Prostate | ***PROpel and PROfound***

The only PARPi FDA-approved as a combination therapy and monotherapy in mCRPC with rPFS and OS data included in the label

PROpel: Combination therapy
In combination with abi/pred in *BRCA*m* mCRPC

PROfound: Monotherapy
Following progression on prior enza or abi in HRRm* mCRPC, including *BRCA*m

CHOOSE THE #1 PRESCRIBED PARPi **for patients with prostate cancer†**

*Select patients for this indication based on an FDA-approved companion diagnostic for LYNPARZA.

†IQVIA LAAD (Longitudinal Access and Adjudication Dataset) prescription claims data, National Prescription Audit as of April 2024. #1 for new prescriptions and for total prescriptions.

abi=abiraterone; abi/pred=abiraterone plus prednisone or prednisolone; *BRCA*m=*BRCA*-mutated or *BRCA* mutation(s); enza=enzalutamide; g*BRCA*m=germline *BRCA*-mutated; HRRm=homologous recombination repair gene–mutated; mCRPC=metastatic castration-resistant prostate cancer; OS=overall survival; PARPi=poly (ADP-ribose) polymerase inhibitor; rPFS=radiological progression-free survival.

Important Safety Information

CONTRAINDICATIONS

There are no contraindications for LYNPARZA.

WARNINGS AND PRECAUTIONS

Myelodysplastic Syndrome/Acute Myeloid Leukemia (MDS/AML): Occurred in approximately 1.2% of patients with various *BRCA*m, g*BRCA*m, HRR gene-mutated or HRD-positive cancers who received LYNPARZA as a single agent or as part of a combination regimen, consistent with the approved indications, and the majority of events had a fatal outcome. The median duration of therapy in patients who developed MDS/AML was approximately 2 years (range: <6 months to >4 years). All of these patients had previous chemotherapy with platinum agents and/or other DNA-damaging agents, including radiotherapy.

In SOLO-1, patients with newly diagnosed advanced *BRCA*m ovarian cancer, the incidence of MDS/AML was 1.9% (5/260) in patients who received LYNPARZA and 0.8% (1/130) in patients who received placebo based on an updated analysis. In PAOLA-1, of patients with newly diagnosed advanced ovarian cancer with HRD-positive status, the incidence of MDS/AML was 1.6% (4/255) in patients who received LYNPARZA and 2.3% (3/131) in the control arm.

In SOLO-2, patients with *BRCA*m platinum-sensitive relapsed ovarian cancer, the incidence of MDS/AML was 8% (15/195) in patients who received LYNPARZA and 4% (4/99) in patients who received placebo. The duration of

Please see additional Important Safety Information throughout and complete Prescribing Information, including Medication Guide.

LYN PI_11.2023: p2/col2/§1.7/¶1/ln4-5; §1.8/¶1/ln3-4

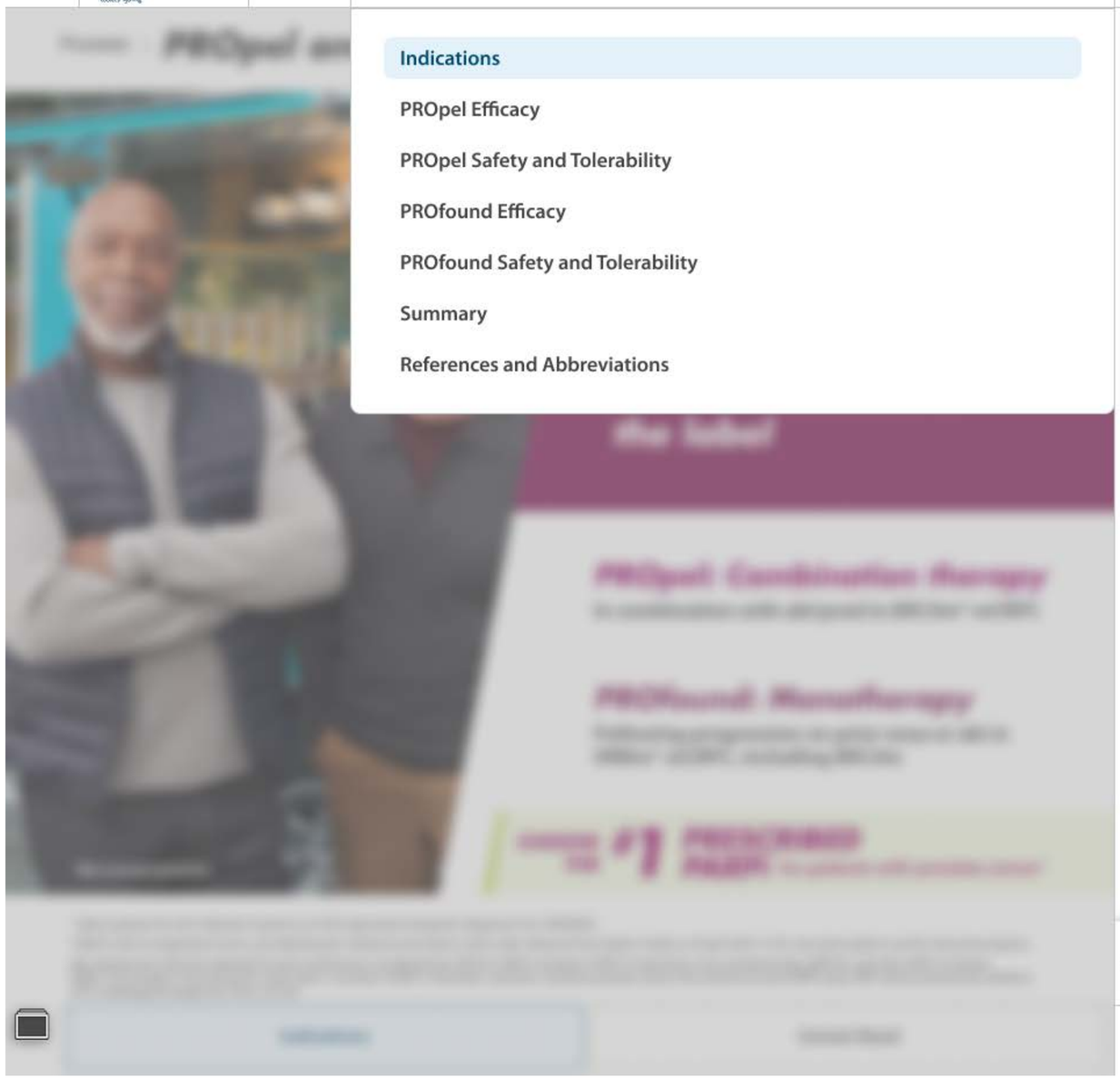
LYN PI_11.2023: p2/col2/§1.8/all

LYN PI_11.2023: p2/col2/§1.7/all

LYN PI_11.2023: p2/col2/§1.7/all

- LYN PI_11.2023: p2/col2/§1.7/all; §1.8/all; p9/col1/§12.1/¶1/ln1-3
- Rubraca PI 6.2023: p2/§1.2/¶1/ln1-4; p11/§12.1/ln1-2; p15/§14.2/¶1/ln1-3
- Talzenna PI 2023: p3/§1; p15/§12.1/¶1/ln1-2
- Zejula PI 4.2023: p2/§1/all; p17/§12.1/ln1-2

Akeega PI 8.2023: p2/sec1/col1/para1/ln1-3; p6/sec12.1/col2/para1/ln1-2; sec14.1/col1/para5/all



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Revised from US-73132, p3 where indicated. All other content is direct lift

LYNPARZA® (olaparib) tablets 150 mg

MENU | Lynparza® olaparib | PI | Indications | Prev Slide | Next Slide

Prostate | PROpel & PROfound

Initial therapy at diagnosis of BRCAm *mCRPC is a pivotal treatment decision*

Tryggvadottir 2007: p930/col2/¶1/ln13-15, ¶4/ln1-2; p931/col1/¶3/ln1-3; p932/col2/¶2/ln1-4, 8-15

mCRPC is more aggressive in *BRCA* mutation carriers

Tryggvadottir 2007: p930/col2/¶1/ln13-15, ¶4/ln1-2; p931/col1/¶3/ln1-3; p932/col2/¶2/ln1-4, 8-15

At diagnosis of prostate cancer, *BRCA* mutation carriers exhibited:

- Lower mean age
- More advanced tumor stage
- Higher tumor grade (Grades 3-4)

From a review of 596 patients diagnosed with prostate cancer in Iceland from 1955-2004, 30 patients with *BRCA2* mutation were matched with 59 control, noncarrier patients.

Among patients with g*BRCA* mutations compared to noncarriers

>2x had Gleason scores ≥8

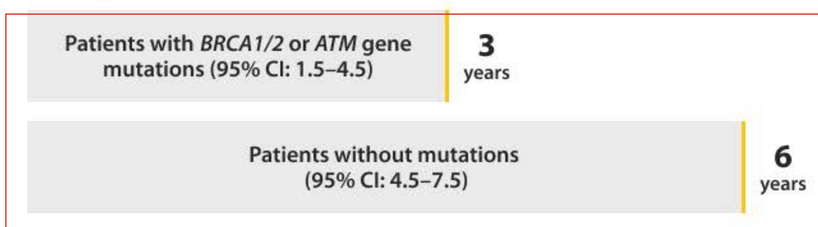
From a retrospective analysis of patients with locally advanced prostate cancer (n=1302) of which 67 patients had a g*BRCA* mutation.

• Na 2017 p3/§2.1/¶1/ln1-3,9-10; p5/§3/¶1/ln3-5; p6/§3/¶3/ln1-6; p12/Fig2C
• CALC: 3 is half of 6

Median survival for those with *BRCA1/2* or *ATM* gene mutations was half that of those without mutations

In a separate retrospective study based on a subgroup analysis of patients with metastatic prostate cancer (n=122)*

Na 2017 p12/Fig2C



• Na 2017 p3/§2.1/¶1/ln1-3; p4/§2.2/¶1/ln1-2; p5/§3/¶1/ln3-5; p6/§3/¶3/ln1-6
CALC: 313+486=799

*Subgroup of patients with metastatic disease at the time of diagnosis (n=122) whose germline DNA was sequenced. From a retrospective case study of patients with prostate cancer (n=799).

Indications | Unmet Need

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Castro 2014: p2/col 1/¶5/ln1-4; p3/col1/¶2/ln1-3; col2/¶1/ln7-10

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Revised from US-73132, p3, replaced previous content with bar chart

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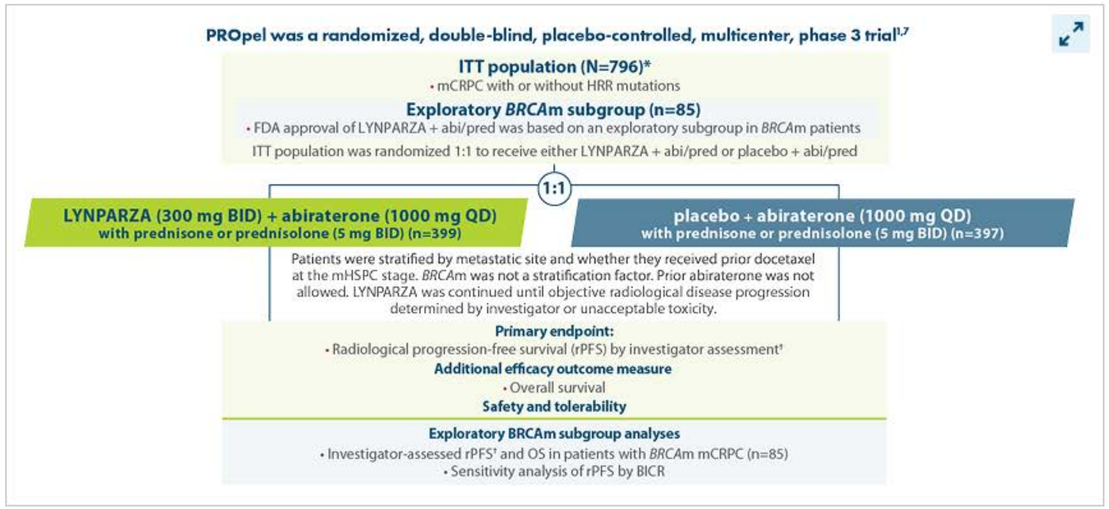
Note to reviewers: This content was originally approved in expired asset US-51240. Content was taken to JC and revised per PRT feedback: US-NM-0404 p3

Please see additional Important Safety Information throughout and complete Prescribing Information, including Medication Guide.

Indications + | Important Safety Information +

PROpel studied LYNPARZA + abi/pred vs placebo + abi/pred (active comparator) in patients with mCRPC



Select Baseline Patient Characteristics >

*All patients received a GnRH analog or had prior bilateral orchiectomy.

†rPFS assessed by investigator per RECIST v1.1 (soft tissue) and PCWG3 (bone) criteria.

BICR=blinded independent central review; BID=twice daily; GnRH=gonadotropin-releasing hormone; ITT=intent-to-treat; mHSPC=metastatic hormone-sensitive prostate cancer; PCWG3=Prostate Cancer Working Group 3; QD=once daily; RECIST=Response Evaluation Criteria in Solid Tumors.

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Revised from US-73132, p3, formatted as pop-up, marked changes, content otherwise is a direct lift

LYNPARZA® (olaparib) tablets 150 mg

MENU | Lynparza® olaparib tablets 150 mg | PI | PROpel Efficacy | Prev Slide | Next Slide

PROpel Study Design

PROpel was a randomized, double-blind, placebo-controlled, multicenter, phase 3 trial[1,7]

ITT population (N=796)*
- mCRPC with or without HRR mutations

Exploratory *BRCA*m subgroup (n=85)
- FDA approval of LYNPARZA + abi/pred was based on an exploratory subgroup in *BRCA*m patients

ITT population was randomized 1:1 to receive either LYNPARZA + abi/pred or placebo + abi/pred

1:1

LYNPARZA (300 mg BID) + abiraterone (1000 mg QD) with prednisone or prednisolone (5 mg BID) (n=399)

placebo + abiraterone (1000 mg QD) with prednisone or prednisolone (5 mg BID) (n=397)

Patients were stratified by metastatic site and whether they received prior docetaxel at the mHSPC stage. *BRCA*m was not a stratification factor. Prior abiraterone was not allowed. LYNPARZA was continued until objective radiological disease progression determined by investigator or unacceptable toxicity.

Primary endpoint:
- Radiological progression-free survival (rPFS) by investigator assessment†

Additional efficacy outcome measure
- Overall survival

Safety and tolerability

Exploratory BRCAm subgroup analyses
- Investigator-assessed rPFS† and OS in patients with *BRCA*m mCRPC (n=85)
- Sensitivity analysis of rPFS by BICR

*All patients received a GnRH analog or had prior bilateral orchiectomy.

†rPFS assessed by investigator per RECIST v1.1 (soft tissue) and PCWG3 (bone) criteria.

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Please see additional Important Safety Information throughout and complete Prescribing Information, including Medication Guide.

•LYN PI_11.2023: p14/col2/§14.8/¶1/ln1-4 •Clarke 2022: p2/col2/¶4/ln1

LYN PI_11.2023: p14/col2/§14.8/¶1/ln4-6
Clarke 2022: p3/col2/Table 1/row 23-26

LYN PI_11.2023: p15/col1/¶3/ln1-2; ¶4-5/all

•LYN PI_11.2023: p3/col1/§*BRCA*-mutated Metastatic Castration-Resistant Prostate Cancer in Combination with Abiraterone and Prednisone or Prednisolone/all; p14/col2/§14.8/¶1/ln4-6; ln8-12

•LYN PI_11.2023: p15/col1/¶2/ln1-3

•LYN PI_11.2023: p15/col1/¶2/ln3

•LYN PI_11.2023: p7/col2/§PROpel/¶1/ln1-2; ¶2/all; ¶3-6/all; p8/col1/¶1/all; Table16

•LYN PI_11.2023: p15/col1/¶3/ln1-2; ¶5/all, Table 28

LYN PI_11.2023: p14/col2/§14.8/¶1/ln6-8

Clarke 2022: p3/col1/¶2/all

LYN PI_11.2023: p15/col1/¶2/ln1-3
Clarke 2022: p2/col2/¶4/ln10-14

Revised from US-73132, p36, marked changes, content otherwise is a direct lift

LYN PI_11.2023: p14/col2/ §14.8/¶1/ln4-6

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MENU | Lynparza olaparib | PI | PROpel Efficacy | Prev Slide | Next Slide

PROpel

Select patient baseline characteristics

		ITT LYNPARZA + abi/pred (n=399)	ITT placebo + abi/pred (n=397)
***BRCA*m status, n (%)**	*BRCA*m	47 (11.8)	38 (9.6)
	*BRCA*m not identified	352 (88.2)	359 (90.4)

*BRCA*m status was assessed after randomization and before primary analysis by both NGS-based tumor tissue and ctDNA tests. *BRCA*m classification criteria in line with the FDA-approved assays were used to determine the deleterious and suspected deleterious germline or somatic mutation status of patients.

		ITT LYNPARZA + abi/pred (n=399)	ITT placebo + abi/pred (n=397)	*BRCA*m subgroup LYNPARZA + abi/pred (n=47)	*BRCA*m subgroup placebo + abi/pred (n=38)
Age, median (range) years		69 (43-91)	70 (46-88)	67 (43-83)	70 (46-85)
Race (%)	White	70		72	
	Asian	17		22	
	Hispanic or Latino	17		13	
	Black or African American	3		2	
Gleason score, n (%)	≥8	265 (66.4)	258 (65.0)	34 (72.4)	25 (65.8)
	Missing	13 (3.3)	5 (1.3)	3 (6.4)	1 (2.6)
ECOG performance status, n (%)	0	286 (71.7)	272 (68.5)	36 (76.6)	20 (52.6)
	1	112 (28.1)	124 (31.2)	11 (23.4)	18 (47.4)
	Missing	1 (0.3)	1 (0.3)	0	0
Symptomatic (BPI-SF ≥4 and/or opiate use), n (%)		103 (25.8)	80 (20.2)	15 (31.9)	10 (26.3)
Site of metastases, n (%)	Bone only	217 (54.4)	217 (54.7)	25 (53.2)	20 (52.6)
	Visceral	53 (13.3)	52 (13.1)	5 (10.6)	8 (21.1)
	Other	129 (32.3)	128 (32.2)	17 (36.2)	10 (26.3)
Docetaxel treatment at mHSPC stage, n (%)		95 (23.8)	94 (23.7)	10 (21.3)	11 (28.9)
Median PSA, µg/L (IQR)		17.9 (6.1–67.0)	16.8 (6.3–53.3)	29.0 (7.0–78.8)	22.5 (8.1–53.0)

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Indications + | Important Safety Information +

Clarke 2022: p3/col2/Table1/ rows 25, 27-28
CALC:
LYN BRCAm: 38+9=47
placebo BRCAm: 35+3=38
BRCAm unknown=HRRm unknown
LYN non-BRCAm: 399-(47+9)=343
placebo non-BRCAm: 397-(38+9)=350

LYN PI_11.2023: p15/col1/¶1/all

LYN PI_11.2023: p15/col1/ Table28/row1

ODAC Sponsor Briefing Document_29Mar2023 /p98/Table D1/col5-6/ row5

Clarke 2022: p3/col2/Table1/ row 2

LYN PI_11.2023: p15/col1/ ¶3/ln3-4

ODAC Sponsor Briefing Document_29Mar2023/p98/Table D1/col5-6/row12
Calc:
LYN+abi pts (n=47)
with missing score:
47 - (34+10)=3
3/47=0.64x100%=6.4%
Placebo+abi pts (n=38)
with missing score:
38 - (25+12)=1
1/38=0.026x100%=2.6%

ODAC Sponsor Briefing Document_29Mar2023/p98/Table D1/col5-6/row9-10

ODAC Sponsor Briefing Document_29Mar2023 /p98/Table D1/col5-6/ row15-17

DOF PROpel 2023: p5/ Table 1B/"Docetaxel"

LYN PI_11.2023: p14/col2/ §14.8/¶1/ln4-6

Clarke 2022: p3/col2/Table1/ row 2

DOF PROpel 2023: p5/ Table 1B/"Race"/row 3

Clarke 2022: p6/Fig2/all 3 rows before last row
CALC:
White: 282
+275=557/796=0.699 or 70%
Asian: 66+72=138/796=0.173 or 17%
Black or African American:
14+11=25/796=0.031 or 3%

Clarke 2022: p3/col2/Table1/ rows 3-5

Clarke 2022: p3/col2/Table 1/rows 6-9

DOF PROpel 2023: p5/ Table 1B/"Symptomatic"

Clarke 2022: p6/Fig2/row 6-8
CALC:
LYN:
217/399=0.544 or 54.4%
53/399=0.133 or 13.3%
129/399=0.323 or 32.3%
placebo:
217/397=0.547 or 54.7%
52/397=0.131 or 13.1%
128/397=0.322 or 32.2%

Clarke 2022: p6/Fig2/row 9
CALC:
LYN: 95/399=0.238 or 23.8%
placebo: 94/397=0.237 or 23.7%

Clarke 2022: p3/col2/Table 1/row29

DOF PROpel 2023: p5/Table 1B/"Median PSA"

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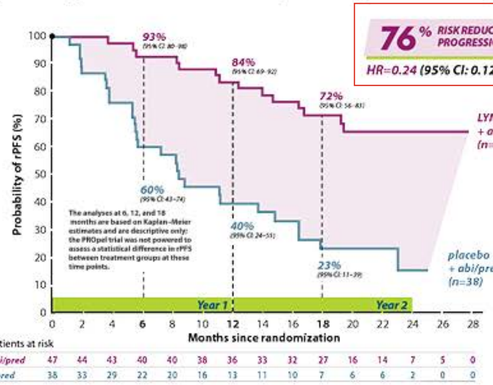
MENU | Lynparza olaparib | PI | PROpel Efficacy | Prev Slide | Next Slide

Prostate | PROpel: Combination Therapy

FDA approval was based on an exploratory *BRCA*m subgroup

LYNPARZA + abi/pred demonstrated improvement in rPFS vs placebo + abi/pred in patients with BRCAm mCRPC

rPFS by investigator assessment in exploratory BRCA*m subgroup*



Median rPFS

LYNPARZA + abi/pred	placebo + abi/pred
Not reached	8 months
(95% CI: NR–NR)	(95% CI: 6–15)

***BRCA*m subgroup (n=85)**
Events, n (%): 14/47 (30) with LYNPARZA + abi/pred and 28/38 (74) with placebo + abi/pred. Results from the BICR assessment were consistent with the investigator-assessed rPFS results. *BRCA*m status was not a stratification factor in PROpel, and analysis was not controlled for Type 1 error.

ITT population (n=796)
Statistically significant improvement in rPFS* was observed for LYNPARZA + abi/pred compared with placebo + abi/pred.

Patients without an identified *BRCA*m (n=711)
Results from an exploratory analysis in this subgroup (HR=0.77 [95% CI: 0.63–0.96]) indicated that the improvement in the ITT population was primarily attributed to the results seen in the *BRCA*m subgroup.

* rPFS assessed by investigator per RECIST v1.1 (soft tissue) and PCWG3 (bone) criteria.

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Study Design | rPFS | Overall Survival | Indications + | Important Safety Information +

LYN PI_11.2023: p15/col1/¶3/ln1-2; ¶4-5/all

LYN PI_11.2023: p14/col2/§14.8 title ("BRCAm mCRPC"); p15/col1/¶4/all; Table 28/row2-5

LYN PI_11.2023: p15/col1/Table 28/col2-3/row3-5; Figure 12

LYN PI_11.2023: p15/col1/Table 28/col2-3/row 5
CALC: 100%-24%
HR=76% reduced risk

LYN PI_11.2023: p15/col1/Table 28/col2-3/row 1

LYN PI_11.2023: p15/col1/Table 28/col2-3/row 1,3
CALC: 47 + 38 = 85
n=85

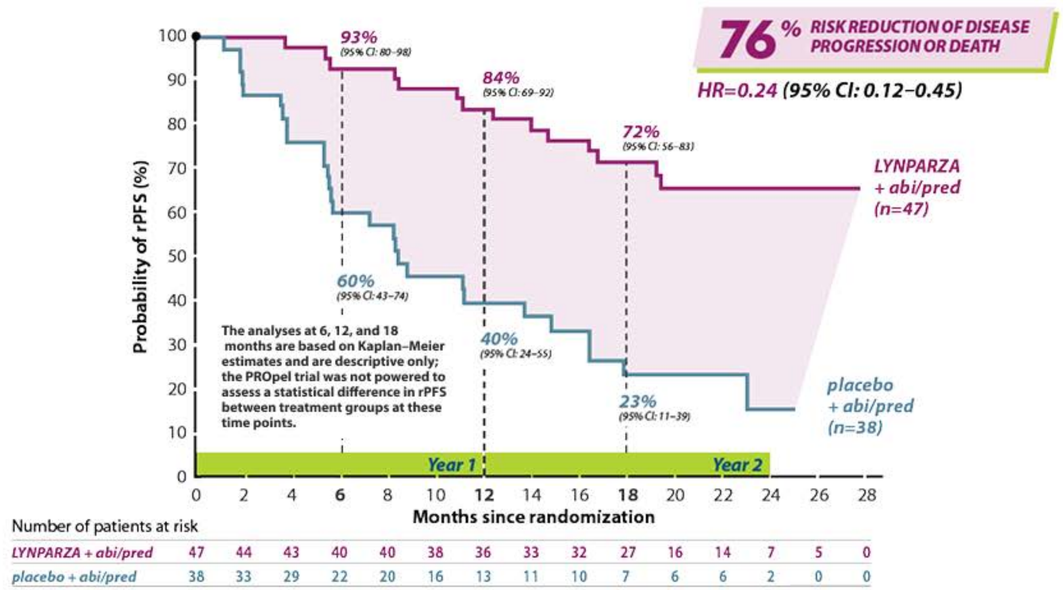
LYN PI_11.2023: p15/col1/¶6/all

LYN PI_11.2023: p14/sect14.8/col2/¶1/ln10-11

LYN PI_11.2023: p14/col2/§14.8/¶1/ln4; p15/col1/¶4/ln1-2

LYN PI_11.2023: p15/col1/¶4/all

~4.7 years median PFS with LYNPARZA and ~1.2 years with placebo



Number of patients at risk

LYNPARZA + abi/pred	47	44	43	40	40	38	36	33	32	27	16	14	7	5	0
placebo + abi/pred	38	33	29	22	20	16	13	11	10	7	6	6	2	0	0

Important Safety Information

CONTRAINDICATIONS

There are no contraindications for LYNPARZA.

WARNINGS AND PRECAUTIONS

Myelodysplastic Syndrome/Acute Myeloid Leukemia (MDS/AML): Occurred in approximately 1.2% of patients with various *BRCA*m, g*BRCA*m, HRR gene-mutated or HRD-positive cancers who received LYNPARZA as a single agent or as part of a combination regimen, consistent with the approved indications, and the majority of events had a fatal outcome. The median duration of therapy in patients who developed MDS/AML was approximately 2 years (range: <6 months to >4 years). All of these patients had previous chemotherapy with platinum agents and/or other DNA-damaging agents, including radiotherapy.

In SOLO-1, patients with newly diagnosed advanced *BRCA*m ovarian cancer, the incidence of MDS/AML was 1.9% (5/260) in patients who received LYNPARZA and 0.8% (1/130) in patients who received placebo based on an updated analysis. In PAOLA-1, of patients with newly diagnosed advanced ovarian cancer with HRD-positive status, the incidence of MDS/AML was 1.6% (4/255) in patients who received LYNPARZA and 2.3% (3/131) in the control arm.

In SOLO-2, patients with *BRCA*m platinum-sensitive relapsed ovarian cancer, the incidence of MDS/AML was 8% (15/195) in patients who received LYNPARZA and 4% (4/99) in patients who received placebo. The duration of

Please see additional Important Safety Information throughout and complete Prescribing Information, including Medication Guide.

LYN PI_11.2023: p15/col1/¶3/ln1-2; ¶4-5/all

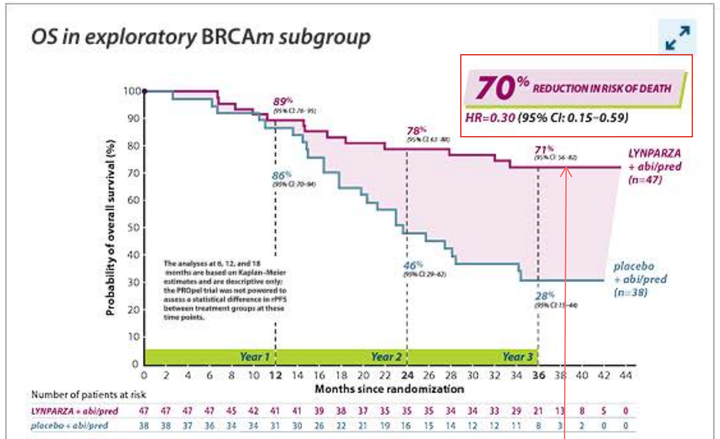
FDA approval was based on an exploratory *BRCA*m subgroup

LYN PI_11.2023: p15/col1/§14.8/¶3/ln3; ¶4/ln2-5

Overall survival for LYNPARZA + abi/pred vs placebo + abi/pred in patients with BRCAm *mCRPC*

LYN PI_11.2023: p15/col1/Table 28/col2-3/row 1, 6-9; Figure 13

OS in exploratory BRCA*m subgroup*



LYN PI_11.2023: p15/col1/Table 28/col2-3/row 9
CALC: 100%-30%
HR=70% reduced risk

Median OS

LYNPARZA + abi/pred	placebo + abi/pred
Not reached	23 months
(95% CI: NR–NR)	(95% CI: 18–34)

***BRCA*m subgroup (n=85)**
Events, n (%): 13/47 (28) with LYNPARZA + abi/pred and 25/38 (66) with placebo + abi/pred. *BRCA*m status was not a stratification factor in PROpel, and analysis was not controlled for Type 1 error.

ITT population (n=796)
OS for LYNPARZA + abi/pred compared to placebo + abi/pred did not reach statistical significance in the ITT population.

Patients without an identified *BRCA*m (n=711)
Results from an exploratory analysis in this subgroup (HR=0.92 [95% CI: 0.74–1.14]) indicated that the improvement in the ITT population was primarily attributed to the results seen in the *BRCA*m subgroup.

In PROpel, crossover from placebo to receive LYNPARZA + abi/pred was not allowed.

Important Safety Information

CONTRAINDICATIONS

There are no contraindications for LYNPARZA.

WARNINGS AND PRECAUTIONS

LYN PI_11.2023: p15/col1/Table 28/col2-3/row 1, 6-9; Figure 13

LYN PI_11.2023: p15/col1/Table 28/col2-3/row 1,7
CALC: 47+38=85

Myelodysplastic Syndrome/Acute Myeloid Leukemia (MDS/AML): Occurred in approximately 1.2% of patients with various *BRCA*m, g*BRCA*m, HRR gene-mutated or HRD-positive cancers who received LYNPARZA as a single agent or as part of a combination regimen, consistent with the approved indications, and the majority of events had a fatal outcome. The median duration of therapy in patients who developed MDS/AML was approximately 2 years (range: <6 months to >4 years). All of these patients had previous chemotherapy with platinum agents and/or other DNA-damaging agents, including radiotherapy.

LYN PI_11.2023: p14/col2/sect14.8/¶1/ln10-11

In SOLO-1, patients with newly diagnosed advanced *BRCA*m ovarian cancer, the incidence of MDS/AML was 1.9% (5/260) in patients who received LYNPARZA and 0.8% (1/130) in patients who received placebo based on an updated analysis. In PAOLA-1, of patients with newly diagnosed advanced ovarian cancer with HRD-positive status, the incidence of MDS/AML was 1.6% (4/255) in patients who received LYNPARZA and 2.3% (3/131) in the control arm.

LYN PI_11.2023: p14/col2/sect14.8/para1/ln4
Clarke 2022: p15/col1/¶2/ln5-7

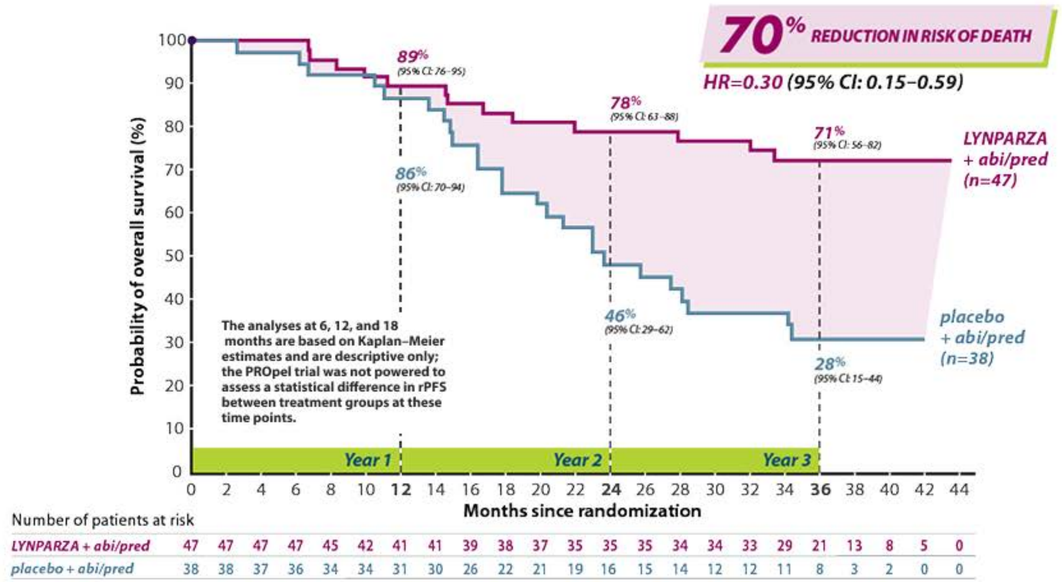
In SOLO-2, patients with *BRCA*m platinum-sensitive relapsed ovarian cancer, the incidence of MDS/AML was 8% (15/195) in patients who received LYNPARZA and 4% (4/99) in patients who received placebo. The duration of

LYN PI_11.2023: p15/col1/¶4/all

Clarke 2022: p3/col1/¶1/ln8-9

Please see additional Important Safety Information throughout and complete Prescribing Information, including Medication Guide.

OS in exploratory BRCA*m subgroup*



Number of patients at risk

LYNPARZA + abi/pred	47	47	47	47	45	42	41	41	39	38	37	35	35	35	34	34	33	29	21	13	8	5	0
placebo + abi/pred	38	38	37	36	34	34	31	30	26	22	21	19	16	15	14	12	12	11	8	3	2	0	0

Important Safety Information

CONTRAINDICATIONS

There are no contraindications for LYNPARZA.

WARNINGS AND PRECAUTIONS

Myelodysplastic Syndrome/Acute Myeloid Leukemia (MDS/AML): Occurred in approximately 1.2% of patients with various *BRCA*m, g*BRCA*m, HRR gene-mutated or HRD-positive cancers who received LYNPARZA as a single agent or as part of a combination regimen, consistent with the approved indications, and the majority of events had a fatal outcome. The median duration of therapy in patients who developed MDS/AML was approximately 2 years (range: <6 months to >4 years). All of these patients had previous chemotherapy with platinum agents and/or other DNA-damaging agents, including radiotherapy.

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Please see additional Important Safety Information throughout and complete Prescribing Information, including Medication Guide.

Revised from US-73132, p6, marked changes, content otherwise is a direct lift

In the full study population

Select adverse reactions in PROpel

LYNPARZA + abi/pred (n=398) | placebo + abi/pred (n=396)

Adverse Reactions*	Grades 1–4 (%)	Grades 3–4 (%)
Blood and Lymphatic Disorders		
Anemia	48 18	16 3.3
Lymphopenia	14 6	5 1.8
General Disorders and Administration Site Conditions		
Fatigue (including asthenia)	38 30	2.3 1.5
Gastrointestinal Disorders		
Nausea	30 14	0.3 0.3
Diarrhea	19 10	1 0.3
Abdominal pain§	13 7	0 0.5
Metabolism and Nutrition Disorders		
Decreased appetite	16 7	1 0

Adverse reactions reported in ≥10% of patients who received LYNPARZA (with a difference of ≥5% vs placebo)

- **Fatal adverse reactions** occurred in 6% of patients, including COVID-19 (3%) and pneumonias (0.5%)
- **Serious adverse reactions** occurred in 39% of patients. Serious adverse reactions reported in >2% of patients included anemia (6%), COVID-19 (6%), pneumonia (4.5%), pulmonary embolism (3.5%), and urinary tract infection (3%)
- **Venous thromboembolism** (VTE), including severe or fatal pulmonary embolism (PE), occurred in patients treated with LYNPARZA. In the combined data of two randomized, placebo-controlled clinical studies (PROfound and PROpel) in patients with metastatic castration-resistant prostate cancer (N=1180), VTE occurred in 8% of patients who received LYNPARZA, including pulmonary embolism in 6%. In the control arms, VTE occurred in 2.5%, including pulmonary embolism in 1.5%

* Graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE), version 4.03.
† Includes anemia, anemia macrocytic, and red blood cell count decreased.
‡ Includes lymphocyte count decreased and lymphopenia.
§ Includes abdominal discomfort, abdominal pain, abdominal pain upper, and abdominal pain lower.
‖ Includes dizziness and vertigo.

LYN PI 11.2023: p7/col2/PROpel/para2/all

LYN PI 11.2023: p7/col2/PROpel/para3/all

LYN PI 11.2023: p3/col2/sec5.3/para1/all

LYN PI_11.2023: p8/col1/Table 16

LYN PI_11.2023: p8/col1/Table 16/footnotes

In the full study population

Select adverse reactions in PROpel

LYNPARZA + abi/pred (n=398) placebo + abi/pred (n=396)

Adverse Reactions*	Grades 1–4 (%)	Grades 3–4 (%)
Lymphopenia	14 6	5 1.8
General Disorders and Administration Site Conditions		
Fatigue (including asthenia)	38 30	2.3 1.5
Gastrointestinal Disorders		
Nausea	30 14	0.3 0.3
Diarrhea	19 10	1 0.3
Abdominal pain§	13 7	0 0.5
Metabolism and Nutrition Disorders		
Decreased appetite	16 7	1 0
Nervous System Disorders		
Dizziness‖	14 7	0.3 0

Adverse reactions reported in ≥10% of patients who received LYNPARZA (with a difference of ≥5% vs placebo)

- **Fatal adverse reactions** occurred in 6% of patients, including COVID-19 (3%) and pneumonias (0.5%)
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† Includes anemia, anemia macrocytic, and red blood cell count decreased.
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§ Includes abdominal discomfort, abdominal pain, abdominal pain upper, and abdominal pain lower.
‖ Includes dizziness and vertigo.

Revised from US-73132, p7, marked changes, content otherwise is a direct lift

LYN PI_11.2023: p8/col1/ Table 17

In the full study population

Select laboratory abnormalities reported in ≥20% of patients in PROpel

LYNPARZA + abi/pred (n=398) placebo + abi/pred (n=396)

Laboratory Parameter	Grades 1–4 (%)	Grades 3–4 (%)
Decrease in hemoglobin	97 81	12 1.3
Decrease in lymphocytes	70 49	23 11
Decrease in platelets	23 20	1.2 0.3
Decrease in absolute neutrophil count	23 6	5 0

LYN PI_11.2023: p8/col1/ Table 17/footnote

* This number represents the safety population. The derived values in the table are based on the total number of evaluable patients for each laboratory parameter.

Revised from US-73132, p8, marked changes, content otherwise is a direct lift

LYN PI_11.2023: p7/col1/§PROpel/¶1/ln1-2; /¶4/all;¶5/all; ¶6/all

In the full study population

Dose modifications in PROpel

Changes due to adverse reactions	LYNPARZA + abi/pred (n=398)
Dose interruptions due to ARs	48%
Dose reductions due to ARs	21%
Discontinuations due to ARs	16%

LYN PI_11.2023: p7/col2 §PROpel/¶1/ln1-2; ¶2/all, ¶4/ln1-2
Calc: 100%-16%=84%

In PROpel, the majority of patients remained on treatment without discontinuing due to adverse reactions (84% for LYNPARZA + abi/pred)

The most common (>2%) adverse reactions requiring dosage interruption of LYNPARZA were anemia (16%), COVID-19 (6%), fatigue (3.5%), nausea (2.8%), pulmonary embolism (2.3%), and diarrhea (2.3%). The most common (>2%) adverse reactions requiring dosage reductions of LYNPARZA were anemia (11%) and fatigue (2.5%). The most common adverse reactions that resulted in permanent discontinuation of LYNPARZA were anemia (4.3%) and pneumonia (1.5%).

Revised from US-73132, p14, marked changes, content otherwise is a direct lift

•LYN PI_11.2023: p13/col2/§14.7/¶1/all; ¶2/ln1-2
de Bono 2020 p2/col1/¶2/ln1-4; col2/¶3/ln1-2

PROfound studied LYNPARZA vs investigator's choice of enza or abi (active comparator) in patients with HRRm mCRPC (including BRCAm)

PROfound was a prospective, multicenter, randomized, open-label, phase 3 trial

KEY ELIGIBILITY CRITERIA: mCRPC; progression on prior enzalutamide or abiraterone for the treatment of metastatic prostate cancer and/or CRPC; a tumor mutation in at least 1 of 15 genes involved in the HRR pathway

Randomization was stratified by prior receipt of taxane chemotherapy and presence of measurable disease by RECIST v1.1

COHORT A
BRCA1/2 or *ATM* gene mutation (n=245)[†‡]
LYNPARZA 300 mg BID[‡‖] (n=162)
2:1 randomization open label
Investigator's choice of enzalutamide or abiraterone[‡‖] (n=83)

Primary endpoint:
Cohort A: rPFS as determined by BICR using RECIST v1.1 and PCWG3 (bone) criteria

Select secondary endpoints (tested sequentially within a hierarchical statistical analysis):
- **Cohort A:** Confirmed objective response rate (ORR)
- **Cohort A+B:** rPFS as assessed by BICR
- **Cohort A:** OS

COHORT B
Other HRR gene mutations (n=142)[†§]
LYNPARZA 300 mg BID[‡‖] (n=94)
2:1 randomization open label
Investigator's choice of enzalutamide or abiraterone[‡‖] (n=48)

Patients with mCRPC were eligible for PROfound regardless of previous taxane use.
Although patients with *PPP2R2A* gene mutations were enrolled in the trial, LYNPARZA is not indicated for the treatment of patients with this gene mutation due to unfavorable risk-benefit ratio.

Select Baseline Patient Characteristics >

* HRR gene mutations (*BRCA1*, *BRCA2*, *ATM*, *BARD1*, *BRIP1*, *CDK12*, *CHEK1*, *CHEK2*, *FANCL*, *PALB2*, *PPP2R2A*, *RAD51B*, *RAD51C*, *RAD51D*, and/or *RAD54L*) were identified by tissue-based testing using the Foundation Medicine FoundationOne® clinical trial HRR assay performed at a central laboratory. No patients were enrolled who had mutations in 2 of the 15 prespecified HRR genes: FANCL and RAD51C.

† Patients with co-mutations (*BRCA1*, *BRCA2*, or *ATM* plus a Cohort B gene) were assigned to Cohort A.

‡ All patients received a GnRH analog or had prior bilateral orchiectomy.

§ *BARD1*, *BRIP1*, *CDK12*, *CHEK1*, *CHEK2*, *FANCL*, *PALB2*, *PPP2R2A*, *RAD51B*, *RAD51C*, *RAD51D*, and/or *RAD54L*

‖ Treatment was continued until objective radiological disease progression as determined by BICR. Upon radiological progression confirmed by BICR, patients randomized to enzalutamide or abiraterone were given the option to switch to LYNPARZA.

CRPC=castration-resistant prostate cancer.

Important Safety Information

CONTRAINDICATIONS

There are no contraindications for LYNPARZA.

WARNINGS AND PRECAUTIONS

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Study Design

rPFS

Exploratory Subgroup Analysis for rPFS

Overall Survival

Exploratory Subgroup Analysis for OS

rPFS for Cohort A+B

Important Safety Information

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Randomization was stratified by prior receipt of taxane chemotherapy and presence of measurable disease by RECIST v1.1

COHORT A

***BRCA1/2* or *ATM* gene mutation (n=245)†‡**

LYNPARZA 300 mg BID‡‖ (n=162)

2:1 randomization open label

Investigator's choice of enzalutamide or abiraterone‡‖ (n=83)

Primary endpoint:

Cohort A: rPFS as determined by BICR using RECIST v1.1 and PCWG3 (bone) criteria

Select secondary endpoints (tested sequentially within a hierarchical statistical analysis):

- **Cohort A:** Confirmed objective response rate (ORR)
- **Cohort A+B:** rPFS as assessed by BICR
- **Cohort A:** OS

COHORT B

Other HRR gene mutations (n=142)‡§

LYNPARZA 300 mg BID‡‖ (n=94)

2:1 randomization open label

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* HRR gene mutations (*BRCA1*, *BRCA2*, *ATM*, *BARD1*, *BRIP1*, *CDK12*, *CHEK1*, *CHEK2*, *FANCL*, *PALB2*, *PPP2R2A*, *RAD51B*, *RAD51C*, *RAD51D*, and/or *RAD54L*) were identified by tissue-based testing using the Foundation Medicine FoundationOne® clinical trial HRR assay performed at a central laboratory. No patients were enrolled who had mutations in 2 of the 15 prespecified HRR genes: FANCL and RAD51C.

† Patients with co-mutations (*BRCA1*, *BRCA2*, or *ATM* plus a Cohort B gene) were assigned to Cohort A.

‡ All patients received a GnRH analog or had prior bilateral orchiectomy.

§ Upon radiological progression confirmed by BICR, patients randomized to enzalutamide or abiraterone were given the option to switch to LYNPARZA.

‖ Treatment was continued until objective radiological disease progression as determined by BICR. Upon radiological progression confirmed by BICR, patients randomized to enzalutamide or abiraterone were given the option to switch to LYNPARZA.

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LYN PI_11.2023: p13/col2/§14.7/¶1/all; ¶2/ln1-2 de Bono 2020 p2/col1/¶2/ln1-6; col2/¶3/ln1-4

LYN PI_11.2023: p2/col2/§1.7/all; p13/col2/§14.7/¶1/ln5-8

LYN PI_11.2023: p13/col2/§14.7/¶2/ln12-13

LYN PI_11.2023: p3/col1/§2.2/¶1/all; p13/col2/§14.7/¶2/ln1-2,8-10; ¶6/ln1-3

LYN PI_11.2023: p3/col1/§2.2/¶1/all; p13/col2/§14.7/¶2/ln1-2,8-10; ¶6/ln1-3

LYN PI_11.2023: p13/col2/§14.7/¶1/ln1-4; ¶2/ln11-12 de Bono 2020: p2/col2/para4/line8-9

LYN PI_11.2023: p13/col2/§14.7¶2/ln6-8

LYN PI_11.2023: p13/col2/§14.7/¶2/ln1-6,16-18; ¶3/ln6-7

LYN PI_11.2023: p13/col2/§14.7/¶2/ln5-6

•LYN PI_11.2023: p13/col2/§14.7/¶5/all; p14/col1/Table26 de Bono 2020: p3/col2/¶4/ln2-5; p4/col1/¶1/ln1-6

LYN PI_11.2023: p3/col1/§2.2/¶1/all; p13/col2/§14.7/¶2/ln2-5,11-12; ¶6/line1-3

LYN PI_11.2023: p3/col1/§2.2/¶1/all; p13/col2/§14.7/¶2/ln2-5,11-12; ¶6/line1-3

LYN PI_11.2023: p13/col2/§14.7/¶1/ln4-5

LYN PI_11.2023: p13/col2/§14.7/¶2/ln14-16

p13/sec14.7/col2/para2/ln13-16

Revised from US-71899, p6: chart split across 2 pages with relevant footnotes on each page, reformatted to align to style of PROpel table

PROfound

Patient baseline characteristics

LYN PI 11.2023: p13/col2/§14.7/¶1/ln2-3
de Bono 2020: p5/Table1/col2-5/row1

Select patient characteristics*	Cohort A		Cohort A+B	
	LYNPARZA (n=162)	Investigator's choice of enzalutamide or abiraterone (n=83)	LYNPARZA (n=256)	Investigator's choice of enzalutamide or abiraterone (n=131)
Patients with alteration(s) in a single HRR gene, n (%)†				
BRCA1	8 (5)	5 (6)	8 (3)	5 (4)
BRCA2	80 (49)	47 (57)	81 (32)	47 (36)
ATM	60 (37)	24 (29)	62 (24)	24 (18)
Median age at randomization (range), years	68 (47–86)	67 (49–86)	69 (47–91)	69 (49–87)
Metastatic disease at initial diagnosis, n (%)	38 (23)	19 (23)	66 (26)	25 (19)
Metastases at baseline, n (%)				
Bone only	57 (35)	23 (28)	86 (34)	38 (29)
Visceral: lung or liver	46 (28)	32 (39)	68 (27)	44 (34)
Other	49 (30)	23 (28)	88 (34)	41 (31)
Measurable disease at baseline, n (%)‡	95 (59)	46 (55)	149 (58)	72 (55)
Median PSA at baseline (IQR), µg/L	62.2 (21.9, 280.4)	112.9 (34.3, 317.7)	68.2 (24.1, 294.4)	106.5 (37.2, 326.6)

de Bono 2020: p5/Table1/col2-5/row7-10
de Bono 2020: p5/Table1/col2-5/row2
de Bono 2020: p5/Table1/col2-5/row4
LYN PI 11.2023: p13/col2/§14.7/¶1/ln2-3
de Bono 2020: p5/Table1/col2-5/row14-17
de Bono 2020: p5/Table1/col2-5/row13
de Bono 2020: p5/Table1/col2-5/row12

*Cohort A included patients with at least 1 alteration in *BRCA1*, *BRCA2*, or *ATM*. Cohort B included patients with alterations in any of 12 other prespecifed genes: BRIP1, *BARD1*, *CDK12*, *CHEK1*, *CHEK2*, *FANCL*, *PALB2*, *PPP2R2A*, *RAD51B*, *RAD51C*, *RAD51D*, and *RAD54L*. Patients with co-mutations (*BRCA1*, *BRCA2*, or *ATM* plus a Cohort B gene) were assigned to Cohort A. In both cohorts, patients in the control group received the physician's choice of enzalutamide or abiraterone.

†A total of 28 patients (21 in cohort A and 7 in cohort B) had mutations in more than 1 gene. A total of 4 patients were incorrectly assigned to cohort B (1 in the olaparib group had an alteration in *BRCA2*, 1 in the control group had alterations in *BRCA2* and *CDK12*, and 2 in the olaparib group had alterations in *ATM*).

‡Data were derived from electronic case-report forms as assessed by the investigator.

§A total of 13 patients received a new hormonal agent for disease before diagnosis of mCRPC; all others received a new hormonal agent after the development of mCRPC.

‖One patient recieved paclitaxel.

de Bono 2020: p5/Table1/section symbol and paragraph symbol footnotes

de Bono 2020: p5/Table1/col1-5/row31

Important Safety Information

CONTRAINDICATIONS

There are no contraindications for LYNPARZA.

WARNINGS AND PRECAUTIONS

Myelodysplastic Syndrome/Acute Myeloid Leukemia (MDS/AML): Occurred in approximately 1.2% of patients with various *BRCA*m, g*BRCA*m, HRR gene-mutated or HRD-positive cancers who received LYNPARZA as a single agent or as part of a combination regimen, consistent with the approved indications, and the majority of events had a fatal outcome. The median duration of therapy in patients who developed MDS/AML was approximately 2 years (range: <6 months to >4 years). All of these patients had previous chemotherapy with platinum agents and/or other DNA-damaging agents, including radiotherapy.

In SOLO-1, patients with newly diagnosed advanced *BRCA*m ovarian cancer, the incidence of MDS/AML was 1.9% (5/260) in patients who received LYNPARZA and 0.8% (1/130) in patients who received placebo based on an updated analysis. In PAOLA-1, of patients with newly diagnosed advanced ovarian cancer with HRD-positive status, the incidence of MDS/AML was 1.6% (4/255) in patients who received LYNPARZA and 2.3% (3/131) in the control arm.

In SOLO-2, patients with *BRCA*m platinum-sensitive relapsed ovarian cancer, the incidence of MDS/AML was 8% (15/195) in patients who received LYNPARZA and 4% (4/99) in patients who received placebo. The duration of

Please see additional Important Safety Information throughout and complete Prescribing Information, including Medication Guide.

de Bono 2020: p5/Table1/asterisk and double dagger footnotes

Indications + | Important Safety Information +

PROfound

Patient baseline characteristics

Select patient characteristics*	Cohort A		Cohort A+B	
	LYNPARZA (n=162)	Investigator's choice of enzalutamide or abiraterone (n=83)	LYNPARZA (n=256)	Investigator's choice of enzalutamide or abiraterone (n=131)
Metastases at baseline, n (%)				
Bone only	57 (35)	23 (28)	86 (34)	38 (29)
Visceral: lung or liver	46 (28)	32 (39)	68 (27)	44 (34)
Other	49 (30)	23 (28)	88 (34)	41 (31)
Measurable disease at baseline, n (%)‡	95 (59)	46 (55)	149 (58)	72 (55)
Median PSA at baseline (IQR), µg/L	62.2 (21.9, 280.4)	112.9 (34.3, 317.7)	68.2 (24.1, 294.4)	106.5 (37.2, 326.6)
ECOG performance status 0-1, n (%)	151 (93)	80 (96)	243 (95)	126 (96)
Previous new hormonal agent§				
Enzalutamide	68 (42)	40 (48)	105 (41)	54 (41)
Abiraterone	62 (38)	29 (35)	100 (39)	54 (41)
Abiraterone+ enzalutamide	32 (20)	14 (17)	51 (20)	23 (18)
Previous taxane use, n (%)	106 (65)‖	52 (63)	170 (66)‖	84 (64)

de Bono 2020: p5/ Table1/col2-5/ row18-20
CALC:
84+67=151, n=151
52+41=93, n=93%
34+46=80, n=80
41+55=96, n=96%
131+112=243, n=243
51+44=95, n=95%
55+71=126, n=126
42+54=96, n=96%

de Bono 2020: p5/ Table1/col2-5/row27

de Bono 2020: p5/ Table1/col2-5/ row23-26

* Cohort A included patients with at least 1 alteration in *BRCA1*, *BRCA2*, or *ATM*. Cohort B included patients with alterations in any of 12 other prespecifed genes: BRIP1, *BARD1*, *CDK12*, *CHEK1*, *CHEK2*, *FANCL*, *PALB2*, *PPP2R2A*, *RAD51B*, *RAD51C*, *RAD51D*, and *RAD54L*. Patients with co-mutations (*BRCA1*, *BRCA2*, or *ATM* plus a Cohort B gene) were assigned to Cohort A. In both cohorts, patients in the control group received the physician's choice of enzalutamide or abiraterone.

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§ A total of 13 patients received a new hormonal agent for disease before diagnosis of mCRPC; all others received a new hormonal agent after the development of mCRPC.

‖ One patient recieved paclitaxel.

Important Safety Information

CONTRAINDICATIONS

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WARNINGS AND PRECAUTIONS

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In SOLO-1, patients with newly diagnosed advanced *BRCA*m ovarian cancer, the incidence of MDS/AML was 1.9% (5/260) in patients who received LYNPARZA and 0.8% (1/130) in patients who received placebo based on an updated analysis. In PAOLA-1, of patients with newly diagnosed advanced ovarian cancer with HRD-positive status, the incidence of MDS/AML was 1.6% (4/255) in patients who received LYNPARZA and 2.3% (3/131) in the control arm.

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Please see additional Important Safety Information throughout and complete Prescribing Information, including Medication Guide.

Indications +

Important Safety Information +

Revised from US-73132, p16, headline changed from "more than doubled median rPFS; marked changes, content otherwise is a direct lift

Replaced old headline which read "Primary endpoint in PROfound: rPFS in Cohort A[1]" -Pulled and revised headline from callout copy on the right which read "In patients with *BRCA1/2*- or *ATM*-mutated mCRPC >2x median rPFS with LYNPARZA vs investigator's choice of enzalutimide or abiraterone"

also adjusted chart header to match 2x claim

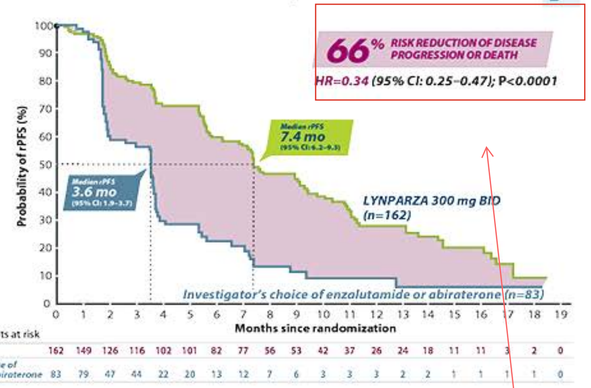
In patients with *BRCA1/2*- or *ATM*-mutated mCRPC (Cohort A)

LYNPARZA demonstrated superior rPFS vs investigator's choice of enza or abi

•LYN PI_11.2023: p13/col2/§14.7/¶2/ln1-2; ¶6/ln1-3; p14/col1/Table26/col2-3/row4
CALC: 3.6 x 2=7.2; 7.4 > 3.6 x 2

•LYN PI_11.2023: p13/col2/§14.7/¶6/ln1-3; p14/col1/Table26/col2-3/row1,2-6; Fig10

LYNPARZA doubled median rPFS vs comparator



•LYN PI_11.2023: p14/col1/Table 26/col2-3/row5-6
CALC: 100 - 34 = 66; HR=0.34

rPFS in Cohort A: Determined by BICR using RECIST version 1.1 and PCWG3 (bone) criteria.

Events, n (%): 106/162 (65) with LYNPARZA and 68/83 (82) with investigator's choice of enzalutamide or abiraterone.

Consistent results were observed in exploratory analyses of rPFS:

- For patients who received or did not receive prior taxane therapy
- For those with germline *BRCA* mutations identified using the Myriad BRACAnalysis CDx® assay compared with those with *BRCA* mutations identified using the Foundation Medicine F1CDx assay

Important Safety Information

CONTRAINDICATIONS

There are no contraindications for LYNPARZA.

WARNINGS AND PRECAUTIONS

LYN PI_11.2023: p13/col2/§14.7/¶5/ln1-3

Myelodysplastic Syndrome/Acute Myeloid Leukemia (MDS/AML): Occurred in approximately 1.2% of patients with various *BRCA*m, g*BRCA*m, HRR gene-mutated or HRD-positive cancers who received LYNPARZA as a single agent or as part of a combination regimen, consistent with the approved indications, and the majority of events had a fatal outcome. The median duration of therapy in patients who developed MDS/AML was approximately 2 years (range: <6 months to >4 years). All of these patients had previous chemotherapy with platinum agents and/or other DNA-damaging agents, including radiotherapy.

LYN PI 11.2023: p14/sec14.7/col1/table 26

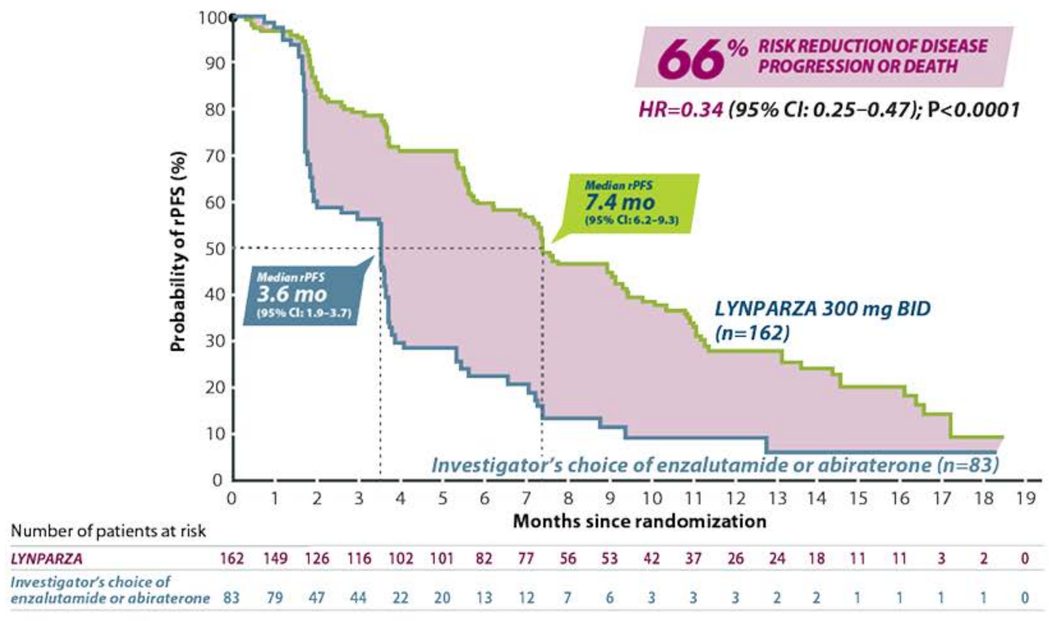
LYN PI_11.2023: p13/col2/§14.7/¶3/ln1-5

In SOLO-1, patients with newly diagnosed advanced *BRCA*m ovarian cancer, the incidence of MDS/AML was 1.9% (5/260) in patients who received LYNPARZA and 0.8% (1/130) in patients who received placebo based on an updated analysis. In PAOLA-1, of patients with newly diagnosed advanced ovarian cancer with HRD-positive status, the incidence of MDS/AML was 1.6% (4/255) in patients who received LYNPARZA and 2.3% (3/131) in the control arm.

In SOLO-2, patients with *BRCA*m platinum-sensitive relapsed ovarian cancer, the incidence of MDS/AML was 8% (15/195) in patients who received LYNPARZA and 4% (4/99) in patients who received placebo. The duration of

Please see additional Important Safety Information throughout and complete Prescribing Information, including Medication Guide.

LYNPARZA doubled median rPFS vs comparator



Number of patients at risk

LYNPARZA	162	149	126	116	102	101	82	77	56	53	42	37	26	24	18	11	11	3	2	0
Investigator's choice of enzalutamide or abiraterone	83	79	47	44	22	20	13	12	7	6	3	3	3	2	2	1	1	1	1	0

Important Safety Information

CONTRAINDICATIONS

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WARNINGS AND PRECAUTIONS

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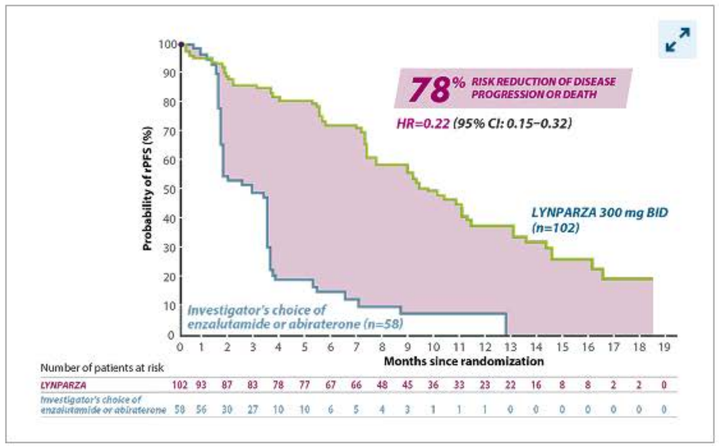
Revised from US-73132, p16, marked changes, content otherwise is a direct lift

Exploratory subgroup analysis

rPFS in patients with BRCAm *mCRPC*



These exploratory subgroup analyses are descriptive only. The PROfound trial was not designed to assess statistical significance in rPFS between treatment arms in the *BRCA*m or *ATM*-mutated subgroups. Results should be interpreted with caution.

rPFS in patients with *BRCA*m mCRPC:
Events, n(%): 62/102 (60.8) with LYNPARZA and 51/58 (87.9) with investigator's choice of enzalutamide or abiraterone.

rPFS in patients with *ATM*m mCRPC:
Events, n(%): 46/62 (74.2) with LYNPARZA and 17/24 (70.8) with investigator's choice of enzalutamide or abiraterone: 4% increased risk of progression or death; HR=1.04 (95% CI: 0.61–1.87).

Important Safety Information

CONTRAINDICATIONS

There are no contraindications for LYNPARZA.

WARNINGS AND PRECAUTIONS

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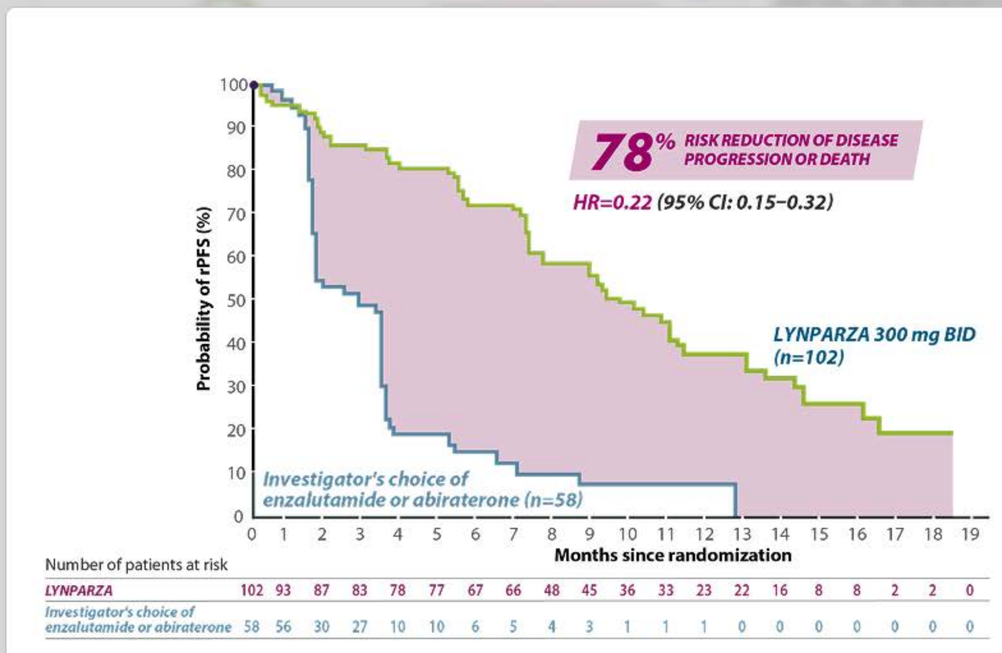
de Bono 2020 Appendix: p18 (pdf pg 19)/Figure S5/(A)/Chart Left
CALC: 100%-22%= 78% HR=0.22

Mateo 2023: p6/ Fig2A/legend

CALC:
62/102 =0.6078
51/58 =0.879

de Bono 2020 Appendix: p18 (pdf p19)/Figure S5/legend (B) ATM; p19 (pdf p20)/Figure B/Chart Left
CALC: 100%-104%= -4% HR=1.04

DAP: US-97600/ OA_LYN-04474



Important Safety Information

CONTRAINDICATIONS

There are no contraindications for LYNPARZA.

WARNINGS AND PRECAUTIONS

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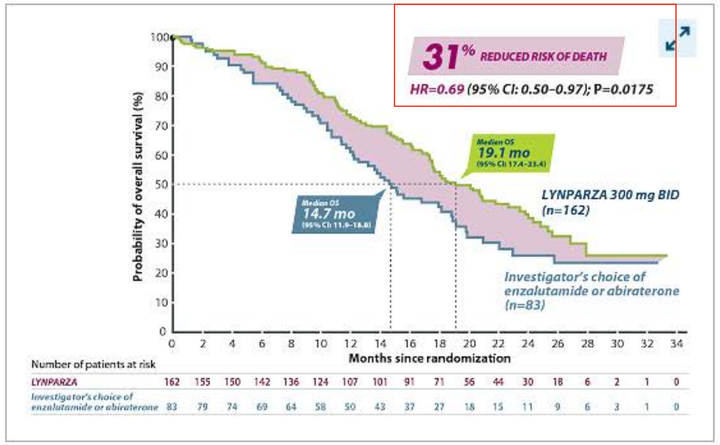
Prostate | PROfound: Monotherapy

In patients with *BRCA1/2*- or *ATM*-mutated mCRPC (Cohort A)

LYNPARZA demonstrated superior overall survival vs investigator's choice of enza or abi



OS in Cohort A: LYNPARZA demonstrated an OS benefit vs investigator's choice of enzalutamide or abiraterone.

Events, n (%): 91/162 (56) with LYNPARZA and 57/83 (69) with investigator's choice of enzalutamide or abiraterone.

PROfound was powered to evaluate several secondary endpoints within a hierarchical statistical analysis, including:

- ORR in Cohort A
- rPFS in Cohort A+B
- OS in Cohort A

Important Safety Information

CONTRAINDICATIONS

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WARNINGS AND PRECAUTIONS

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LYN PI_11.2023: p14/col1/Table26/col2-3/row15-16
CALC: 100%-69%
HR=31% reduced risk

LYN PI_11.2023: p14/col1/¶1/all

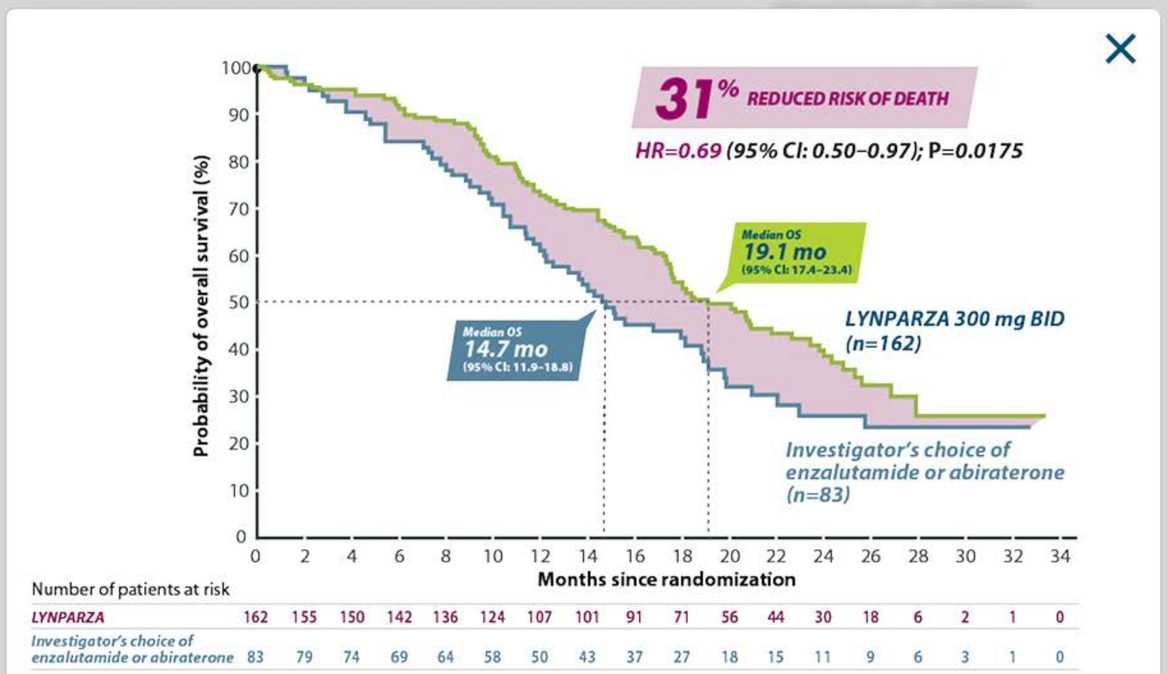
LYN PI 11.2023: p14/Table 26

•LYN PI_11.2023: p13/col2/§14.7/¶2/ln1-2; ¶5/ln3-5; ¶6/ln5-7; p14/col1/Table26/col2-3/row7-11
de Bono 2020/p4/col2/¶2/ln1-6

•LYN PI_11.2023: p13/col2/§14.7/¶2/ln1-2, 8-12; ¶5/ln3-5; p14/col1/Table26/col2-3/row12-16; col2/figure 11

LYN PI_11.2023: p13/col2/§14.7/¶5/ln3-5; p14/¶1/all
de Bono 2020; p3/col2/¶4/ln2-5;p4/col1/¶1/ln1-6

•LYN PI_11.2023: p13/col2/§14.7/¶5/ln3-5; ¶6/ln1-3, 5-7; p14/col1/Table26/row2-6;
de Bono 2020: p4/col2/¶4/all; p7/col1/¶1/ln1-2



Important Safety Information

CONTRAINDICATIONS

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this is new data incorporated into this piece from the 2023 Mateo JCO paper.

LYNPARZA® (olaparib) tablets 150 mg

MENU | Lynparza olaparib | PI | PROfound Efficacy | Prev Slide | Next Slide

Prostate | PROfound: Monotherapy

Exploratory subgroup analysis

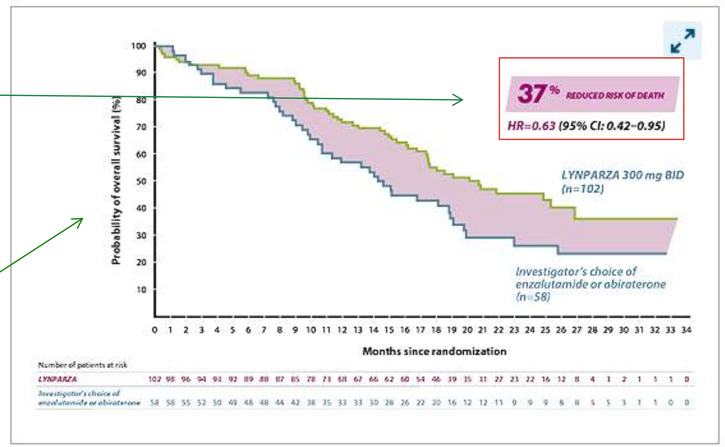
Overall survival in patients with BRCAm mCRPC

Mateo 2023: p6/ Fig2B

Mateo 2023: p5/ col1/para7/ln1-4; p6/Fig2B/legend

CALC: 100% - 63% = 37% reduced risk of death

Mateo 2023: p6/ Fig2B



Exploratory analyses are descriptive only. The PROfound trial was not designed to assess statistical significance in gene-by-gene subgroup analysis. Results should be interpreted with caution.

OS in patients with *BRCA*m mCRPC: Events, n(%): 53/102 (52) with LYNPARZA and 41/58 (70.7) with investigator's choice of enzalutamide or abiraterone.

OS in patients with *ATM* mCRPC: Events, n(%): 39/62 (62.9) with LYNPARZA and 15/24 (62.5) with investigator's choice of enzalutamide or abiraterone: 7% reduced risk of death; HR=0.93 (95% CI: 0.53–1.75).

Hussain 2020: NEJM suppl appendix/Fig S5B

Important Safety Information

CONTRAINDICATIONS

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WARNINGS AND PRECAUTIONS

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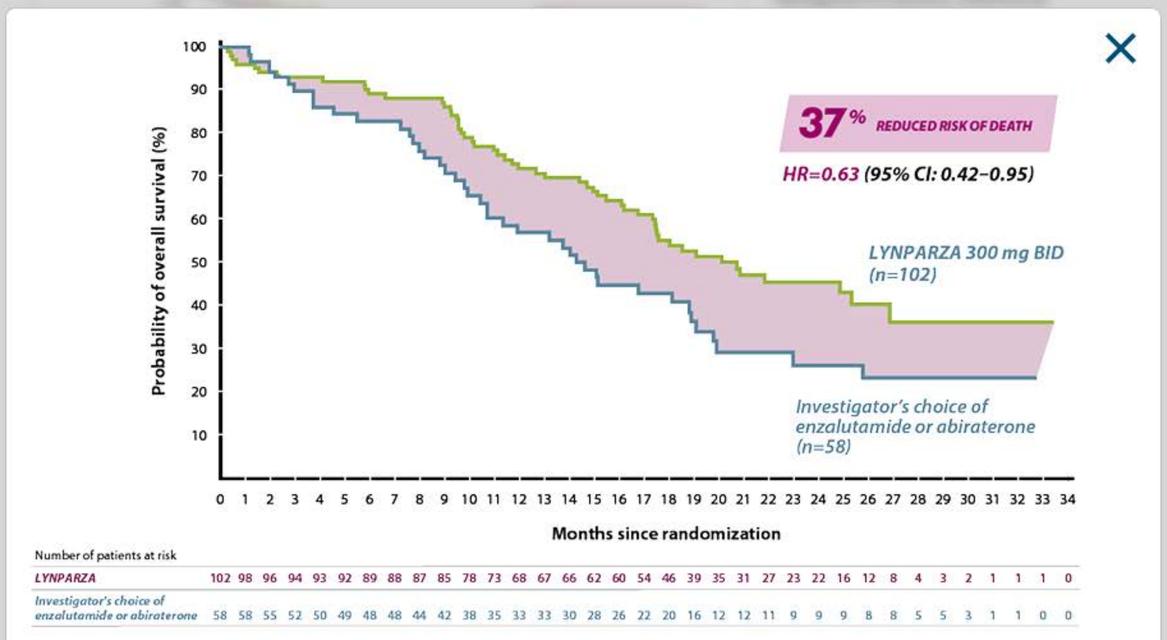
More | Overall Survival | Exploratory Subgroup Analysis for OS | rPFS for Cohort A+B | Indications + | Important Safety Information +



Important Safety Information

CONTRAINDICATIONS

There are no contraindications for LYNPARZA.

WARNINGS AND PRECAUTIONS

Myelodysplastic Syndrome/Acute Myeloid Leukemia (MDS/AML): Occurred in approximately 1.2% of patients with various *BRCA*m, g*BRCA*m, HRR gene-mutated or HRD-positive cancers who received LYNPARZA as a single agent or as part of a combination regimen, consistent with the approved indications, and the majority of events had a fatal outcome. The median duration of therapy in patients who developed MDS/AML was approximately 2 years (range: <6 months to >4 years). All of these patients had previous chemotherapy with platinum agents and/or other DNA-damaging agents, including radiotherapy.

In SOLO-1, patients with newly diagnosed advanced *BRCA*m ovarian cancer, the incidence of MDS/AML was 1.9% (5/260) in patients who received LYNPARZA and 0.8% (1/130) in patients who received placebo based on an updated analysis. In PAOLA-1, of patients with newly diagnosed advanced ovarian cancer with HRD-positive status, the incidence of MDS/AML was 1.6% (4/255) in patients who received LYNPARZA and 2.3% (3/131) in the control arm.

In SOLO-2, patients with *BRCA*m platinum-sensitive relapsed ovarian cancer, the incidence of MDS/AML was 8% (15/195) in patients who received LYNPARZA and 4% (4/99) in patients who received placebo. The duration of

Please see additional Important Safety Information throughout and complete Prescribing Information, including Medication Guide.

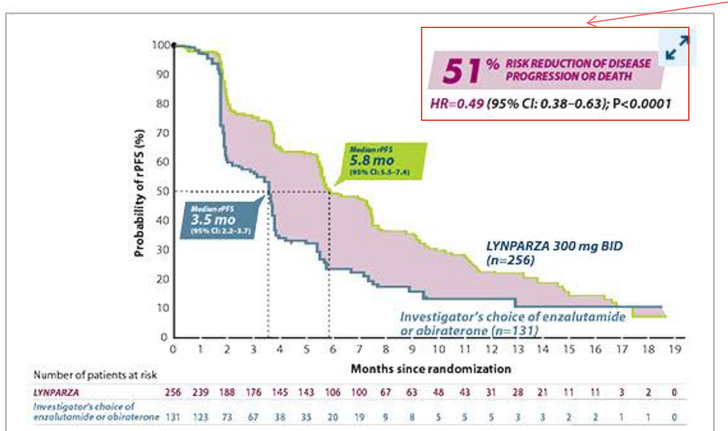
LYNPARZA® (olaparib) tablets 150 mg

MENU | Lynparza olaparib | PI | PROfound Efficacy | Prev Slide | Next Slide

Prostate | PROfound: Monotherapy

In patients with HRRm mCRPC (Cohort A+B)

LYNPARZA demonstrated superior rPFS vs investigator's choice of enza or abi



rPFS in Cohort A+B was assessed by BICR.

Genes included in Cohort A+B:

BRCA1, BRCA2, ATM, BARD1, BRIP1, CDK12, CHEK1, CHEK2, FANCL, PALB2, PPP2R2A,* RAD51B, RAD51C, RAD51D, and RAD54L.

*Although patients with *PPP2R2A* mutations were included in all analyses of Cohort A+B, LYNPARZA is not indicated for this population due to an unfavorable risk-benefit ratio.

PROfound was powered to evaluate several secondary endpoints within a hierarchical statistical analysis, including:

- ORR in Cohort A
- rPFS in Cohort A+B
- OS in Cohort A

Important Safety Information

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More | Overall Survival | Exploratory Subgroup Analysis for OS | rPFS for Cohort A+B | Indications + | Important Safety Information +

LYN PI 11.2023: p13/sec14.7/col2/para6/ln1-3; p14/table26

LYN PI 11.2023: p13/col2/§14.7/¶1/ln2-3; ¶5/ln3-5; p14/col1/Table26/col4-5/row2-6

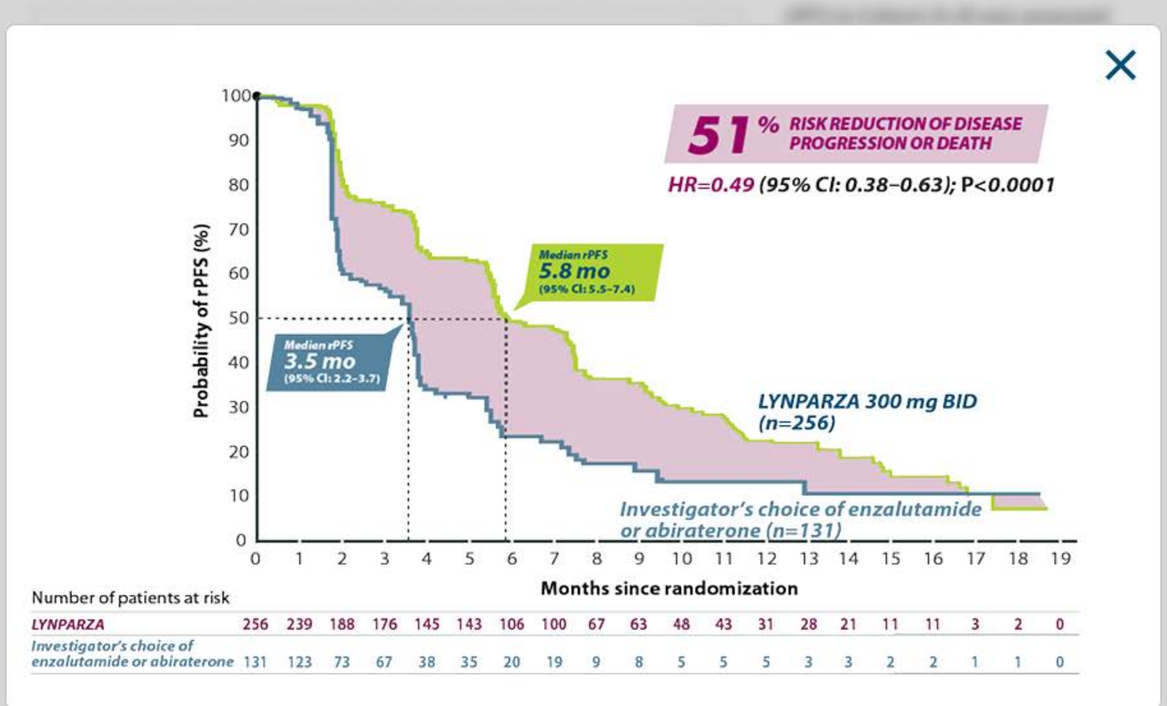
RRR CALC: 100%-49% HR=51% RRR

LYN PI 11.2023: p13/col2/§14.7/¶5/ln3-5

LYN PI 11.2023: p13/col2/§14.7/¶2/ln1-6

LYN PI 11.2023: p13/col2/§14.7/¶2/ln1-8

de Bono 2020 p3/col2/¶4/all; p4/¶1/ln1-6



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Revised from US-73132, p20, marked changes, content otherwise is a direct lift

LYNPARZA® (olaparib) tablets 150 mg

MENU | Lynparza olaparib | PI | PROfound Safety and Tolerability | Prev Slide | Next Slide

Prostate | PROfound: Monotherapy

Revised from headline that read "Adverse reaction reported in ≥10% of patients in PROfound (Cohorts A+B)[1]"

Select adverse reactions in PROfound (Cohort A+B)

LYNPARZA (n=256) | Investigator's choice of enzalutamide or abiraterone (n=130)

Adverse Reactions*	Grades 1–4 (%)	Grades 3–4 (%)
Blood and Lymphatic Disorders		
Anemia†	46 15	21 5
Thrombocytopenia‡	12 3	4 0
Gastrointestinal Disorders		
Nausea	41 19	1 0
Diarrhea	21 7	1 0
Vomiting	18 12	2 1
General Disorders and Administration Site Conditions		
Fatigue (including asthenia)	41 32	3 5
Metabolism and Nutrition Disorders		
Decreased appetite	30 18	1 1
Respiratory, Thoracic, and Mediastinal Disorders		

Adverse reactions reported in ≥10% of patients who received LYNPARZA

LYN PI_11.2023: p7/col2/ §PROfound/Table 14; Table15

- **Fatal adverse reactions** occurred in 4% of patients treated with LYNPARZA. These included pneumonia (1.2%), cardiopulmonary failure (0.4%), aspiration pneumonia (0.4%), intestinal diverticulum (0.4%), septic shock (0.4%), Budd-Chiari syndrome (0.4%), sudden death (0.4%), and acute cardiac failure (0.4%)

LYN PI 11.2023: p7/col1/PROfound/ para2/all

- **Serious adverse reactions** occurred in 36% of patients receiving LYNPARZA. The most frequent serious adverse reactions (≥2%) were anemia (9%), pneumonia (4%), pulmonary embolism (2%), fatigue/asthenia (2%), and urinary tract infection (2%)

LYN PI 11.2023: p7/col1/PROfound/ para3/all

- **Venous thromboembolism** (VTE), including severe or fatal pulmonary embolism (PE), occurred in patients treated with LYNPARZA. In the combined data of two randomized, placebo-controlled clinical studies (PROfound and PROpel) in patients with metastatic castration-resistant prostate cancer (N=1180), VTE occurred in 8% of patients who received LYNPARZA, including pulmonary embolism in 6%. In the control arms, VTE occurred in 2.5%, including pulmonary embolism in 1.5%

LYN PI 11.2023: p3/col2/sec5.3/ para1/all

*Graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE), version 4.03.
†Includes anemia and hemoglobin decreased.
‡Includes platelet count decreased and thrombocytopenia.

LYN PI_11.2023: p7/col2/ §PROfound/Table 14/ footnotes/all

Please see additional Important Safety Information throughout and complete Prescribing Information, including Medication Guide.

Select adverse reactions in PROfound (Cohort A+B)

LYNPARZA (n=256) Investigator's choice of enzalutamide or abiraterone (n=130)

Adverse Reactions*	Grades 1–4 (%)	Grades 3–4 (%)
Thrombocytopenia‡	12 3	4 0
Gastrointestinal Disorders		
Nausea	41 19	1 0
Diarrhea	21 7	1 0
Vomiting	18 12	2 1
General Disorders and Administration Site Conditions		
Fatigue (including asthenia)	41 32	3 5
Metabolism and Nutrition Disorders		
Decreased appetite	30 18	1 1
Respiratory, Thoracic, and Mediastinal Disorders		
Cough	11 2	0 0
Dyspnea	10 3	2 0

Adverse reactions reported in ≥10% of patients who received LYNPARZA

- **Fatal adverse reactions** occurred in 4% of patients treated with LYNPARZA. These included pneumonia (1.2%), cardiopulmonary failure (0.4%), aspiration pneumonia (0.4%), intestinal diverticulum (0.4%), septic shock (0.4%), Budd-Chiari syndrome (0.4%), sudden death (0.4%), and acute cardiac failure (0.4%)
- **Serious adverse reactions** occurred in 36% of patients receiving LYNPARZA. The most frequent serious adverse reactions (≥2%) were anemia (9%), pneumonia (4%), pulmonary embolism (2%), fatigue/asthenia (2%), and urinary tract infection (2%)
- **Venous thromboembolism** (VTE), including severe or fatal pulmonary embolism (PE), occurred in patients treated with LYNPARZA. In the combined data of two randomized, placebo-controlled clinical studies (PROfound and PROpel) in patients with metastatic castration-resistant prostate cancer (N=1180), VTE occurred in 8% of patients who received LYNPARZA, including pulmonary embolism in 6%. In the control arms, VTE occurred in 2.5%, including pulmonary embolism in 1.5%

*Graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE), version 4.03.

†Includes anemia and hemoglobin decreased.

‡Includes platelet count decreased and thrombocytopenia.

Laboratory abnormalities reported in ≥25% of patients in PROfound (Cohort A+B)

LYNPARZA (n=256)* Investigator's choice of enzalutamide or abiraterone (n=130)*

Laboratory Parameter†	Grades 1–4 (%)	Grades 3–4 (%)
Decrease in hemoglobin	98 73	13 4
Decrease in lymphocytes	62 34	23 13
Decrease in leukocytes	53 21	4 0
Decrease in absolute neutrophil count	34 9	3 0

LYN PI_11.2023: p7/col2/ §PROfound/ Table15, footnotes

Reorganized copy to align to style of PROpel table

* This number represents the safety population. The derived values in the table are based on the total number of evaluable patients for each laboratory parameter.
† Patients were allowed to enter clinical studies with laboratory values of CTCAE Grade 1.

Revised from US-71899, p13, formatted to align to PROpel table, other changes marked, content otherwise is a direct lift

Dose modifications in PROfound

Changes due to adverse reactions	LYNPARZA (n=256)
Dose interruptions due to ARs	**45%**
Dose reduction due to ARs	**22%**
Discontinuations due to ARs	**18%**

The most frequent adverse reactions leading to dose interruption of LYNPARZA were anemia (25%) and thrombocytopenia (6%), and the most frequent adverse reaction leading to reduction was anemia (16%). The adverse reaction that most frequently led to discontinuation of LYNPARZA was anemia (7%).

Reorganized copy to align to style of PROpel table

LYN PI 11.2023: p7/col1/PROfound/para4/all

LYN PI_11.2023: p7/col1/§PROfound/¶4/ln5-6
CALC: 100%-18% = 82%

In PROfound, the majority of patients remained on treatment without discontinuing due to adverse reactions (82% for LYNPARZA)

Replaced the line that read ">8 OUT OF 10 PATIENTS REMAINED ON LYNPARZA WITHOUT DISCONTINUING DUE TO ADVERSE REACTIONS"

This is a summary page conglomerating content from US-73132, p12 and other pages in this deck - indicated where marked - marked changes, content otherwise is a direct lift

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MENU | Lynparza® olaparib | PI | Summary | Prev Slide | Next Slide

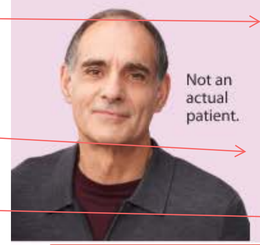
Prostate

LYNPARZA is a targeted treatment option for eligible patients with mCRPC who are at higher risk of aggressive disease

PROpel: Combination Therapy
In combination with abi/pred in BRCAm* mCRPC

FDA approval based on rPFS and OS data in an exploratory BRCA*m subgroup:*

rPFS (n=85)	*OS (n=85)*
76% RISK REDUCTION OF DISEASE PROGRESSION OR DEATH *vs placebo + abi/pred*	**70% REDUCTION IN RISK OF DEATH** *vs placebo + abi/pred*
HR=0.24 (95% CI: 0.12–0.45)	HR=0.30 (95% CI: 0.15–0.59)
Median rPFS with LYNPARZA + abi/pred was not reached (95% CI: NR–NR) vs 8 months with placebo + abi/pred (95% CI: 6–15).	Median OS with LYNPARZA + abi/pred was not reached (95% CI: NR–NR) vs 23 months with placebo + abi/pred (95% CI: 18–34).
	OS did not reach statistical significance in the ITT population

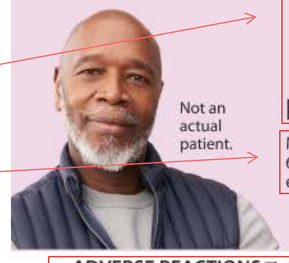

Not an actual patient.

*BRCA*m status was not a stratification factor in PROpel, and analysis was not controlled for Type 1 error.

ADVERSE REACTIONS The most common adverse reactions (≥10%) in patients who received LYNPARZA + abi/pred were anemia (48%), fatigue (38%), nausea (30%), diarrhea (19%), decreased appetite (16%), lymphopenia (14%), dizziness (14%), and abdominal pain (13%).

PROfound: Monotherapy
Following progression on prior enza or abi in HRRm* mCRPC

*Primary Endpoint: Statistically significant rPFS in Cohort A (*BRCA*m/ATMm; n=245)*	*Select secondary endpoint: Statistically significant OS in Cohort A (*BRCA*m/ATMm; n=245)*
66% RISK REDUCTION OF DISEASE PROGRESSION OR DEATH *vs investigator's choice of enza or abi*	**31% REDUCTION IN RISK OF DEATH** *vs investigator's choice of enza or abi*
HR=0.34 (95% CI: 0.25–0.47); *P*<0.0001	HR=0.69 (95% CI: 0.50–0.97); *P*=0.0175
Median rPFS with LYNPARZA was 7.4 months (95% CI: 6.2-9.3) vs 3.6 months with investigator's choice of enza or abi (95% CI: 1.9–3.7).	Median OS with LYNPARZA was 19.1 months (95% CI: 17.4–23.4) vs 14.7 months with investigator's choice of enza or abi/pred (95% CI: 11.9–18.8).
	PROfound was powered to evaluate several secondary endpoints within a hierarchical statistical analysis including ORR in Cohort A, rPFS in Cohort A+B, and OS in Cohort A.


Not an actual patient.

ADVERSE REACTIONS The most common adverse reactions (≥10%) in patients who received LYNPARZA were anemia (46%), fatigue (41%), nausea (41%), decreased appetite (30%), diarrhea (21%), vomiting (18%), thrombocytopenia (12%), cough (11%), and dyspnea (10%).

*Select patients for this indication based on an FDA-approved companion diagnostic for LYNPARZA.[1]

Important Safety Information

CONTRAINDICATIONS

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WARNINGS AND PRECAUTIONS

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In SOLO-1, patients with newly diagnosed advanced *BRCA*m ovarian cancer, the incidence of MDS/AML was 1.9% (5/260) in patients who received LYNPARZA and 0.8% (1/130) in patients who received placebo based on an updated analysis. In PAOLA-1, of patients with newly diagnosed advanced ovarian cancer with HRD-positive status, the incidence of MDS/AML was 1.6% (4/255) in patients who received LYNPARZA and 2.3% (3/131) in the control arm.

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Indications + | Important Safety Information +

LYN PI_11.2023: p2/col2/§1.8/all

LYN PI_11.2023: p15/col1/Table 28/col2-3/row 5
CALC: 100%-24%
HR=76% reduced risk

LYN PI_11.2023: p15/col1/Table28; col2-3/row4-5

LYN PI_11.2023: p14/col2/sect14.8/¶1/ln10-11

LYN PI_11.2023: p8/col1/Table 16

LYN PI_11.2023: p2/col2/§1.7/all

•LYN PI_11.2023: p13/col2/§14.7/¶2/ln1-2, ¶5/ln1-2, ¶6/ln1-3; p14/col1/Table 26/col2-3/row1 CALC: 162 + 83 = 245; n=245

•LYN PI_11.2023: p14/col1/Table 26/col2-3/row5-6 CALC: 100 - 34 = 66; HR=0.34

•LYN PI_11.2023: p14/col1/Table26/col2-3/row4

LYN PI_11.2023: p7/col2/Table14/col1-2/all

LYN PI_11.2023: p2/col2/§1.7/¶1/ln4-5; §1.8/¶1/ln3-4

LYN PI_11.2023: p2/col2/§1.7-1.8/all
ADD
Clarke
DiBono

LYN PI_11.2023: p15/col1/¶3/ln1-2; ¶4-5/all; Table 28/col2-3/row 1
CALC: 47+38=85
n=85

LYN PI_11.2023: p15/col1/Table 28/col2-3/row 9
CALC: 100%-30%
HR=70% reduced risk

LYN PI_11.2023: p15/col1/Table 28/col2-3/row 8

Clarke 2022: p15/col1/¶2/ln5-7

•LYN PI_11.2023: p13/col2/§14.7/¶2/ln1-2; ¶5/ln1-2; ¶6/ln1-3; p14/col1/Table 26/col2-3/row1 CALC: 162 + 83 = 245; n=245

LYN PI_11.2023: p14/col1/Table26/col2-3/row15-16
CALC: 100%-69%
HR=31% reduced risk

•LYN PI_11.2023: p14/col1/Table26/col2-3/row12-16

•LYN PI_11.2023: p13/col2/§14.7/¶2/ln1-6; ¶5/ln3-5; ¶6/ln1-7; p14/col1/¶1/all, Table26/col2-6/row7-11
de Bono 2020 p3/col2/¶4/ln2-5; p4/col1/¶1/ln1-6, col2/¶2/ln1-6, ¶4/all; p7/col1/¶1/ln1-2

Prostate

References

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Prostate

Abbreviations

abi/pred = abiraterone plus prednisone or prednisolone
AR = adverse reaction
*ATM*m= *ATM*-mutated
BICR = blinded independent central review
BID = twice daily
*BRCA*m = *BRCA*-mutated
CDx = companion diagnostic
CI = confidence interval
CR = complete response
DCO = data cutoff
ECOG = Eastern Cooperative Oncology Group
enza = enzalutamide
g*BRCA*m = germline BRCA–mutated or germline BRCA mutation(s)
GnRH = gonadotropin-releasing hormone
HR = hazard ratio
HRD = homologous recombination deficiency
HRR = homologous recombination repair
HRRm = homologous recombination repair gene-mutated
ITT = intent-to-treat
IV = intravenous
mCRPC = metastatic castration-resistent prostate cancer
mHSPC = metastatic hormone-sensitive prostate cancer
mPC = metastatic prostate cancer
mPFS = median progression-free survival
NCI CTCAE = National Cancer Institute Common Terminology Criteria for Adverse Events
NR = not reached
OS = overall survival
PARPi = poly (ADP-ribose) polymerase (PARP) inhibitor
PCWG3 = Prostate Cancer Working Group 3
PFS = progression-free survival
PR = partial response
PS = performance status
QD = once daily
RECIST = Response Evaluation Criteria in Solid Tumors
rPFS = radiological progression-free survival
t*BRCA* = tumor *BRCA*
UTI = urinary tract infection

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