Intralesional Injection of IL-2 Prior to Surgery in Early-Stage Triple-Negative Breast Cancer

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BACKGROUND

Triple-negative breast cancer (TNBC) is a relatively uncommon but aggressive breast cancer subtype.



TNBC accounts for approximately **15-20%** of all newly diagnosed **breast cancer cases annually**.



This subtype exhibits a **high mutational burden**, **dense** tumor-infiltrating lymphocytes **(TILs)**, and **elevated** programmed death-ligand 1 **(PD-L1) expression.**

TNBC is associated with an **increased risk of distant metastasis** and **reduced survival rates** compared to other forms of the disease[1].

Figure 1. Characteristics of TNBC.

IMMUNOTHERAPY

Systemic immunotherapy is approved as a **first-line treatment** for ***metastatic and unresectable*** TNBC.

KEYNOTE-522 trial demonstrates improved clinical response and survival rates in ***earlier-stage, resectable*** disease[2].



The growing use of systemic therapy in small, early-stage tumors must be balanced against the risk of **rare** but **potentially life-threatening side effects**.

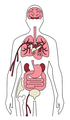




Adrenal insufficiency



Pneumonitis leading to respiratory failure



Multi-organ dysfunction syndrome

Figure 2. Systemic immunotherapy treatment landscape.

INTERLEUKIN-2

- **Interleukin-2 (IL-2)**, one of the first immunomodulating agents approved for cancer therapy, has significant toxicity when administered systemically[3].
- **Intralesional delivery** can achieve **high local concentrations** with **manageable side effects**.
- While published IL-2 protocols are largely based on melanoma studies[4], case reports suggest that intralesional IL-2 may also achieve a **pathologic complete response (pCR)** in metastatic or unresectable TNBC[5].

OBJECTIVE

Evaluate the ability of intralesional IL-2 to induce a pathologic response and alter the tumor microenvironment in early-stage TNBC.



PRIMARY ENDPOINT

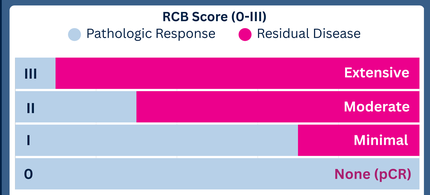


Figure 3. Pathological complete response (pCR) defined by the residual cancer burden (RCB) index (O-III).

SECONDARY ENDPOINTS

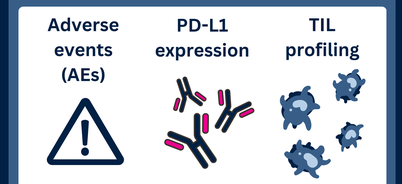
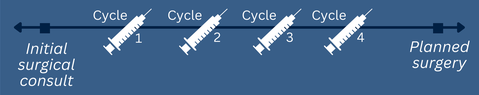


Figure 4. Trial endpoints including other pathological descriptors of treatment effect.

INTERVENTION

This regimen is designed to utilize the **4–6 week wait-time** between initial consultation and upfront surgery as a **'window of opportunity'**.



1 intralesional injection is administered each week/cycle, for up to 4 cycles while awaiting surgery.

Figure 5. Intralesional IL-2 injection timeline.

Dosing

500,000 IU (5 million IU/mL)
per millimetre of tumor at index presentation

Maximum tumor dimension used

E.g., 10 mm tumor injected with 1 ml or 5 million IU (5 million IU/ml)

STUDY DESIGN

SINGLE-CENTRE | SINGLE ARM | NON-RANDOMIZED EXPERIMENTAL TRIAL

Design	Details
Location	Breast Health Clinic, IWK Health Centre, Halifax, Nova Scotia, Canada
Population	• Adult women (18–90 years) with biopsy-confirmed **cT1N0 TNBC (≤2 cm)** • Upfront surgery planned (due to stage (cT1N0) or medical ineligibility for NAT)
Recruitment	**Ongoing** with the clinical care team at the Breast Health Clinic
Sample Size	Enrollment will conclude once **10 patients** complete IL-2 injections and surgery with full pathology, or 20 participants are enrolled, whichever occurs first

1. Participants will provide **written informed consent** and **complete screening** for IL-2 contraindications, including autoimmune disease or organ function tests.
2. In the **perioperative window** after initial surgical consultation, eligibile patients will be scheduled to receive **weekly (x4) ultrasound-guided intralesional injections**.
3. During each cycle, an injection of IL-2 is administered by a radiologist in two equal portions:
½ to the **lesion center** and ½ to the **periphery**.
4. Follow-up phone calls after each cycle **assess for AEs** and **confirm suitability** for **subsequent dosing**, continuing through all four injections until surgery, which concludes study participation.



Figure 6. Intralesional delivery of immunotherapy.

CONCLUSION

- This pilot trial will provide **preliminary data on the potential efficacy** of intralesional IL-2 in patients with early-stage TNBC and provide key data to **inform** whether a **phase II study** is warranted.
- Future experimental trials may investigate additional intralesional immunotherapies, such as PD-L1 inhibitors, to further enhance treatment response.
- Phase II trials could also further evaluate the feasibility of intralesional IL-2, refine biomarker selection, and identify the patients most likely to benefit.

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