Window of Opportunity

2022 Portfolio Trials

Call for Concepts

PURPOSE

This document is intended to guide Investigators applying to the OICR Window of Opportunity (WOO) Network for funding support for **pre-surgical immune-modulatory WOO trials** in **treatment-naïve or early disease patients.**

WINDOW OF OPPORTUNITY NETWORK

The Ontario Institute for Cancer Research (OICR) was established in 2005 to mobilize and reinforce provincial excellence in the fight against cancer, realize the local economic value of cancer discoveries, and make Ontario a major global address for cancer research and innovation. As Ontario's facilitator of translational cancer research, OICR brings together researchers, clinicians, patients and caregivers, health system partners, industry, and funders to drive solutions to cancer needs and accelerate the advancement of discoveries to improve cancer prevention, detection, diagnosis, and treatment.

OICR's Strategic Plan 2021-2026 focuses on developing the knowledge and tools to implement cancer precision medicine, where patients are diagnosed as early as possible, treated precisely, and monitored proactively. In order to drive an innovative clinical-translational research platform where novel therapies can be tested in newly diagnosed treatment-naive patients in order to support a deep molecular understanding of how these therapies can fight cancer, the OICR established a WOO Network.

The OICR WOO Network is co-led by Drs. Angel Arnaout (The Ottawa Hospital) and Melanie Spears (OICR), with governance from a provincial Steering Committee and oversight by a Scientific Advisory Committee. It is a collaboration between clinicians, scientists, and patient partners to drive a clinical-translational research program where novel therapies are quickly tested in cancer patients prior to surgery during WOO trials. It provides prioritized WOO studies with support for trial development and translational analysis. Importantly, the Network builds provincial capacity in WOO trials through mentoring of new investigators. Pharma engagement will be a cornerstone of the Network, partnering with industry to support access to novel agents.

MISSION: Support a portfolio of integrated pre-surgical WOO clinical trials to accelerate development of personalized, biomarker driven, immune inductive therapies for patients with early cancer.

VISION: To improve the biological understanding of immunomodulation through the rigorous study of novel immune inductive therapies.

The initial scientific focus of the Network is immunomodulation - understanding the biology of how therapeutics can elicit an immune response and alter the immune environment in tumours which is critical to make immunotherapy more effective, less toxic, and more durable. It will examine novel immunomodulatory agents across a portfolio of trials, integrating comprehensive molecular screening and multi-omic biomarker analysis. Single agents or drug combinations targeting pathways that trigger antigen release and presentation, T-cell priming and activation, TIL recruitment and function are the focus of the current Network approach to optimizing novel immuno- oncology therapies. Importantly, the Network will provide a unique opportunity to generate data across multiple tumour types and targeted interventions and build a framework for powerful approaches for novel neoadjuvant therapies for primary-diagnosed invasive cancers by offering a platform to quickly and efficiently test new drugs and/or combinations, and their effects in the primary pre-surgical setting.

Benefits of the Network to the provincial cancer research community include:

- Collaboration with experts in translational science and leading-edge technologies.

- Guidance to promote efficient implementation, data collection, and translational analysis.
- Consultation with patient partners and experienced WOO trialists throughout the study process.
- Support in profiling the tumour and the immune environment using multi-omic technologies.
- Pan-cancer and pan-therapy comparisons amongst a portfolio of Network trials.
- Funding support for prioritized WOO trials that meet funding criteria.

WINDOW OF OPPORTUNITY TRIALS

WOO trials exploit the 'window' of time after cancer diagnosis, typically prior to initiation of cancer therapy (usually surgery with curative intent). In pre-surgical WOO trials, patients with treatment naïve or early-stage disease are treated for a brief "window" period with a novel therapy followed by surgical resection. Unlike neoadjuvant trials, the "window" period is kept short (few weeks) to ensure that surgery is not delayed.

The WOO study design has increasingly become part of drug development. Pre-surgical WOO trials with agents with proven safety profiles:

- take advantage of treatment-naïve tumors
- rapidly characterize mechanism of action (MOA) for novel therapeutic approaches
- de-risk Phase 2-3 trials
- inform go/no-go decisions for new therapeutic approaches and their combinations
- further precision medicine by identifying biomarkers that predict which patients benefit from novel therapy

Key criteria for WOO Network trials:

- pre-surgical design
- small, multi-centre, with less than 100 patients
- focus on immunomodulation with identification of novel biomarkers of immune response
- demonstrated drug safety profile
- highly engaged Principal Investigators and Co-Investigators, including surgeons and oncologists
- embedded patient engagement
- feasibility for patient accrual completed within two years, with ethics approval, study start-up and first patient accrued within the first two quarters after funding approval

It is important to note that study data from funded WOO trials will be made available for sharing in a WOO Network database.

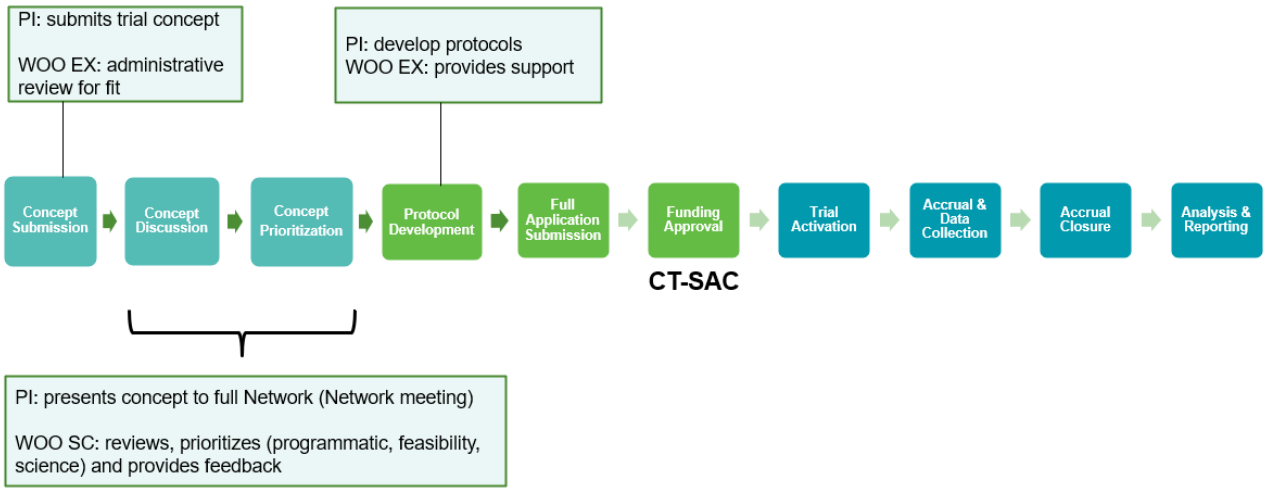
Out of scope WOO trials:

- Perioperative window designs.
- Neoadjuvant window designs.

WOO TRIAL DEVELOPMENT

Network trial development is facilitated and iterative (see Figure 1). Submissions begin as concepts which undergo review by the Executive of the WOO Steering Committee (WOO EX) for fit against key WOO criteria. Eligible concepts are approved for presentation at the next WOO Network Meeting. During the meeting, concepts are discussed with provincial Network members and prioritized by the WOO Steering Committee (WOO SC) for further development and submission to the Scientific Advisory Committee of OICR's Clinical Translation (CT-SAC) for final review and funding decision.

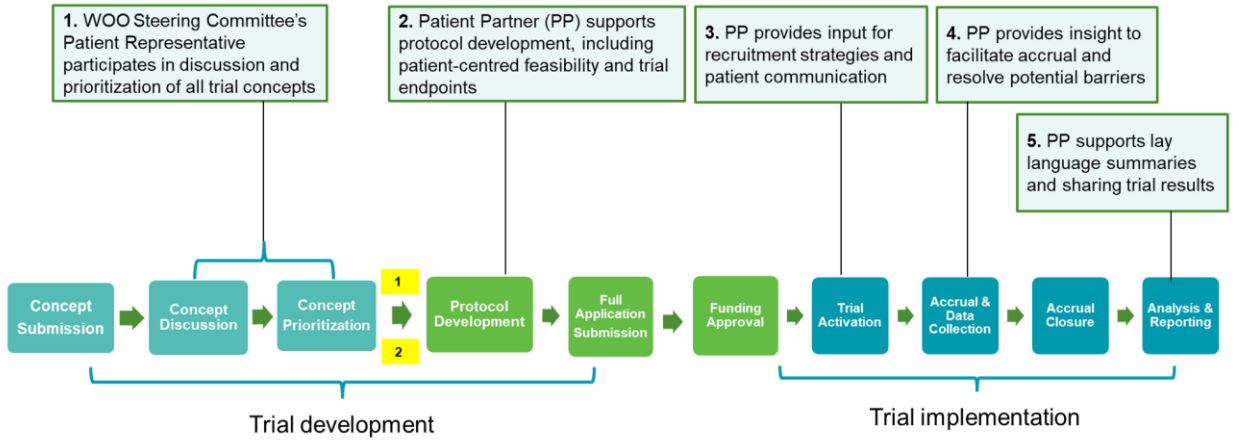
Figure 1. Trial development: facilitated and iterative



PATIENT PARTNERSHIP

Integrating patient perspectives and insight can be transformative to research planning and successful execution. The WOO Network, together with OICR's Patient and Family Advisory Council (PFAC), ensures that each WOO trial integrates patient partnership throughout the development and implementation phase of a WOO trial (see Figure 2).

Figure 2. Patient Partnership: engagement throughout the WOO trial lifecycle



1: Patient Partner Engagement Form is completed by the PI and submitted to PFAC for identification of an appropriate Patient partner.
2: Trial PI meets with the PP for trial orientation and to support protocol development. When possible, the same partner will continue to be involved throughout the full trial. If the PP needs to change, then a new PP is identified, orientation provided, and patient engagement continues.

For the WOO Network, patient partnership begins with a Patient Representative member as part of the WOO SC, reviewing and prioritizing submitted trial concepts. Additional roles for patient partners in WOO studies, include, but are not limited to, supporting i) protocol design (e.g. inclusion of patient-centred endpoints, identifying potential challenges of protocol design to

participating patients, input into accrual strategy and patient-facing materials such as consent forms), ii) clinical trial execution (e.g. identifying solutions to potential patient barriers, developing plans to reach patient communities), and iii) results reporting (e.g. developing lay-language communication material and disseminating results to patient networks).

Resources for best practices in involving patients and the public in research are provided by the Canadian Cancer Clinical Trials Network (https://3ctn.ca/for-researchers/patient-public-involvement/) or the Clinical Trials Transformation Initiative (https://www.ctti-clinicaltrials.org/). Importantly, assistance on developing patient partnership within the proposed WOO trial and connecting with patient partners is available through Justin Noble, Patient Partnership and New Initiatives Lead, OICR justin.noble@oicr.on.ca.

TRIAL CONCEPT

Concept submission

Concepts are to be submitted to WOONetwork@oicr.on.ca using the **WOO_2022 Portfolio_Concept Form**, which captures details including:

- Study background, rationale, and specific immunomodulation hypothesis.
- Study synopsis, schema, and timelines.
- Trial feasibility details.
- Pharma engagement details and drug safety profile.
- Capacity building details, especially patient partnership plan. It is important to note that OICR's Patient and Family Advisory Committee can assist with this.

Forms (and associated documents) are to be submitted by the deadline listed in Table 1 below.

Table 1. Timelines

Activity	2022 Dates
Concept	
Deadline	February 7, 12 p.m. EST
Review by WOO Executive	February 9 - February 22
Feedback communicated	February 24
Updated concept submitted	March 1
Review by WOO Steering Committee	March 2 - March 22
Presentation of proposed concept by Lead PIs at Network Meeting; Prioritization by WOO Steering Committee. **Lead PI's must attend the Network Meeting.**	March 29, 10 a.m. – 12 p.m. (WOO Network Meeting)
Results communicated	April 4
Protocol development period	April 5 - May 15
Full Application	
Deadline	May 16, 12 p.m.
Review by WOO Executive	May 17 - 30
WOO Executive feedback and support period	May 31 – June 12
Deadline: updated submission	June 13
Review by CT-SAC	Early July
Notification of results	End of July
Funding start	September 1, 2022

Concept review and prioritization

Upon submission, an administrative review will be conducted to assess the concept for conformity with this document. The network Executive will review concepts for fit/suitability and readiness to present at the upcoming WOO Network Meeting. Feedback will be shared with the PI to allow for submission of an improved concept.

During the Network Meeting, lead investigators will present their concept to the full Network. This will be followed by a discussion period with the aim of identifying potential improvements or the involvement of additional provincial cancer centres.

At the end of the Network meeting, during a closed session, the WOO SC will prioritize concepts based on the criteria below.

Prioritization Criteria

Programmatic:

- appropriate study design
- aligned with WOO Network's focus on immunomodulation
- primary goal is to investigate agent MOA and associated tumour and immune response biomarkers

Capacity building:

- multi-site study
- surgeon led or co-led (with oncologist)
- patient partnership

Feasibility:

- study is brief in nature, with the appropriate staff and resources to support a study that can **complete patient accrual within two years**
- available patient population to support accrual
- minimal impact from competing trials
- industry-partner commitment for study agent
- established drug safety profile

Following the meeting, results will be communicated to applicants. Concepts prioritized for protocol development and full application submission will be provided with a summary of details discussed during the closed SC session. Should it be necessary, lead investigators may be asked to address key comments prior to developing a protocol as part of a full application. During the period of protocol development, members of the WOO Executive will be available for support, especially for developing the translational research component of the study.

FULL APPLICATION

Full applications are to be submitted by the deadline in Table 1 above using:

- **WOO_2022 Portfolio_FA_Form I_Summary**
- **WOO_2022 Portfolio Trials_FA_Form II_D/M**
- **WOO_2022 Portfolio Trials_FA_Form III_Budget**

1. **Summary:** Using **Form I**, provide a summary of the WOO trial, including the information below. Submit in Word format.

- *Background and rationale*: Describe the study background, rationale, and specific hypothesis. Provide a brief summary of current knowledge relative to the proposed study. Include information of the agent and its safety profile. Outline how the study fits into the goals and focus of the WOO Network. Explain the study's "path to clinical impact" (e.g., by informing future, larger neoadjuvant trials; by informing drug discovery directions).
- *Translational biomarker investigations*: Outline the planned biomarker analyses and their significance to the study. Outline linkage to the WOO Network's core biomarker analyses platform (at OICR) to allow future cross trial comparisons.
- *Study synopsis*: Provide a brief study synopsis which includes study design, objectives, endpoints (primary, secondary), patient population, main inclusion criteria, and sample size. **Note that a penultimate protocol, that has been reviewed and approved by all partner site co-investigators, patient partners and pharma partners (if applicable), MUST be attached as outlined below. Please include trial schema in appendix.**
- *Statistical analysis plan*: Outline the principal features of the statistical analysis of the study (clinical and correlative) data. Include justification for the choice of primary outcomes(s) and sample size.
- *Team details*: Identify leadership at lead site and participating sites; identify patient partner. Include information on experience of the lead Investigator and clinical teams, and patient partner as they relate to the study. In line with the OICR, the WOO Network is focused on developing and supporting the next generation of cancer researchers, and strongly encourages applicants to include early career investigators/clinicians as part of the team.
- *Study initiation and management*: Outline the role of involved teams (lead site, participating sites) with regards to study initiation and management. Describe existing available resources and how they will be used to ensure timely success of the study. Describe plan for engaging partner sites. Letters of support from committed co-investigators at participating sites must be included with the application. ***Letters must attest to the review and approval of the study protocol.*** Identify potential risks to trial success and describe possible mitigation plans.
- *Recruitment plan*: outline the planned monthly patient recruitment rate and demonstrate that the eligible population of patients is available at the participating institutions. Where applicable, describe any competing studies and how they will be managed to ensure success of the current study. Include go/no go decision points for opening additional study sites to ensure patient accrual and timelines are met.
- *Accrual strategy*: outline an accrual strategy for patient engagement and retention that will support the recruitment plan. Outline any potential barriers to enrollment and how they would be addressed.
- *Patient partnership plan:* outline a patient partnership plan that will engage patients at the various stages of trial development and implementation, as described above.
- *Equity, Diversity, and Inclusion (EDI) considerations***:** WOO trials are expected to embrace the principles of EDI in order to:
  - Ensure research serves cancer patients from all communities, in particular those that are historically underrepresented.
  - Foster a more diverse and inclusive research community.
  - Create an environment where all can thrive and feel included.

  Describe how the study will aim to incorporate principles of EDI in the study team, study design and/or patient accrual.
- *Study drug plan:* Provide evidence of access to investigational agent including information of commitment from pharma. This must be reinforced through a Letter of Support from the pharma partner with details of drug access and availability timeline. Include information about drug storage, labelling, and distribution to all study sites.

2. **Deliverables and milestones (D/Ms):** using **Form II**, include D/Ms which will allow tracking of trial timelines and progress. Submit in Excel format.

   In situations where trials are not progressing towards achievement of deliverable or accruing on target, the study lead will be expected to meet with WOO Network and/or CT leadership and outline a remediation plan to ensure study success. If the study continues to encounter issues, OICR can consider closing the study. D/Ms must include but are not limited to:
   - final protocol completion and approval
   - ethics submission and approval
     - visit the Ontario Cancer Research Ethics Board website https://ocreb.ca/ to understand and prepare for ethics submission requirements and timelines
   - study activation (at lead and partnering sites)
   - first patient accrued (at lead and partnering sites)
   - interim analysis (if applicable)
   - meetings of the Data Safety Monitoring Board
   - last patient accrued (at lead and participating sites)
   - correlative sample collection and analysis
   - study lock
   - clinical data analysis

Where possible, include milestones that specify go/no-go decision points.

3. **Budget:** Use **Form III** to complete the budget request details. Submit in Excel format.

Successful WOO trials will be funded to a **maximum of $450,000 CAD.**

The total budget should represent the OICR contribution. Additional contributions committed from other funding sources or collaborators should be included as co-funding (use Co-funding Worksheet). Line-item descriptions must be brief. Line-item justifications are required and should provide a high-level explanation of the expenses and how they are calculated.

Notes
- OICR does not provide overhead for clinical trials.
- Funding is contingent upon available funding from the Government of Ontario.

4. **Attachments:** The following items should be attached to the application:
- *Figures and tables*: submit in PDF format.
- *References*: submit in PDF format.
- *Protocol:* attach a penultimate protocol that has been reviewed and approved by all partner site co-investigators, patient partners and pharma partners (if applicable); submit in PDF format.
- *Letters of Support:* submit as one PDF.

FULL APPLICATION REVIEW

Administrative review
An administrative review will be completed in order to assess the submission for conformity with this document. Relevant points from the administrative review will be shared with the PI.

Review by the WOO Executive
Full applications will be reviewed by the WOO Executive to ensure applications are ready for submission to the CT-SAC for final approval and funding recommendation.

Patient and Family Advisory Council
The Executive and WOO Network Senior Project Manager will work with OICR's PFAC to ensure that the patient partnership plan is appropriate and supportive of a successful WOO trial.

NOTIFICATION OF AWARDS

Applications recommended for funding by the CT-SAC will receive a Notice of Award outlining next steps in order to accept the award and establish a funding agreement.

ESTABLISHMENT OF AGREEMENTS

Following approval of the project, OICR will establish a funding agreement with the Host Institution of the Lead PI. The agreement will cover the general principles regarding the conduct of research activities, eligible research expenses, terms and conditions regarding the disbursement of funds, agreements with third-party funders, financial and progress reporting, PI covenants, intellectual property, commercialization, publications, and communication policies.

REPORTING REQUIREMENTS

Financial and operational status reporting

The following schedule (Table 2) will be used for financial and operational status reporting. Note that the deadlines indicated are moved to the next business day if they fall on a non-working day. A quarterly reporting template and instructions will be available on the OICR online financial reporting system, CaAwardNet.

Financial Officers of the Lead Institution will be required to provide quarterly updates on budget versus actual expenditures as per the table below.

When reporting on the operational status of a trial (Quarterly Expense Report Narrative), an explanation of variances of greater than ±15 per cent and mitigation plans to address the budget gaps must be provided.

Table 2: Financial and operational status reporting

Period covered	Responsible party and action	
	Financial Officer	PI at Lead Institution (or designate)
Q1-Q4	Quarterly expenditure reports are due 45 days post each quarter end.	Review and submit quarterly financial expenditure report and QER Narrative. Due 45 days post each quarter end.
Q1-Q4	Annual fiscal year financial report: *Due August 31*	Review and submit fiscal year financial report. *Due August 31.*

Progress and Key Performance Indicator (KPI) Reporting

All trials will be included in the reporting process as required by the Government of Ontario according to the schedule below (Table 3). Note that the deadlines indicated are moved to the next business day if they fall on a non-working day.

Table 3: Progress/KPI Reporting

Period covered	PI at Lead Institution (or designate)
Q1-Q2	Provide Biannual Progress Reports, including status updates on patient accrual and D/Ms to CT leadership via WOONetwork@oicr.on.ca: *Due 45 days post Q2 end*
Q3-Q4	Provide Biannual Progress Reports, including status updates on patient accrual and D/Ms to CT leadership via WOONetwork@oicr.on.ca: *Due 45 days post Q4 end.*
Q1-Q4 Apr-Mar	Provide quantitative KPIs using ReportNet (OICR's online KPI reporting system): *Due April 30*

Communication with OICR

The obligations of the investigators to advise OICR of anticipated public dissemination, publications, and media announcements will be outlined in the research agreement.

ACKNOWLEDGEMENT AND RECOGNITION OF SUPPORT

All investigators and the recipient institutions must acknowledge and credit the contribution/support, in whole or part, of OICR and the Government of Ontario to the projects in any promotional material, including, without limitation, scientific publications of whatever nature or kind, and in any communication materials or publications supported by OICR funding by referencing the projects with the following statement: "This project was conducted with the support of the Ontario Institute for Cancer Research through funding provided by the Government of Ontario."

CONTACT INFORMATION

Email: WOONetwork@oicr.on.ca