POWER OF ONE

N-of-1 Clinical Trials
As opposed to traditional methodologies, which test a specific drug in a group of participants with the same type of cancer, N-of-1 trials recognize that no two cancers are the same and study them on a patient-by-patient basis. Each patient is matched to one or more drugs based on the molecular characteristics of their tumor. Rather than using DNA mutations to identify candidate “targeted” therapies, however, the new approach uses supercomputers to predict each tumor’s response to all clinically available drugs based on its RNA. RNA is the molecule responsible for making proteins based on the instructions encoded in the cell’s DNA.

At Columbia University Irving Medical Center, a multidisciplinary research team is conducting a series of innovative oncology studies called N-of-1 clinical trials.
For covered tumor types, enrollment in an N-of-1 trial—including molecular profiling, analysis with the new OncoTreat and OncoTarget methodologies, tumor transplantation in a mouse (PDX), and PDX treatment—is at no cost to the participant. This N-of-1 study is not an interventional trial. Whether patients will be able to receive the treatment(s) identified by the study is at the complete discretion of their treating oncologist.

The N-of-1 trials at Columbia University Irving Medical Center focus on both rare and untreatable cancers, including:

- Neuroendocrine
- Bladder
- Ovarian
- Prostate
- Glioblastoma
- Meningioma
- Breast
- Pancreatic
- GIST sarcoma
- Breast
- Breast
The N-of-1 trials leverage techniques from a new field called “systems biology” to predict protein activity based on the RNA profile of an individual patient’s tumor, which can be accurately and inexpensively obtained. This allows us to identify the key master regulator proteins that are critical for the cancer cell’s survival.

Extensive research has shown that targeting master regulator proteins is catastrophic for the tumor, making it virtually impossible for its cells to effectively survive and proliferate.

“We call these proteins master regulators and have developed innovative methodologies that allow their systematic discovery on an individual patient basis and the prediction of individualized therapies that target them.”

—Andrea Califano, Dr, Lead PI
N-of-1 trials at Columbia are exploring whether these methodologies could be used within a clinical context to improve precision medicine. Specifically, the researchers use super computers and high-throughput drug screens to pinpoint the master regulators of an individual tumor that are critical for its survival and to identify the drugs and drug combinations that are best suited to target them.

Only FDA-approved drugs and other investigational compounds that have already been shown to be safe in humans are being considered, thus allowing any potential findings to provide actionable options to the treating oncologist.

“This is a whole new approach that will forever change cancer therapeutics.”
–Gary Schwartz, MD, co-PI

This is a promising approach. Master Regulator analysis has already led to several discoveries that are being tested in the clinics. To name a few:

➤ It was used to discover a combination therapy (ruxolitinib and trastuzumab) for HER2-positive metastatic breast cancer, specifically for patients whose tumors no longer responded to trastuzumab alone.

➤ It helped select entinostat as a powerful treatment for a specific type of metastatic neuroendocrine tumors; this led to rapid IND approval by the FDA for a clinical trial with Syndax.

➤ It led to discovery of HDAC6 as a novel target for inflammatory breast cancer, resulting in a phase Ib clinical trial.

➤ It led to phase II clinical trials in patients with recurrent pancreatic ductal carcinoma and metastatic prostate cancer, as well as preclinical studies in osteosarcoma, the most commonly diagnosed bone tumor in children.

“A more comprehensive understanding of tumors, a systems view, might lead us to our goal of curing your cancer.”
–Hanina Hibshoosh, MD, co-PI
N-of-1 Clinical Trials
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