HHS Public Access

Author manuscript

*Pharmacotherapy*. Author manuscript; available in PMC 2018 September 01.

Published in final edited form as:

*Pharmacotherapy*. 2017 September ; 37(9): 988–989. doi:10.1002/phar.1975.

# Perspective on Precision Medicine in Oncology

**Tali M. Johnson**

Senior Clinical Research Pharmacist, Pharmaceutical Management Branch, Cancer Therapy Evaluation Program, Division of Cancer Treatment and Diagnosis, National Cancer Institute, National Institutes of Health, Bethesda, Maryland

## Abstract

The topic of precision medicine is increasingly more prevalent in the general medical literature with oncology research leading the way. Many factors, such as, availability of targeted drugs, advances in laboratory science, and improved information systems, converged to make precision medicine research possible on a large scale at the National Cancer Institute. The resultant big data will spur new kinds of research in the decades to come, but until then, all clinicians are challenged to make sense of an overabundance of information when managing individual patients.

### Keywords

The Cancer Genome Atlas; National Cancer Institute; Molecular Tumor Board

Significant scientific and medical milestones, exponential advances in genetic research, and investment in computer technology led the National Cancer Institute (NCI) to commit considerable resources toward precision medicine initiatives. By its very nature, precision medicine prompts researchers to redesign the traditional clinical trial framework that methodically tested therapies in populations of patients by using tumor histology to define eligibility. Precision medicine's master protocol concept—using biomarker profiling to define eligibility with speed and complexity—challenges the existing clinical trial infrastructure. Researchers can screen small subpopulations of patients rapidly for somatic mutations of interest, assign them to one or more targeted agents, and expand the study of targeted mutations and agents with relative ease. However, this type of trial design makes increasing demands on laboratory and bioinformatics resources as more and more infrequent mutations of interest are sought out. Large numbers of screened patients and smart trial designs are required to efficiently use these resources.[1]

Several ongoing trials at the NCI Division of Cancer Treatment and Diagnosis employ this type of master protocol concept.[1] For example, The Cancer Genome Atlas results facilitated "umbrella," biomarker-driven treatment trials with a "genotype to phenotype" approach in a single disease such as the NCI's Lung-MAP, Adjuvant Lung Cancer Enrichment Marker Identification and Sequencing Trials (ALCHEMIST), and Metastatic Papillary Renal

**For correspondence:** Tali M. Johnson, National Cancer Institute, National Institutes of Health, 9609 Medical Center Drive, Room 5W236, MSC 9725, Bethesda, MD 20892; Phone: 240-276-6575; tmjohnson@mail.nih.gov.

The author has no potential conflicts of interest.

Carcinoma (PAPMET). Several organizations are conducting “basket” studies, testing specific agents across varied tumor histologies with the same mutation of interest. NCI-Molecular Analysis for Therapy Choice (NCI-MATCH) is an ambitious, signal-finding “hybrid” study that will screen 6000 adults with advanced refractory cancers by using standard validated assays and match them to one of 20 or more targeted agents.[2,3,4] The NCI Exceptional Responders Initiative, a “phenotype to genotype” approach, collects tumor tissue and data from patients who experienced an exceptional response to standard and/or targeted therapy in the setting of otherwise underwhelming overall response rates. NCI Pediatric MATCH will screen hundreds of children with refractory pediatric malignancies and match them to one of several targeted therapies starting in 2017. Data generated from NCI precision medicine studies will be publicly available.[5] The NCI Genomic Data Commons (GDC) is a centralized system for data sharing that will likely generate prognostic and predictive information about particular treatments and even detect rare cancer drivers, which may be clinically important when selecting treatment regimens.[5]

Access to a national database may be one source for community clinicians who are challenged to manage patients effectively, as scientific findings, novel testing platforms, and a robust drug pipeline result in an overabundance of information. A multitude of United States Food and Drug Administration–approved targeted agents with companion diagnostics are available,[6] but in the absence of regulatory approval, clinicians are cautioned against off-label use of targeted agents based merely on the molecular test report of a patient’s tumor. Negative results in the SHIVA trial and underwhelming results in others point to precision medicine as a complex science that remains mostly elusive since it is the rare patient that responds exceptionally well to biomarker-driven targeted therapy used off-label.[7] Ideally, patients would be enrolled in one of many precision medicine trials, or they could receive off-label targeted therapy for a specific mutation based on sufficient evidence. A molecular tumor board can aid the clinician by recommending treatments based on available literature and interdisciplinary expertise. They are increasingly employed to interpret these highly specialized molecular testing reports, as there is variability in laboratory reporting, read depth, tissue sources, assay type, and many other factors.[8]

The molecular tumor board is to molecular testing reports as an institution’s infectious disease department is to antimicrobial susceptibility testing: the testing results and resistance patterns are interpreted by the infectious disease specialists, and the prepared antibiogram is integrated into routine practice by all clinicians. As such, the interpretation of molecular test results will become an integral component of the patient’s electronic medical record, just as routine laboratory results are now. Clinicians will encounter oncology patients in the chronic disease setting more frequently since many cancers are managed with oral agents, and patients will be subject to repeated molecular testing as resistance mechanisms are identified. Patients’ cancers develop resistance, and although agent resistance is not a concern within the population of patients with cancer like it is for antimicrobials, patient-specific agent sequencing is important for some diseases and agents already. Continuous surveillance of the latest precision medicine data will help ensure a systematic approach to the choice of agent that will optimize safe and effective medication delivery regardless of what other agent-related variables are discovered along the way in our quest for precision medicine.

## Acknowledgments

**Disclosures:** No funding was received for the development of this manuscript.

## References

1. Redmond MW, Allegra CJ. The master protocol concept. Semin Oncol. 2015; 42:724–730. [PubMed: 26433553]
2. National Cancer Institute NCI-Molecular Analysis for Therapy Choice (NCI-MATCH) Trial. Available from https://www.cancer.gov/about-cancer/treatment/clinical-trials/nci-supported/nci-match. Accessed November 5, 2016
3. Conley BA, Doroshow JH. Molecular analysis for therapy choice: NCI-MATCH. Semin Oncol. 2014; 41:297–299. [PubMed: 25023344]
4. Siu LL, Conley BA, Boerner S, et al. Next-generation sequencing to guide clinical trials. Clin Cancer Res. 2015; 21:4536–4544. [PubMed: 26473189]
5. Grossman RL, Heath AP, Ferretti V, et al. Toward a shared vision for cancer genomic data. N Engl J Med. 2016; 375:12.
6. FDA list of cleared or approved companion diagnostic devices. Available from https://www.fda.gov/medicaldevices/productsandmedicalprocedures/invitrodiagnostics/ucm301431.htm Accessed March 3, 2017
7. Fojo T. Precision oncology: a strategy we were not ready to deploy. Semin Oncol. 2016; 43:9–12. [PubMed: 26970119]
8. Knepper TC, Bell GC, Hicks JK, et al. Key lessons learned from Moffitt's molecular tumor board: the Clinical Genomics Action Committee experience. Oncologist. 2017; 22:144–151. [PubMed: 28179575]