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Talazoparib plus enzalutamide in first-line metastatic castration-resistant prostate cancer:

TALAPRO-2 Phase III study design

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Objective and rationale

Primary objective

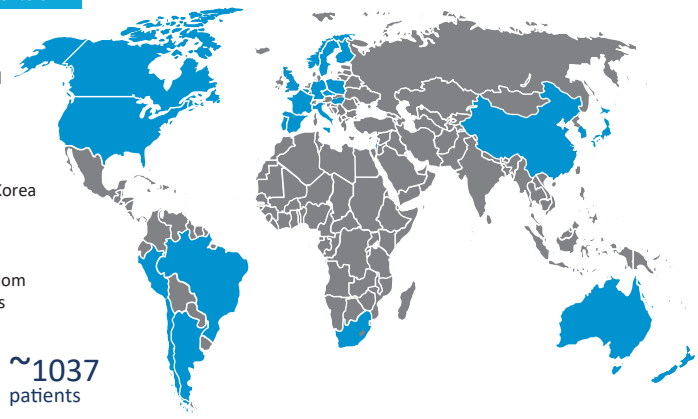
Demonstrate that talazoparib plus enzalutamide is superior to placebo plus enzalutamide in prolonging BICR-assessed rPFS in patients with mCRPC unselected for DDR status and in patients with mCRPC harboring DDR alterations

Rationale

Previous studies suggest that a PARP inhibitor in combination with an AR inhibitor may be efficacious in the treatment of mCRPC regardless of DDR alteration status [1-5]

Countries with investigative centers

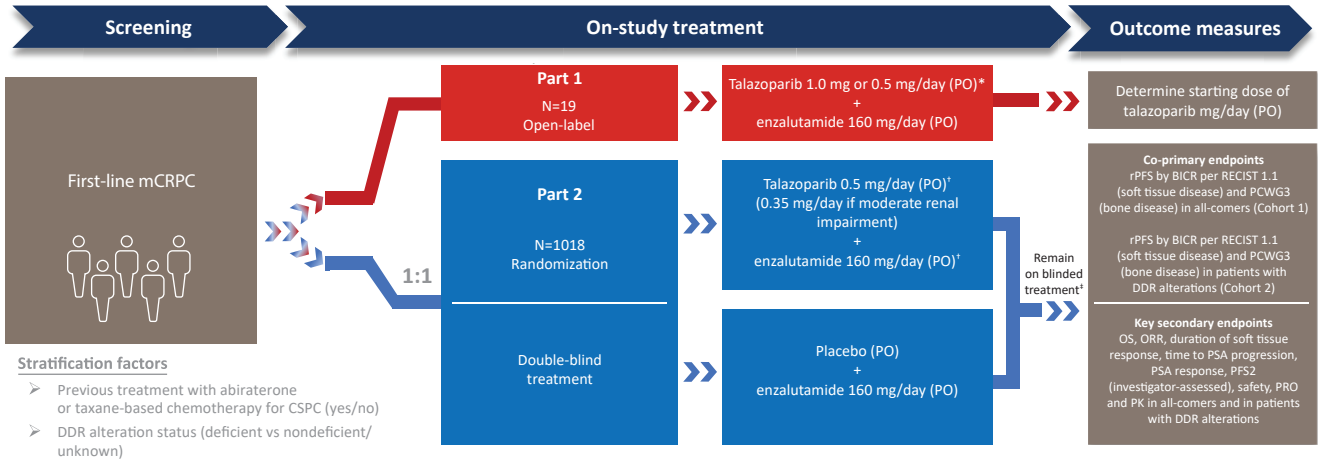
Argentina	Italy
Australia	Japan
Belgium	New Zealand
Brazil	Norway
Canada	Peru
Chile	Poland
China	Portugal
Czech Republic	Republic of Korea
Finland	South Africa
France	Spain
Germany	Sweden
Hungary	United Kingdom
Israel	United States



26 countries

~1037 patients

Study design



Key eligibility criteria

- Men aged ≥18 years§
- Histologically or cytologically confirmed adenocarcinoma of the prostate
- Asymptomatic or mildly symptomatic first-line mCRPC
- Prospective assessment of DDR alteration status by a gene alteration biomarker panel using blood or tumor tissue
- Bilateral orchiectomy or ongoing ADT with a GnRH agonist/antagonist, with serum testosterone ≤50 ng/dL (≤1.73 nmol/L) at screening‖
- ECOG performance status 0 or 1
- Progressive disease at study entry defined as at least one of the following:
  - PSA progression
  - Bone progression
  - Soft tissue progression

Glossary: *Patients initially received a talazoparib starting dose of 1.0 mg/day prior to dose reduction to 0.5 mg/day based on safety and PK data. †Dose of talazoparib 0.5 mg/day plus enzalutamide 160 mg/day was determined in Part 1 as providing the same talazoparib exposure as talazoparib 1.0 mg/day monotherapy. ‡Remain on blinded treatment until radiographic progression and no longer clinically benefiting as per investigator opinion, the occurrence of an AE leading to permanent discontinuation, patient decision to discontinue treatment, or death. §≥20 years in Japan. ‖ADT must continue throughout the study for patients who have not undergone bilateral orchiectomy. ADT: Androgen deprivation; AE: Adverse event; therapy; AR: Androgen receptor; BICR: Blinded independent central review; CSPC: Castration-sensitive prostate cancer; DDR: DNA damage response; ECOG: Eastern Cooperative Oncology Group; GnRH: Gonadotropin-releasing hormone; mCRPC: Metastatic castration-resistant prostate cancer; ORR: Objective response rate; OS: Overall survival; PARP: Poly(ADP-ribose) polymerase; PCWG3: Prostate Cancer Working Group 3; PFS2: Time from randomization to the date of documented progression on the first subsequent antineoplastic therapy, or death from any cause, whichever occurs first (investigator-assessed); PK: Pharmacokinetics; PO: By mouth; PRO: Patient-reported outcomes; PSA: Prostate-specific antigen; RECIST: Response Evaluation Criteria in Solid Tumors; rPFS: Radiographic progression-free survival.

References

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