Perilymphatic IRX-2 cytokine therapy to enhance tumor infiltrating lymphocytes and PD-L1 expression preceding curative-intent therapy in early stage breast cancer

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Abstract #1625  Tumor infiltrating lymphocyte recruitment after peri-lymphatic IRX-2 cytokine immunotherapy in resectable breast and head and neck carcinoma

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Background

IRX-2 is an injectable cytokine-based immunotherapy containing multiple cytokines derived from ex vivo phytohemagglutinin-stimulated donor lymphocytes.

- Measurable constituents include: IFN gamma, IL-2, IL-1beta, TNFalpha, IL-6, IL-8, GM-CSF, and G-CSF.
- In preclinical models, IRX-2 activates T cells and natural killer cells, and facilitates dendritic cell maturation.
- In a phase I trial, neoadjuvant IRX-2 increased tumor-infiltrating lymphocytes (TILs) and shrank tumors in resectable headneck squamous carcinoma (HNSCC).
- Stomal TILs (sTILs) are associated with improved survival in early stage breast cancer (EBBC).

Primary Endpoint: Feasibility

No treatment-related grade 3/4 toxicities

Hypothesis

To assess the feasibility of preoperative IRX-2, and its effect on TIL recruitment and immune priming within breast and HNN tumors, regional lymphatics, and peripheral blood.

Methods

- Patients with early stage (I/II) breast cancer were enrolled preoperatively.
- Patients received low dose of cyclophosphamide (300 mg/m²) to facilitate Tregulatory (Treg) depletion. Followed by 10 days of subcutaneous peri-areolar subcutaneous IRX-2 into the affected breast (1 mL) 2x at tumor axis and at 90°.
- Similar to sentinel lymph node mapping methodology.
- Subjects also received oral indomethacin, which may reverse immunosuppression by modulating maturation.

Primary endpoint: feasibility.

Secondary endpoints: limited assessment of sTILs by the 2015 San Antonio working group criteria.

Exploratory endpoints: comprehensive immune monitoring.

Figure 1: Regimen

Figure 2: sTILs increases After IRX-2 Therapy

Figure 3: PD-L1 increases After IRX-2 Therapy (IHC and NanosT).

Exploratory Endpoints: Immune Monitoring

Figure 5: Effects on peripheral T-cells

Figure 4: IRX-2 Increases immune checkpoint, cytotoxic T-cells and leukocyte genes expression

Conclusions and Further Directions

- IRX-2 was well tolerated, with no treatment-related grade 3 or 4 toxicities or surgical delays.
- In breast cancer, IRX-2 enhances TIL recruitment and PD-L1 expression (by mRNA and IHC).
- Peripheral immune changes were associated with Cy administration but not IRX-2 injections.
- These preliminary findings will be further explored in a follow-up clinical trial that compares anti-PD-1/-L1 vs. IRX-2 as induction therapy preceding neoadjuvant chemotherapy in stage II/III triple negative breast cancer, with a primary endpoint of pathologic complete response rate.

References


Legend: Cy = cyclophosphamide; Be = bevacizumab; MIBC = muscle-invasive bladder carcinoma.