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• For a full list of adverse events (AEs), please refer to the United Kingdom SmPC here.
Adverse events should be reported. Reporting forms and information can be found at yellowcard.mhra.gov.uk. Adverse events should also be reported to AstraZeneca on +44 (0)800 0191 627 or to medsafe@astrazeneca.com or MSD on +44 (0)1992 467272 or medicalsafety@uk.msd.com.

• Click on the following link to view the United Kingdom Prescribing Information for LYNPARZA (olaparib) here.

# LYNPARZA® (olaparib) in prostate cancer:

## Managing adverse events

Lynparza® (olaparib)

### LYNPARZA (olaparib) is indicated:

- In combination with abiraterone and prednisone or prednisolone for the treatment of adult patients with metastatic castration-resistant prostate cancer (mCRPC) in whom chemotherapy is not clinically indicated and who have mild or moderate pain from their prostate cancer that is not sufficiently painful to warrant regular use of opioid analgesics or whose prostate cancer is not sufficiently symptomatic to warrant chemotherapy, following prior therapy that included a new hormonal agent (NHA)[1]

### ✓ NICE recommended/SMC accepted

- LYNPARZA in combination with abiraterone and prednisone or prednisolone is NICE recommended and SMC accepted for treatment of adult patients with mCRPC in whom chemotherapy is not clinically indicated[1,2]
- LYNPARZA monotherapy is recommended by NICE and accepted by SMC for treating hormone-relapsed prostate, with BRCA1/2 mutations that has progressed after NHA (such as abiraterone or enzalutamide)[1,3]

### LYNPARZA is a PARP inhibitor:

- Developed to specifically **target DNA repair pathways**[4-7]
- Acts on the principle of **synthetic lethality** in cancer cells with compromised for a range of indications, including prostate cancer, breast cancer, ovarian cancer, pancreatic cancer and metastatic castration resistant prostate cancer[1]
- Indicated as monotherapy for the treatment of patients with **metastatic castration-resistant prostate cancer** and **deleterious BRCA1/2 and/or BRCA2 mutations** (germline and/or somatic) who have progressed after prior therapy that included a NHA[1]
- Also indicated in combination with abiraterone and prednisone or prednisolone for the treatment of adult patients with mCRPC in whom chemotherapy is not clinically indicated[1]

### LYNPARZA clinical trials

PROfound was a Phase III, randomised, open-label, multicentre study that evaluated the efficacy and safety of LYNPARZA versus investigator's choice of NHA in patients with mCRPC.[8,9,10]

**PROfound study design[8,9]**

PROfound was a Phase III, randomised, double-blind, placebo-controlled, multicentre study evaluating the efficacy and safety of LYNPARZA in combination with abiraterone and prednisone or prednisolone vs placebo in combination with abiraterone and prednisone or prednisolone in patients with mCRPC in the first-line setting[11,12]

**PROpel study design[13,14]**

### Are associated with LYNPARZA are generally of mild or moderate severity (CTCAE grade 1 or 2)

When LYNPARZA is used in combination with abiraterone and prednisone or prednisolone for mCRPC, the safety profile is generally consistent with that of the individual therapies

Anaemia, fatigue and nausea are most commonly associated with PARPi[15]

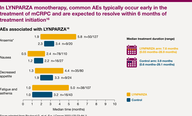
- Very common (≥10%) all-grade AEs reported with abiraterone and LYNPARZA in the Phase III PROpel study were anaemia (49%), nausea (47%), hypertension (38%), fatigue (36%), vomiting (29%), AST increased (28%), constipation (26%), thrombocytopenia (21%), decreased appetite (19.8%), dyspnea (19.3%), arthralgia (18.6%), COVID-19 (12.8%), peripheral oedema (12.3%), dizziness (12.3%), cough (11.8%) and urinary tract infection (11.8%)[16]

**Haematological toxicity and pneumonitis are included as special warnings on the LYNPARZA SmPC, and hypertension is included on the abiraterone SmPC for this combination**

Please refer to the SmPCs for more information on other adverse events associated with LYNPARZA and abiraterone and their management, including those not included in this material, such as those related to cardiovascular events, renal events, and fluid retention.

### Blood, GI, general disorders and respiratory disorders are the most frequently reported AEs after treatment with LYNPARZA[16]

**Frequency of selected blood, GI, general and vascular grade ≥3 AEs[1]**




**AEs observed with LYNPARZA monotherapy in PROfound[1]**

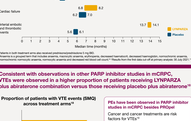
**AEs observed with LYNPARZA plus abiraterone and prednisone or prednisolone in PROpel[16]**

Very common (≥1/10 people) Common (1/100 to <1/10 people)

AEs with special warnings and precautions associated with LYNPARZA can be found below in the assessment. For a full list of AEs, please see the SmPC.

### In LYNPARZA monotherapy, common AEs typically occur early in the treatment of mCRPC and are expected to resolve within 6 months of treatment initiation[16]

**AEs associated with LYNPARZA[16]**

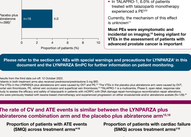



*Grade 3 anaemia: 7% (LYNPARZA) vs 1% (control)

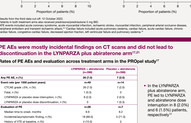
Figure adapted from Fizazi et al. Ann Oncol 2021;72:62-71.

### In LYNPARZA plus abiraterone combination treatment of mCRPC, common AEs typically occur early and are expected to resolve within 9 months of treatment initiation[1]

**AEs associated with LYNPARZA[16]**




**AEs associated with abiraterone[16]**




Adverse events are based on pooled safety analysis of patients who received LYNPARZA 300 mg twice daily (n=1174) and placebo (n=1088) in combination with abiraterone and prednisone/prednisolone. Treatment-emergent adverse events, regardless of treatment relationship, occurring in ≥5% of patients in the LYNPARZA arm and with a difference between treatment groups of ≥2% for any grade or ≥1% for grade ≥3 were included in the analysis.

### Consistent with observations in other PARP inhibitor studies in mCRPC, VTEs were observed at a higher proportion of patients receiving LYNPARZA plus abiraterone combination versus those receiving placebo plus abiraterone[16]

**Proportion of patients with VTE events (SMQ across treatment arms[16])**

**PEs have been observed in PARP inhibitor studies in mCRPC based on PROpel**

Cancer and cancer treatments are risk factors for VTE[17]

- In PROfound, 4.3% of patients treated with LYNPARZA monotherapy and 0.8% of patients in the control arm treated with abiraterone or enzalutamide developed PE[18]
- In OLAPARIS, 5.8% of patients treated with olaparib monotherapy experienced PE[19]

Currently, the mechanism of this effect is unknown

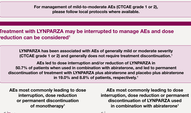
**Most PEs were asymptomatic and incidental on imaging,[20] being eligible for VTEs in the assessment of patients with advanced prostate cancer is important.**

**Please refer to the section on AEs with special warnings and precautions for LYNPARZA in this document and the LYNPARZA SmPC for further information on patient monitoring.**

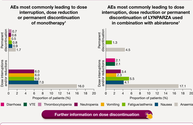
Based on pooled data from both LYNPARZA arms (n=1174) and placebo (n=1088) in combination with abiraterone and prednisone/prednisolone. Treatment-emergent adverse events were identified using standardised MedDRA queries (SMQ) across treatment arms. The VTEs in the placebo arm included events in the SMQ venous thromboembolism, PE, retinal vein occlusion and superficial vein thrombosis.[16] The MPR[21] is a multivariate, Phase II, open-label, regulatory-mandated study in patients with metastatic castration-resistant prostate cancer who have progressed on androgen deprivation therapy and have ≥1 cardiovascular risk factor, designed to evaluate the safety of LYNPARZA plus abiraterone and prednisone versus abiraterone and prednisone.

### The rate of CV and ATE events is similar between the LYNPARZA plus abiraterone combination arm and the placebo plus abiraterone arm[16]

**Proportion of patients with ATE events (SMQ across treatment arms[16])**




**Proportion of patients with cardiac failure (SMQ across treatment arms[16])**




Results from the third data cut-off, 13 October 2021.

Cardiac failure includes cardiac failure, cardiac failure congestive and pulmonary oedema, myocardial infarction, peripheral arterial occlusive disease, venous thrombosis and transient ischaemic attack.[16] Cardiac failure included acute pulmonary oedema, cardiac failure, acute cardiac failure, chronic congestive cardiac failure, cardiogenic shock, ventricular dysfunction, congestive cardiomyopathy, and cardiomyopathy.[16]

### PE AEs were mostly incidental findings on CT scans and did not lead to discontinuation in the LYNPARZA combination arm[16,20]

**Rates of PE AEs and avoidance treatment discontinuation in the PROpel study[16]**

| | Abiraterone + placebo (n=488) | Abiraterone + olaparib (n=488) |
|---|---|---|
| Any PE AE (%) | 1.0 | 2.4 |
| Grade ≥3 PE AE (patient year) | 0.2 | 0.4 |
| CTCAE grade ≥3% n (%) | 2/1.0 | 1/2.0 |
| Fatal n (%) | 0/0 | 1/0.2 |
| LYNPARZA or placebo dose interruption n (%) | 0/0 | 1/0.2 |
| LYNPARZA or placebo dose reduction n (%) | 0/0 | 0/0 |
| **Evaluation of PE** | | |
| Median time to onset, months | 9.1 | 6.1 |
| Median treatment duration, months | 5.6 | 8.3 |
| Rate of PE events per 100 patient years | 0.2 | 0.4 |
| Administration of DTC prior to PE, n (%) | 1/0 | 1/0 |
| Administration of DTC post PE, n (%) | 1/0 | 1/0 |

- In the LYNPARZA plus abiraterone arm, PE led to LYNPARZA and abiraterone dose interruption in 0.2% and 0.1.5% patients, respectively

**Most patients recovered from the event and were able to continue LYNPARZA with the introduction of anticoagulant treatment based on standard medical practice.[1]**

Patients in both treatment arms did not received prophylaxis/treatment for a VTE.
Rates of PE events are based on patient years of exposure.

### Overview of the LYNPARZA AE management process[1,11,16]

Based on the LYNPARZA SmPC and the PROpel study design

### Managing AEs related to LYNPARZA in prostate cancer

*Successful management of AEs may result in treatment continuation*

- In most cases, AEs can be managed by interrupting treatment, providing supportive care and considering dose reduction[1,11]

**Anaemia**

Median time to first onset of anaemia was approximately 4 weeks (approximately 2 weeks for CTCAE grade ≥3 anemia)[1]

- Carry out baseline, dose interruption, dose reduction and permanent discontinuation

Baseline testing, followed by monthly monitoring of complete blood counts, is recommended prior to the start of treatment and periodically after this time to monitor for clinically significant changes in the parameter during treatment

**Nausea and vomiting**

First onset of nausea and vomiting was observed within the first month and first 2 months of treatment, respectively[1]

Can be managed with prophylactic or reactive antiemetic therapy[1]

Antiemetic prophylaxis is not required, but supportive therapy should be considered for patients presenting symptoms[22]

**For management of mild-to-moderate AEs (CTCAE grade 1 or 2), consider the following non-pharmacological protocols where available**

### Treatment with LYNPARZA may be interrupted to manage AEs and dose reduction can be considered[1]

**LYNPARZA has been associated with AEs of generally mild or moderate severity (CTCAE grade 1 or 2) and generally does not require treatment discontinuation.[1]**

**AEs led to dose interruption and/or reduction of LYNPARZA in 39.7% and 10.6% of patients, respectively, and to permanent discontinuation of treatment with LYNPARZA plus abiraterone and prednisone plus abiraterone in 19.0% and 8.8% of patients, respectively.[1]**

**AEs most commonly leading to dose interruption, dose reduction or permanent discontinuation of monotherapy[1]**

**AEs most commonly leading to dose interruption, dose reduction or permanent discontinuation of LYNPARZA used in combination with abiraterone[1]**

**Should dose reduction be required, the recommended initial reduction is 200 mg twice daily.[1] If further dose reduction is needed, then a reduction to 100 mg twice daily is recommended.[1]**

**Further information on dose reduction**

### AEs with special warnings and precautions for LYNPARZA[1]

Always AEs related to LYNPARZA are generally mild or moderate in severity and usually do not require treatment discontinuation, there are certain situations involving specific risk and specified precautions:

**Severe haematological toxicity**

- Anaemia was the most common CTCAE grade ≥3 adverse reaction reported in clinical trials of LYNPARZA. In patients treated with the tablet formulation, the incidence of CTCAE grade 3 anaemia was 14.8%
- If a patient develops unexpected hematological toxicity or blood transfusion dependence, consider referral to a haematologist, interrupt and appropriate haematological testing initiated[1]
- If the blood parameters remain clinically abnormal after 4 weeks of LYNPARZA dose interruption, further dose reduction of LYNPARZA (drug) (olaparib) tablets are recommended[1]

**MDS/AML**

- MDS/AML occurred in 0.3% of patients in clinical studies of LYNPARZA across indications, with a cumulative incidence of monotherapy at 5 therapeutic dose[1]
- If MDS/AML is suspected, the patient should be referred to a haematologist for further investigations, including bone marrow examination and cytogenetic testing. Interrupt and should be permanently discontinued if confirmed, investigation of prolonged haematologic toxicity, LYNPARZA should be discontinued and the patient treated appropriately[1]

**Pneumonitis**

- Pneumonitis has been reported in <1.0% of patients treated with LYNPARZA in clinical studies[1]
- If patients present with new or worsening respiratory symptoms and fever, interrupt treatment, perform a chest x-ray and radiological finding is observed, LYNPARZA should be interrupted and appropriate investigation initiated
- If pneumonitis is confirmed, LYNPARZA should be discontinued and the patient treated appropriately[1]

**VTEs**

- Monitor patients for clinical signs and symptoms of venous thrombosis and PE and treat as medically appropriate[1]
- Patients with a prior history of VTE may be at risk for VTE in the LYNPARZA monotherapy at therapeutic dose[1]
- If MDS/AML is suspected, the patient should be referred to a haematologist for further investigations, including bone marrow examination and cytogenetic testing. Interrupt and should be permanent discontinued if confirmed, investigation of prolonged haematologic toxicity, LYNPARZA should be discontinued and the patient treated appropriately[1]
- In the PROpel and PROfound studies, most PEs were asymptomatic and incidental on imaging[20]

**Hepatotoxicity**

- If clinical symptoms or signs suggestive of hepatotoxicity develop, prompt clinical evaluation of the patient and treatment of the LYNPARZA should be permanent[1]
- In case of suspected DILI, treatment should be interrupted. In case of severe DILI, treatment discontinuation should be considered as clinically appropriate[1]

Please refer to LYNPARZA's SmPC for further information.

**LYNPARZA has been associated with AEs generally of mild or moderate severity (CTCAE grade 1 or 2) and generally does not require treatment discontinuation.[1]**

**Please refer to the LYNPARZA SmPC for a full list of AEs, including uncommon and rare AEs.**


AE, adverse of interest; AML, acute myeloid leukaemia; ATE, arterial thrombosis event; BID, twice daily; CI, confidence interval; CRPC, castration-resistant prostate cancer; CTCAE, Common Terminology Criteria for Adverse Events; CV, cardiovascular; DILI, drug induced liver injury; DTC, dose-time curve; GI, gastrointestinal; HR, hazard ratio; mCRPC, metastatic castration-resistant prostate cancer; MDS, myelodysplastic syndrome; MPR, multivariate platform randomised; NICE, National Institute for Health and Care Excellence; OS, overall survival; PE, pulmonary embolism; PFS, progression-free survival; SMC, Scottish Medicines Consortium; SmPC, Summary of Product Characteristics; SMQ, Standardised MedDRA Query; VTE, venous thrombosis event; VTE, venous thromboembolism.

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# PROfound study design[1,9,11]

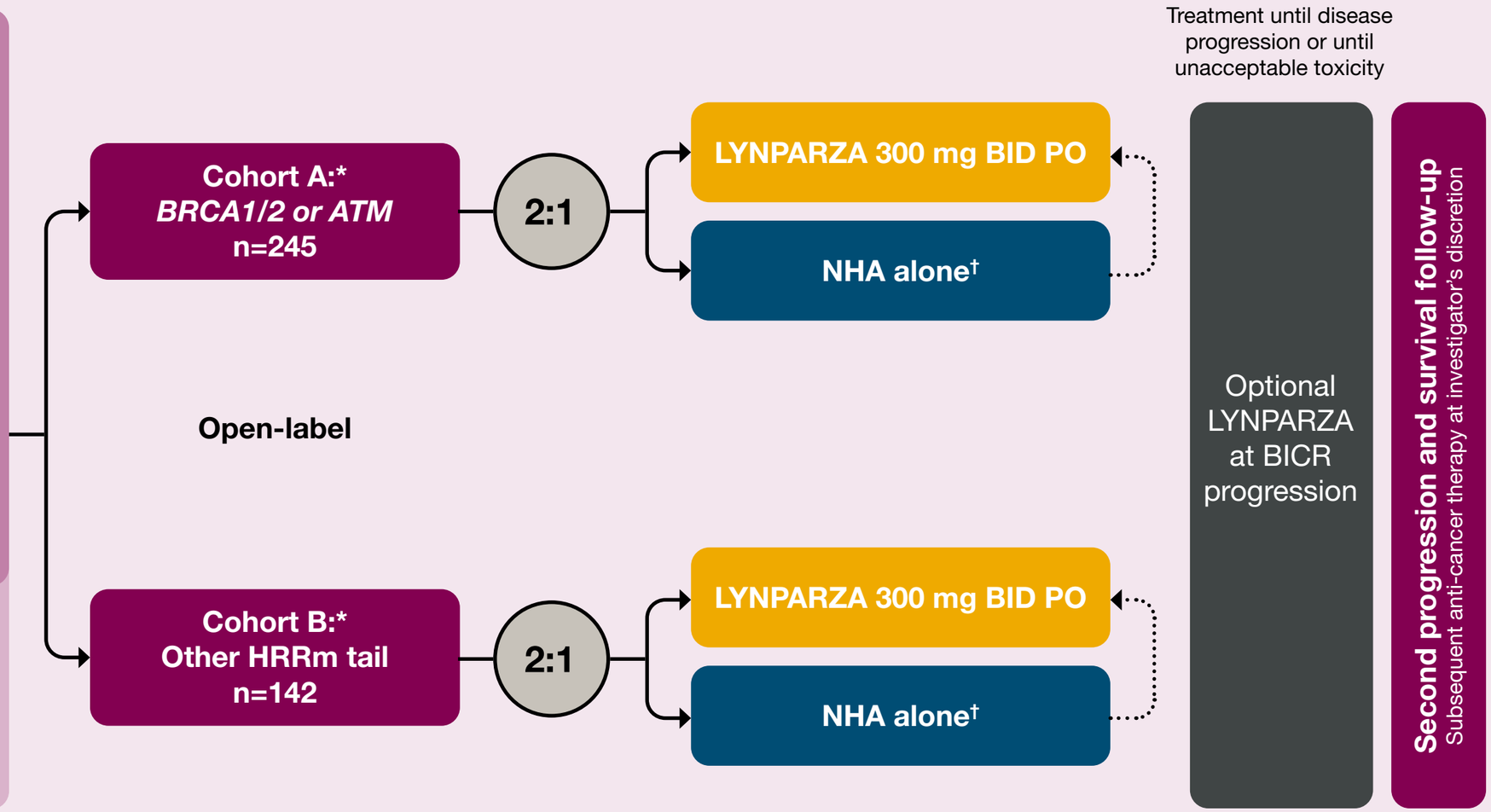
**N=387**

**Patient population**

- Documented mCRPC
- Qualifying HRR mutation
- Investigator-assessed progression on NHA for metastatic prostate cancer and/or CRPC
- Radiographic progression at study entry while on ADT (or after bilateral orchiectomy)
- ECOG PS 0–2
- No prior treatment with a PARPi/any DNA-damaging cytotoxic chemotherapy for prostate cancer

**Stratification factors**

- Previous taxane therapy (yes or no)
- Measurable disease at baseline v1.1 (yes or no)




**Primary endpoint**

- rPFS by BICR in Cohort A, using RECIST v1.1 (soft tissue) and PCWG3 (bone) criteria

**Key secondary endpoint**

- BICR-confirmed ORR (Cohort A)
- rPFS by BICR (Cohorts A + B)
- TTPP (Cohort A)
- OS (Cohort A)
- Safety and tolerability

*Cohort A included patients with *BRCA1, BRCA2 or ATM mutations, Cohort B* included patients with *BARD1, BRIP1, CDK12, CHEK1, CHEK2, FANCL, PALB2, PPP2R2A, RAD51B, RAD51C, RAD51D or RAD54L* mutations.[9]

†Physician's choice of enzalutamide (160 mg QD) or abiraterone (1000 mg QD plus prednisone at 5 mg BID).[9]

BICR, blinded independent central review; BID, twice daily; CRPC, castration-resistant prostate cancer; ECOG, Eastern Cooperative Oncology Group; HRR, homologous recombination repair; mCRPC, metastatic castration-resistant prostate cancer; NHA, new hormonal agent; ORR, objective response rate; OS, overall survival; PCWG3, Prostate Cancer Clinical Trials Working Group 3; RECIST, Response Evaluation Criteria in Solid Tumours; rPFS, radiographic progression-free survival; TTPP, time to pain progression.

# PROpel study design[12,13]

**N=796**

**Patient population**

- First-line mCRPC
- Docetaxel during neoadjuvant/adjuvant treatment for localised prostate cancer and mHSPC was permitted
- Other NHAs permitted if treatment was stopped >12 months prior to randomisation*
- ECOG PS 0–1

**Stratification factors**

- Metastases: bone only vs visceral vs other
- Docetaxel treatment at mHSPC stage: yes or no

**1:1**

**Double-blind**

**LYNPARZA 300 mg BID†**
**+**
**Abiraterone 1000 mg QD†**
**+**
**prednisone/prednisolone 5 mg BID**
n=399

**Placebo**
**+**
**Abiraterone 1000 mg QD†**
**+**
**prednisone/prednisolone 5 mg BID**
n=397

Treatment was initiated with full doses of LYNPARZA and abiraterone, maximising the effectiveness of the combination

**Primary endpoint**

- rPFS by investigator assessment§
- Pre-specified sensitivity analysis of rPFS by BICR

**Key secondary endpoint**

- OS

**Additional endpoints:**

- TFST
- PFS2
- HRQoL (FACT-P)
- ORR
- Time to an SSRE
- CTC conversion
- Time to opiate use
- HRRm prevalence (pre-defined, post-randomisation testing)
- Safety and tolerability

*Except abiraterone; †Both therapies were used at full dose, equivalent to monotherapy regimens;[12] ‡Following objective disease progression, further treatment was at investigator discretion; §rPFS assessed by investigator per RECIST 1.1 (soft tissue) and PCWG-3 (bone) criteria; ¶AEs and serious AEs as defined by CTCAE version 4.03.[12]
BICR, blinded independent central review; BID, twice daily; ECOG, Eastern Cooperative Oncology Group; HRQoL, health-related quality of life; HRR, homologous recombination repair; mCRPC, metastatic castration-resistant prostate cancer; mHSPC, metastatic hormone-sensitive prostate cancer; OS, overall survival; PFS2, time to second progression or death; rPFS, radiographic progression-free survival; TFST, time to first subsequent therapy or death.

## CTCAE[14]

- A descriptive terminology used for AE reporting
- A grading (severity) scale is provided for each AE term

**Mild**
- Asymptomatic or mild symptoms
- Clinical or diagnostic observations only
- Intervention not indicated

**Severe or medically significant, but not immediately life-threatening**
- Hospitalisation or prolongation of hospitalisation indicated
- Disabling and limiting self-care ADL*

Grade 1 — Grade 2 — Grade 3 — Grade 4 — Grade 5

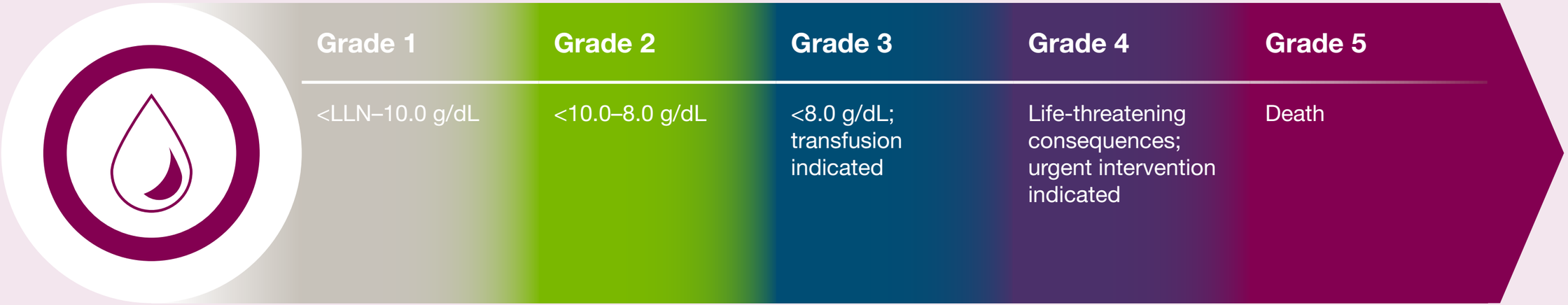
**Moderate**
- Minimal, local or non-invasive intervention indicated
- Limiting age-appropriate instrumental ADL†

**Life-threatening consequences**
- Urgent intervention indicated

**Death**
- Related to AE

*Self-care ADL refers to bathing, dressing and undressing, feeding self, using the toilet, taking medications and not bedridden; †Instrumental ADL refers to preparing meals, shopping for groceries or clothes, using the telephone, managing money, etc.
ADL, activities of daily living; AE, adverse event; CTCAE, Common Terminology Criteria for Adverse Events.

## **Anaemia:** A reduction in the amount of haemoglobin in the blood[14]




## **Signs and symptoms:** Pallor of skin and mucous membranes, shortness of breath, heart palpitations, soft systolic murmurs, lethargy and fatigability[14]

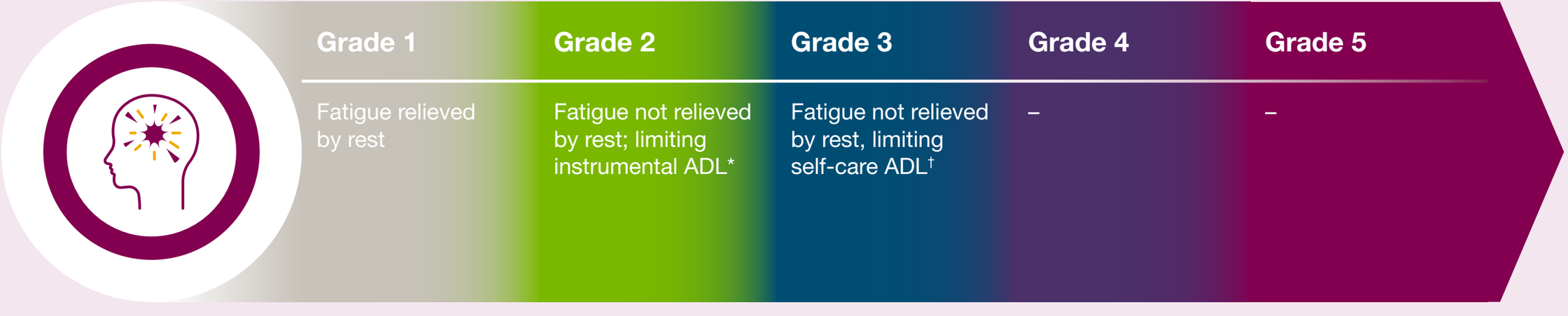
LLN, lower limit of normal.

## **Nausea:** A queasy sensation, with or without the urge to vomit[14]

| Grade 1 | Grade 2 | Grade 3 | Grade 4 | Grade 5 |
|---|---|---|---|---|
| Loss of appetite without alteration in eating habits | Oral intake decreased without significant weight loss, dehydration or malnutrition | Inadequate oral caloric or fluid intake; tube feeding, total parenteral nutrition or hospitalisation indicated | – | – |

*A dash (–) indicates a grade is not available. Not all grades are appropriate for all AEs.*
AE, adverse event.

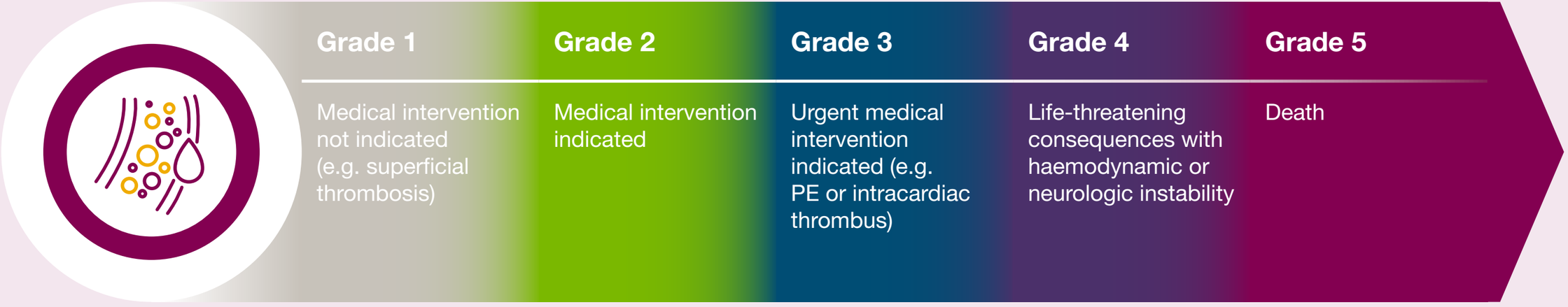
## **Fatigue:** A state of generalised weakness with a pronounced inability to summon sufficient energy to accomplish daily activities[14]



| Grade 1 | Grade 2 | Grade 3 | Grade 4 | Grade 5 |
|---|---|---|---|---|
| Fatigue relieved by rest | Fatigue not relieved by rest; limiting instrumental ADL* | Fatigue not relieved by rest, limiting self-care ADL† | – | – |

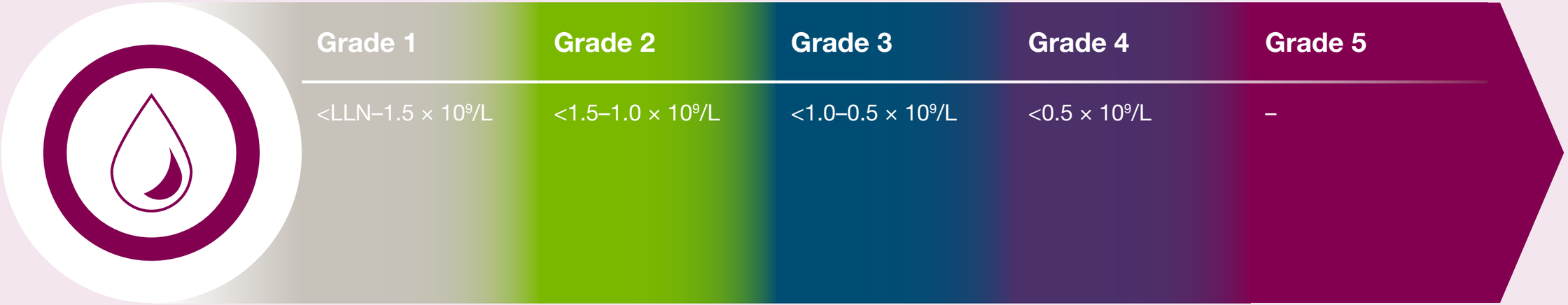
*Instrumental ADL refers to preparing meals, shopping for groceries or clothes, using the telephone, managing money, etc; †Self-care ADL refers to bathing, dressing and undressing, feeding self, using the toilet, taking medications and not bedridden.
*A dash (–) indicates a grade is not available. Not all grades are appropriate for all AEs.*
ADL, activities of daily living; AE, adverse event.

## **VTE:** An occlusion of a vessel by a thrombus that has migrated from a distal site via the blood stream[14]



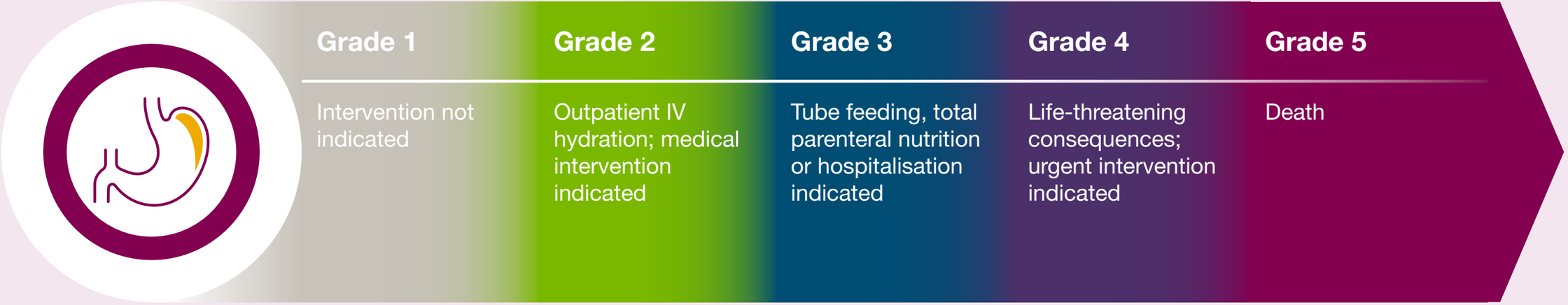

PE, pulmonary embolism; VTE, venous thromboembolism.

## **Neutropenia:** A decrease in the number of neutrophils in the blood[14]




*A dash (–) indicates a grade is not available. Not all grades are appropriate for all AEs.*
AE, adverse event; LLN, lower limit of normal.

## **Vomiting:** The reflexive act of ejecting the contents of the stomach through the mouth[14]



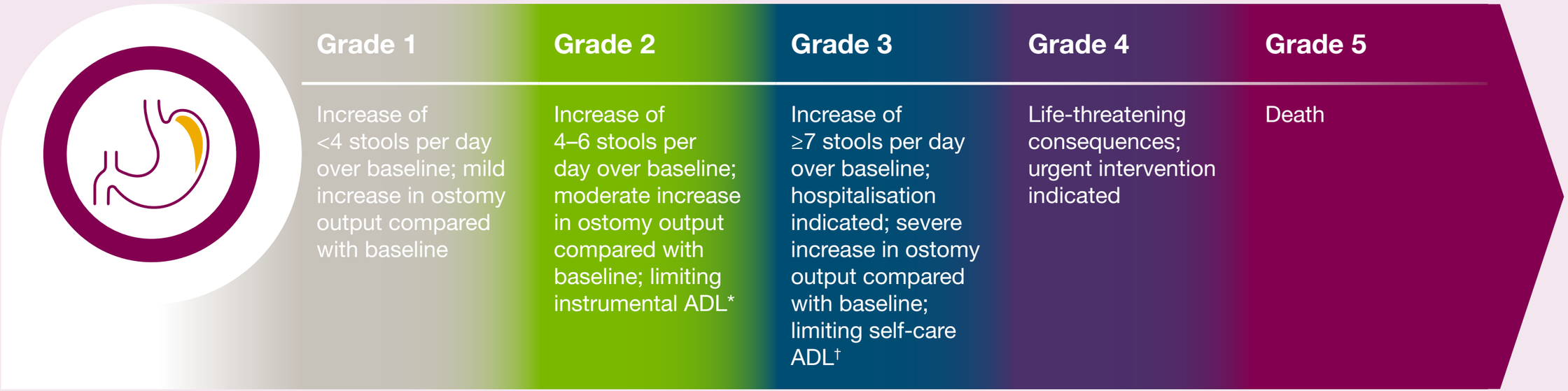

IV, intravenous.

## **Thrombocytopenia:** A decrease in the number of platelets in the blood[14]

| Grade 1 | Grade 2 | Grade 3 | Grade 4 | Grade 5 |
|---|---|---|---|---|
| <LLN–75.0 × $10^9$/L | <75.0–50.0 × $10^9$/L | <50.0–25.0 × $10^9$/L | <25.0 × $10^9$/L | – |

*A dash (–) indicates a grade is not available. Not all grades are appropriate for all AEs.*
AE, adverse event; LLN, lower limit of normal.

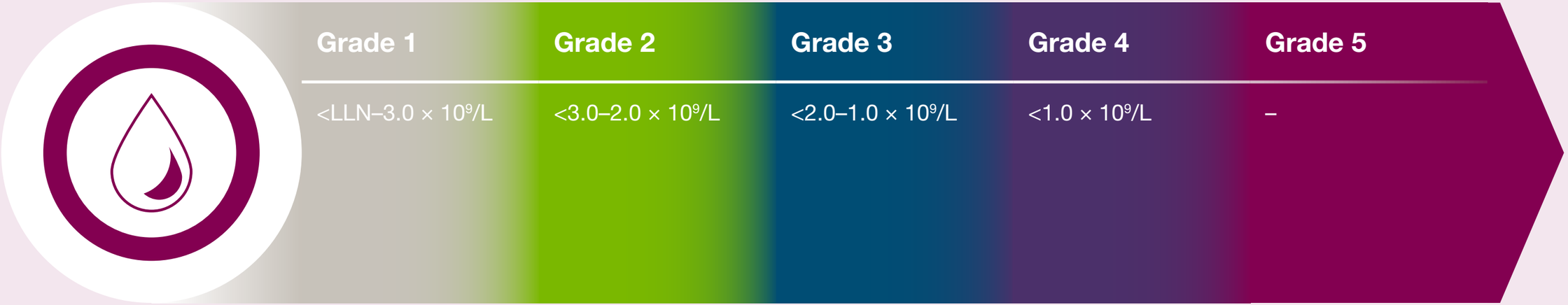
## **Diarrhoea:** An increase in the frequency of or loose or watery bowel movements[14]



| Grade 1 | Grade 2 | Grade 3 | Grade 4 | Grade 5 |
|---|---|---|---|---|
| Increase of <4 stools per day over baseline; mild increase in ostomy output compared with baseline | Increase of 4–6 stools per day over baseline; moderate increase in ostomy output compared with baseline; limiting instrumental ADL* | Increase of ≥7 stools per day over baseline; hospitalisation indicated; severe increase in ostomy output compared with baseline; limiting self-care ADL† | Life-threatening consequences; urgent intervention indicated | Death |

*Instrumental ADL refers to preparing meals, shopping for groceries or clothes, using the telephone, managing money, etc; †Self-care ADL refers to bathing, dressing and undressing, feeding self, using the toilet, taking medications and not bedridden.
ADL, activities of daily living.

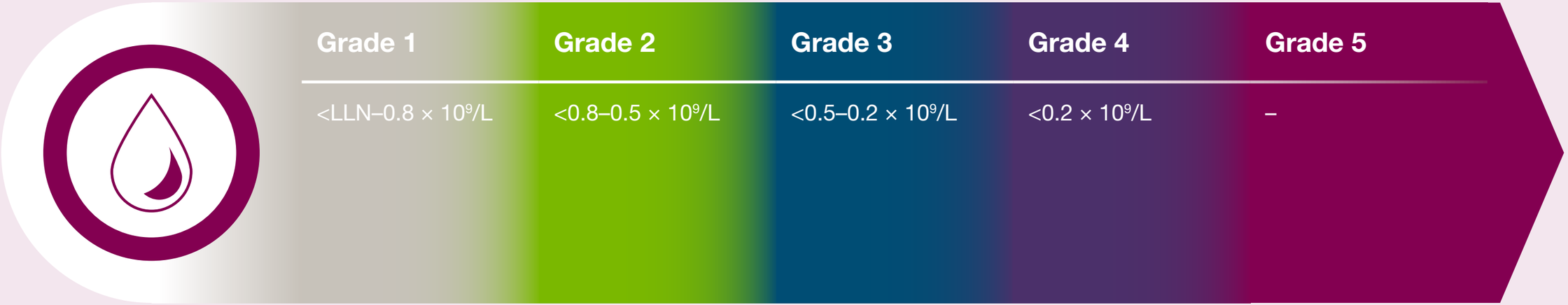
## **Leukopenia:** A decrease in the number of white blood cells in the blood[14]



| Grade 1 | Grade 2 | Grade 3 | Grade 4 | Grade 5 |
|---|---|---|---|---|
| <LLN–3.0 × $10^9$/L | <3.0–2.0 × $10^9$/L | <2.0–1.0 × $10^9$/L | <1.0 × $10^9$/L | – |

*A dash (–) indicates a grade is not available. Not all grades are appropriate for all AEs.*
AE, adverse event; LLN, lower limit of normal.

## **Lymphopenia:** A decrease in the number of lymphocytes in the blood[14]



| Grade 1 | Grade 2 | Grade 3 | Grade 4 | Grade 5 |
|---|---|---|---|---|
| <LLN–0.8 × $10^9$/L | <0.8–0.5 × $10^9$/L | <0.5–0.2 × $10^9$/L | <0.2 × $10^9$/L | – |

*A dash (–) indicates a grade is not available. Not all grades are appropriate for all AEs.*
AE, adverse event; LLN, lower limit of normal.

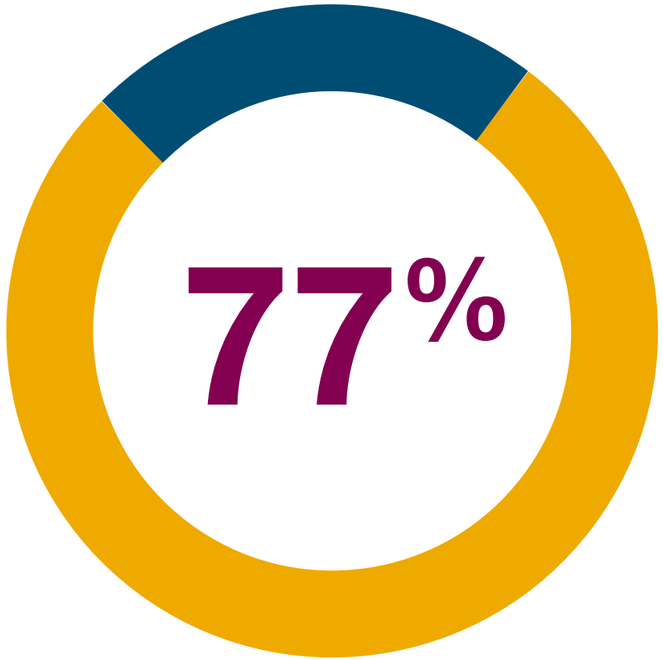
## AEs observed in the LYNPARZA monotherapy arm of the PROfound study[22]

| AE, n (%) | All grades | Grade ≥3 |
|---|---|---|
| **Anaemia** | 127 (50) | 58 (23) |
| **Nausea** | 110 (43) | 4 (2) |
| **Fatigue or asthenia** | 107 (42) | 8 (3) |
| **Decreased appetite** | 80 (31) | 4 (2) |
| **Diarrhoea** | 55 (21) | 2 (<1) |
| **Constipation** | 49 (19) | 0 |
| **Back pain** | 34 (14) | 2 (<1) |
| **Peripheral oedema** | 34 (13) | 0 |
| **Cough** | 29 (11) | 0 |
| **Dyspnoea** | 27 (11) | 6 (2) |
| **Vomiting** | 51 (20) | 6 (2) |
| **Arthralgia** | 26 (10) | 1 (<1) |
| **Urinary tract infection** | 21 (8) | 5 (2) |

n=256.
AE, adverse event.

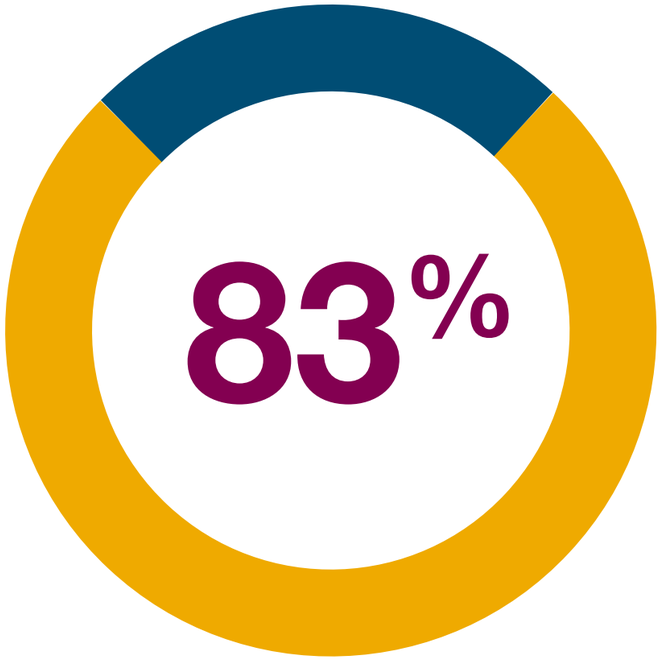
## In the LYNPARZA plus abiraterone combination arm of the PROpel study, 8 out of 10 patients remained on LYNPARZA without discontinuation due to AEs[23]

### No dose reduction




of patients **remained on the full dose of LYNPARZA** without needing a dose reduction due to AEs

### No discontinuation

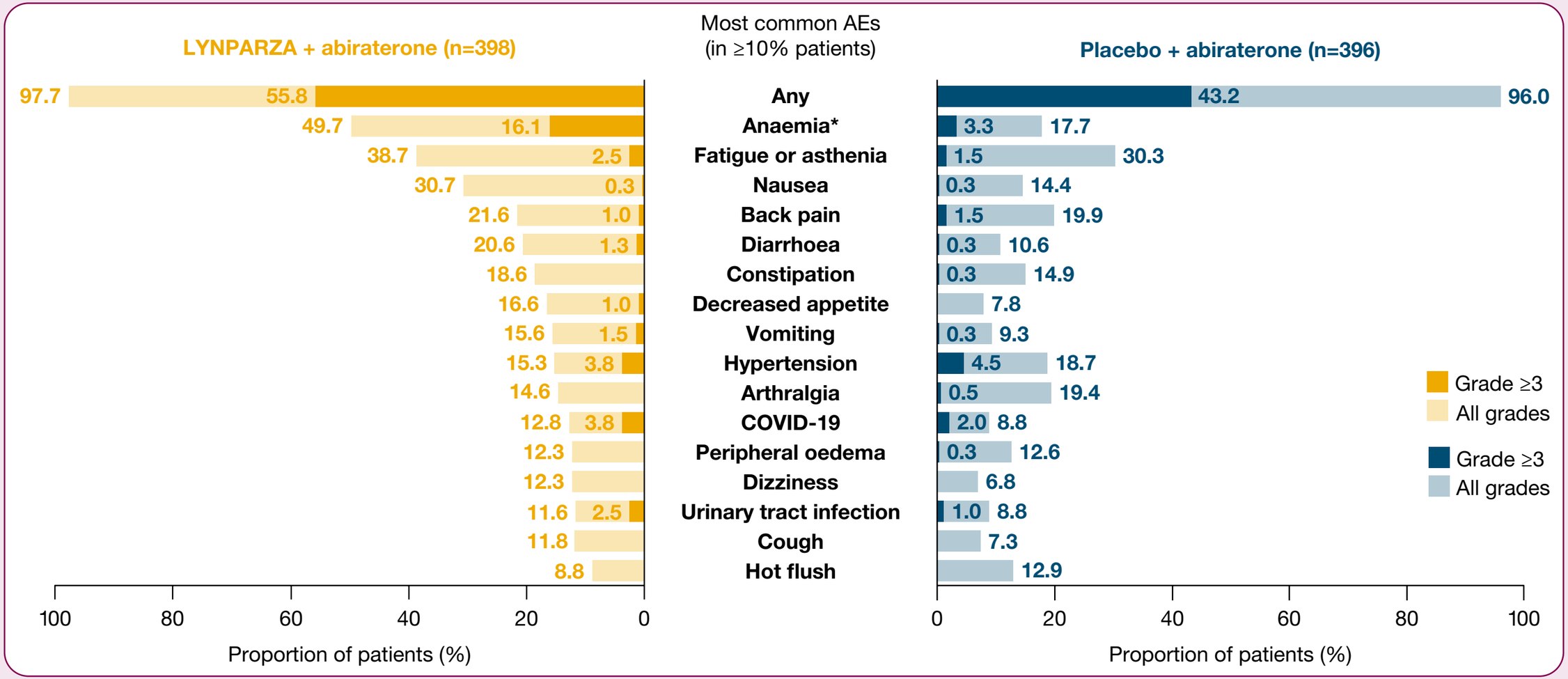



of patients **remained on LYNPARZA** without discontinuation due to AEs

Patients in both treatment arms also received prednisone/prednisolone 5 mg BID.
Results from the data cut-off at final pre-specified analysis: 12 October 2022.
AE, adverse event.

**Patients should be monitored regularly during treatment for any clinically significant changes which may require dose interruption or reduction and/or further treatment. Please refer to the SmPC for full information.**

# AEs observed in the LYNPARZA plus abiraterone combination arm of the PROpel study[15]




Results from the third data cut-off at primary analysis: 12 October 2022.
Safety was assessed through the reporting of AEs according to the NCI CTCAE v4.03 and laboratory assessments.
Patients in both treatment arms also received prednisone/prednisolone 5 mg BID.
*Anaemia category includes anaemia, decreased haemoglobin level, decreased red blood cell count, decreased haematocrit level, erythropenia, macrocytic anaemia, normochromic anaemia, normochromic normocytic anaemia and normocytic anaemia.
AE, adverse event.

## Posology[1,13]

**Recommended dose[1]** →

**Two 150 mg tablets** → **300 mg twice daily**

**If dose reduction is required to manage AEs**

**Dose reduction[1]** →

**One 150 mg tablet and one 100 mg tablet** → **250 mg twice daily**

**Following dose reduction, the patient cannot recommence the starting dose at any point[13]**

**Further dose reduction[1]** →

**Two 100 mg tablets** → **200 mg twice daily**

**There are only two dose reductions indicated for LYNPARZA**

**Tablets not to scale.**
**For concomitant administration with CYP3A inhibitors, or for patients with hepatic or renal impairment, please consult the LYNPARZA 100 mg and 150 mg tablet SmPC for specific dose reductions.**
AE, adverse event; CYP3A, cytochrome P450, family 3, subfamily A; SmPC, Summary of Product Characteristics.