Investor science conference call: European Society for Medical Oncology (ESMO) Congress 2021

Conference call for investors and analysts

20 September 2021
Forward-looking statements

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Speakers

Dr Sara Hurvitz
Senior Investigator, DESTINY-Breast03 and Professor at David Geffen School of Medicine at UCLA

Dave Fredrickson
Executive Vice President, Oncology Business Unit

Sunil Verma
Vice President, Oncology R&D, Late-Stage Development Breast Cancer

Susan Galbraith
Executive Vice President, Oncology R&D

Cristian Massacesi
Chief Medical Officer & Oncology Chief Development Officer

Chris Sheldon
Vice President, Head of Investor Relations
Introduction: AstraZeneca @ ESMO 2021

Enhertu (T-DXd) Phase III DESTINY-Breast03 trial

What's next for Enhertu?

ESMO 2021 other highlights: Enhertu and Imfinzi

Closing and Q&A
Introduction

Susan Galbraith
Executive Vice President, Oncology R&D
Comprehensive portfolio to combat cancer

Diverse pipeline with potential for orthogonal combinations

- **Immune engagers**
  - Redirect local immunity
  - Awaken dormant immune cells

- **Cell therapy**
  - Build synthetic immunity
  - Infuse with engineered T cells

- **Oncolytic virus**
  - Targeted delivery of medicines that recruit immunity

- **Activate immune system**
  - Build on PDx
  - Overcome immune suppression

- **Immuno-oncology**
  - Microenvironment

- **DNA damage response**
  - Synthetic lethality exploiting impaired DNA damage response

- **Tumour drivers and resistance**
  - Oncogenic truncal drivers and mechanisms of resistance

- **Direct killing**
  - Tumour

- **Radioimmuno-conjugates**

- **Nanomedicines**

- **Epigenetics**
  - Reprogramming tumour cells

- **Antibody drug conjugates**

Source: AstraZeneca.
65 abstracts with 20 oral presentations

• One Presidential presentation
• Eight Proffered paper oral presentations
• 11 Mini oral presentations
• 45 Posters
• 65 Abstracts

Data highlights

• Enhertu in breast cancer
  DESTINY-Breast03

• Enhertu in other cancers
  DESTINY-Gastric02, DESTINY-Lung01

• Imfinzi
  COAST, CASPIAN, PACIFIC-R

• Tagrisso, Lynparza,
  datopotamab deruxtecan and capivasertib

*Alliance presentations. Source: ESMO 2021 accepted abstracts. 23 additional presentations at ESMO 2021 will feature AstraZeneca medicines and potential new medicines but were not supported by AstraZeneca.
Enhertu (T-DXd)
DESTINY-Breast03

Dr Sara Hurvitz
Senior Investigator,
DESTINY-Breast03
Phase III trial
DESTINY-Breast03: first randomised phase III trial of T-DXd
An open-label, multicentre study (NCT03529110)

Patients
- Unresectable or metastatic HER2-positive breast cancer
- Previously treated with trastuzumab and taxane in advanced/metastatic setting
- Could have clinically stable, treated brain metastases

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

Interim analysis for PFS (data cutoff: May 21, 2021)
- Efficacy boundary for superiority: P < 0.000204 (based on 245 events)
- IDMC recommendation to unblind study (July 30, 2021)

Key secondary endpoint, OS: boundary for efficacy: P < 0.000265 (based on 86 events)

T-DXd, trastuzumab deruxtecan; T-DM1, ado-trastuzumab emtansine; BICR, blinded independent central review; DOR, duration of response; HER2, human epidermal growth factor receptor 2; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; Q3W, every 3 weeks.

1. HER2 IHC3+ or IHC2+/ISH+ based on central confirmation. 2. Progression during or <6 months after completing adjuvant therapy involving trastuzumab and taxane.
Patient disposition

**Screened (n = 699)**

**Randomised (n = 524)**

- **Randomised to T-DXd (n = 261)**
  - Treated (n = 257)
    - Ongoing study treatment (n = 132)
    - Discontinued study treatment (n = 125)
      - Death (n = 3)
      - Adverse event (n = 35)
      - Progressive disease (n = 66)
      - Clinical progression (n = 4)
      - Withdrawal by subject (n = 13)
      - Physician decision (n = 2)
      - Other (n = 2)

- **Randomised to T-DM1 (n = 263)**
  - Treated (n = 261)
    - Ongoing study treatment (n = 47)
    - Discontinued study treatment (n = 214)
      - Death (n = 3)
      - Adverse event (n = 17)
      - Progressive disease (n = 158)
      - Clinical progression (n = 12)
      - Withdrawal by subject (n = 11)
      - Physician decision (n = 8)
      - Other (n = 5)

**Median follow up for T-DXd was 16.2 months and for T-DM1 was 15.3 months**
Efficacy: confirmed ORR and best overall response

T-DXd (n = 245)\(^1\)

T-DM1 (n = 228)\(^1\)

<table>
<thead>
<tr>
<th></th>
<th>T-DXd (n = 261)</th>
<th>T-DM1 (n = 263)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Confirmed ORR n (%)(^2)</td>
<td>208 (79.7) [74.3-84.4]</td>
<td>90 (34.2) [28.5-40.3]</td>
</tr>
<tr>
<td>CR</td>
<td>42 (16.1)</td>
<td>23 (8.7)</td>
</tr>
<tr>
<td>PR</td>
<td>166 (63.6)</td>
<td>67 (25.5)</td>
</tr>
<tr>
<td>SD</td>
<td>44 (16.9)</td>
<td>112 (42.6)</td>
</tr>
<tr>
<td>PD</td>
<td>3 (1.1)</td>
<td>46 (17.5)</td>
</tr>
<tr>
<td>Not evaluable</td>
<td>6 (2.3)</td>
<td>15 (5.7)</td>
</tr>
<tr>
<td>CR + PR + SD (DCR)</td>
<td>252 (96.6)</td>
<td>202 (76.8)</td>
</tr>
</tbody>
</table>

CI, confidence interval; CR, complete response; DCR, disease control rate; PD, progressive disease; PR, partial response; SD, stable disease.

1. Only subjects with measurable disease at baseline and at least one postbaseline target lesion assessment are included. 2. Based on BICR.

Red line at 20% indicates progressive disease; black line at -30% indicates partial response.
Primary endpoint: PFS by BICR

Median PFS follow up for T-DXd was 15.5 months (range, 15.1-16.1) 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.
Secondary Endpoint: PFS by investigator assessment

![Progression-Free Survival probability, %](chart)

<table>
<thead>
<tr>
<th></th>
<th>T-DXd (n = 261)</th>
<th>T-DM1 (n = 263)</th>
</tr>
</thead>
<tbody>
<tr>
<td>mPFS, mo (95% CI)</td>
<td>25.1 (22.1-NE)</td>
<td>7.2 (6.8-8.3)</td>
</tr>
<tr>
<td>12-mo PFS rate, %</td>
<td>76.3 (70.4-81.2)</td>
<td>34.9 (28.8-41.2)</td>
</tr>
<tr>
<td>HR (95% CI)</td>
<td>0.26 (0.20-0.35)</td>
<td>P = 6.5 × 10^{-24}</td>
</tr>
</tbody>
</table>

**Censor**

- 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 0 0 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 6 4 1 1 1 1 1 1 1 0
Key secondary endpoint: overall survival

Early OS data with relatively few events (33 in the T-DXd arm, 53 in the T-DM1 arm)

- T-DXd (n = 261)
- T-DM1 (n = 263)

<table>
<thead>
<tr>
<th>Time, months</th>
<th>Overall survival probability, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>1</td>
<td>97.6</td>
</tr>
<tr>
<td>2</td>
<td>93.6</td>
</tr>
<tr>
<td>3</td>
<td>89.1</td>
</tr>
<tr>
<td>4</td>
<td>84.7</td>
</tr>
<tr>
<td>5</td>
<td>80.3</td>
</tr>
<tr>
<td>6</td>
<td>76.0</td>
</tr>
<tr>
<td>7</td>
<td>71.7</td>
</tr>
<tr>
<td>8</td>
<td>67.4</td>
</tr>
<tr>
<td>9</td>
<td>63.1</td>
</tr>
<tr>
<td>10</td>
<td>58.7</td>
</tr>
<tr>
<td>11</td>
<td>54.4</td>
</tr>
<tr>
<td>12</td>
<td>50.0</td>
</tr>
<tr>
<td>13</td>
<td>45.7</td>
</tr>
<tr>
<td>14</td>
<td>41.3</td>
</tr>
<tr>
<td>15</td>
<td>37.0</td>
</tr>
<tr>
<td>16</td>
<td>32.6</td>
</tr>
<tr>
<td>17</td>
<td>28.3</td>
</tr>
<tr>
<td>18</td>
<td>24.0</td>
</tr>
<tr>
<td>19</td>
<td>20.3</td>
</tr>
<tr>
<td>20</td>
<td>17.7</td>
</tr>
<tr>
<td>21</td>
<td>15.0</td>
</tr>
<tr>
<td>22</td>
<td>12.4</td>
</tr>
<tr>
<td>23</td>
<td>10.0</td>
</tr>
<tr>
<td>24</td>
<td>7.7</td>
</tr>
<tr>
<td>25</td>
<td>6.0</td>
</tr>
<tr>
<td>26</td>
<td>4.7</td>
</tr>
<tr>
<td>27</td>
<td>3.7</td>
</tr>
<tr>
<td>28</td>
<td>2.3</td>
</tr>
<tr>
<td>29</td>
<td>1.7</td>
</tr>
<tr>
<td>30</td>
<td>1.0</td>
</tr>
<tr>
<td>31</td>
<td>1.0</td>
</tr>
<tr>
<td>32</td>
<td>1.0</td>
</tr>
<tr>
<td>33</td>
<td>1.0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>HR (95% CI)</th>
<th>0.56 (0.36-0.86)</th>
</tr>
</thead>
<tbody>
<tr>
<td>P</td>
<td>.007172</td>
</tr>
</tbody>
</table>

Overall survival probability, %

- Patients Still at Risk:
  - T-DXd (n = 261)
  - T-DM1 (n = 263)

mOS, mo (95% CI)

- T-DXd: NE (NE-NE)
- T-DM1: NE (NE-NE)

12-mo OS rate, % (95% CI)

- T-DXd: 94.1 (90.3-96.4)
- T-DM1: 85.9 (80.9-89.7)

HR (95% CI)

- T-DXd: 0.56 (0.36-0.86)
- T-DM1: 1.0 (0.6-1.6)

P = .007172

a) P = .007172, but does not cross pre-specified boundary of P < .000265
Drug-related TEAEs in ≥20% of patients

<table>
<thead>
<tr>
<th>System Organ Class</th>
<th>Preferred term, n (%)</th>
<th>T-DXd (n = 257)</th>
<th>T-DM1 (n = 261)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Any Grade</td>
<td>Grade ≥3</td>
<td>Any Grade</td>
<td>Grade ≥3</td>
</tr>
<tr>
<td>Blood and lymphatic system disorders</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neutropenia¹</td>
<td>110 (42.8)</td>
<td>49 (19.1)</td>
<td>29 (11.1)</td>
<td>8 (3.1)</td>
</tr>
<tr>
<td>Anemia²</td>
<td>78 (30.4)</td>
<td>15 (5.8)</td>
<td>37 (14.2)</td>
<td>11 (4.2)</td>
</tr>
<tr>
<td>Leukopenia³</td>
<td>77 (30.0)</td>
<td>17 (6.6)</td>
<td>20 (7.7)</td>
<td>1 (0.4)</td>
</tr>
<tr>
<td>Thrombocytopenia⁴</td>
<td>64 (24.9)</td>
<td>18 (7.0)</td>
<td>135 (51.7)</td>
<td>65 (24.9)</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>187 (72.8)</td>
<td>17 (6.6)</td>
<td>72 (27.6)</td>
<td>1 (0.4)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>113 (44.0)</td>
<td>4 (1.6)</td>
<td>15 (5.7)</td>
<td>1 (0.4)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>61 (23.7)</td>
<td>1 (0.4)</td>
<td>10 (3.8)</td>
<td>1 (0.4)</td>
</tr>
<tr>
<td>Constipation</td>
<td>58 (22.6)</td>
<td>0</td>
<td>25 (9.6)</td>
<td>0</td>
</tr>
<tr>
<td>General disorders</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatigue⁵</td>
<td>115 (44.7)</td>
<td>13 (5.1)</td>
<td>77 (29.5)</td>
<td>2 (0.8)</td>
</tr>
<tr>
<td>Investigations</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AST increased</td>
<td>60 (23.3)</td>
<td>2 (0.8)</td>
<td>97 (37.2)</td>
<td>13 (5.0)</td>
</tr>
<tr>
<td>ALT increased</td>
<td>50 (19.5)</td>
<td>4 (1.6)</td>
<td>71 (27.2)</td>
<td>12 (4.6)</td>
</tr>
<tr>
<td>Metabolism and nutrition disorders</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Decreased appetite</td>
<td>67 (26.1)</td>
<td>3 (1.2)</td>
<td>33 (12.6)</td>
<td>0</td>
</tr>
<tr>
<td>Skin and subcutaneous tissue disorders</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alopecia⁶</td>
<td>93 (36.2)</td>
<td>1 (0.4)</td>
<td>6 (2.3)</td>
<td>0</td>
</tr>
</tbody>
</table>

Most drug-related TEAEs were gastrointestinal or haematological in nature

1. This category includes the preferred terms neutrophil count decreased and neutropenia 2. This category includes the preferred terms hematocrit decreased, red blood cell count decreased, anemia, and hematocrit decreased 3. This category includes the preferred terms white blood cell count decreased and leukopenia 4. This category includes platelet count decreased and thrombocytopenia 5. This category includes the preferred terms fatigue, asthenia, and malaise 6. This category includes: T-DXd = 26.5%; T-DM1 = 2.3%; grade 2, T-DXd = 9.3%.
Adverse events of special interest

### Adjudicated as drug-related ILD/pneumonitis, n (%)

<table>
<thead>
<tr>
<th>n (%)</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
<th>Grade 5</th>
<th>Any Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>T-DXd (n = 257)</td>
<td>7 (2.7)</td>
<td>18 (7.0)</td>
<td>2 (0.8)</td>
<td>0</td>
<td>0</td>
<td>27 (10.5)</td>
</tr>
<tr>
<td>T-DM1 (n = 261)</td>
<td>4 (1.5)</td>
<td>1 (0.4)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>5 (1.9)</td>
</tr>
</tbody>
</table>

- There were no grade 4 or 5 adjudicated drug-related ILD/pneumonitis events observed with T-DXd

### LVEF, n (%)

<table>
<thead>
<tr>
<th>n (%)</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
<th>Grade 5</th>
<th>Any Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>T-DXd (n = 257)</td>
<td>1 (0.4)²</td>
<td>6 (2.3)³</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>7 (2.7)</td>
</tr>
<tr>
<td>T-DM1 (n = 261)</td>
<td>0</td>
<td>1 (0.4)³</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1 (0.4)</td>
</tr>
</tbody>
</table>

- In the T-DXd arm, all LVEF adverse events reported were asymptomatic and no cases of cardiac failure occurred

ILD, interstitial lung disease; LVEF, left-ventricular ejection fraction.

1. Patients with prior history of ILD/pneumonitis requiring steroids were excluded 2. Left ventricular dysfunction 3. Decreased ejection fraction.
Conclusions

In the first randomised Phase III trial in breast cancer, T-DXd demonstrated:

Highly clinically meaningful and statistically significant improvement in PFS compared with T-DM1 in patients with HER2-positive mBC

- PFS HR of 0.28 ($P = 7.8 \times 10^{-22}$)
- Consistent benefit seen across key subgroups and efficacy endpoints, with a confirmed ORR for T-DXd of 79.7% vs 34.2% for T-DM1 (CR, 16.1% vs 8.7%)

Encouraging OS trend at the time of first interim analysis

- 12-month OS rate for T-DXd was 94.1% vs 85.9% for T-DM1

A safety profile that is comparable between the two arms

- Similar rates of all grade and grade ≥3 drug-related TEAEs between arms
- There were no grade 4 or 5 ILD/pneumonitis events in either arm

These data support T-DXd becoming the standard of care for 2L HER2-positive mBC

mBC, metastatic breast cancer.
T-DXd transforms the treatment paradigm for patients with metastatic HER2+ breast cancer

- **1L** Trastuzumab + pertuzumab + taxane, CLEOPATRA\(^1\): mPFS = 18.7 months
- **1L** T-DM1 + pertuzumab, MARIANNE\(^2\): mPFS = 15.2 months
- **2L** T-DXd DESTINY-Breast03\(^3\): mPFS = not yet reached
  - Investigator-assessed PFS: 25.1 months
- **2L+** T-DM1, EMILIA\(^4\): mPFS = 9.6 months
- **3L+** T-DXd DESTINY-Breast01\(^5\): mPFS = 19.4 months

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What’s next for *Enhertu*?

Dave Fredrickson
Executive Vice President,
Oncology Business Unit
Enhertu: a new standard of care for patients with HER2-positive metastatic breast cancer

Today: 3rd-line+ mBC
- Strong launch trajectory: market leader in every major country launched\(^1\)
- >7,000 patients treated to date
- Partnering with healthcare practitioners with treatment-specific guidance

2022: 2nd-line mBC
- DESTINY-Breast03: unprecedented benefit in 2nd line
- Consistent efficacy across all sub-groups
- Safety profile and prolonged PFS benefit supports extended duration on therapy

Future: earlier settings, combinations
- Efficacy and safety profile support development in 1st line and adjuvant settings
- Opens opportunity to treat with curative intent
- An Enhertu option for every patient with HER2+ breast cancer

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1. UK National Health Service – Cancer Drugs Fund, AstraZeneca market studies.
## Enhertu in breast cancer and beyond

Opportunities across treatment settings

<table>
<thead>
<tr>
<th>HER2-positive breast cancer</th>
<th>neo-adjuvant / adjuvant</th>
<th>1st-line metastatic</th>
<th>2nd-line metastatic</th>
<th>3rd-line metastatic</th>
</tr>
</thead>
<tbody>
<tr>
<td>neo-adjuvant</td>
<td>replace chemo + trastuzumab + pertuzumab</td>
<td>replace chemotherapy + trastuzumab + pertuzumab</td>
<td>replace T-DM1 and other standard of care</td>
<td></td>
</tr>
<tr>
<td>post neo-adjuvant</td>
<td>replace T-DM1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>adjuvant</td>
<td>replace chemo + trastuzumab + pertuzumab</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### HER2-low breast cancer

<table>
<thead>
<tr>
<th>HR+: chemotherapy ± endocrine therapy</th>
<th>endocrine ± CDK4/6i</th>
<th>replace/displace chemotherapy and endocrine combinations&lt;sup&gt;1&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR-: chemotherapy +/- IO</td>
<td></td>
<td>replace/displace chemotherapy and evaluate combinations</td>
</tr>
</tbody>
</table>

### Beyond breast cancer

- **broaden** in gastric cancer and **expand** into NSCLC, CRC and other cancers

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1. in endocrine therapy refractory/resistant patients.

**Abbreviations:**
- HR = hormone-receptor positive; CDK4/6i = cyclin-dependent kinase 4/6 inhibitor; HR- = hormone-receptor negative; IO = immuno-oncology. NSCLC = non-small cell lung cancer; CRC = colorectal cancer.
Other ESMO 2021 highlights - *Enhertu* and *Imfinzi*

Susan Galbraith
Executive Vice President, Oncology R&D
Enhertu: extending clinical benefit to other cancers

**Phase II DESTINY-Lung01**
Robust and durable anti-cancer activity in patients with previously treated HER2m NSCLC

**Phase II DESTINY-Gastric02**
Efficacy results demonstrate clinically meaningful and durable responses

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**Overall Survival**

Median OS: 17.8 months (95% CI, 13.8-22.1)

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**Best Percentage Change of Tumour Size from Baseline**

Confirmed ORR: 38% (95% CI, 27.3-49.6)

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Median PFS follow up for T-DXd was 15.5 months (range, 15.1-16.1) and for T-DM1 was 13.9 months (range, 11.8-15.1)

Dashed lines indicate the 95% CI. Of 91 patients, 47 had died by the cutoff date.

Data for 44 patients were censored as indicated by tick marks; patients were censored if they discounted treatment.
### Enhertu: an extensive clinical development programme

**Focusing on HER2+ and HER2-low breast cancer and other cancers**

<table>
<thead>
<tr>
<th>HER2 status</th>
<th>Post-neoadjuvant/Adjuvant</th>
<th>1st line</th>
<th>2nd line</th>
<th>3rd line+</th>
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<tbody>
<tr>
<td><strong>Breast cancer</strong></td>
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<tr>
<td>HER2+</td>
<td>DESTINY-Breast05 Ph III</td>
<td>DESTINY-Breast07 Ph ib/II (Part 2)</td>
<td>DESTINY-Breast03 Ph III</td>
<td>DESTINY-Breast01 Ph II</td>
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<td>DESTINY-Breast09 Ph III</td>
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<td>DESTINY-Breast02 Ph III</td>
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<td>HER2 Low</td>
<td>BEGONIA Ph II</td>
<td>DESTINY-Breast06 Ph III</td>
<td>DESTINY-Breast04 Ph III</td>
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<td></td>
<td>DESTINY-Breast08 Ph ib</td>
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<tr>
<td><strong>Gastric cancer</strong></td>
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<tr>
<td>HER2+</td>
<td></td>
<td>DESTINY-Gastric02 Ph II</td>
<td>DESTINY-Gastric01 Ph II</td>
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<tr>
<td></td>
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<td>DESTINY-Gastric03 Ph ib/II</td>
<td>DESTINY-Gastric06 Ph II</td>
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<td></td>
<td>DESTINY-Gastric04 Ph III</td>
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<tr>
<td><strong>Lung, CRC and other cancers</strong></td>
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<tr>
<td>HER2 mutated</td>
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<td>DESTINY-Lung04 Ph III</td>
<td>DESTINY-Lung02 Ph II</td>
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<td>DESTINY-PanTumor03 Ph II</td>
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<td>DESTINY-Lung01 Ph II</td>
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<td>HER2 expressing</td>
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<td>HUDSON Ph II</td>
<td>DESTINY-CRC01 Ph II</td>
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<td>DESTINY-PanTumor02 Ph II</td>
<td>DESTINY-CRC02 Ph II</td>
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<td>DESTINY-Lung03 Ph Ib</td>
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*monotherapy  combination*
Electronic document page text

Imfinzi in Stage III, unresectable non-small cell lung cancer
Cementing leadership in this potentially curative setting

PACIFIC-R: Real world PFS

*Imfinzi* after CRT for a median duration of ~11 months is effective in a large, real-world cohort of patients with unresectable Stage III NSCLC

<table>
<thead>
<tr>
<th></th>
<th>PACIFIC-R FAS</th>
<th>PACIFIC trial (durva. arm)¹</th>
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<tbody>
<tr>
<td>PFS</td>
<td>N=1,399</td>
<td>N=476</td>
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<tr>
<td>Total events, N (%)</td>
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<td></td>
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<tr>
<td>Progression per RECIST</td>
<td>737 (52.7)</td>
<td>268 (56.3)⁴</td>
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<tr>
<td>Progression per physician assessment</td>
<td>456 (32.6)</td>
<td></td>
</tr>
<tr>
<td>Progression, assessment unknown</td>
<td>170 (12.2)</td>
<td></td>
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<tr>
<td>Deaths in absence of progression</td>
<td>30 (2.1)</td>
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<tr>
<td>Median PFS, months</td>
<td>21.7</td>
<td>16.9</td>
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<tr>
<td>95% CI</td>
<td>19.2–24.5</td>
<td>13.0–23.9</td>
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PFS rate, %

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<table>
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<tbody>
<tr>
<td>12 months</td>
<td>62.4</td>
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<tr>
<td>24 months</td>
<td>48.2</td>
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COAST: PFS by investigator’s analysis

First randomised Phase II to show evidence of improved outcomes with novel IO combinations in the PACIFIC setting

<table>
<thead>
<tr>
<th></th>
<th>D</th>
<th>D+O</th>
<th>D+M</th>
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</thead>
<tbody>
<tr>
<td>Events/patients, n</td>
<td>38/67</td>
<td>22/60</td>
<td>21/62</td>
</tr>
<tr>
<td>mPFS, months (95% CI)²</td>
<td>6.3 (3.7–11.2)</td>
<td>NR (10.4–NE)</td>
<td>15.1 (13.6–NE)</td>
</tr>
<tr>
<td>HR (95% CI)²,³</td>
<td>0.44 (0.26–0.75)</td>
<td>0.65 (0.49–0.85)</td>
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</tbody>
</table>

Data cut-off: 17 May 2021 (median follow-up of 11.5 months; range, 0.4–23.4) D, durvalumab; M, monalizumab; O, oleclumab.

1. Interim analysis performed when all patients had a 10mth min potential follow-up; Kaplan-Meier estimates for PFS, PFS rate and 95% CIs 2. PFS HR and 95% CI estimated by Cox regression model, stratified by histology (adenocarcinoma and non-adenocarcinoma) 3. Compared with the 67 and 64 patients in the D arm enrolled concurrently with patients in the D+O and D+M arms, respectively.


*Range for median follow-up duration = 0–35.6 months; In the PACIFIC trial, PFS was assessed by BICR per RECIST v1.1; Per local regulations. FAS, full analysis set; rw, real-world; UK, United Kingdom.
**Imfinzi**: extending IO leadership through portfolio combinations

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**ADCs**

POC: BEGONIA mBC 1L HER2-low/HR-

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**CD73, NKG2A**

POC: COAST – Stg III UR NSCLC (below) / Study 5 (PDAC)

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**PARP inhibitor**

POC: MEDIOLA BRCAwt PSR ovarian (below) / BAYOU (UC)

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**CTLA4**

POC: POSEIDON (adv NSCLC)/Study 22 (HCC)/MEDI5752 Ph II

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**TIGIT**

POC: BEGONIA mBC 1L HER2-low/HR-

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**ATR inhibitor**

POC: POSEIDON (adv NSCLC)/Study 22 (HCC)/MEDI5752 Ph II

---

**PARP inhibitor**

POC: MEDIOLA BRCAwt PSR ovarian (below) / BAYOU (UC)

---

**TIGIT**

Imfinzi + domvamalimab

Phase III (PACIFIC-8)

AZD2936

Phase I/II (ARTEMIDE-01)

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ADCs = antibody drug conjugates; CD73 = cluster of differentiation 73; NKG2A = natural killer group 2 member A; PARP = poly(ADP-ribose) polymerase; CTLA4 = cytotoxic T-lymphocyte-associated protein 4; HCC = hepatocellular carcinoma; TIGIT = T cell immunoreceptor with Ig and ITIM domains; ATR = ataxia telangiectasia and rad3-related; POC = proof of concept; UR = unresectable; NSCLC = non small cell lung cancer; BRCAwt = breast cancer gene wildtype; PSR = platinum sensitive relapsed; PDAC = pancreatic ductal adenocarcinoma; UC = urothelial cancer; adv = advanced.
Closing and Q&A
Appendix
Enhertu: DESTINY-Lung01 trial design
Multi-centre, international, 2-cohort Phase II trial (NCT03505710)

**Key eligibility criteria**
- Unresectable/metastatic nonsquamous NSCLC
- Relapsed from or is refractory to standard treatment
- Measurable disease by RECIST v1.1
- Asymptomatic CNS metastases at baseline
- ECOG PS of 0 or 1
- Locally reported HER2 mutation (for Cohort 2)

**Data cutoff: May 3, 2021**
- 91 patients with HER2m NSCLC were enrolled and treated with T-DXd
- 15 patients (16.5%) remain on treatment to date
- 76 patients (83.5%) discontinued, primarily for progressive disease (37.4%) and adverse events (29.7%)

**Primary end point**
- Confirmed ORR by ICR

**Secondary end points**
- DOR
- PFS
- OS
- DCR
- Safety

**Exploratory end point**
- Biomarkers of response

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1. Patients with asymptomatic brain metastases not requiring ongoing steroid or anticonvulsant therapy were allowed to enrol
2. HER2 mutation documented solely from a liquid biopsy could not be used for enrolment
3. HER2 overexpression without known HER2 mutation was assessed by local assessment of archival tissue and centrally confirmed
4. Per RECIST v1.1

ECOG PS = Eastern Cooperative Oncology Group performance status; ICR = independent central review; IHC = immunohistochemistry; q3w, every 3 weeks; RECIST v1.1, Response Evaluation Criteria in Solid Tumours version 1.1.
Enhertu: DESTINY-Gastric02 trial design

Open-label, multicentre Phase II trial in Western patients with HER2+ gastric or GEJ cancer (NCT04014075)

Key eligibility criteria
- Pathologically documented, unresectable or metastatic gastric or GEJ cancer
- Centrally confirmed HER2 positive disease (defined as IHC 3+ or IHC 2+/ISH+) on biopsy after progression on first-line trastuzumab-containing regimen
- ECOG PS 0 or 1

Primary endpoint
- Confirmed ORR by ICR

Secondary endpoints²
- PFS by ICR
- OS
- DOR by ICR
- Safety and tolerability

T-DXd 6.4 mg/kg Q3W
N = 79¹

- DESTINY-Gastric02 is the first study focused only on second-line T-DXd monotherapy in Western patients with HER2+ gastric/GEJ cancer who have progressed on a trastuzumab-containing regimen
- It is the follow-on study to DESTINY-Gastric01, which evaluated T-DXd third-line or later in Asian patients³
- Patients were enrolled in Europe (Belgium, Great Britain, Italy, Spain) and the United States (data cutoff: April 9, 2021)

¹ Enrollment of 80 patients was planned; actual enrollment was 79 patients ² Other secondary endpoints were ORR, PFS, and DOR by investigator assessment, pharmacokinetics, anti-drug antibodies, and patient-reported outcomes ³ Shitara K et al. N Engl J Med. 2020;382:2419-30.

GEJ = gastroesophageal junction; ISH = in situ hybridisation.
Imfinzi: COAST trial design

A Phase II, randomised open-label trial

- A planned sample size of 60 patients per arm was designed to provide acceptable precision in estimating antitumour activities in an early phase setting
- Between Jan 2019 and Jul 2020, 189 patients were randomised of whom 186 received D (n=66), D+O (n=59) or D+M (n=61)
- As of 17 May 2021, all patients had a minimum of 10 months potential follow-up and the median actual follow-up was 11.5 months (range, 0.4–23.4; all patients)

IV = intravenous; PK = pharmacokinetics.
Imfinzi: Propensity score matching of COAST (durvalumab arm) with PACIFIC (durvalumab arm)

- **Matching variables**: Age (<75, ≥75), Race (Asian, Other), Prior therapy (Carboplatin, Cisplatin), Time from last radiation to randomisation (<14 days, ≥14 days), Best response to prior therapies (PR, SD) and Disease stage at entry (IIIA, IIIB, IIIC)

<table>
<thead>
<tr>
<th>Events/patients, n</th>
<th>COAST (D)</th>
<th>PACIFIC (D)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PFS-10 months</td>
<td>32/61</td>
<td>31/60</td>
</tr>
<tr>
<td>(95% CI)</td>
<td>38.0%</td>
<td>44.6%</td>
</tr>
<tr>
<td></td>
<td>(24.5–51.3%)</td>
<td>(31.3–57.1%)</td>
</tr>
<tr>
<td>ORR (conf + unconf), %</td>
<td>24.6%</td>
<td>24.6%</td>
</tr>
<tr>
<td>(n)</td>
<td>(15)</td>
<td>(15)</td>
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