Investor science conference call: American Society of Clinical Oncology Genitourinary (ASCO GU) Cancers Symposium 2022

Conference call for investors and analysts

23 February 2022
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Speakers

Dr Fred Saad
Principal Investigator PROpel,
Professor and Chief of Urology,
University of Montreal Hospital Centre, Canada

Dave Fredrickson
Executive Vice President,
Oncology Business Unit

Andy Barnett
Global Franchise Head, GU and GYN Cancers, DDR and Established Oncology (for Q&A)

Susan Galbraith
Executive Vice President,
Oncology R&D

Sunil Verma
Senior Vice President,
Global Head of Oncology, Medical (for Q&A)
Introduction: AstraZeneca @ ASCO GU 2022

Lynparza Phase III PROpel trial

Opportunity and unmet need in mCRPC

Other ASCO GU highlights

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**
- **Cell therapy**
- **Activate immune system**
- **Oncolytic virus**
- **Immuno-oncology**

**Microenvironment**

- Redirect local immunity
  - Awaken dormant immune cells
- Build synthetic immunity
  - Infuse with engineered T cells
- Targeted delivery of medicines that recruit immunity
- Build on PDx
  - Overcome immune suppression

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

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

**Direct killing**

- Tumour
- Tumour microenvironment

**Radioimmuno-conjugates**
- Nanomedicines
- Antibody drug conjugates

**Epigenetics**
- Reprogramming tumour cells

**Oncogenic truncal drivers**
- With targeted delivery of toxic molecules

**Source:** AstraZeneca.
19 abstracts with three oral presentations

- **Two** Oral presentations
- **One** Mini-oral presentation
- **16** Posters
- **19** Abstracts accepted

Data highlights

- **Lynparza + abiraterone** in 1st-line mCRPC PROpel Phase III trial
- **Lynparza + Imfinzi** in 1st-line urothelial carcinoma BAYOU Phase II trial
- **Enhertu + nivolumab** in HER2+ urothelial carcinoma U105 Phase Ib trial

Source: ASCO GU 2022 accepted abstracts. Inclusive of externally sponsored research and partner-led trials. mCRPC = metastatic castration resistant prostate cancer; HER2+ = human epidermal receptor 2 positive.
**Lynparza and abiraterone**

Success in Study 08 paved the way for PROpel in 1st-line mCRPC

### Study 08

**Phase II trial**

**Graph:**
- **Olaparib and abiraterone (n=71):**
  - 71 (0)
  - 58 (5)
  - 50 (6)
  - 42 (8)
  - 32 (12)
  - 26 (12)
  - 18 (12)
  - 12 (17)
  - 8 (19)
  - 0 (25)

- **Placebo and abiraterone (n=71):**
  - 71 (0)
  - 48 (3)
  - 39 (4)
  - 25 (5)
  - 21 (7)
  - 19 (7)
  - 15 (7)
  - 14 (7)
  - 10 (8)
  - 7 (19)
  - 0 (17)

**Significant rPFS benefit regardless of HRRm status**

35% risk reduction

**PARP-signaling and AR-signaling pathway interaction**

may explain combined effect


**rPFS:** radiographic progression free survival;

**HRR:** homologous recombination repair;

**HRRm:** HRR gene mutation;

**PARP:** poly adenosine diphosphate-ribose polymerase;

**AR:** androgen receptor;

**NHA:** new hormonal agents.
Lynparza PROpel

Dr Fred Saad
Principal Investigator,
PROpel Phase III trial
PROpel
A global randomised double-blind Phase III trial

Patient population
• 1L mCRPC
• Docetaxel allowed at mHSPC stage
• No prior abiraterone
• Other NHAs allowed if stopped ≥12 months prior to enrollment
• Ongoing ADT
• ECOG 0–1

Stratification factors
• Site of distant metastases: bone only vs visceral vs other
• Prior taxane at mHSPC: yes vs no

Olaparib 300 mg bid + abiraterone 1000 mg qd*
n=399
Full dose of olaparib and abiraterone used

Placebo + abiraterone 1000 mg qd*
n=397
Full dose of abiraterone used

Primary endpoint
• Radiographic progression or death (rPFS)
  by investigator assessment

Key secondary endpoint
• Overall survival (alpha control)

Additional endpoints
• Time to first subsequent therapy or death (TFST)
• Time to second progression or death (PFS2)
• Objective response rate (ORR)
• HRRm† prevalence (retrospective testing)
• Health-related quality of life
• Safety and tolerability

First patient randomized: Nov 2018; Last patient randomized: Mar 2020; DCD1: July 30, 2021, for interim analysis of rPFS and OS.
Multiple testing procedure is used in this study: 1-sided alpha of 0.025 fully allocated to rPFS. If the rPFS result is statistically significant, OS to be tested in a hierarchical fashion with alpha passed on to OS.
†Please access the Supplement at https://bit.ly/3r50msO for more details.

*In combination with prednisone or prednisolone 5 mg bid. †HRRm, homologous recombination repair mutation, including 14 genes panel.
ADT = androgen deprivation therapy; bid = twice daily; ECOG = Eastern Cooperative Oncology Group; mHSPC = metastatic hormone sensitive prostate cancer.
Baseline patient characteristics

Well-balanced between treatment arms

<table>
<thead>
<tr>
<th></th>
<th>Olaparib + abiraterone (n=399)</th>
<th>Placebo + abiraterone (n=397)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median (range) age, years</td>
<td>69.0 (43–91)</td>
<td>70.0 (46–88)</td>
</tr>
<tr>
<td>ECOG performance status, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>286 (71.7)</td>
<td>272 (68.5)</td>
</tr>
<tr>
<td>1</td>
<td>112 (28.1)</td>
<td>124 (31.2)</td>
</tr>
<tr>
<td>Symptomatic,* n (%)</td>
<td>103 (25.8)</td>
<td>80 (20.2)</td>
</tr>
<tr>
<td>Site of metastases, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bone</td>
<td>349 (87.5)</td>
<td>339 (85.4)</td>
</tr>
<tr>
<td>Distant lymph nodes</td>
<td>133 (33.3)</td>
<td>119 (30.0)</td>
</tr>
<tr>
<td>Locoregional lymph nodes</td>
<td>82 (20.6)</td>
<td>89 (22.4)</td>
</tr>
<tr>
<td>Lung</td>
<td>40 (10.0)</td>
<td>42 (10.6)</td>
</tr>
<tr>
<td>Liver</td>
<td>15 (3.8)</td>
<td>18 (4.5)</td>
</tr>
<tr>
<td>Docetaxel treatment at mHSPC stage, n (%)</td>
<td>90 (22.6)</td>
<td>89 (22.4)</td>
</tr>
<tr>
<td>Median PSA, ug/L (IQR)</td>
<td>17.90 (6.09–67.00)</td>
<td>16.81 (6.26–53.30)</td>
</tr>
<tr>
<td>HRRm status†</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HRRm</td>
<td>111 (27.8)</td>
<td>115 (29.0)</td>
</tr>
<tr>
<td>Non-HRRm</td>
<td>279 (69.9)</td>
<td>273 (68.8)</td>
</tr>
<tr>
<td>HRRm unknown</td>
<td>9 (2.3)</td>
<td>9 (2.3)</td>
</tr>
</tbody>
</table>

*Patients with symptomatic pain at baseline: BPI-SF item #3 score ≥4 and/or opiate use at baseline.

†The HRRm status of patients in PROpel was determined retrospectively using results from tumor tissue and plasma ctDNA HRRm tests. Patients were classified as HRRm if (one or more) HRR gene mutation was detected by either test; patients were classified as non-HRRm if no HRR gene mutation was detected by either test; patients were classified as unknown HRRm if no valid HRR test result from either test was achieved. Please access the Supplement via the QR code at the end of this presentation for more details.

BPI-SF = Brief Pain Inventory – Short Form; ctDNA = circulating tumor DNA; IQR = interquartile range; PSA = prostate-specific antigen.
Primary endpoint: rPFS by investigator-assessment

34% risk reduction of progression or death with olaparib + abiraterone

12-month rate

71.8%
63.4%

24-month rate

51.4%
33.6%

Events, n (%)

Olaparib + abiraterone (n=399)
Placebo + abiraterone (n=397)

168 (42.1) 226 (56.9)

Median rPFS (months)

24.8 16.6

HR (95% CI)

0.66 (0.54–0.81); P<0.0001

Pre-specified 2-sided alpha: 0.0324
Secondary endpoint: rPFS by blinded independent central review*  
39% risk reduction of progression or death, highly consistent with the primary analysis

**Graph: Probability of rPFS**

- **12-month rate**
  - Olaparib + abiraterone: 73.8%
  - Placebo + abiraterone: 60.6%

- **24-month rate**
  - Olaparib + abiraterone: 53.7%
  - Placebo + abiraterone: 34.1%

**Events, n (%)**

<table>
<thead>
<tr>
<th></th>
<th>Olaparib + abiraterone (n=399)</th>
<th>Placebo + abiraterone (n=397)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median rPFS</td>
<td>27.6</td>
<td>16.4</td>
</tr>
<tr>
<td>HR (95% CI)</td>
<td>0.61 (0.49–0.74) P&lt;0.0001†</td>
<td></td>
</tr>
</tbody>
</table>

Median rPFS improvement of 11.2 months favors olaparib + abiraterone‡

*Predefined sensitivity analysis. †Nominal. ‡In combination with prednisone or prednisolone.
Subgroup analysis of rPFS

rPFS benefit observed across all pre-specified subgroups

<table>
<thead>
<tr>
<th>Number of patients, n</th>
<th>Median rPFS, months</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients 796</td>
<td>24.8 16.6</td>
<td>0.66 (0.54–0.81)</td>
</tr>
<tr>
<td>Age at randomization</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;65 227</td>
<td>NR 16.4</td>
<td>0.51 (0.35–0.75)</td>
</tr>
<tr>
<td>≥65 569</td>
<td>22.0 16.7</td>
<td>0.78 (0.62–0.98)</td>
</tr>
<tr>
<td>ECOG performance status at baseline</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 558</td>
<td>24.9 16.8</td>
<td>0.67 (0.52–0.85)</td>
</tr>
<tr>
<td>1 236</td>
<td>17.5 14.6</td>
<td>0.75 (0.53–1.06)</td>
</tr>
<tr>
<td>Site of distant metastases</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bone only 434</td>
<td>27.6 22.2</td>
<td>0.73 (0.54–0.98)</td>
</tr>
<tr>
<td>Visceral 105</td>
<td>13.7 10.9</td>
<td>0.62 (0.39–0.99)</td>
</tr>
<tr>
<td>Other 257</td>
<td>20.5 13.7</td>
<td>0.62 (0.44–0.85)</td>
</tr>
<tr>
<td>Docetaxel treatment at mHSPC stage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes 189</td>
<td>27.6 13.8</td>
<td>0.61 (0.40–0.92)</td>
</tr>
<tr>
<td>No 607</td>
<td>24.8 16.8</td>
<td>0.71 (0.56–0.89)</td>
</tr>
<tr>
<td>Baseline PSA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Below median baseline PSA 396</td>
<td>25.2 22.0</td>
<td>0.75 (0.55–1.02)</td>
</tr>
<tr>
<td>Above or equal to median baseline PSA 397</td>
<td>18.5 13.8</td>
<td>0.63 (0.48–0.82)</td>
</tr>
<tr>
<td>HRRm status*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HRRm 226</td>
<td>NR 13.9</td>
<td>0.50 (0.34–0.73)</td>
</tr>
<tr>
<td>Non-HRRm 570</td>
<td>24.1 19.0</td>
<td>0.76 (0.60–0.97)</td>
</tr>
</tbody>
</table>

Global interaction test not significant at 10% level. *The HRRm status of patients in PROpel was determined retrospectively using results from tumor tissue and plasma ctDNA HRRm tests. Patients were classified as HRRm if (one or more) HRR gene mutation was detected by either test; patients were classified as non-HRRm patients if no HRR gene mutation was detected by either test; patients were classified as unknown: HRRm if no valid HRR test result from either test was achieved. 18 patients did not have a valid HRR testing result from either a tumor tissue or ctDNA test and were excluded from the subgroup analysis. This subgroup analysis is post hoc exploratory analysis. Please access the Supplement via the QR code at the end of this presentation for more details. NR = not reached.
Secondary endpoint: overall survival

28.6% maturity; trend towards improved OS with olaparib + abiraterone
Secondary endpoints: TFST and PFS2
TFST and PFS2 results support longer-term benefit with olaparib + abiraterone

<table>
<thead>
<tr>
<th>Time to first subsequent therapy or death (TFST)</th>
<th>Time to second progression or death (PFS2)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Probability of not experiencing first subsequent therapy or death</strong></td>
<td><strong>Probability of second progression-free survival</strong></td>
</tr>
<tr>
<td><strong>Olaparib + abiraterone (n=399)</strong></td>
<td><strong>Olaparib + abiraterone (n=399)</strong></td>
</tr>
<tr>
<td>Events, n (%)</td>
<td>183 (45.9)</td>
</tr>
<tr>
<td>Median TFST (months)</td>
<td>25.0</td>
</tr>
<tr>
<td>HR (95% CI)</td>
<td>0.74 (0.61–0.90)</td>
</tr>
<tr>
<td>P = 0.004*</td>
<td>P = 0.0184*</td>
</tr>
</tbody>
</table>

| **Placebo + abiraterone (n=397)** | **Placebo + abiraterone (n=397)** |
| Events, n (%) | 221 (55.7) | 94 (23.7) |
| Median PFS2 (months) | 19.9 | NR |
| HR (95% CI) | NR | NR |

*Nominal.
Overall safety profile

A relatively small increase in discontinuations for olaparib vs placebo, discontinuation with abiraterone was similar between treatment arms

<table>
<thead>
<tr>
<th>n (%)</th>
<th>Olaparib + abiraterone (n=399)</th>
<th>Placebo + abiraterone (n=397)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any AE</td>
<td>387 (97.2)</td>
<td>376 (94.9)</td>
</tr>
<tr>
<td>Any AE CTCAE Grade ≥3</td>
<td>188 (47.2)</td>
<td>152 (38.4)</td>
</tr>
<tr>
<td>Death due to an AE</td>
<td>16 (4.0)</td>
<td>17 (4.3)</td>
</tr>
<tr>
<td>Any AE leading to:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dose interruption of olaparib/placebo</td>
<td>178 (44.7)</td>
<td>100 (25.3)</td>
</tr>
<tr>
<td>Dose reduction of olaparib/placebo</td>
<td>80 (20.1)</td>
<td>22 (5.6)</td>
</tr>
<tr>
<td>Discontinuation of olaparib/placebo</td>
<td>55 (13.8)</td>
<td>31 (7.8)</td>
</tr>
<tr>
<td>Discontinuation of abiraterone</td>
<td>34 (8.5)</td>
<td>35 (8.8)</td>
</tr>
</tbody>
</table>

AEs of special interest for olaparib
- No MDS/AML reported
- Incidence of new primary malignancies and pneumonitis were balanced between treatment arms
Cardiac and thromboembolic adverse events

Cardiac failure and arterial thromboembolic events were balanced between the two arms.

Numerically higher venous thromboembolic events were reported for olaparib + abiraterone.

- Pulmonary embolism was the most commonly reported venous thromboembolic event.
- Pulmonary embolism events were mostly incidental findings by CT scans and did not lead to discontinuation of olaparib or abiraterone.

<table>
<thead>
<tr>
<th>n (%)</th>
<th>Olaparib + abiraterone (n=399)</th>
<th>Placebo + abiraterone (n=397)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac failure SMQ</td>
<td>6 (1.5)</td>
<td>5 (1.3)</td>
</tr>
<tr>
<td>Embolic and thrombotic events, arterial SMQ</td>
<td>8 (2.0)</td>
<td>10 (2.5)</td>
</tr>
<tr>
<td>Embolic and thrombotic events, venous SMQ</td>
<td>29 (7.3)</td>
<td>13 (3.3)</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>26 (6.5)</td>
<td>7 (1.8)</td>
</tr>
</tbody>
</table>

CT = computerised tomography; SMQ = Standardised MedDRA Query.
Most common adverse events

AE profile was consistent with the known toxicity profiles for the individual drugs

Safety was assessed through the reporting of AEs according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE v4.03) and laboratory assessments.

*Anemia category includes anemia, decreased hemoglobin level, decreased red-cell count, decreased hematocrit level, erythropenia, macrocytic anemia, normochromic anemia, normochromic normocytic anemia, and normocytic anemia.

Safety was assessed through the reporting of AEs according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE v4.03) and laboratory assessments.
Conclusions

Olaparib + abiraterone led to a significant and clinically meaningful improvement in rPFS (HR 0.66 [95% CI 0.54–0.81]) over placebo + abiraterone in 1L mCRPC

- Benefit observed led to a median rPFS beyond 2 years
- Benefit was observed irrespective of HRRm status

Secondary and exploratory endpoints support the treatment benefit of olaparib + abiraterone over placebo + abiraterone in the overall patient population

The safety profile of olaparib + abiraterone was consistent with the safety profile for the individual drugs and there was no detriment to quality of life allowing most patients to stay on therapy

The Phase III PROpel study is the first combination approach to deliver consistent clinical benefits for patients in the 1L mCRPC setting, irrespective of HRRm status
Opportunity and unmet need in mCRPC

Dave Fredrickson
Executive Vice President, Oncology Business Unit
Prostate is the second most common cancer in male patients. mCRPC therapies are limited; mostly monotherapy, including in first line.

<table>
<thead>
<tr>
<th></th>
<th>Hormone sensitive</th>
<th>Castration resistant</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Urologist-led</td>
<td>Urologists and oncologists</td>
</tr>
<tr>
<td></td>
<td>Primary/</td>
<td>mHSPC</td>
</tr>
<tr>
<td>mCRPC</td>
<td>adjuvant</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Biochemical</td>
<td>nmCRPC</td>
</tr>
<tr>
<td>recurrence</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>1st-line metastatic</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2nd-line+ metastatic</td>
</tr>
<tr>
<td></td>
<td>Recurrent</td>
<td>De-novo</td>
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<tr>
<td></td>
<td>ADT +/-</td>
<td>docetaxel/other</td>
</tr>
<tr>
<td></td>
<td>docetaxel +/-</td>
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<td></td>
<td>RTx</td>
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<td></td>
<td>ADT +/ NHA</td>
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<td></td>
<td>ADT + NHA</td>
<td>NHA</td>
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<tr>
<td></td>
<td>NHA or docetaxel</td>
<td>Lynparza (PROfound)</td>
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<tr>
<td></td>
<td></td>
<td>HRRm 20-30%</td>
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<tr>
<td></td>
<td></td>
<td>NHA or docetaxel</td>
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<td></td>
<td></td>
<td>chemo/palliative care</td>
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<td>Lynparza (PROfound)</td>
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<td></td>
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<td>NHA or docetaxel</td>
</tr>
<tr>
<td></td>
<td></td>
<td>chemo/palliative care</td>
</tr>
</tbody>
</table>

NHA naïve at mCRPC ~50%
NHA experienced in mCRPC ~50%

~80% diagnosed here
~20% diagnosed here


ADT = androgen deprivation therapy; RTx = radiation therapy; nmCRPC = non-metastatic castration resistant prostate cancer
PROpel - unprecedented clinical benefit without compromising quality of life - a potential new SoC in mCRPC

**Outcomes remain poor**
in advanced prostate cancer

**40%**
of patients with prostate cancer will develop metastatic disease<sup>1-3</sup>

**30%**
the 5-year survival rate for patients with metastatic disease<sup>4</sup>

**3 years**
median OS for mCRPC patients in the first-line setting<sup>5-9</sup>

**50%**
of patients receive only one line of active therapy in mCRPC<sup>10</sup>

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**PROpel**
building on the success of PROfound

- Representational real-world population - simple trial design
- All-comers ITT population
- Retrospective HRR testing via tissue and ctDNA testing<sup>11</sup>
- Primary endpoint: radiographic progression free survival
- Key secondary endpoints: Overall survival, time to first subsequent therapy, time to second progression or death

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**300 mg Lynparza™ + abiraterone**
a potential new standard of care

- Clinically meaningful and consistent efficacy across subgroups
- Despite OS immaturity, strong secondary endpoint results provide confidence
- Class-leading tolerability - full 300mg Lynparza dose in combination with abiraterone
- Quality of life maintained, allowing adoption of upfront combination therapy

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**8.2-month median rPFS benefit over abiraterone alone**

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OS = overall survival; ITT = intent-to-treat.
After almost a decade, the addition of Lynparza achieves a similar absolute rPFS improvement compared to the pivotal trial that established abiraterone as first-line SoC.

<table>
<thead>
<tr>
<th>COU-AA-302(^1) (2012)</th>
<th>PROpel (2022)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Median rPFS</strong></td>
<td></td>
</tr>
<tr>
<td>control</td>
<td>abiraterone</td>
</tr>
<tr>
<td></td>
<td>Dif.</td>
</tr>
<tr>
<td></td>
<td>abiraterone</td>
</tr>
<tr>
<td></td>
<td>Dif.</td>
</tr>
<tr>
<td><strong>8.2m</strong></td>
<td><strong>16.4m</strong></td>
</tr>
<tr>
<td><strong>8.2m</strong></td>
<td><strong>16.6m</strong></td>
</tr>
<tr>
<td><strong>24.8m</strong></td>
<td><strong>8.2m</strong></td>
</tr>
</tbody>
</table>

**PROpel median rPFS**

<table>
<thead>
<tr>
<th></th>
<th>abiraterone</th>
<th><em>Lynparza</em> + abiraterone</th>
<th>HR</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Investigator assessment</strong></td>
<td>16.6m</td>
<td>24.8m</td>
<td>0.66 (0.54-0.81)</td>
</tr>
<tr>
<td><strong>HRRm</strong></td>
<td>13.9m</td>
<td>NR</td>
<td>0.50 (0.34-0.73)</td>
</tr>
<tr>
<td><strong>Non-HRRm</strong></td>
<td>19.0m</td>
<td>24.1m</td>
<td>0.76 (0.60-0.97)</td>
</tr>
<tr>
<td><strong>BICR</strong></td>
<td>16.4m</td>
<td>27.6m</td>
<td>0.61 (0.49-0.74)</td>
</tr>
</tbody>
</table>

PROpel: a new treatment approach in 1st-line mCRPC

A clear option for NHA-naïve patients regardless of HRRm status

The first combination trial to demonstrate consistent clinical benefit in 1st-line mCRPC

Lynparza and abiraterone demonstrates a clear clinical benefit vs. abiraterone alone in first line patients who are NHA naïve

For NHA experienced patients, Lynparza and abiraterone offers a well tolerated, chemo-free treatment option

Source: AstraZeneca estimates. 1. Pending health authority authorisation. The PROpel trial data is not currently approved in any jurisdiction.
Other ASCO GU highlights

Susan Galbraith
Executive Vice President, Oncology R&D
New advances in urothelial carcinoma
Phase II data advancing understanding of this aggressive cancer

**Imfinzi + Lynparza: Phase II BAYOU trial**
Platinum-ineligible patients with mUC

<table>
<thead>
<tr>
<th></th>
<th>D+O</th>
<th>D+PBO</th>
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</thead>
<tbody>
<tr>
<td><strong>ITT population</strong></td>
<td>n=78</td>
<td>n=76</td>
</tr>
<tr>
<td><strong>Median PFS, mo (95% CI)</strong></td>
<td>4.2 (3.6–5.6)</td>
<td>3.5 (1.9–5.1)</td>
</tr>
<tr>
<td><strong>HR (95% CI)</strong></td>
<td>0.94 (0.64–1.39)</td>
<td></td>
</tr>
<tr>
<td><strong>Log-rank p-value</strong></td>
<td>0.789</td>
<td></td>
</tr>
<tr>
<td><strong>HRRm subset</strong></td>
<td>n=17</td>
<td>n=14</td>
</tr>
<tr>
<td><strong>Median PFS, mo (95% CI)</strong></td>
<td>5.6 (1.9–8.1)</td>
<td>1.8 (1.7–2.2)</td>
</tr>
<tr>
<td><strong>HR (95% CI)</strong></td>
<td>0.18 (0.06–0.47)</td>
<td></td>
</tr>
<tr>
<td><strong>Log-rank p-value</strong></td>
<td>&lt;0.001</td>
<td></td>
</tr>
</tbody>
</table>

Data suggests a role for PARP inhibition in HRRm UC

**Enhertu: Phase II U105 trial**
Combination with nivolumab

HER2+ UC included in DESTINY-PanTumor02

mUC = metastatic urothelial carcinoma; UC = urothelial carcinoma; T-DXd = trastuzumab deruxtecan (Enhertu).
Closing and Q&A
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Appendix
Olaparib and abiraterone: A randomised Phase II trial

- Patients with mCRPC, unselected by HRRm status, with prior docetaxel treatment
- Randomized 1:1 to full dose of olaparib + abiraterone vs placebo + abiraterone
- Statistically significant improvement in rPFS with olaparib + abiraterone, irrespective of HRRm status


* Dashed line and shaded area show HR and 95% CI, respectively, for the intent to treat population.

Please access the Supplement at https://bit.ly/3r50msO for more details including the full citations and further details on the HRRm partially characterised subgroup.
ORR in patients with measurable disease
10% improvement in ORR with olaparib + abiraterone

321/796 patients (40.3%) had measurable disease by RECIST v1.1 criteria at baseline

OR 1.60 (95% CI 1.02‒2.53)

P=0.0409*

ORR
58.4%

ORR
48.1%

CR = complete response; OR = odds ratio; ORR = overall response rate; PD = progressive disease; PR = partial response; RECIST = Response Evaluation Criteria in Solid Tumors; SD = stable disease.
FACT-P quality of life over time
Quality of life comparable between treatment arms

Least-squares mean change from baseline in FACT-P total score*

Analysis visit (weeks)

Olaparib + abiraterone (n=399)
Placebo + abiraterone (n=397)

*Plot includes 95% confidence limits. FACT-P total score change from baseline values can be a minimum of -156 and a maximum of 156. A clinically meaningful change in FACT-P total score is 1015,16

FACT-P = Functional Assessment of Cancer Therapy-Prostate.
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