

NEOIRX: A PHASE II TRIAL OF LOCOREGIONAL CYTOKINE THERAPY TO PROMOTE IMMUNOLOGIC PRIMING AND CLINICAL RESPONSE TO NEOADJUVANT PEMBROLIZUMAB PLUS CHEMOTHERAPY IN TRIPLE NEGATIVE BREAST CANCER (TNBC)

<http://dx.doi.org/10.1136/jitc-2021-SITC2021.398>

¹Katherine Sanchez*, ²Alison Conlin, ³Parvin Peddi, ²Sasha Stanton, ⁴Janet Ruzich, ²Kelly Perlewitz, ²Yaping Wu, ²Nicole Moxon, ²Staci Mellinger, ²Zhaoyu Sun, ²William Redmond, ²David Page. ¹Baylor College of Medicine, Houston, TX, USA; ²Providence Cancer Institute, Portland, OR, USA; ³St John Cancer Institute, Santa Monica, CA, USA; ⁴Providence Cancer Institute Newberg, Clackamas, OR, USA

Background Background: The FDA has approved pembrolizumab in combination with neoadjuvant chemotherapy (doxorubicin, cyclophosphamide, paclitaxel [ACT], and carboplatin) for stage II/III TNBC, on the basis of improved event free survival (EFS) and pathologic complete response (pCR) rate in the Keynote-522 study.¹ Novel combination immunotherapy strategies may further improve outcomes and allow the opportunity to de-escalate the chemotherapy backbone, potentially mitigating grade III/IV toxicities which occurred in 81% of recipients. We have previously reported safety and feasibility of pre-operative IRX-2, a novel cytokine biotherapeutic, that is administered locoregionally in the peri-areolar tissue to enhance the immune microenvironment within the sentinel lymph nodes, the putative site of antigen presentation.² In this phase Ib study, pre-operative IRX-2 was safe and was associated with increased tumor infiltrating lymphocytes (sTILs, by H&E and multispectral immunofluorescence [mIF]), PD-L1 expression (Ventana SP142 assay, mIF), and lymphocyte activation (by RNA sequencing). Similar effects were observed in a pre-operative head and neck carcinoma trial. These findings support further study of IRX-2 in combination with anti-PD-1 in early stage TNBC.

Methods

Methods neoIRX is an open-label, phase II trial to evaluate the clinical and immunological activity of induction IRX-2 plus pembrolizumab, followed by de-escalated chemotherapy (ACT) and pembrolizumab as neoadjuvant therapy in TNBC. Patients are randomized to receive pembrolizumab induction (single dose 200mg IV, n=15), versus pembrolizumab + IRX-2 induction (1mL SQ x 2 daily, x 10 days, n=15), followed by research biopsy. All patients will then receive neoadjuvant pembrolizumab plus ACT every three 3 weeks. Eligible subjects will have previously untreated, resectable stage II/III TNBC. The primary endpoint is pCR. The secondary endpoint is safety. On-treatment biopsies will permit a prospective, randomized validation of previously reported immunomodulatory effects of IRX-2 (sTILs, PD-L1, lymphocyte RNA signatures). As of 7/28/2021, n=7/30 subjects are enrolled (Providence Cancer Institute, Portland, OR, Providence St. John's Cancer Institute, Santa Monica, CA, Baylor Medicine, Houston, TX).

Trial Registration NCT04373031

REFERENCES

1. Schmid PN. *Engl J Med* 2020; **382**:810–821.
2. Page DB. *Clinical Cancer Research* 26.7(2020):1595–1605.

Ethics Approval The study protocol was approved by the Providence Portland Medical Center IRB committee and was conducted in accordance with the ethical standards established by the Declaration of Helsinki, PH&S IRB# 2019000486. Written informed consent was obtained for all trial participants.