Preliminary plans for NCI’s next generation of precision medicine trials

Courtesy of Jeff Moscow, M.D.
Investigational Drug Branch, CTEP, DCTD, NCI
National precision medicine trials to succeed MATCH

- MATCH trial is not accepting new arms and eventually all arms will close.
- The ComboMATCH is a successor trial in development:
  - **ComboMATCH** focuses on drug combinations versus single agent focus of MATCH.
    - No immunotherapy.
- There will also be an iMATCH and a master trial for AML/MDS.
ComboMATCH protocol organization

All trials structured with a master protocol run by one of the cooperative groups and substudies run by any or all of the cooperative groups.

ECOG-ACRIN administrative coordination

EA ComboMATCH master protocol (Contains rules for assignment of patients to treatment arms)
ComboMATCH

- Led by ECOG-ACRIN
- Extramural co-leads: Funda Meric-Bernstam and Jim Ford
- NCI co-leads: Lyndsay Harris, Jeff Moscow

**Premise:** Drug combinations are more likely to provide clinical benefit than single agents in most scenarios, so the successor trial to MATCH will focus on drug combinations

**Hypothesis:** Pre-clinical data from *in vivo* models of drug combinations can predict clinical benefit in defined patient groups
NCI central support for ComboMATCH

- **Molecular Diagnostics Network** - MDNet a network of laboratories that will provide both CLIA and non-CLIA lab support
- **Precision Medicine Analysis and Coordination Center** – PMACC - a data center that will provide data coordination, decision-making and communications support
- A common biobank
- CTEP IND
- All agents brought in under CRADA
- CTEP will provide scientific review of master protocols and substudies
- NCI-CIRB will be IRB of record
NRG Representation for ComboMATCH

NRG Representatives: R O’Cearbhaill (Steering), T Yap, K Moore, P Konstantinopoulos

Protocol Logistics: N Soto, R O’Cearbhaill

Molecular Assays: K Moore

Precision Molecular Analysis Coordinating Center: H Day

17 concepts were presented on behalf of NRG

Email any concepts to ocearbhr@mskcc.org
Pre-clinical evidence for combination

**Required:** ≥2 xenograft models that show both
1) at least additive antitumor activity of the multi-agent combination in comparison to the individual agents
2) at least prolonged stable disease, if not tumor regression, of the proposed combination.*

*Evidence can include the use of agents of the same class as the agent in the proposed trial

**Requested:** In vitro or in vivo evidence of the mechanism of action of combo

Clinical evidence for single agents and proposed combination

**Requested:** Demonstrated clinical activity of agents (or similar agents) alone or together (if available) in target population (if available)
Clinical evidence of tolerability

**Required:** AE profile of each agent and potential overlapping toxicities
Potential drug:drug interactions of each agent and combo

**Requested:** Phase 1 data of the combination if available
Phase 2 data of the combination if available

**Brief proposed schema**

**Required:** Target population – selection criteria (integral biomarker)*
- Line of therapy (2\textsuperscript{nd} or later)
- Phase 2 ready vs safety run-in needed vs phase 1 needed?
- Proposed schedule of administration
- Proposed cohorts if more than one

* Integrated and exploratory biomarkers will be performed post-hoc and analyzed by trial outcome and comparison with initial biomarker assay