COMBATTING FUTURE BIOLOGICAL THREATS – HOST-DIRECTED INTERVENTIONS TO EMERGING THREATS FOR RAPID RESPONSE

The Ards Expansion Of The I-SPY Covid Platform Clinical Trial

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The I-SPY COVID Trial has been running for 4 years and is now transitioning to a multi-cause acute respiratory distress syndrome (ARDS) patient population. The trial leveraged more than 15 years of prior work from the successful I-SPY2 Trial in breast cancer that has tested 24 agents, 4 of which have been FDA approved for use in breast cancer (pertuzumab, pembrolizumab, TDM-1, and carboplatin). The I-SPY COVID trial was active at 42 clinical sites, enrolled more than 3,000 study participants, and evaluated 12 different interventional agent arms. The platform trial approach was significantly faster and more efficient than conducting 12 individual clinical trials, allowing for the evaluation of 11 agent arms in only 1.5 years. A major advantage to our approach is that a platform trial creates value during non-pandemic time periods. Having all of the platform trial infrastructure in place and ready to pivot in a matter of days or weeks as opposed to months is the ideal way to be prepared for the next pandemic or national security threat.

ARDS is the common, and often fatal, result of exposure to a variety of threats, including most aerosolized chemicals, chemical weapons, particulate matter, infectious pathogens etc. Quantum Leap Healthcare Collaborative (QLHC), the trial sponsor, is implementing new innovative strategies aimed at improving the success rate for new therapeutics in ARDS. Our investigators have developed biomarker-based subphenotypes in ARDS that can predict patient responses to treatment. We have enrolled more than 200 study participants in an ongoing noninterventional biomarker study of patients with the newly expanded global definition of ARDS. Preliminary biomarker data from this study shows that approximately 25% of these patients have a hyperinflammatory phenotype and 75% have a hypoinflammatory phenotype suggesting different treatment approaches will have higher likelihoods of success in different patients.

The expanded trial will identify agents that reduce mortality and time on invasive mechanical ventilation or advanced respiratory support. The trial currently has more than 30 trial sites across the US. This trial will build on a foundation of innovations common to the I-SPY family of trials: a central IRB, common control arms, universal eligibility criteria, Bayesian design, biomarker analyses, early endpoints, and QLHC-developed technology solutions to enhance operational efficiency. I-SPY ARDS is designed to test more interventions more rapidly and at lower cost than traditional trials while also prospectively identifying baseline ARDS subphenotypes, enabling our investigators to identify agents that benefit a specific subset of patients. Our ultimate goal is to identify safer and more effective treatments for ARDS patients as rapidly as possible.

The I-SPY platform trial approach has now been successfully applied in two settings: cancer (non-pandemic) and infectious disease (pandemic). QLHC is also currently expanding into additional disease areas with separate platform trials such as our new trial in ductal carcinoma in situ (NCT06075953) and we plan to continue to work with various stakeholders, including DTRA, to continue to explore expanding into other therapeutic areas where the platform trial approach would be advantageous, such as antimicrobials.

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