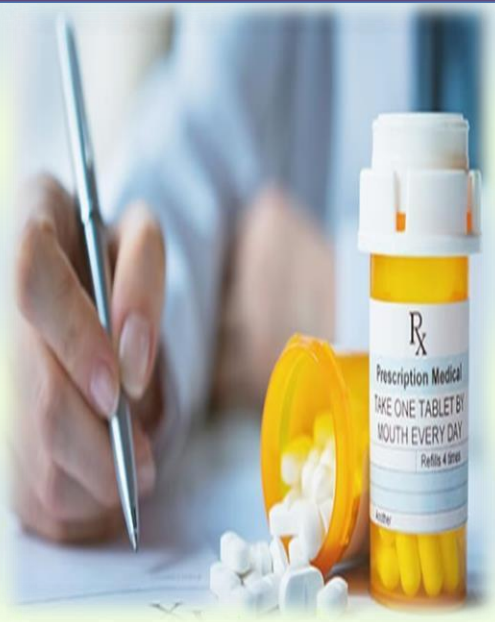
RESEARCHER LEAFLET



IPIROC

INTERMITTENT PARP INHIBITOR REGIMEN IN OVARIAN CANCER

What is IPIROC

PARP inhibitors (PARPi) have revolutionized the treatment of ovarian and other cancers with mutations in the BRCA genes and homologous-recombination deficiency (HRD). However, majority of women globally cannot afford the cost of the recommended daily dosing of PARPi, leading to financial burden and health disparity. Hematological or blood cell related toxicities associated with daily dosing of PARPi, especially in women with lower body weight or pre-existing anemia, pose a significant challenge. Laboratory studies have shown that a single dose of the PARPi rucaparib can inhibit PARP beyond 72 hours, providing a proof- of-concept for optimal scheduling with a less frequent dosing regimen. Our pilot trial (CRUK-DBT funded) confirms that intermittent bi-weekly (2 days a week) scheduling can significantly reduce the side effects and the cost of treatment (1/4th). Some women have attained long-term disease-free period with this well-tolerated regimen; however, larger clinical trials are needed to generate further evidence on optimized dosing schedules rather than using empirical dose-reduction practices without any pre- clinical scientific data. This is the goal for our IPIROC Umbrella studies (KolGO-PROVAR 002).

Funding support:

- Phase 2 study and PARPi registry: ICMR (Indian Council of Medical Research)
- Physician survey- Global Health Equity Grant,University of Michigan, USA
- Intermittent single arm study-CRUK DBT seed corngrant
- Willingness to pay and patient survey: ICMR andNewcastle University (CRUK-DBT)
- Drug support: BDR Pharmaceuticals Int'l Pvt Ltd.

About us

Study sponsor: Kolkata Gynecological Oncology Trials and Translational Research Group (KolGOTrg)

KolGOTrg is a research group (ISO certified SIRO) dedicated to conducting high-quality research in women's cancer in India through a collaborative platform between scientists and clinicians across the region and focusing on research areas which are relevant to the need of women residing in resource poor settings.

It isthe first research group from India to become a member group of GCIG (Gynecologic Cancer InterGroup) and a partner organization of the IGCS (International Gynecologic Cancer Society)

Contact Us

If you want to know more about the study or want to take part in some or all the studies under the IPIROC umbrella series, please contact us directly:

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'IPIROC series'

We are initiating a number of studies under the IPIROC Umbrella ranging from patient and clinician surveys to randomized and non-randomized studies on optimal dosing and scheduling of PARP inhibitors (PARPi) in cancer, ensuring a flexible and patient-centric approach

Aims of the study

i. To provide proof-of-concept evidence that intermittent dosing of specific PARP inhibitors (rucaparib) is non-inferior to daily dosing for toxicity (including financial)and quality-of-life-adjusted survival endpoints.

ii. Capacity building for biomarker-driven novel study designs/conduct of trials in a cost-efficient manner.

Rucaparib, also known as Rubraca®, was developed by the Newcastle University research team, UK (including Study PI, Dr Asima Mukhopadhyay) and is one of the first PARPi to enter anticancer clinical trials; currently, its generic form is widely prescribed in India.

Our pre-clinical studies (DST-UKIERI grant) (Cancers, DOI: 10.3390/cancers14225559) show that compared to other PARP inhibitors, only rucaparib has the unique property of inhibiting PARP for more than 72 hours after a single dose, making it suitable for intermittent scheduling

How can you participate?

*There are one or multiple ways you can participate under the IPIROC Umbrella series of studies: click to **REGISTER HERE***

1. Physician survey on the current practice of prescribing standard of care (SOC) PARPi.

2. Patient survey on their viewpoints for use of PARPi and the actual uptake including willingness to pay for the same.

3. Phase 2 randomized controlled trial (RCT) in platinum-sensitive relapse setting (BRCA/HRD) for PARPi maintenance with daily versus intermittent (2 days a week) arms of PARPi scheduling (drug-funded).

4. Single arm intermittent dosing PARPi maintenance study in relapse setting, where rucaparib is given 2 days a week when patient is not willing/suitable for the RCT (drug-funded).

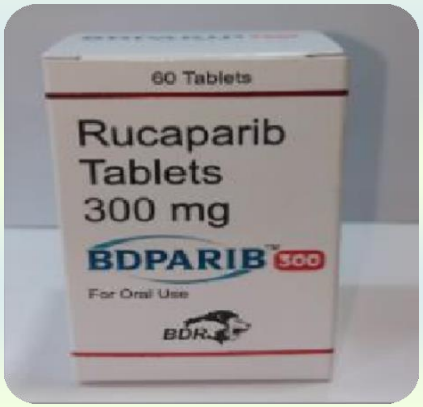
5. Observational study on SOC daily dosing of PARPi maintenance in relapse setting where patient prefers this option for maintenance (self-funded).

6. Observational study on Physician's choice of maintenance or no maintenance and clinical follow-up in relapse setting.

7. Implementation research project on de-escalation trials (EASE model).

8. Contributing to an ICMR-KolGOTrg PARPi registry.

9. Frontline maintenance: Phase 2/3 RCT on daily versus intermittent PARPi regimen and other platforms (in preparation).



Study drug: Made in India generic

How will it benefit you?

- Opportunity to be a part of a ground-breaking ICMR funded project which aims to reduce toxicity and cost of PARPi and investigate PK/PD/PG guided dosing approaches.
- Developing future clinical trial pipelines for made-in-India PARPi initiatives (HCP-40 Program, CSIR).
- Co-developing novel study design/methodologies (adaptive designs) for conducting trials and studies in resource-adapted-settings using KolGOTrg R2CT approach (Rationalizing and Reducing the Cost of running randomized control Trials) and GCIG trials.
- Application of this concept to other targeted agents like immunotherapy or other HRD cancers (basket trials).
- Co-authorship in the multicenter collaborative study and policy making publications.
- Participation as a co-investigator in KolGOTrg biomarker discovery, biobank and translational studies

How can you participate?

There are one or multiple ways you can participate under the IPIROC Umbrella series of studies: click to ***REGISTER HERE***

Website: www.kolgotrg.org/ipiroc/

Study participation options (non–interventional)

- Systematic review on EDI in PARPi trials
- Survey: Physician and patient on current practice of SOC
- Survey: Willingness to pay for cost–benefit analysis
- Registry: PARPi use in cancer

Pragmatic Trial participation platforms for maintenance PARPi (interventional)

- Arm 1: Accepts to continue SOC (daily dosing) but does not consent for randomisation Observational cohort 1
- Arm 2: Accepts to continue SOC and consents to be randomised in trial Daily arm
- Arm 3: Accepts to continue SOC and consents to be randomised in trial Intermittent arm
- Arm 4: Patient does not accept/ cannot tolerate SOC daily, but is willing to accept a trial for new SOC
  – Single arm non–randomised Intermittent arm
- Arm 5: Does not accept/tolerate SOC daily and is not willing to participate in any PARPi trial
  – Single arm physician's choice/ no maintenanc–e Observational cohort 2

IPIROC Master protocol July 2024