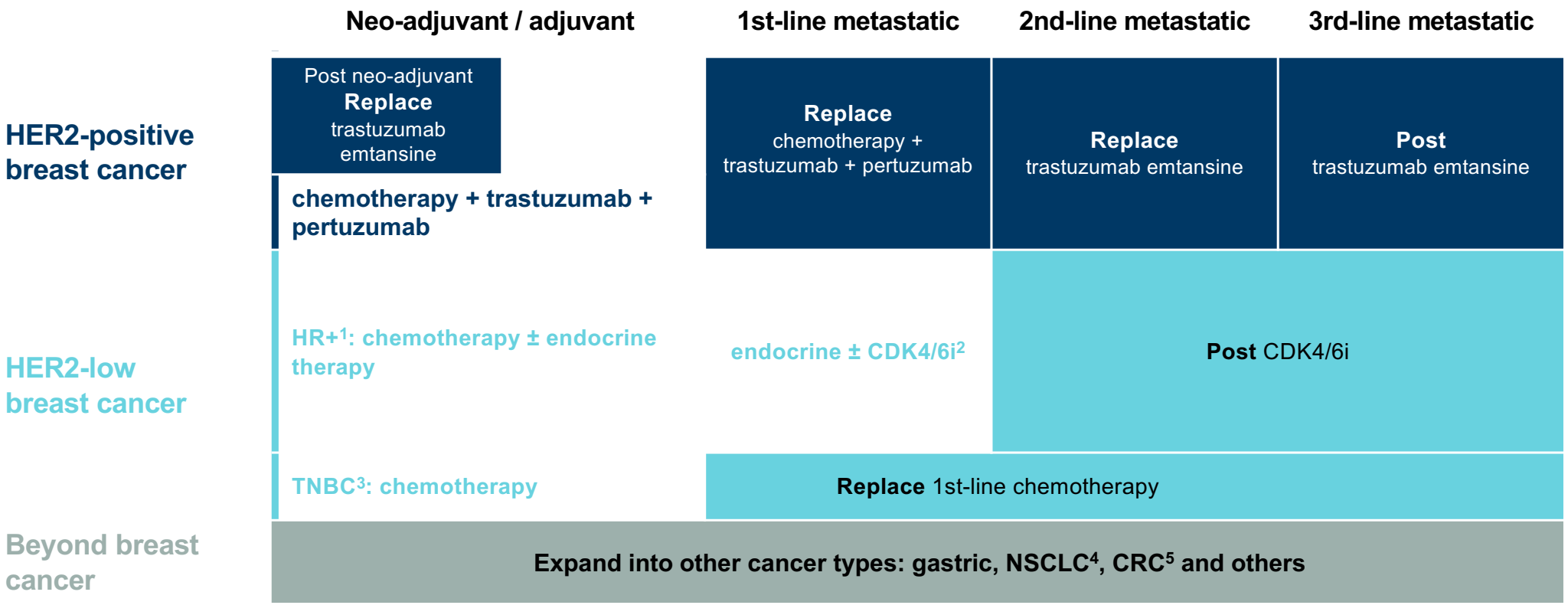
Phase II trial met primary endpoint in HER2+ breast cancer

Source: Phase I, Tamura et al., *The Lancet Oncology*, 2019.

1. Disease control was calculated as the proportion of patients demonstrating complete response, partial response, or stable disease for a minimum of five weeks from the first dosing date 2. Not estimable.

Trastuzumab deruxtecan in breast cancer and beyond

Opportunities across treatment settings in breast cancer

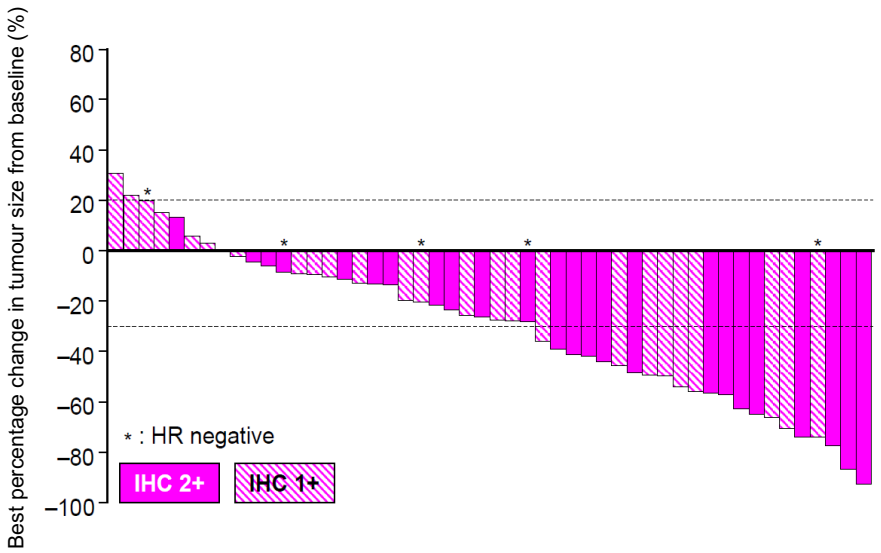


1.Hormone-receptor positive 2. Cyclin-dependent kinase 4/6 inhibitor 3. Triple-negative breast cancer 4. Non-small cell lung cancer 5. Colorectal cancer.

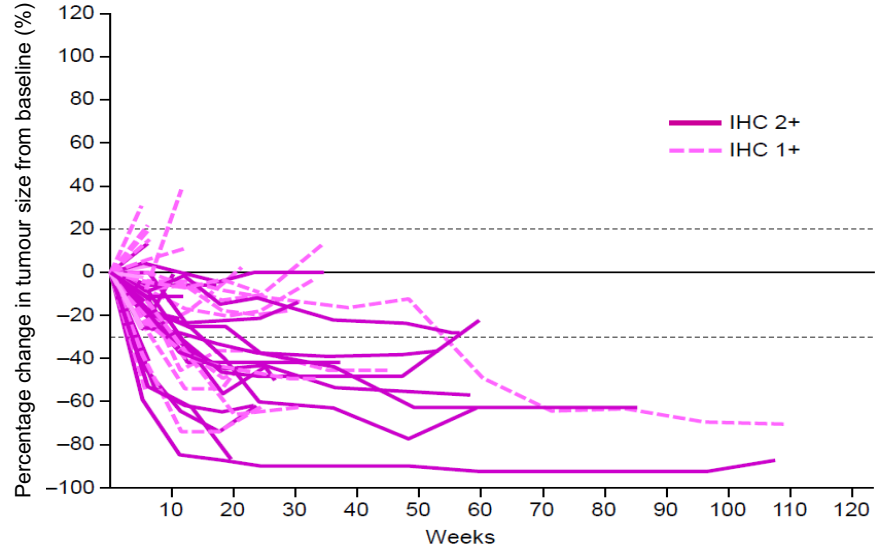
Trastuzumab deruxtecan

Encouraging efficacy in HER2-low breast cancer

HER2-low breast cancer efficacy



44.2% objective response rate



Dotted lines denote 30% decrease and 20% increase in tumor size cutoffs for partial response and progressive disease, respectively.
IHC, immunohistochemistry.

9.4 months DoR[2], 7.6 months median PFS[3]

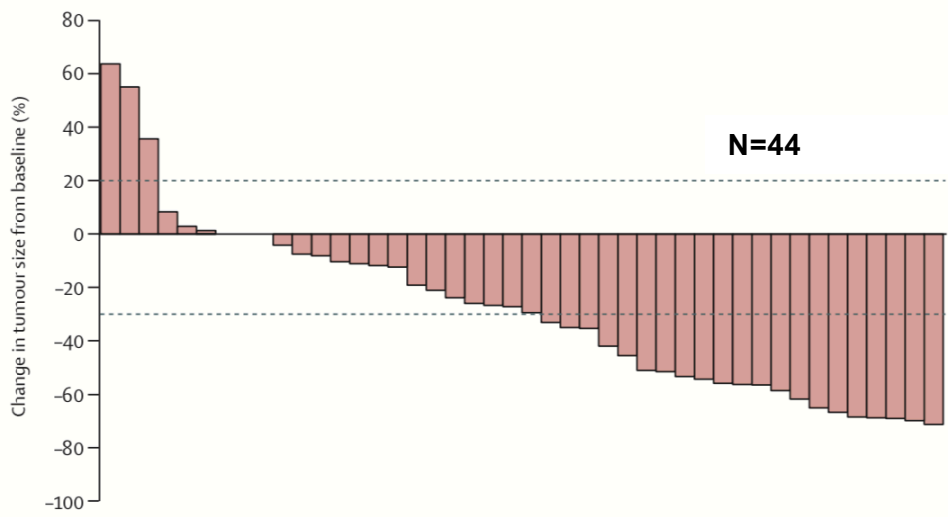
HR: hormone receptor.
IHC: immunohistochemistry.
Source: poster # p6-17-02, SABCS 2018 (based on 12 October 2018 data cut off).

2. Duration of response.
3. Progression-free survival.

Trastuzumab deruxtecan

Compelling efficacy in other cancer types

HER2-positive gastric cancer

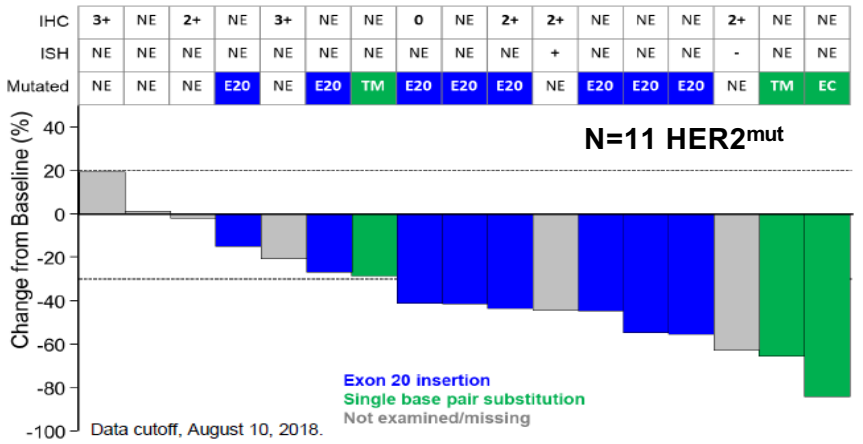


Three average lines of prior treatment

43% ORR
5.6 months median PFS

Source: Phase I, Shitara et al., *The Lancet Oncology*.

HER2-positive and HER2-mutated NSCLC

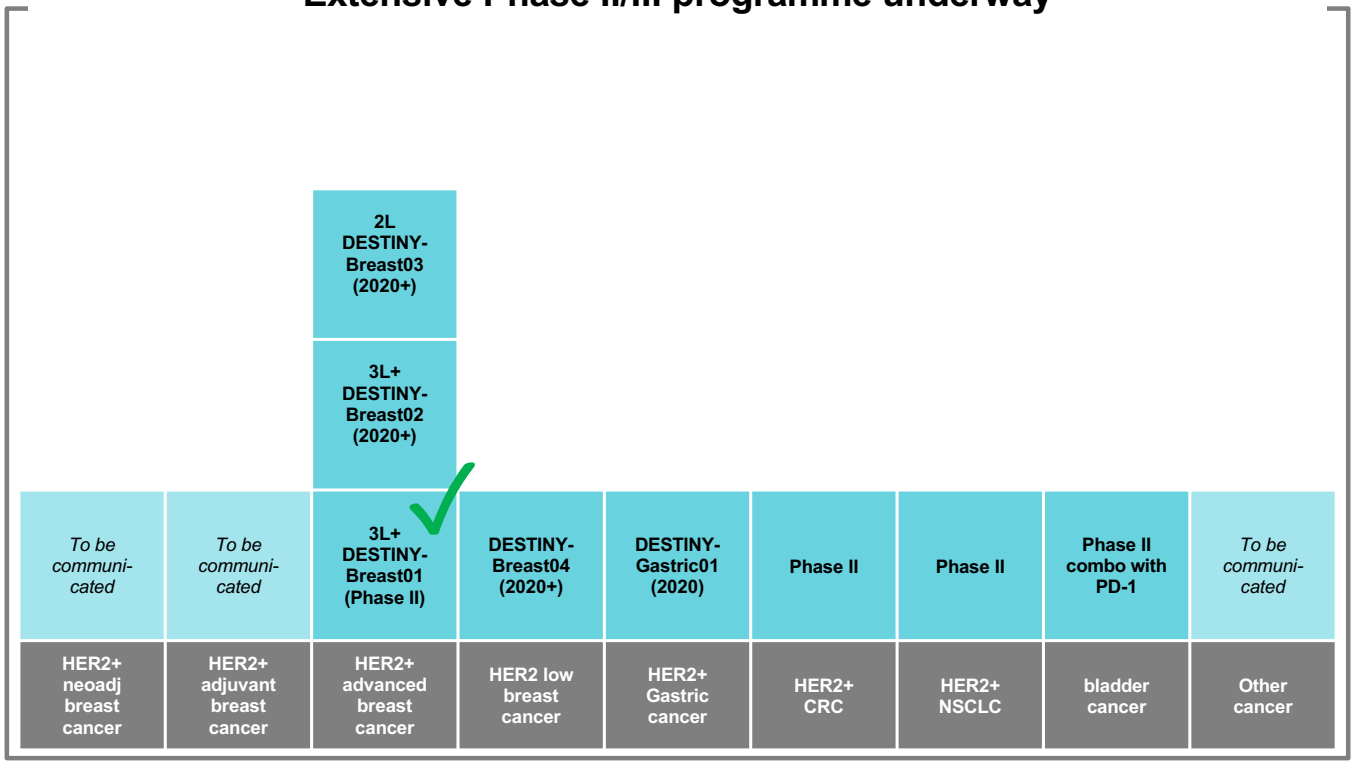


73% ORR[1]
14.1 months median PFS[1]

Source: abstract #13325, Tsurutani et al, WCLC 2018.
1. HER2-mutated NSCLC only.

Trastuzumab deruxtecan
Development plans and news flow

Extensive Phase II/III programme underway



News flow

- US FDA BTD[2] granted in Aug 2017
- DESTINY-Breast01 data presentation in H2 2019
- Regulatory decision anticipated in 2020
- Further Phase III starts anticipated in 2019-2020

US regulatory submission anticipated in H2 2019

Source: AstraZeneca data on file.

2. Breakthrough Therapy Designation.

Q&A

Use of AstraZeneca conference call, webcast and presentation slides