

A Seamless Cancer Drug Development Paradigm: View from the FDA

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Major Challenges in Oncology Drug Development



- Clinical development can't keep up with rapidly evolving science
- Traditional Phase 1,2,3 progression can't provide enough information as cancers and their therapies are splintered into multiple subgroups and treatment categories
- Maturity of diagnostics lags behind individual therapeutic development
- Cost issues: need to improve success rate in development, drive rapidly toward curative interventions

Design Innovations to Address Challenges



- Master protocols
 - Study a disease or disease subset, not a particular drug
 - Objective: continuous improvement in patient outcomes
 - A highly evolved MP could evaluate new diagnostic markers as well as new therapies, regimens, combos, decision trees for therapeutic approaches
- Seamless adaptive designs
 - Important element of many master protocols
 - Single drug development programs also would benefit from adaptive designs for dose-finding, adding (or dropping) certain patient cohorts, transition from exploratory to definitive trial

Regulatory Advances

- Oncology Center of Excellence
 - Tightly integrate diagnostic and therapeutic evaluation
 - Intensive interaction with the scientific, medical and patient communities
 - Multiple regulatory innovations expected from this group
- New endpoints
 - Patient reported outcomes including QOL
 - Immunotherapies—RECIST, ORR may not capture effect
 - Other metrics—e.g., tumor volume for everolimus for sub-ependymal giant cell astrocytoma—have been used recently
- Totality of evidence
 - In vitro data on mechanism will be increasingly utilized, as well as pharmacology, modeling, experience in the market with similar agents and so forth

Use of Real World Evidence

- FDA just published “Real-World Evidence—What Is It and What Can It Tell Us?” NEJM Dec 6, 2016
 - Contemplates use of data from patient care for regulatory purposes
 - Considers possibility of randomizing within care setting
- Oncology is leading the way, with several groups integrating lab, e-HR, claims data from practice and generating data on how targeted therapies are being used, outcomes of treatment, adverse events, subsequent therapies
- Well-documented data could be used for subsequent indications of approved drugs in subgroups
- Ultimately may be able to merge practice setting and trial setting, so that the barriers to trial setup and data collection are minimized, and more patients in the US can participate in trials intended to optimize disease outcomes

Advances in Diagnostics

- Understanding the performance of various diagnostics with respect to drug therapy remains a challenge
- Next generation sequencing—Precision Medicine Initiative
- Moonshot—biospecimens and data banks
- However, more formal exploration of diagnostic's performance should be incorporated into clinical trials of therapeutics—perhaps in an adaptive fashion



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