ComboMATCH Request for Sub-Protocol Proposals

Dear ECOG-ACRIN Members and Community,

ECOG-ACRIN introduced the concept of ComboMATCH to the wider scientific community on June 2, 2019 at the annual meeting of the American Society of Clinical Oncology (ASCO). Subsequent to this meeting, ECOG-ACRIN is soliciting ideas for possible ComboMATCH sub-protocols.

The hypothesis behind this trial is that in vivo evidence, in particular PDX and cell line derived xenograft data, can be used to predict the benefit of drug combination therapy in multiple specified patient subgroups.

Like MATCH, ComboMATCH is conceived as a signal-seeking study. To distinguish this trial from the original MATCH trial, this trial will focus on rational combinations of agents supported by preclinical in vivo evidence.

The trial is envisioned as having an overall Master Control document managed by ECOG-ACRIN that will coordinate separate NCTN group-specific treatment “cassettes” and each cassette will have 4-6 sub-protocols. Therefore, each cassette and up to 4-6 sub-protocols will be administratively managed by each of the cooperative groups in coordination with EA. Like with NCI-MATCH, we hope to have multiple investigators involved in each arm with junior and senior investigators and translational researchers.

Sub-protocol proposals will be reviewed by the ComboMATCH Agents and Genes Working Group (C-AGWG). This will consist of 4 members from each cooperative group along with additional members with developmental therapeutics and precision oncology expertise. Accepted sub-protocols will be assembled into the different cassettes by this committee in coordination with each of the cooperative groups.

We would like to follow up now with a solicitation for ideas for ComboMATCH sub-protocols and potentially cassettes. Attached please find a brief application form.

We would like to request that members of NCTN send their suggestions to the ComboMATCH representatives of each NCTN group listed below:

ECOG-ACRIN  Peter O’Dwyer  odywer.peter@jimmy.harvard.edu
(CC: emendelsohn@ecog-acrin.org)

SWOG  Gary Lyman  glyman@fredhutch.org

Alliance  Geoff Shapiro  geoffrey_shapiro@dfci.harvard.edu

NRG  Roisin O’Cearbhaill  ocearbhr@mskcc.org
Brief scientific principles:

- Sub-protocol proposals must be supported by both a strong scientific rationale and in vivo evidence of efficacy.
- Combination therapy proposals are desired. There should be evidence that both agents in the combination are required for efficacy. The proposed need to have safety data available or justification of why a short run-in design may be considered
- Single arm, sequential or randomized designs can be considered
- Selected monotherapy arms can be considered for agents with strong rationale or preliminary signal of efficacy
- Combinations involving immunotherapy agents are discouraged unless they are supported by pre-clinical models. A separate NCI initiative is being planned that will provide relevant immune-oncology diagnostic support for signal-seeking studies involving immune-oncology agents.
- Combinations with strong preclinical data but lacking safety data can be considered for future arms after safety data is obtained. Such combinations may be referred to the ETCTN for phase 1 study by the C-AGWG.

In vivo preclinical data should demonstrate enhancement of tumor growth inhibition with a combination compared to either agent alone with tumor regression and stabilization with increased time to tumor progression. Promising agent combinations with inadequate pre-clinical data maybe referred by the C-GAWG to PDXNet for possible additional studies and data generation.

Thanks in advance for your valuable contributions.

ECOG-ACRIN