HemaSphere

EHA EUROPEAN HEMATOLOGY ASSOCIATION

P555 A PHASE 1B/2 STUDY OF THE CD123-TARGETING ANTIBODY-DRUG CONJUGATE PIVEKIMAB SUNIRINE (IMGN632) IN COMBINATION WITH VENETOCLAX (VEN) AND AZACITIDINE (AZA) FOR PATIENTS WITH CD123-POSITIVE AML

Topic: 04. Acute myeloid leukemia - Clinical

Naval G. Daver[1], Pau Montesinos[2], Ahmed Aribi[3], Giovanni Martinelli[4], Jessica Altman[5], Gail Roboz[6], Eunice S. Wang[7], Patrick W. Burke[8], Deepa Jeyakumar[9], Roland B. Walter[10], Daniel J. DeAngelo[11], Harry P. Erba[12], Anjali Advani[13], Lauris Gastaud[14], Xavier Thomas[15], Elisabetta Todisco[16], Naveen Pemmaraju[1], Lordes Mendez[17], Adolfo de la Fuente[18], Gianluca Gaidano[19], Antonio Curti[20], Nicolas Boissel[21], Christian Recher[22], Christoph Schliemann[23], Paresh Vyas[24], Callum M. Sloss[25], Jiuzhou Wang[25], Kara A. Malcolm[25], Patrick A. Zweidler-McKay[25], Kendra L. Sweet[26]

[1] Department of Leukemia, The University of Texas MD Anderson, Houston, United States;[2] Hospital Universitari i Politècnic La Fe, Valencia, Spain;[3] Gehr Family Center for Leukemia Research, City of Hope, Duarte, United States;[4] Department of Experimental, Diagnostic and Specialty Medicine, Institute of Hematology "L. e A. Seràgnoli", Bologna, Italy;[5] Division of Hematology and Oncology, Northwestern University Feinberg School of Medicine, Chicago, United States;[6] Division of Hematology & Medical Oncology, Weill Cornell Medicine/New York Presbyterian Hospital, New York, United States;[7] Roswell Park Comprehensive Cancer Center, Buffalo, United States;[8] Department of Internal Medicine, Division of Hematology/Oncology, University of Michigan, Ann Arbor, United States;[9] University of California Irvine, Chao Family Comprehensive Cancer Center, Orange, United States;[10] Fred Hutchinson Cancer Research Center, Seattle, United States;[11] Department of Medical Oncology, Harvard Medical School, Dana-Farber Cancer Institute, Boston, United States;[12] Division of Hematologic Malignancies and Cellular Therapy, Duke University, Durham, United States;[13] Taussig Cancer Institute, Cleveland Clinic, Cleveland, United States;[14] Medical Oncology Department, Antoine Lacassagne Hospital, Nice, France;[15] Department of Hematology, Hospices Civils de Lyon, Lyon-Sud Hospital, Lyon, France;[16] Division of Onco-Hematology, European Institute of Oncology IRCCS, Milano, Italy;[17] Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, United States;[18] MD Anderson Cancer Center Madrid, Madrid, Spain;[19] Division of Hematology, Department of Translational Medicine, Università del Piemonte Orientale, Novara, Italy;[20] IRCCS Azienda ospedaliero-universitaria di Bologna, Istituto di Ematologia "Seràgnoli", Bologna, Italy;[21] Université de Paris, Service Hématologie, Hôpital Saint-Louis, Paris, France;[22] Service d'Hématologie, CHU de Toulouse - Institut Universitaire du Cancer Toulouse Oncopole, Toulouse, France;[23] Department of Medicine A, Hematology, Oncology and Pneumology, University Hospital Muenster, Muenster, Germany;[24] MRC Molecular Haematology Unit, Weatherall Institute of Molecular Medicine, University of Oxford, Oxford NIHR Biomedical Research Centre, and Oxford University Hospitals NHS Trust, Oxford, United Kingdom;[25] ImmunoGen, Inc., Waltham, United States;[26] Department of Malignant Hematology, H. Lee Moffitt Cancer Center and Research Institute, Tampa, United States

Background:

Overexpression of CD123 occurs in multiple hematological malignancies, including acute myeloid leukemia (AML), blastic plasmacytoid dendritic cell neoplasm (BPDCN), acute lymphoblastic leukemia (ALL) and others. With limited expression on normal hematopoietic progenitor cells, the CD123 antigen is an attractive target for new therapeutics. IMGN632 is a CD123-targeting antibody-drug conjugate (ADC) comprising a novel anti-CD123 antibody coupled, via a peptide linker, to a unique DNA-alkylating cytotoxic payload of the IGN (indolinobenzodiazepine pseudodimer) class. In preclinical models of AML, IMGN632 exhibited potent anti-leukemia activity, with a wide therapeutic index. Confirming preclinical expectations, encouraging single-agent activity has emerged for IMGN632 in the ongoing Phase I trial in patients with CD123-positive BPDCN and AML (Daver. Blood (2019) 134 (Supplement_1):734.).

Preclinical data have demonstrated increased activity with the addition of IMGN632 to AZA alone and to AZA+VEN in multiple AML xenograft and PDX models, leading to improved survival in these models (Kuruvilla. Blood (2019) 134 (Supplement_1):1375.). We have reported compelling activity (ORR 59% and CCR rate 38%) of the IMGN632 triplet in relapsed or refractory AML patients (Daver. ASH 2021 Abstract #372). The safety profile of the triplet

Abstract Book Citations: Authors, Title, HemaSphere, 2022;6:(S3):pages. The individual abstract DOIs can be found at https://journals.lww.com/hemasphere/pages/default.aspx.

included rates of cytopenias similar to those observed with AZA+VEN; additional low-grade adverse events included infusion-related reactions, dyspnea, fatigue, gastrointestinal toxicities, electrolyte imbalances, and pneumonia.

Aims: This Phase 1b/2 study is designed to determine the safety, tolerability, and preliminary anti-leukemia activity of IMGN632 when administered in combination with AZA and VEN to patients with relapsed and frontline CD123-positive AML.

Methods: Dose escalation for the IMGN632+AZA+VEN triplet is complete. The Recommended Phase 2 Dose levels are: IMGN632 45 mcg/kg given on day 7 with 14 days of VEN, and either AZA 50 OR 75 mg/m2 for 7 days of a 28-day cycle.

Results: N/A

Summary/Conclusion: Phase 2 expansion cohorts for patients with untreated/frontline and relapsed AML are enrolling to further characterize the safety profile and assess the antileukemic activity. NCT04086264

Copyright Information: (Online) ISSN: 2572-9241

Abstract Book Citations: Authors, Title, HemaSphere, 2022;6:(S3):pages. The individual abstract DOIs can be found at https://journals.lww.com/hemasphere/pages/default.aspx.