# PS4-08-15 Towards Personalized Medicine

# Patient-Derived Breast Tumor Grafts as Predictors of Relapse and Response to Therapy: Final Results.

Vaklavas C, Matsen CB, Chu Z, Boucher KM, Scherer SD, Pathi S, Beck A, Brownson KE, Buys SS, Chittoria N, D'Astous E, Gulbahce HE, Henry NL, Kimani S, Porretta J, Rosenthal R, Ward J, Wei M, Welm BE, Welm AL

Huntsman Cancer Institute, University of Utah

## Background

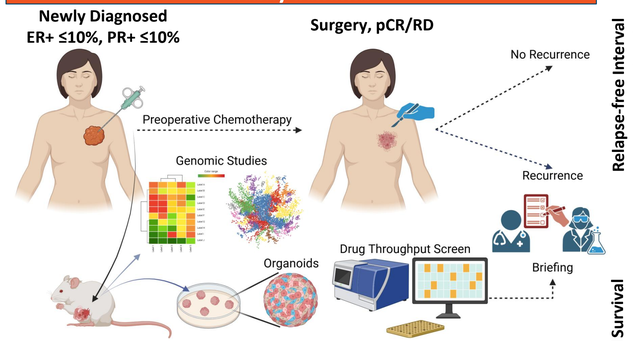
The high attrition rate of new oncology drugs has propelled the development of patient-derived xenografts (PDXs) for preclinical studies. PDXs retain most of the phenotypic and molecular features of the originating tumors, allowing for more accurate predictions about the activity of novel drugs in the clinic.

Not all tumors can engraft[1]. Across multiple tumor types, engraftment correlates with a more aggressive natural history and poor clinical outcomes[2].

In non-metastatic high-risk breast cancer, the achievement of pathologic complete response (pCR) with preoperative therapy is associated with better long-term outcomes. However, not all patients with residual disease (RD) relapse and patients who achieve a pCR still harbor a risk for recurrence, albeit small. Better biomarkers are needed to identify patients at high risk for recurrence, and better models are needed to develop regimens specifically for those with a true high risk of recurrence.

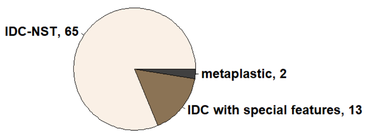
In the TOWARDS clinical trial, we systematically investigated whether PDX engraftment could prospectively predict disease recurrence. The secondary endpoint of disease-free survival (DFS) in 1 year has been previously reported[2]. We now report on the primary endpoint, DFS in 3 years.

## Study Schema




Tumor tissue was acquired from patients with a new diagnosis of non-metastatic hormone receptor-low (≤10%) or negative breast cancer who were planned to receive preoperative chemotherapy. Tumor fragments were surgically implanted into the cleared inguinal mammary fat pad of NOD/SCID mice. In the course of the study, we developed a PDX-derived organoid-based functional precision oncology platform to inform treatment selection upon disease recurrence[2-4].

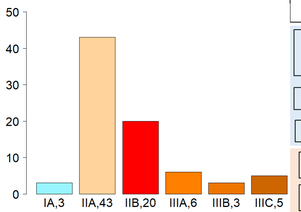
## Patient Characteristics & CONSORT Diagram




Assessed for eligibility (n=89)

Excluded (n=9)
a. Consent withdrawal (n=3)
b. Metastatic disease (n=2)
c. Unable to collect tissue (n=2)
d. HR(+) disease (n=1)
e. Invalid consent (n=1)

**Clinical Stage at Diagnosis (Stage, n)**

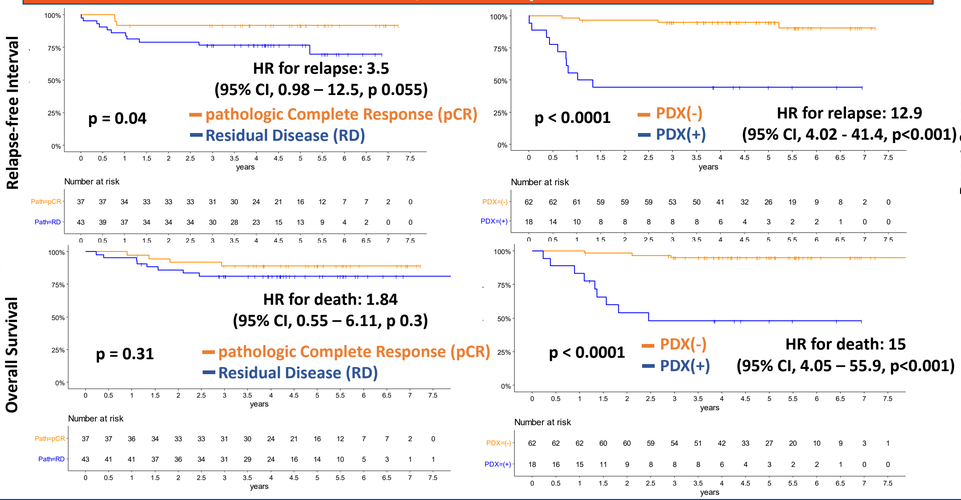



**80** patients eligible proceeded with tissue acquisition & tumor engraftment
**80** patients underwent definitive surgery

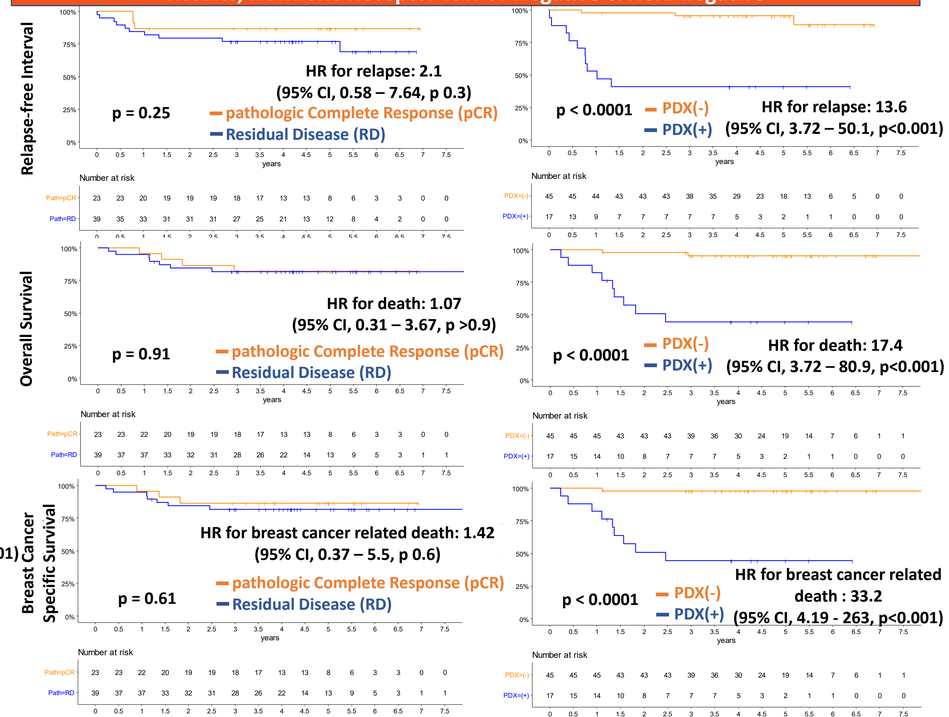
| TNBC n = 51 | HR low/Her2(-) n = 10 | HR low/Her2(+) n = 7<br>HR(-)/Her2(+) n = 11 | Mixed n = 1 |
|---|---|---|---|
| PDX(+), 14 \| PDX(-), 37 | PDX(+), 3 \| PDX(-), 7 | PDX(+), 1 \| PDX(-), 17 | PDX(-), 1 |
| RD, 16 \| pCR, 35 | RD, 3 \| pCR, 7 | RD, 4 \| pCR, 14 | RD, 1 |

Successful engraftment (PDX(+)), n = 18
Residual Disease (RD), n = 43
No engraftment (PDX(-)), n = 62
Achievement of pCR, n = 37

## Results, Overall Population




## Results, Hormone Receptor-low or Negative & Her2 negative




## Discussion & Conclusions

A. With longer follow up (3.6 years since definitive surgery of the last enrolled patient), the association between PDX engraftment and recurrence, overall and breast cancer specific survival remains strong. PDX(+) patients who relapsed had early recurrence and their survival following relapse did not exceed 1 year.

B. Strength of the study is that patients received uniform treatments as per standard of care. Notable limitation is the change in the standard of care in early-stage TNBC with the incorporation of immunotherapy and adoption of carboplatin since this trial ended. Our ongoing TOWARDS-II clinical trial (NCT05464082) aims to determine whether PDX engraftment still correlates with clinical outcomes in HR-low or negative/Her2 negative non-metastatic breast cancer and prospectively develop patient derived models to inform treatment selection upon recurrence.

## Contact

Christos Vaklavas
Huntsman Cancer Institute
Email: christos.vaklavas@hci.utah.edu
Website: https://uofuhealth.utah.edu/huntsman/labs/welm-labs
Phone: 801 213 8477

## References

1. DeRose YS, *et al.* **Tumor grafts derived from women with breast cancer authentically reflect tumor pathology, growth, metastasis and disease outcomes**. Nat Med. Oct 23 2011;17(11):1514-20. .
2. Vaklavas C, *et al.* **TOWARDS Study: Patient-Derived Xenograft Engraftment Predicts Poor Survival in Patients With Newly Diagnosed Triple-Negative Breast Cancer**. JCO Prec Oncol. 2024 Jul:8:e2300724.
3. Scherer SD, *et al.* **Breast cancer PDxO cultures for drug discovery and functional precision oncology.** STAR Protoc 2023 Sep 15;4(3):102402.
4. Guillen KP, *et al.* **A human breast cancer-derived xenograft and organoid platform for drug discovery and precision oncology.** Nat Cancer 2022 Feb;3(2):232-250.
5. Images created at **BioRender.com**

This presentation is the intellectual property of the author/presenter. Contact them at christos.vaklavas@hci.utah.edu for permission to reprint and/or distribute.

© Poster Template by Genigraphics® 1.800.790.4001 www.genigraphics.com