AML-262

Pivekimab Sunirine (PVEK, IMGN632) Triplet With Azacitidine and Venetoclax Shows Broad Activity in Adverse Genetic Subsets of Relapsed/ Refractory Acute Myeloid Leukemia and Reduced Infusion-Related Reactions

Naval Daver MD1, Pau Montesinos MD, PhD2, Ahmed Aribi MD3, Giovanni Martinelli MD4, Jessica K. Altman MD5, Eunice S. Wang MD6, Gail J. Roboz MD7, Patrick W. Burke MD8, Gianluca Gaidano MD9, Roland B. Walter MD, PhD, MS10, Xavier Thomas MD, PhD11, Deepa Jeyakumar MD12, Daniel J. DeAngelo MD, PhD13, Harry P. Erba MD, PhD14, Elisabetta Todisco MD, PhD15, Kebede Begna MD16, Anjali Advani MD17, Lauris Gastaud MD18, Adolfo de la Fuente MD19, Antonio Curti MD, PhD20, Lourdes M. Mendez MD, PhD21, Paresh Vyas MD22, Nicolas Boissel MD, PhD23, Norbert Vey MD24, Christian Recher MD, PhD25, Thomas Longval MD26, Uwe Platzbecker MD27, Silke Kapp-Schwörer MD28, Christoph Schliemann MD29, Marina Konopleva MD, PhD1, Laura Torres MD2, David A. Sallman MD30, Guido Marcucci MD3, Giovanni Marconi MD4, Hagop Kantarjian MD1, Callum M. Sloss PhD31, Karen E. Malcolm RN31, Patrick A. Zweidler-McKay MD, PhD31, Kendra Sweet MD30

1The University of Texas, MD Anderson Cancer Center, Houston, USA. 2Hospital Universitario La Fe de Valencia, Valencia, Spain. 3City of Hope, Duarte, USA. 4Institute of Hematology “L. e A. Seràgnoli”, Bologna, Italy. 5Northwestern University, Chicago, USA. 6Roswell Park Comprehensive Cancer Center, Buffalo, USA. 7Weill Cornell Medical College, New York, USA. 8University of Michigan, Ann Arbor, USA. 9Università del Piemonte Orientale, Novara, Italy. 10Fred Hutchinson Cancer Center, Seattle, USA. 11Hospices Civils de Lyon, Lyon-Sud Hospital, Lyon, France. 12University of California Irvine, Orange, USA. 13Dana-Farber Cancer Institute, Boston, USA. 14Duke University Health System, Durham, USA. 15European Institute of Oncology IRCCS, Milano, Italy. 16Mayo Clinic, Rochester, USA. 17Taussig Cancer Institute, Cleveland Clinic, Cleveland, USA. 18Antoine Lacassagne Hospital, Nice, France. 19The University of Texas MD Anderson Cancer Center Madrid, Madrid, Spain. 20IRCCS Azienda ospedaliero-universitaria di Bologna, Bologna, Italy. 21Beth Israel Deaconess Medical Center, Boston, USA. 22Churchill Hospital, Headington, Oxford, United Kingdom. 23Hôspital Saint-Louis, Paris, France. 24Institute Paoli-Calmettes, Marseilles, France. 25CHU de Toulouse, Toulouse, France. 26Hôpital André Mignot, Versailles, France. 27University of Leipzig Medical Center, Leipzig, Germany. 28Universitätsklinikum Ul, Ulm, Germany. 29University Hospital Muenster, Muenster, Germany. 30H. Lee Moffitt Cancer Center, Tampa, USA. 31ImmunoGen, Inc., Waltham, USA

Context: Pivekimab sunirine (PVEK, IMGN632) is a fi rst-in- class ADC comprising a CD123 high-affinity antibody, a cleavable linker, and an IGN (indolinobenzodiazepine pseudodimer) payload. PVEK with azacitidine (AZA) and venetoclax (VEN) is a novel triplet that has demonstrated anti-leukemia activity in relapsed/ refractory AML patients. Objectiv e: Evaluate the anti-leukemia activity in genetic subgroups of AML and safety of the triplet. Intervention: Patients with relapsed/refractory AML received PVEK+AZA+VEN in a three-drug escalation over a 28-day cycle: PVEK 0.015 or 0.045 mg/kg day 7, AZA 50 or 75 mg/m 2 days 1–7, and VEN 400 mg for 8, 14, or 21 days. Results: Twenty-nine patients (median age 67 y, ELN adverse 62%, prior VEN 48%) were in higher-intensity cohorts (PVEK 0.045 mg/kg and/or VEN for 14 or 21 days). The overall response rate (ORR) was 59% (4 CR, 6 CRh, 1 CRp,

6 MLFS) and the composite complete remission rate (CCR, CR+CRh+CRp+CRi) was 38%. Higher rates are seen in patients with FLT3-ITD (n=9, ORR 89%, CCR 78%), IDH2 (n=4, ORR 75%, CCR 75%), and WT1 (n=7, ORR 57%, CCR 43%) mutations. Lower rates are seen in patients with monosomy 7/abn7q (n=6, ORR 17%, CCR 17%), TP53 (n=4, ORR 25%, CCR 25%), and ASXL1 (n=6, ORR 6 7%, CCR 17%) deletions or mutations. The safety profile for the PVEK triplet is similar to AZA+VEN. No VOD, TLS, or CRS was reported. IRRs were reported in 33% (n=17, one grade 4) of patients given 1 dose of dexamethasone (8 mg) as premedication (n=51); these IRRs were most frequently tachycardia and chills, with no anaphylactic reactions reported. Following the data cut-off, there was a second grade 4 IRR, and the prophylactic regimen was increased with two additional doses of dexamethasone on the day prior to the PVEK dose. The IRR rate has dropped to 8% (3 of 38), with no grade 3+; all were grades 1–2 that resolved with limited intervention ($P<0.01$). Conclusions: The PVEK triplet with AZA+VEN demonstrates anti-leukemic activity across multiple high-risk genetic subsets of relapsed/refractory AML. Prophylactic steroids added on day −1 have significantly reduced IRRs. Expansion cohorts are now enrolling for untreated and relapsed AML patients.