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General AML

FDA lifts clinical hold on the phase I trial of UCART123 in AML

Cynthia Umukoro | Nov 09, 2017

On 6th November 2017, the U.S. Food and Drug Administration (FDA) lifted the clinical hold on clinical trials of the allogenic gene-edited Chimeric Antigen Receptor (CAR) T-cell therapy targeting CD123, UCART123, for Acute Myeloid Leukemia (AML) patients. UCART123 had previously been granted Investigational New Drug approval by the FDA for the treatment of AML which was reported here.

In September 2017, the AML Global Portal (AGP) reported on the clinical hold placed on the phase I trials of UCART123 by the FDA after the drug manufacturer's, Cellectis, reported the death of a patient with Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN) who was enrolled in the phase I ABC123 study (NCT03203369). They also reported the adverse events observed in an AML patient enrolled in the phase I AML123 study (NCT03190278).

The FDA agreed to lift the clinical hold on these two trials following revisions in the phase I UCART123 trials protocol by the drug manufacturers. The adjustments in the protocol include:

- Decrease of the cohort dose level to $6.25x10^4$ UCART123 cells/kg
- Decrease of the cyclophosphamide dose of the lympho-depleting regimen to 750 mg/m²/day over three days with a maximum daily dose of 1.33 grams of cyclophosphamide
- Inclusion of specific criteria at Day 0, the day of UCART123 infusion, such as no new uncontrolled infection after receipt of lymphodepletion, afebrile, off all but replacement dose of corticosteroids, no organ dysfunction since eligibility screening
- Provision to ensure that the next three patients to be treated in each protocol will be under the age of 65
- Provision to ensure that the enrollment will be staggered across the UCART123 protocols AML123 and ABC123: at least 28 days should elapse between the enrollments of two patients across the two studies

Cellectis say that they are "working with the investigators and clinical sites to obtain IRB's approval on the revised protocols and resume patient enrolment.

References

1. Business Wire: FDA Lifts Clinical Hold on Cellectis Phase 1 Clinical Trials with UCART123 in AML and BPDCN. 2017 Nov 6 http://www.businesswire.com/news/home/20171106006562/en/FDA-Lifts-Clinical-Hold-Cellectis-Phase-1 . [Accessed 2017 Nov 8].