Meet AZN management: ASCO 2020
Virtual breakout 3: Lynparza

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IR moderator: Nick Stone

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Webinar is being recorded
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**Lynparza: ovarian cancer**

The most comprehensive PARPi\(^1\) development programme in ovarian cancer

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**Study 19: 3L+**

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**SOLO-1: 1L maintenance**

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**ASCO 2020: continued advancement of science supporting Lynparza**

- **Phase III SOLO2**
  - Final OS for maintenance treatment in BRCA\(^3\)-mutated PSR\(^4\) OC\(^5\)

- **Other**
  - Phase IIIb OPINION IA\(^6\): maintenance of non-germline BRCA1/2-mutated PSR OC
  - Phase III: *Lynparza* or the combination of cediranib and *Lynparza* to standard platinum-based CTx\(^7\) in recurrent platinum-sensitive OC
  - Phase II LIGHT: PSR ovarian cancer by BRCA mutation and HRD status

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**SOLO-2: 2L maintenance**

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**PAOLA-1: 1L (HRD+ve\(^2\))**

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Source: Study 19, abstract SS01, ASCO 2016; and SOLO-2, 2 - Late Breaking Abstract, SGO 2017.

1. Poly ADP ribose polymerase (PARP) inhibitor.
2. Homologous recombination deficiency (HRD) positive, including tBRCAm.
3. Breast cancer susceptibility gene 1/2 mutation
4. Platinum-sensitive relapsed
5. Ovarian cancer
6. Interim analysis
7. Chemotherapy.

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Source: Study 19, abstract SS01, ASCO 2016; and SOLO-1, ESMO 2018; and PAOLA-1, ESMO 2019.
**Lynparza: SOLO2 final OS**

**Maintenance treatment for PSR OC patients with gBRCA positive tumours**

**PFS: 63% maturity with a median follow up ~22 months**

SOLO2: median OS improved by 12.9 months with maintenance Lynparza over placebo (p-value: 0.0537)

- **TFST**: 28% of patients (vs. 13% of placebo patients) were alive and had not received subsequent therapy at 5 years

1. Time to first subsequent therapy.


2. Prespecified adjusted OS analysis (RPSFT model, re-censored): to adjust for subsequent PARPi inhibitor therapy in placebo group. The RPSFT model (re-censored) adjusts for the 38% of placebo patients who received subsequent PARPi inhibitor therapy. RPSFT: rank preserving structural failure time model. Source: abstract 6002, ASCO 2020.

Adjusting for subsequent PARPi therapy in placebo patients median OS improved by 16.3 months for Lynparza vs. placebo; HR 0.56 (0.35–0.97)²
**Lynparza: PAOLA-1**

1L maintenance treatment with bevacizumab

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**PAOLA-1: 1L ovarian cancer**

1L (complete response; partial response; or non-evidence of disease)

Randomisation (2:1)

- **Lynparza (two years) + bevacizumab**
- **Placebo (two years) + bevacizumab**

Progression-free survival (PFS1)

Follow up for second progression (PFS2) or death

Overall survival

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**PAOLA-1: biomarker subgroups**

**~1 in 2**

Women with advanced OC are HRD+ve

**Approved**

1L maintenance treatment in the US with bevacizumab for HRD+ve advanced OC

HRD-ve\(^3\):
- n=277; 34%

HRD+ve:
- n=387; 48%

HRD status unknown:
- n=142; 18%

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PAOLA-1 demonstrated the predictive value of HRD testing

>37 months mPFS for patients treated with **Lynparza** + bevacizumab

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1. Bevacizumab: 15mg/kg, every 3 weeks for a total of 15 months, including when administered with chemotherapy
2. Secondary endpoints.
3. HRD negative.


Source: ESMO 2019.
**Lynparza: PAOLA-1 and PRIMA**

Maintenance treatment essential; HRD testing critical to obtain longest mPFS

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**Indirect treatment comparison of PAOLA-1 and PRIMA PFS: HRD+ve**

After adjustment, in HRD+ve patients, the benefit was greatest with *Lynparza* + bevacizumab combination therapy.

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**Indirect treatment comparison of PAOLA-1 and PRIMA PFS: HRD-ve**

After adjustment, in HRD-ve patients, the benefit was greatest with either of the bevacizumab containing regimens (bevacizumab alone or *Lynparza* + bevacizumab).

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2. Adjusted analysis, formal matching analysis of the PAOLA-1 patients’ characteristics to the PRIMA patients’ characteristics, in the absence of randomized controlled trial. Source: poster 223, ASCO 2020.

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Lynparza: ovarian cancer
Continued global expansion

+69%
Product sales growth Q1 2020

$397m
Product sales Q1 2020

Product sales by region

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Under regulatory review

Patient focus: health economic analysis in Italy to demonstrate the added benefit that Lynparza offers to patients

AstraZeneca showed the cost-effectiveness of a preventive testing strategy in relatives of patients with BRCA mutated ovarian cancer versus a no testing strategy. The evaluation showed how it is cost-effective to include BRCA tests for patients and family of those with a family history of breast/ovarian cancer.
**Lynparza:** the only PARPi to improve overall survival in prostate cancer patients\(^1\)

PROfound, cohort A

What’s now: Phase III lifecycle management, major

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1. Lynparza vs. enzalutamide or abiraterone in a biomarker-based subset BRCA1/2 or ATM\(^2\)-mutations.
2. Ataxia telangiectasia mutated.


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1L castration-resistant prostate cancer: data readout, regulatory submission

2L prostate cancer: regulatory decision (JP)

Adjuvant breast cancer:

2021

Adjuvant breast cancer:

2021

1L advanced ovarian cancer: data readout

2021+

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1. Lynparza vs. enzalutamide or abiraterone in a biomarker-based subset BRCA1/2 or ATM\(^2\)-mutatations.
2. Ataxia telangiectasia mutated.

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*6 - Toggle mute/unmute
*9 - Raise hand
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