Poster Number - CT055

PAVO: A Phase-II, Open Label, Single Arm Study of Niraparib in Patients with Locally Advanced/Metastatic *PALB2* Mutated Tumors

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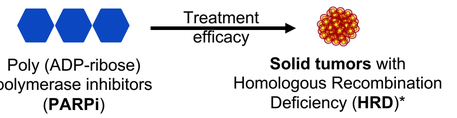
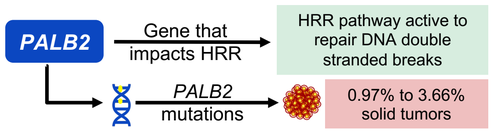
BACKGROUND



* inability to repair DNA double-stranded breaks via the Homologous Recombination Repair (HRR) pathway

While *BRCA1/2* mutations are main drivers of HRR deficiency, mutations in other genes such as *PALB2* are also associated with susceptibility to various cancers.



Hypothesis: Patients with germline or somatic *PALB2* mutations may benefit from PARPi treatment, as a potential tumor agnostic therapy option.

STUDY RATIONALE

The purpose of this study is to evaluate the efficacy and safety of niraparib in patients with locally advanced/metastatic solid tumors harboring a pathogenic or likely pathogenic *PALB2* (t*PALB2*) mutation

POPULATION

Key Inclusion Criteria

- ✓ Locally advanced or metastatic solid tumor(s)
- ✓ Confirmed pathogenic or likely pathogenic somatic or germline *PALB2* mutation
- ✓ Received all standard of care (SOC) therapy for tumor type, or are unlikely to derive benefit from SOC therapy
- ✓ ECOG performance status - 0 or 1

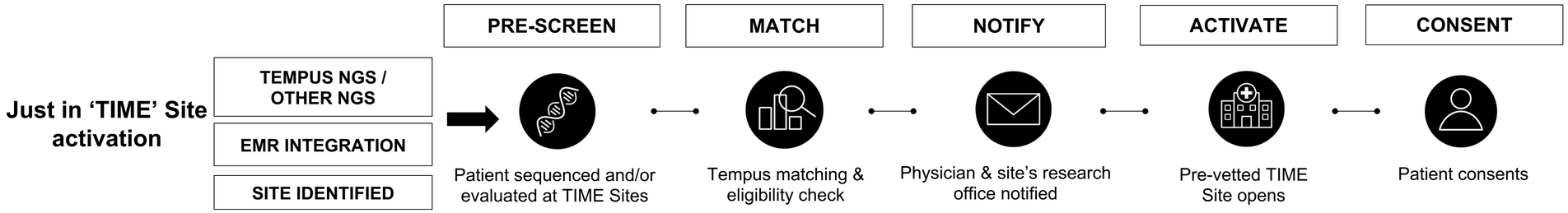
Key Exclusion Criteria

- ✓ Confirmed *BRCA1/2* mutation
- ✓ Prior treatment with any PARPi
- ✓ Ovarian or prostate cancer
- ✓ Rapid progression while on platinum-based therapy in the metastatic setting

STUDY DESIGN AND PRESCREENING ALGORITHM

Tempus molecular data tracking and the TIME Trial program enable precision-medicine guided identification and prescreening of patients with rare t*PALB2* alterations

Enrollment occurs through a combination of TIME and other clinical sites, where individualized prescreening models are in development



Non-TIME Site Patient Pre-screening

EMR Review
EMR data pre-screen at participating sites for potential patient matches to PAVO

NGS Testing
Patients pre-screened for molecular eligibility

+

Local Site Review
Site identifies potential match and initiates screening process

→

Patient Enrollment
Identified patients enroll at clinical site

Trial Summary: Methods, Endpoints, and Statistics

Multi-center, open label study

Enrolling solid tumors with tPALB2 mutations

Up to 110 subjects

Niraparib, daily dosing

CT / MRI evaluation every 8 weeks

Study treatment until:
- Documented radiographic progression,
- Unacceptable toxicity,
- Death, or
- Consent withdrawal

Study endpoints

Primary endpoint - Overall response rate (ORR) using RECIST 1.1

Key Secondary Endpoints:
- Duration of response (DOR)
- Progression-free survival (PFS)
- Clinical Benefit Rate (CBR)
- Safety and tolerability (adverse events) per NCI-CTCAE v5.0

Statistical / Interim analyses: Primary efficacy endpoint (ORR) will be assessed using the Bayesian Optimal Phase 2 (BOP2) design, with interim analysis planned when 40 participants have completed their assessment of efficacy (ORR as assessed by Independent Radiology Central Review).

Protocol Number - TMPS-101
Compound Name - Niraparib (GSK3985771)
Clinical Trial Registry - **NCT05169437**

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CURRENT STATUS

- Trial open since March 2022
- Currently 13 open sites
- Enrollment, new site identification, referral to opened sites, and molecular prescreening activities are all ongoing.

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