PS5-12-19 PRE-ISPY Phase I/Ib Oncology Platform Program (PRE-I-SPY-P1) NCT 05868226 – Trial in progress

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BACKGROUND

Many promising agents or combinations regimens relevant to breast cancer and other solid malignancies lack sufficient clinical information for use in the neoadjuvant setting. To enable acceleration of drug development by reducing time and cost of clinical trial planning and conduct, the Phase I initiative PRE-ISPY Program was created.

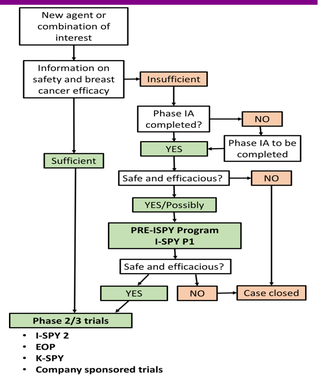


Figure 1: PRE-I-SPY study rationale

METHODS

The PRE-ISPY trial was envisioned as part of the growing I-SPY network of trials, leveraging its efficiencies in streamlined regulatory pathways and trial design processes, including contracting, activation, enrollment, data gathering and analysis. The goals of designing the PRE-ISPY trial were to support investigators and industry partners in meeting safety and preliminary efficacy qualifications for phase II/III studies and gathering translational data to identify the optimal clinical development setting in a timely fashion. The primary aims of the trial are to assess drug toxicity/safety, to determine the Maximum Tolerated Dose (MTD) and Recommended Phase 2 Dose (RP2D), to evaluate preliminary treatment efficacy via Overall Response Rate and Clinical Benefit Rate; and biospecimen acquisition, while gaining experience with the drug/regimen in patients with advanced/recurrent solid malignancies. Arms are independent and may have additional specific aims. Sample size depends on the arm design, number of dose-finding cohorts, and number of expansion cohorts. The minimum sample size for an arm is 15 patients, with no maximum. Study arms include dose finding (Part 1) and dose expansion (Part 2) components. Part 1 is optional if MTD and RP2D have already been established. Each study arm may have specific criteria for transitioning from Part 1 to Part 2. Pre-specified exploratory and qualifying transcriptomic, proteomic and phosphoprotein biomarkers will be analyzed.

RESULTS

Infrastructure & Oversight
- Sponsored by Quantum Leap Healthcare Collaborative (QLHC)
- Established site network, US only
- PRE-ISPY uses a master protocol to evaluate multiple regimens in parallel
- Standardized process to implement regimens or arms when proposed by industry or investigators

Centralized Operations
- Centralized contracting (cost analysis, budgeting, industry contract management)
- Centralized and unified process for study activation (IRB: Wake Forest; SRC: UMINN)
- Centralized coordination of data management with remote and real-time EDC
- Centralized coordination of drug management
- Open and frequent communication with pharma partners on all key decisions

Data & Safety Management
- Study data (EDC)
- Safety (Safety DB) and DSMB
- Biospecimens (LIMs)

Logistics & Biobanking
- Drug and lab kit shipments are coordinated via a unified logistics system
- Centralized biobanking infrastructure for consistency in sample handling and storage

Eligibility
- General eligibility includes adults with advanced/metastatic or recurrent solid tumors, adequate performance status, and organ function
- Arm-specific criteria detail additional requirements for tumor histology, treatment history, and organ function

Program Transition Pathways
- Graduation of a PRE-ISPY regimen to I-SPY2 (neoadjuvant breast cancer trial) or K-SPY (colorectal trial) is *not mandatory*

Trial Activation & Site Network
- The PRE-ISPY trial was activated for enrollment in Feb 2023
- As of November 2025, seven main sites and two satellite sites are activated, with twelve additional site activations planned from Q1 2026 to Q4 2026
- All sites are academic centers affiliated with NCI-Designated Comprehensive Cancer Centers

SITE NETWORK

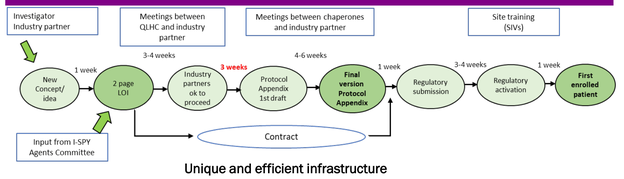
7 Main Sites, 2 Satellites Activated
12 New Site Activations In Progress



Active Sites
- Emory Winship Cancer Institute
- Moffitt Cancer Center
- University of Alabama Birmingham Comp. Cancer Center
- University of Minnesota Masonic Cancer Center
- University of Chicago Comp. Cancer Center
- University of Colorado Comp. Cancer Center
- University of Texas MD Anderson Cancer Center

Upcoming Sites
- City of Hope Comp. Cancer Center
- Columbia University
- Dartmouth Cancer Center
- Georgetown University Comp. Cancer Center
- Mayo Clinic: Arizona, Minnesota, Florida
- NYU Langone Health
- Penn Medicine Abramson Cancer Center
- RWJ Barnabas Health Rutgers
- The Ohio State Univ. Comp. Cancer Center
- UCSF Comp. Cancer Center
- Vanderbilt-Ingram Cancer Center
- Washington University St. Louis

TIMELINE AND TARGET MILESTONES



Unique and efficient infrastructure
- From accepted LOI to full protocol: 3-5 weeks
- Final protocol version to study arm activation requires 6-9 weeks

PRE-I-SPY DESIGN

PART 1 DOSE FINDING
- ✓ Escalation or de-Escalation
- ✓ N number of dose levels
- ✓ N number of administration schedules to be tested
- ✓ This PART is not mandatory

PART 2 DOSE EXPANSION
- ✓ At least one cohort expands in breast cancer
- ✓ N number of administration schedules to be expanded

STUDY ARMS

Two active and three upcoming arms:

PRE1	ALX148 + T-DXd in T-DXd naïve HER2+ and HER2low metastatic breast cancer
PRE2	Zanidatamab + Tucatinib in T-DXd previously treated, HER2+ metastatic breast cancer
PRE3	Vidutolimod + Cemiplimab in patients with HER2 negative breast cancer
PRE4	Undisclosed regimen
PRE5	Undisclosed regimen

PRE-I-SPY TRIAL POTENTIAL ARM DESIGNS

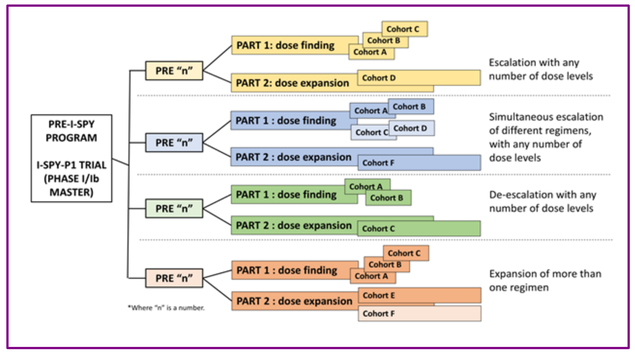


Figure 2: PRE-I-SPY study schema Example of I-SPY-P1 study design with potential Arm designs

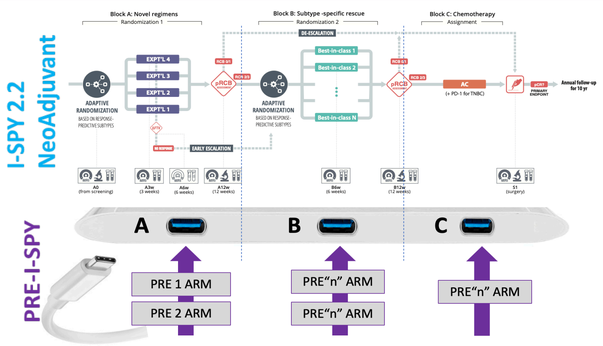


Figure 3: Plug and play into the neoadjuvant I-SPY 2.2 study

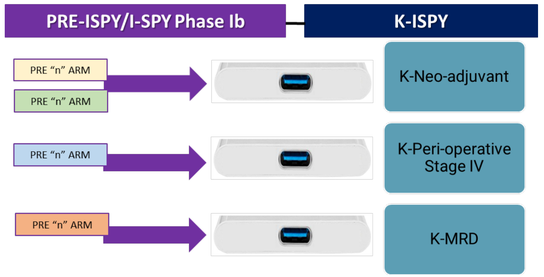


Figure 4: Plug and play into the K-SPY study

CONCLUSIONS

- The PRE-ISPY phase I/Ib trial has been successfully implemented nationally as part of the Consortium of I-SPY trials.
- Once safety is established, promising regimens can be rapidly transitioned to I-SPY2.2, K-SPY or other phase II/III trials.

ACKNOWLEDGEMENTS:

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Quantum Leap Healthcare Collaborative