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616.ACUTE MYELOID LEUKEMIAS: INVESTIGATIONAL THERAPIES, EXCLUDING TRANSPLANTATION AND CELLULAR IMMUNOTHERAPIES

Ongoing Phase III Randomized Trial of Salvage DFP-10917 Vs. Non-Intensive Reinduction or Intensive Reinduction for Acute Myelogenous Leukemia (AML)

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Background: DFP-10917 is a deoxycytidine analogue with a novel structure. It contains a side chain cyanide (CN) group at the 2 carbon of deoxyribose that induces DNA damage in a manner unique from structurally related nucleoside analogues (eg, cytarabine, decitabine, or gemcitabine). When administered at high doses, DFP-10917 inactivates deoxyribonucleic acid (DNA) polymerase leading to S-phase arrest similar to cytarabine. When administered at low concentrations by continuous infusion, it displays an alternative, potentially advantageous, mechanism of action - DNA strand breakage leading to G2/M phase arrest and ultimately cell apoptosis. The strand breakage occurs via a spontaneous beta elimination reaction that requires no additional enzymatic activity.

There is no current standard treatment for patients with relapsed/refractory (R/R) AML. Results of a completed Phase I/II study in R/R AML (D11-11002; NCT01702155) demonstrated preliminary efficacy of DFP-10917 in this indication, with a ~50% complete response (CR) rate in Phase II. Five of 14 patients who achieved CR proceeded to stem cell transplantation. Based on completed studies, risks associated with DFP-10917 are predominantly hematological (eg, neutropenia, anemia, febrile neutropenia, leukopenia, lymphopenia, thrombocytopenia).

Study Design and Methods: Based on promising Phase II results, the Sponsor initiated Study D18-11141 (NCT03926624), a Phase III, randomized, controlled study to compare the rate and duration of CR in patients with AML R/R to 2-4 prior induction regimens. Patients receive either DFP-10917 or non-intensive reinduction (low-dose cytarabine [LoDAC], azacitidine, decitabine, venetoclax + LoDAC or azacitidine or decitabine) or intensive reinduction (high and intermediate dose cytarabine regimens). Patients assigned to DFP-10917 receive 6 mg/m ^{2}/day by continuous infusion for 14 days followed by a 14-day rest period. Control treatment is administered per physician's decision.

Adults aged ≥18 years with histologically or pathologically confirmed diagnosis of AML based on World Health Organization classification and adequate performance status (≤2) and organ function are eligible.

Study Status: The study is ongoing at 34 study centers in the United States. As of July 2023, 162 patients were enrolled, with 82 assigned to DFP-10917. A majority of the patients are male (57.4%) and aged <75 years (83.3%). Overall, 44% have AML with myelodysplasia-related changes; 36% have AML not otherwise specified; and <20% have AML with recurrent genetic abnormalities or therapy-related myeloid neoplasms. Enrollment and management of patients were affected from 2020 to 2021 by COVID-19 restrictions.

A prospectively-planned interim analysis will occur after the 150 th patient randomized is followed for >2 months. Based on recruitment projections, this analysis is scheduled for 09/2023. At that time, the Data Safety Monitoring Board will review an unblinded estimate of the treatment effect for the primary endpoint of CR, with the study either stopped for superiority or futility or continuing to a final analysis. If continued, the number of patients required for the final analysis will range from 300 to 450, in increments of 50, with the number determined based on the size of the interim treatment effect for the primary endpoint of CR or the secondary endpoint of overall survival.

Disclosures Pardee: *AbbVie Pharmaceuticals:* Membership on an entity's Board of Directors or advisory committees; *Cornerstone Pharmaceuticals:* Consultancy, Research Funding; *Genentech Pharmaceuticals:* Membership on an entity's Board of Directors or advisory committees. **Keng:** *Amgen:* Research Funding. **Eshima:** *Delta-Fly Pharmaceuticals:* Current Employment. **Iizuka:** *Delta-Fly Pharmaceuticals:* Current Employment. **Zhang:** *Delta-Fly Pharmaceuticals:* Current Employment.

OffLabel Disclosure: DFP-10917 is not yet approved for the treatment of any disease.

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