HemaSphere

EHA EUROPEAN HEMATOLOGY ASSOCIATION

S248 SIERRA TRIAL RESULTS WITH A TARGETED RADIOTHERAPY, IOMAB-B, A MYELOABLATIVE CONDITIONING WITH REDUCED INTENSITY TOLERABILITY YIELDS HIGH CR, LONG TERM SURVIVAL IN HSCT INELIGIBLE ACTIVE R/R AML

Topic: SCT clinical

Boglarka Gyurkocza[1], Stuart Seropian[2], Hannah Choe*[3], Mark Litzow[4], Camille Abboud[5], Nebu Koshy[6], Patrick Stiff[7], Benjamin Tomlinson[8], Sunil Abhyankar[9], James M Foran[4], Parameswaran Hari[10], George Chen[11], Zaid Al-Kadhimi[12], Partow Kebriaei[11], Mitchell Sabloff[13], Johnnie Orozco[14], Katarzyna Jamieson[15], Margarida Silverman[16], Koen Van Besien[17], Michael Schuster[18], Arjun Law[19], Sameem Abedin[20], Karilyn Larkin, Scott Rowley[21], Pashna Munshi[22], Rachel Cook[23], Sebastian Mayer[24], Moshe Yair Levy[25], Hillard Lazarus[26], Brenda Sandmaier[27], Vijay Reddy[28,29], Jennifer Spross[29], Kathleen Mcnamara[29], Elaina Haeuber[29], Madhuri Vusirikala[29], Akash Nahar[29], John Pagel[30], Sergio Giralt[1], Avinash Desai[29], Rajneesh Nath[31]

[1]Memorial Sloan Kettering Cancer Center, United States; [2]Yale University School Of Medicine, United States; [3]Division Of Hematology, The Ohio State University, United States; [4]Mayo Clinic; [5]Medicine, Division Of Oncology, Washington University School Of Medicine; [6]Clinical Oncology Research, Charles A. Sammons Cancer Center, United States; [7]Loyola University Medical Center; [8]Seidman Cancer Center, University Hospitals Cleveland Medical Center, United States; [9]Division Of Hematologic Malignancies And Cellular Therapeutics, Kansas University Medical Center, United States; [10]Iovance Biotherapeutics, Inc., United States; [11]Md Anderson Cancer Center; [12]University Of Alabama At Birmingham, United States; [13]Ottawa Blood Disease Centre, The Ottawa Hospital, Canada; [14]Department Of Medicine, Fred Hutchinson Cancer Research Center, United States; [15]Lineberger Comprehensive Cancer Center, University Of North Carolina, United States; [16]University Of Iowa Hospitals & Clinics, United States; [17]University Hospitals Cleveland Medical Center; [18]Stony Brook University Hospital; [19]Princess Margaret Cancer Centre; [20]Division Of Hematology And Oncology, Medical College Of Wisconsin; [21]John Theurer Cancer Center, Adult Blood And Marrow Transplantation Program, Hackensack University Medical Center; [22]Georgetown Lombardi Comprehensive Cancer Center; [23]Oregon Health & Science University; [24]Division Of Hematology And Oncology, Weill Cornell Medicine, New York Presbyterian Hospital; [25]Baylor University Medical Center; [26]Case Western Reserve University; [27]Fred Hutchinson Cancer Research Center; [28]Redbud Medicine, China; [29]Actinium Pharmaceuticals, United States; [30]Loxo Oncology At Lilly, United States; [31]Stem Cell Transplant Cellular Therapy And Acute Leukemia, Banner Md Anderson Cancer Center, United States

Background:

Despite recent advances in the treatment of acute myeloid leukemia (AML), prognosis for patients with relapsed, refractory (R/R) disease remains poor. The only potentially curative option for these patients is allogeneic hematopoietic stem cell transplantation (HSCT). However, only a minority reach complete remission (CR) or sufficient disease control to allow for HSCT, and moreover induction and conditioning regimens are poorly tolerated in the older population. Iomab-B (^{131}I-apamistamab) is an anti-CD45 radioimmunoconjugate delivering targeted myeloablative radioactivity to stem cells and leukemic blasts with reduced intensity tolerability.

Aims:

SIERRA (NCT02665065) is a multi-centre, randomized, controlled phase 3 study comparing the efficacy of Iomab-B based conditioning versus physician's choice of conventional care (CC) in older, R/R AML with active disease routinely ineligible for HSCT. Primary endpoint was durable CR (dCR), defined as CR ≥6 mos with or without platelet recovery (CRp).

Methods:

Pts ≥55 years of age with active R/R AML were randomized (1:1) to CC or Iomab-B with fludarabine and total body irradiation (2 Gy) followed by HSCT. CC pts achieving CR received physician's choice conditioning and HSCT. Pts not achieving CR could crossover (CO) to Iomab-B-based conditioning followed by HSCT. Assessment

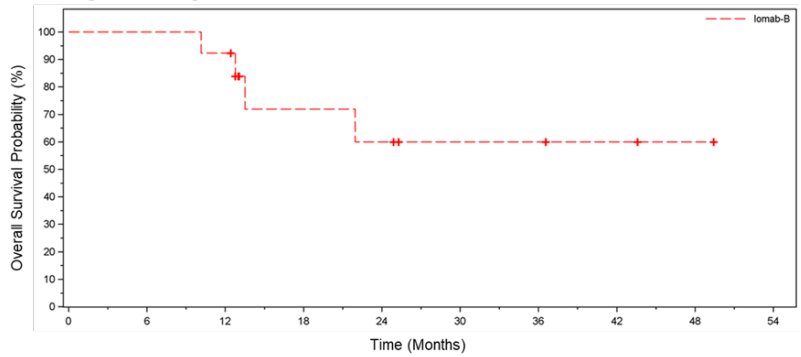
Abstract Book Citations: Authors, Title, HemaSphere, 2023;7(S3):pages. The individual abstract DOIs can be found at https://journals.lww.com/hemasphere/pages/default.aspx.

for CR/CRp occurred between days 28-56 post HSCT or initiation of therapy on the CC arm. Pts in CR/CRp were evaluated for the primary endpoint of dCR 6 mos after achieving initial CR/CRp.

Results:

Baseline pt characteristics were balanced between both arms. 61% pts failed targeted therapies prior to enrolment, of whom 66% received venetoclax-based therapy. Median time to HSCT was 29 and 66.5 days on Iomab-B and CC arms (CC pts who had CR/CRp), respectively. The median infused activity of Iomab-B was 664.4 and 613.3 mCi in Iomab-B and CO arms respectively with median dose to marrow of 16 Gy in both arms. All pts who received the therapeutic dose of Iomab-B (n=66) underwent HSCT vs 14 (18.2%) on CC arm. Of evaluable pts (Iomab: 59; CC: 64), 44 (74.6%) pts on the Iomab-B arm achieved initial CR/CRp compared to 4 (6.3%) on CC. Durable CR rates were 22% vs 0% (95% CI; 12.29, 34.73; p<0.0001). The median overall survival (OS) was 6.4 vs 3.2 mos for pts receiving Iomab-B-based conditioning followed by HSCT vs non-CO pts on CC arm, respectively. Median OS in the CO vs non-CO cohorts on the CC arm was 7.1 vs 3.2 mos (HR=0.51; 95% CI [0.31, 0.85]; p=0.0078). OS in pts receiving Iomab-B and HSCT achieving dCR (n=13) was 92% and 60% at 1 and 2 yrs respectively (Figure 1). Event-free survival (EFS) at 6 mos on Iomab-B vs CC was 26% vs 0.2% (HR=0.22; 95% CI [0.15, 0.34]; p<0.0001). Iomab-B-based conditioning followed by HSCT was well tolerated with a favourable safety profile, with lower rates of sepsis in pts receiving Iomab-B based conditioning vs pts undergoing standard of care HSCT.

Figure 1: Long-Term Survival in Patients with dCR



Summary/Conclusion:

In pts ≥55 yrs with active R/R AML, Iomab-B was able to safely deliver myeloablative doses of targeted radiation to bone marrow. Iomab-B based conditioning with HSCT resulted in rapid engraftment and high initial CR/CRp rates, a favourable toxicity profile and resulted in statistically significant improvement in the pre-specified primary endpoint of dCR. The majority of pts who achieved dCR are long term survivors, in whom OS and EFS was significant. Iomab-B based conditioning was well-tolerated and provided access to HSCT with curative potential in a vulnerable pt population traditionally not considered eligible for HSCT.