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## **Two Phase 3 Trials in Progress: HDAC Inhibitor Pracinostat in Combination with Azacitidine; NEDD Inhibitor Pevonedistat + Aza**

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I am Guillermo Garcia-Manero, I am a Professor in the Department of Leukemia at the University of Texas MD Anderson Cancer Center in Houston, Texas. I am also the head of the Myelodysplastic Section at MD Anderson. I am going to talk today about two important presentations in the trials-in-progress session at the ASCO meeting here in Chicago in 2018.

The first one is the phase 3 randomized trial of azacitidine with or without pracinostat. This is a study on which I have the honor to serve as the principal investigator. It is a very large trial for patients with acute myelogenous leukemia. We plan to enroll close to 500 patients. This is a study basically for older patients with AML (older than 75 years of age) or patients that had not been a candidate for intensive chemotherapy. Pracinostat is a histone deacetylase inhibitor that we have tested at MD Anderson from the single-agent phase 1 to the phase 2 randomized trial, and now in phase 3. The study that led to the development of the phase 3 trial was conducted in a multi-academic program, where we treated 50 patients with azacitidine and pracinostat. In that study, we saw a complete remission rate of 42% and an overall response rate close to 50%. What was really important from that trial is that the median survival of these older patients with acute myelogenous leukemia was over 19 months; that is really an exceptional number, considering that the standard of care with azacitidine or decitabine is well below 12 months. Right now, the study is open at many centers all over the world, and of course, this is an important trial that may give us a new doublet for older patients with acute myelogenous leukemia.

The second study that I would like to mention is a study that is also ongoing with the combination of azacitidine and a compound that is known as a NEDD inhibitor, pevonedistat. This is a very interesting concept. This is a very recent publication with the phase 1 trial of azacitidine and pevonedistat in patients with myelodysplastic syndrome or chronic myelomonocytic leukemia that indicates that the response rate of this combination is close to 45%, and also with a longer duration of response. These two studies, one in older AML and one in myelodysplastic syndrome, are actually quite important and it shows the interest we have in developing new therapy for our patients.

Thank you very much for this opportunity.

**Abstracts:**

Garcia-Manero G, Fong CY, Venditti A, et al. A phase 3, randomized study of pracinostat (PRAN) in combination with azacitidine (AZA) versus placebo in patients  $\geq 18$  years with newly diagnosed acute myeloid leukemia (AML) unfit for standard induction chemotherapy (IC) ASCO 2018. Abstract TPS7078.

<https://meetinglibrary.asco.org/record/165456/abstract>

Sekeres M, Fram R, Hua Z, et al. Phase 3 study of first line pevonedistat (PEV) + azacitidine (AZA) versus single-agent AZA in patients with higher-risk myelodysplastic syndromes (HR MDS), chronic myelomonocytic leukemia (CMML) or low-blast acute myelogenous leukemia (AML) ASCO 2018. Abstract TPS7077.

<https://meetinglibrary.asco.org/record/165469/abstract>