

TO: Clinical Research Associates and Investigators with Patients for EA9161

FROM: ECOG-ACRIN Operations Office

DATE: May 24, 2021

SUBJECT: Protocol Notice: EA9161 COVID Related Events

EA9161 - A Randomized Phase III Study of the Addition of Venetoclax to Ibrutinib and Obinutuzumab versus Ibrutinib and Obinutuzumab in Untreated Younger Patients with Chronic Lymphocytic Leukemia (CLL)

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Dear ECOG-ACRIN Investigators and Study Staff,

We want to provide an update on COVID-related deaths among participants in the EA9161 trial.

Although the reported rates of COVID-19 infection between the two arms of the EA9161 appear similar, there may be a difference in the rate of COVID-related deaths. As of 5/14/21, there are 3 reported deaths due to COVID-19 among the 381 participants randomized to the ibrutinib-obinutuzumab arm (Arm B) and 10 reported deaths due to COVID-19 among the 380 participants randomized to the ibrutinib-venetoclax-obinutuzumab arm (Arm A).

To our knowledge, this has not been seen on other randomized studies using these treatments in CLL. We asked the ECOG-ACRIN Data Safety Monitoring Committee (DSMC) to evaluate this finding. The ECOG-ACRIN DSMC has met and reviewed this information and agrees with continuing the study as designed. These findings do not appear to be related to treatment assignment or to study participation per se. The DSMC will be reevaluating the study more frequently to assure safety of participants. The next evaluation will be in July.

In the meanwhile, it is important that participants in EA9161 **who develop COVID-19 infection be referred** for immediate expert COVID-19 care which may include use of monoclonal anti-bodies (outpatients) or administration of anti-viral therapy (i.e. remdesivir) with or without dexamethasone (hospitalized) in keeping with CDC recommendations.

Also, it is recommended that participants be reminded of the CDC guidelines for high-risk individuals due to CLL and its treatment, and any other features they may have such as age or healthcare disparities. The CDC emphasizes that preventive measures for COVID-19 for high-risk individuals, such as those with CLL, is particularly important. This includes vaccination, wearing a mask and social distancing. The new guidelines for not wearing masks does not apply to high-risk individuals such as those participating on EA9161.

[\(https://www.covid19treatmentguidelines.nih.gov/therapeutic-management/\)](https://www.covid19treatmentguidelines.nih.gov/therapeutic-management/)

All participants are to be made aware of this information. To facilitate discussions with participants enrolled in EA9161, a letter has been developed that can be distributed to them. The participant letter is posted on the ECOG-ACRIN website, and its use is at your discretion.

The participant letter and listings can be accessed using the following link:

<https://webapps.ecog.org/UnblindPatTxListing/EA9161Tx>