

NCI-MATCH precision medicine clinical trial releases new findings

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The National Cancer Institute's Molecular Analysis for Therapy Choice (NCI-MATCH) trial, the largest precision medicine trial of its kind, has achieved a milestone with the release of results from several treatment arms, or sub-studies, of the trial. The new results offer findings of interest for future cancer research that could ultimately play a role in bringing targeted treatments to patients with certain gene abnormalities, regardless of their cancer type.

"NCI-MATCH represents the first attempt to systematically leverage next-generation sequencing to explore so many therapies in parallel," said ECOG-ACRIN study chair Keith T. Flaherty, M.D., a medical oncologist at Massachusetts General Hospital Cancer Center in Boston. "By focusing our investigational effort on new biomarker-guided therapies in understudied [cancer](#) types, we have accelerated the opportunity to find signals of efficacy."

Findings from three arms were released at this year's American Society of Clinical Oncology (ASCO) annual meeting in Chicago, adding to findings from one arm [released in November 2017](#). The study was co-developed by NCI, part of the National Institutes of Health, and the ECOG-ACRIN Cancer Research Group, part of the NCI-sponsored National Clinical Trials Network (NCTN). ECOG-ACRIN and NCI are co-leading the trial.

NCI-MATCH, a phase 2 clinical trial, seeks to determine whether targeted therapies for people whose tumors have certain gene mutations

will be effective regardless of their [cancer type](#). Researchers use a DNA sequencing test to identify gene mutations in patients' tumors. The test looks for mutations in 143 genes associated with cancer that can be targeted by one of the drugs being studied in the trial. The trial launched in August 2015 and has nearly 40 treatment arms, each of which aims to enroll at least 35 patients whose tumors have a specific genetic change. As the first findings are released at ASCO, many other arms are still enrolling patients and several additional arms are in development for possible opening later in 2018.

"The outcomes data being released today from this groundbreaking precision medicine trial are an exciting step for NCI-MATCH," said Lyndsay Harris, M.D., of NCI's Cancer Diagnosis Program and NCI study chair. "These findings represent a large collection of data in populations of patients who may not have been studied in conventional [clinical trials](#), and they will have important implications for future precision medicine [trials](#)."

Highlights from the findings from the three arms announced at ASCO include:

Arm I studied the drug taselisib in 65 patients with mutations in the PIK3CA gene. There were no objective responses to the drug, meaning the tumors did not shrink substantially. However, 24 percent of the patients had progression-free survival—or prolonged stable disease—of greater than six months. This prolonged stable disease was seen even in patients with aggressive cancer types, including lung cancer and cholangiocarcinoma (bile duct) cancer. The observation of prolonged disease control in these cancer types suggests the drug warrants further research.

In Arm Q, the drug ado-trastuzumab emtansine (T-DM1) was studied in patients with HER2- overexpressing tumors, excluding breast and

gastric/gastroesophageal junction cancers. Partial responses (at least 30 percent shrinkage of the tumor) were seen in three of the 37 patients, each of whom had a rare cancer: mucoepidermoid carcinoma of the parotid gland, squamous cell cancer of the parotid gland, and extramammary Paget disease of the scrotum. In addition, 46 percent of the patients had stable disease, including patients with ovarian, uterine, and colorectal cancers. The researchers concluded that the findings warrant further study, particularly in certain rare cancers.

Arm W tested the drug AZD4547 in 50 patients with mutations in the FGFR pathway. Ten percent of patients had a partial response. Among four patients who had a partial response, whose tumors all had different sites of origin, two had point mutations in the FGFR2/3 gene and the other two had FGFR3 gene fusions, in which part of the FGFR gene is joined to part of another gene. This suggests that these mutations may be particularly sensitive to the drug, warranting further studies in tumors harboring these fusions.

Many of the patients in these three arms had been treated with more than three lines of therapy before entering the trial (Arm I: 37 percent, Arm Q: 33 percent, Arm W: 50 percent), so the results are particularly encouraging. It suggests that future studies in populations with earlier-stage disease could potentially see more responses.

Results of additional treatment arms that have completed accrual will be released on a rolling basis as their data mature. The trial is ongoing and enrolling [patients](#) at more than 1,100 cancer centers and community hospitals in every state, the District of Columbia, and Puerto Rico. All trial sites are either members of the research groups in the NCTN that focus on adult cancers—the Alliance for Clinical Trials in Oncology, ECOG-ACRIN Cancer Research Group, NRG Oncology, and SWOG—or are members of the NCI Community Oncology Research Program (NCORP). Genentech, a member of the Roche group, provided

the study drugs for Arms I and Q, and AstraZeneca provided the drug for Arm W.

Provided by ECOG-ACRIN Cancer Research Group

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