**Introduction to master protocols, innovative clinical trial designs for development of precision oncology drugs**

**Hyeon Jeong (Holly) Yang, Pharm.D. Candidate 2019, Marina Shahat, Pharm.D., Lindsay Brust-Sisti, Pharm.D., BCPS, Michael Toscani, Pharm.D.**

**Ernest Mario School of Pharmacy, Rutgers, The State University of New Jersey, Piscataway, NJ**

---

**Background**

- In recent years with the advances in biomedicine, tumor microenvironment could be fully understood and genetic subtypes could be identified and targeted for cancer therapy.
- **Master protocols** are novel trial designs that transformed the conduct of trials and enabled investigators to study multiple therapies in multiple disease subtypes within a shared clinical trial platform. There are three different designs in Master protocols: 1. **Umbrella trial** studies multiple targeted therapies in the context of a single disease. Patients are assigned to different therapies based on their molecular makeup of cancer. 2. **Basket trial** studies a single targeted therapy in the context of multiple diseases. Patients are screened for target response positive carriers. 3. **Platform trial** studies multiple targeted therapies in the context of a single disease in a seamless manner, with therapies allowed to enter or leave the platform on the basis of a pre-defined algorithm.  
- Many investigators have an increased interest in conducting these trials. As of March 2018, four trials are in preparation for set up. Currently, nine trials are ongoing trials and two trials have been already completed. The feasibility on the use of master protocol designs was not assessed. The implementation aligns with the current advancement in oncology. According to literature, advantages and disadvantages of innovative designs have been studied (see above) and these must be weighed in before initiating a trial.

- **Master protocols** enable investigators to conduct research in a time-efficient manner with multiple treatment arms and diseases, thus allowing new ideas to be explored. According to literature, advantages and disadvantages of innovative designs have been studied (see above) and these must be weighed in before initiating a trial. More research will be needed to evaluate the overall value of these trial designs but this implementation aligns with the current advancement in biomarker findings and the focus in the development of precision oncology.

---

**Method**

- Included trials that have publications of design layouts on clinical trial databases and literature: Beat AM, B225 and BATTLE-2.
- Excluded trials that are in preparation stages that do not yet have publications of protocol designs.
- Compared the number of investigation drugs or combinations that are devised in currently ongoing or completed phase I/II clinical trials and arranged the protocol design into flow charts.

---

**Objective**

- To compare different master protocol designs and evaluate how they are devised in currently ongoing or completed phase II clinical trials.

---

**Results**

- Newly diagnosed acute myeloid leukemia (AML)

**Hematologic**

![Image](file1.png)

**Solid tumors**

![Image](file2.png)

**Umbrella Trial**

- Inter-venti-um

**Basket Trial**

- Inter-venti-um

**Platform Trial**

- Inter-venti-um

---

**Discussion**

- **Advantages**
  - Efficient use of time and resources
  - Provide data source for future research
- **Disadvantages**
  - Need to accommodate new comparators

---

**Limitations**

- The review of these clinical trials was performed from literature published on available databases.
- The feasibility on the use of master protocol designs was not assessed.

---

**Conclusions**

- **Master protocols** enable investigators to conduct research in a time-efficient manner with multiple treatment arms and diseases, thus allowing new ideas to be explored. According to literature, advantages and disadvantages of innovative designs have been studied (see above) and these must be weighed in before initiating a trial.
- More research will be needed to evaluate the overall value of these trial designs but this implementation aligns with the current advancement in biomarker findings and the focus in the development of precision oncology.

---

**References**

5. 3. Gottlieb, S. (2018). Master Protocols to Study Multiple Therapies, Multiple Diseases, or Both. Applied Clinical Trials Online. Available at: https://www.appliedclinicaltrialsonline.com/master-protocols-to-study-multiple-therapies-multiple-diseases-or-both
7. 3. Gottlieb, S. (2018). Master Protocols to Study Multiple Therapies, Multiple Diseases, or Both. Applied Clinical Trials Online. Available at: https://www.appliedclinicaltrialsonline.com/master-protocols-to-study-multiple-therapies-multiple-diseases-or-both
11. 3. Gottlieb, S. (2018). Master Protocols to Study Multiple Therapies, Multiple Diseases, or Both. Applied Clinical Trials Online. Available at: https://www.appliedclinicaltrialsonline.com/master-protocols-to-study-multiple-therapies-multiple-diseases-or-both
15. 3. Gottlieb, S. (2018). Master Protocols to Study Multiple Therapies, Multiple Diseases, or Both. Applied Clinical Trials Online. Available at: https://www.appliedclinicaltrialsonline.com/master-protocols-to-study-multiple-therapies-multiple-diseases-or-both
17. 3. Gottlieb, S. (2018). Master Protocols to Study Multiple Therapies, Multiple Diseases, or Both. Applied Clinical Trials Online. Available at: https://www.appliedclinicaltrialsonline.com/master-protocols-to-study-multiple-therapies-multiple-diseases-or-both
23. 3. Gottlieb, S. (2018). Master Protocols to Study Multiple Therapies, Multiple Diseases, or Both. Applied Clinical Trials Online. Available at: https://www.appliedclinicaltrialsonline.com/master-protocols-to-study-multiple-therapies-multiple-diseases-or-both
25. 3. Gottlieb, S. (2018). Master Protocols to Study Multiple Therapies, Multiple Diseases, or Both. Applied Clinical Trials Online. Available at: https://www.appliedclinicaltrialsonline.com/master-protocols-to-study-multiple-therapies-multiple-diseases-or-both
27. 3. Gottlieb, S. (2018). Master Protocols to Study Multiple Therapies, Multiple Diseases, or Both. Applied Clinical Trials Online. Available at: https://www.appliedclinicaltrialsonline.com/master-protocols-to-study-multiple-therapies-multiple-diseases-or-both
29. 3. Gottlieb, S. (2018). Master Protocols to Study Multiple Therapies, Multiple Diseases, or Both. Applied Clinical Trials Online. Available at: https://www.appliedclinicaltrialsonline.com/master-protocols-to-study-multiple-therapies-multiple-diseases-or-both