**NCI ComboMatch study**

Date Issued: April 8, 2019  
Submission Due Date: May 30th 2019  
Reply to: ocearbhr@mskcc.org

**Summary**  
NRG Oncology is soliciting concepts for the NCI ComboMatch study. This trial will focus on rational combinations of agents supported by preclinical in vivo evidence. Please note that IO combinations are NOT permitted for the ComboMatch study.

NRG Oncology will propose a cassette that includes subprotocols.

Projects are to be implemented by May, 2020.

**Background**

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 subprotocols. Therefore, each cassette and up to 4-6 subprotocols 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.

Subprotocol 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 subprotocols will be assembled into the different cassettes by this committee in coordination with each of the cooperative groups.

Brief scientific principles:

--Subprotocol 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.

The ComboMATCH committee is led by Funda Meric-Bernstam, David Hyman, Lyndsay Harris, Jeff Moscow, Peter O’Dwyer

Instructions for Applicants
We would like to request that you send your suggestions to Roisin O’Cearbhaill, your NRG Oncology representative for the ComboMATCH trial.

Please submit the form on pg 3 below to ocearbhr@mskcc.org by 5pm ET, Wednesday, May 29, 2019. Proposals should include:
• Brief description of the proposed concept, including summary of preclinical data, safety data and rationale for the combination
• Ideally all subprotocols will have a junior investigator and senior mentor.

Looking forward to our future collaborations,

Roisin O’Cearbhaill  ocearbhr@mskcc.org
646-888-4227
Chair, DT committee, NRG Oncology
Combo-Match Concept Sheet

Investigator:

Institution:

Cooperative Group Affiliation:
A) ALLIANCE  
B) ECOG/ACRIN  
C) NRG  
D) SWOG  
E) NONE

Study Design:
A) Combination therapy
B) Monotherapy

Histology and/or molecular target:

Background: (please include scientific rationale as well as in vitro and in vivo preclinical data)

If a Combination, is there 1) Safety data of the combination and 2) Single agent activity of proposed agents in the target population?

Please provide rationale for the use of the drug combination specifically in the proposed biomarker defined population, or if this proposal is for a biomarker unselected population, for the histologic group(s).