Summary Report - 1st Critical Care Academic/Pharmaceutical Industry Symposium

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Introduction:

Developing new treatments for acutely unwell patients in intensive care presents unique challenges due to the heterogeneity of patient populations, the complexity of critical illnesses such as sepsis or acute respiratory distress syndrome (ARDS) and the rapid evolution of treatment modalities.

The recent COVID-19 pandemic presented healthcare services worldwide with an urgent need to rapidly evaluate a myriad of potential treatments and interventions to treat patients requiring treatment on ICU for ARDS. Traditional clinical trial models, characterized by sequential evaluation of interventions, were ill-suited to addressing the urgent and evolving challenges of the pandemic. In response, platform trials emerged as a paradigm shift, allowing for the simultaneous evaluation of multiple interventions within a single trial infrastructure. This approach accelerated the evaluation process enabling the identification of effective treatments like dexamethasone and tocilizumab while efficiently utilizing limited resources.

Platform trials have also had a significant effect on the development and approval of new personalized treatments in other areas such as oncology. Here, adaptive platform trials of neoadjuvant therapy such as I-SPY 2, STAMPEDE and FOCUS4 have offered a glimpse into the future of drug development matching targeted therapies for cancer with the patients most likely to benefit from them.

Emerging evidence of disease endotypes within the traditional broad syndromal definitions and evolving clinical practices necessitate the development of new therapies both now and in anticipation of future pandemics. As a result, there is consensus that adaptive platform trials testing precision medicine approaches could revolutionize drug development in acute illness. What is unclear is the best way to develop successful collaborations between academic institutions and the pharmaceutical industry to allow potential novel treatments to be tested.

In response to this, an inaugural critical care academic/pharmaceutical industry symposium was held in Dublin in June 2023 with the following aims:

1. To understand the industry specific challenges of precision medicine drug development in ARDS
2. To identify the barriers to potential pharmaceutical companies entering the critical care space including research and development, market access and commercial considerations
3. Understand the opportunities and challenges for industry involvement in planned academic Phase 2 platform trials in ARDS
4. To understand the industry criteria for engagement in planned platform trials in ARDS and other areas of critical care e.g. sepsis
5. Identify potential solutions to barriers for industry involvement into platform trials

Key Recommendations:

1. General Principles

1.1. Successful demonstration of the maintenance of data quality standards acceptable for regulatory and payer submissions in the early phase of any academically sponsored platform trial will be critical to ensure confidence in ongoing industry participation.

1.2. The emergence of multiple parallel ICU platform trials in different global jurisdictions will mean industry partners will be looking for consistency, collaboration and integration between platforms in key areas such as patient selection, sample collection, minimum data sets and endpoints.

1.3. Trial design e.g. blinding, definitions of standard of care, patient population, endpoints etc. must be acceptable for regulatory submission to support a package that reaches the standard for substantial evidence of effectiveness (FDA-2019-D-4964) to regulators and allow progression to pivotal Phase 3.

1.4. Early involvement and engagement with regulators would be helpful in assisting IND submissions as well as clarity over population, endpoints and other clinical development planning

1.5. Planning for a central therapeutics decision committee is essential given the proposals for multiple parallel ICU platform trials. This will allow a clear “horizon scanning” for potential assets from both larger pharmaceutical companies and smaller biotechs and efficiency of decision making for companies regarding the optimal platform to join.

1.6. Platform trials in ICU must ensure academic independence at all times with sponsorship by an academic entity such as a university. This should not detract from industry engagement and collaboration but will ensure the integrity and robustness of results.

2. Governance

2.1. Governance structure and decision-making processes within platform trials must be consistent, transparent and engage industry partners in a robust way. Overall sponsorship for the platform should be led by academic entities with industry collaboration.

2.2. Ownership of data needs to be clear with agreement on who will prepare submission packages and contribute to regulatory interactions.

2.3. Drug-specific responsibility between sponsor and industry should be clearly pre-specified in the master protocol e.g. pharmacovigilance, medical monitoring, specific safety monitoring and reporting, pharmacokinetics.

2.4. Data integrity is essential for ongoing pharmaceutical company involvement including plans for missingness and compatibility as well as inspection readiness.

3. Intellectual property (IP)

3.1. “Firewalling of data” for each individual industry asset is a potential issue that needs to be addressed with specific structures within the platform trial master protocol. Ideally, platform trials be designed in a “modular” approach to help address this need and ensure appropriate confidentiality.

3.2. The “inventor” should be clearly acknowledged at the start of the trial – either the academic sponsor, industry partner or a pre-determined combination? IP and data must be retained by the organization/company that made the inventive step.

3.3. Ownership and responsibility for biological samples should be clearly pre-specified at the start of the trial

4. Reporting

4.1. The platform trial needs to output reports acceptable to regulators including baseline characteristics, endpoints, safety data.

4.2. Timelines for reporting should be clearly established to assist clinical development planning for companies.

5. Ethical transparency

5.1. The highest ethical standards must be maintained with academic and industry leadership in a collaborative framework to ensure the overall ethical integrity of platform trial processes.

5.2. Funding sources should be transparent, open, and auditable. There should be transparency around the contributions from each pharmaceutical company.

5.3. Efficacy and safety decision making should be conducted by independent data monitoring committees without direct industry involvement. For example, final decisions regarding individual arms at interim analyses.