ELSEVIER

Blood 142 (2023) 5938–5940

The 65th ASH Annual Meeting Abstracts

ONLINE PUBLICATION ONLY

615.ACUTE MYELOID LEUKEMIAS: COMMERCIALLY AVAILABLE THERAPIES, EXCLUDING TRANSPLANTATION AND CELLULAR IMMUNOTHERAPIES

Real World Outcomes of Patients with Secondary Acute Myeloid Leukemia Undergoing Allogeneic Hematopoietic Cell Transplantation after Induction with Liposomal Daunorubicin-Cytarabine (CPX-351)

Guneet Kaleka, MD[1], Dat Ngo, PharmD[2], Dongyun Yang, PhD[3], Sally Mokhtari, PhD[4], Guido Marcucci, MD[5], Ryotaro Nakamura, MD[6], Vinod Pullarkat, MD[7], Caspian H. Oliai, MD[8], Amandeep Salhotra, MD[9]

[1] University of California, Los Angeles, Los Angeles, CA
[2] Pharmacy, City of Hope National Medical Center, DUARTE, CA
[3] Computational and Quantitative Medicine, City of Hope National Medical Center, Duarte, CA
[4] Clinical and Translational Project Development, City of Hope National Medical Center, Duarte
[5] Department of Hematological Malignancies Translational Science, Gehr Family Center for Leukemia Research, Hematologic Malignancies and Stem Cell Transplantation Institute, Beckman Research Institute, City of Hope National Medical Center, Duarte, CA
[6] Hematologic Malignancies and Stem Cell Transplantation Institute, City of Hope National Comprehensive Cancer Center, Duarte, CA
[7] Department of Hematology and Hematopoietic Cell Transplantation and Gehr Family Center for Leukemia Research, City of Hope Comprehensive Cancer Center, Duarte, CA
[8] Department of Medicine/Division of Hematology and Oncology, UCLA Medical Center, Los Angeles, CA
[9] Department of Hematology and Hematopoietic Cell Transplantation, City of Hope National Medical Center, Duarte, CA

Background: Liposomal Daunorubicin-Cytarabine (CPX-351 or Vyxeos), is approved for upfront treatment of adult and pediatric patients with secondary Acute Myeloid Leukemia (sAML) based on results of a randomized phase 3 trial comparing CPX-351 to conventional chemotherapy with 7+3 regimen. The study showed CPX-351 treated patients demonstrated superior complete remission (CR) rates and overall survival (OS) [Lancet et al JCO 2018]. In this study, a higher proportion of CPX-351 treated patients underwent allogeneic hematopoietic cell transplantation (alloHCT), and landmark OS analysis favored CPX-351 treated patients (HR=0.46; 95% CI: 0.24-0.89; p=0.009). Herein, we reviewed City of Hope (COH) and University of California Los Angeles Medical Center (UCLA) database for patients with sAML who underwent allogeneic HCT after CPX-351 induction to investigate OS and disease-free survival (DFS) outcomes of alloHCT in CPX-351 treated patients and to investigate if HCT outcomes are impacted by achievement of pre-HCT measurable residual disease (MRD) negative remission.

Methods: We conducted a multi-center retrospective review of 38 consecutive patients who received CPX-351-based induction before allogeneic HCT to treat sAML, at COH (n=10) and UCLA (n=28), between 2017-2021. The primary endpoint was 2-year OS and DFS in all patients. Secondary outcomes included MRD-ve complete remission (CR) after CPX-351 induction. CR was defined as <5% blasts in bone marrow (BM) aspirates. CR with with hematologic recovery (CRh) was defined as absolute neutrophil counts >1000/μL and platelets ≥100,000/μL. Patients without CRh were categorized as CR with incomplete blood recovery (CRi). MRD assessment was done on day-28 BM aspirate using multiparametric flow cytometric (FC) assay with lower limit of sensitivity of 0.01%. OS was defined as the time from the start of therapy to death and patients were censored if alive at the last follow-up, DFS was defined as the time interval from the date of response to relapse or death, whichever occurred first, and patients were censored at the last follow-up if still leukemia free. Descriptive statistics were used to summarize patient demographics, and disease characteristics. Kaplan-Meier curves and log-rank test were used to evaluate OS and LFS.

Results: Patients' demographic and disease features are summarized in Table 1. Briefly, the median age at diagnosis was 65 years (range: 14-77) and median blast percentage in BM at diagnosis was 34% (range: 20-69%). Based on ELN criteria, 25 patients (66%) had adverse risk, 12 (32%) had intermediate risk and one (2.6%) had favorable risk AML. sAML was due to antecedent hematologic disorder (AHD) in majority of patients (n=32; 84%), therapy related in four (10%) and MDS-related changes (MRC) in two patients (5.3%). Following Vyxeos treatment, the composite CR rate (CRh+CRi) was 76% (CRh in 25,

CRi in 4 patients) and 9 patients (23%) were refractory to upfront therapy. Pre-HCT MRD status was available for majority of patients (n=34; 89%). MRD negative remission by FC was achieved in 58% (20/34) patients (Table 2).
The 1- and 2-years OS was 65% (95% CI: 48-78%) and 54% (95% CI: 36-68%), respectively and the 1- and 2-years DFS was 58% (95% CI: 41-71) and 50% (95%CI: 33-64%), respectively (Figure 1). In the 34 patients with available pre-HCT MRD data, no significant difference in OS (50% vs 58%; p=0.4) or DFS (50% vs 48%; p=0.93) was observed based on pre-HCT MRD status. More patients with who were MRD-positive after induction (50%; 7/14) received myeloablative conditioning (MAC) regimen compared to only 15% (3/20) of patients with MRD negative remission.
Conclusion: CPX-351 induction in patients with sAML is associated with high MRD negative remission and promising 2-year OS/DFS after allogeneic HCT. In patients with MRD positive remission status after CPX-351 induction, MAC conditioning regimens may be preferred to reduce relapse incidence after alloHCT.

Disclosures Marcucci: *Ostentus Therapeutics:* Current equity holder in private company, Research Funding. **Nakamura:** *International Consortium:* Other: consortium chair; *Omeros:* Consultancy; *Napajen:* Consultancy; *Blue Bird:* Consultancy; *Miyarisan:* Research Funding; *Jazz Pharmaceuticals:* Consultancy, Other: research collaboration; *Mt. Sinai:* Other: Acute GVHD; *Sanofi:* Consultancy; *NCCN:* Other: guideline panel for HCT; *Leukemia & Lymphoma Society:* Other: grant reviewer; *BMT CTN Steering Committee:* Membership on an entity's Board of Directors or advisory committees; *NCTN Lymphoma Steering Committee:* Membership on an entity's Board of Directors or advisory committees. **Pullarkat:** *Servier:* Consultancy, Speakers Bureau; *Amgen:* Consultancy, Speakers Bureau; *Novartis:* Consultancy, Speakers Bureau; *Jazz Pharmaceuticals:* Consultancy, Speakers Bureau; *Pfizer:* Consultancy, Speakers Bureau; *Genentech:* Consultancy, Speakers Bureau; *AbbVie:* Consultancy, Speakers Bureau. **Oliai:** *Seagen:* Research Funding; *Arog:* Research Funding; *Jazz Pharmaceuticals:* Research Funding; *Pfizer:* Research Funding; *Novartis:* Research Funding; *Orca Bio:* Research Funding. **Salhotra:** *OrcaBio:* Research Funding; *Sanofi:* Speakers Bureau; *Rigel Pharma:* Research Funding; *Sobi:* Membership on an entity's Board of Directors or advisory committees; *Jazz Pharma:* Research Funding; *Kura Oncology:* Research Funding; *Gilead:* Research Funding; *BMS:* Research Funding.

Baseline Characteristics	
Age in years (Median)	65 years (14-77)
AML Subtype (%)	
AML-AHD	32 (86)
t-AML,	4 (10.5)
MRC	2(5)
Cytogenetic Risk Category (%)	
Favorable	1 (2.6)
Intermediate	12 (32)
Adverse	25 (66)
Clinical Outcomes	
Response to Vyxeos (%)	
Complete Remission (CRh)	25 (65.8)
Complete Remission with incomplete recovery (CRi)	4 (10.5)
MRD Negative (MRD -ve)	20 (58)
MRD Positive (MRD +ve)	14 (41)
Refractory	9 (24)
Post-HCT Outcome	
2-year OS	54% (95% CI: 36-68%)
2-year LFS	50% (95%CI: 33-64%)
2-year OS (MRD-ve vs MRD +ve)	50% vs 58% (p=0.4)
2-year LFS (MRD-ve vs MRD +ve)	50% vs 48 (p=0.93)
MAC regimen (MRD -ve vs MRD +ve)	15% vs 50% (p=0.05)

Figure 1

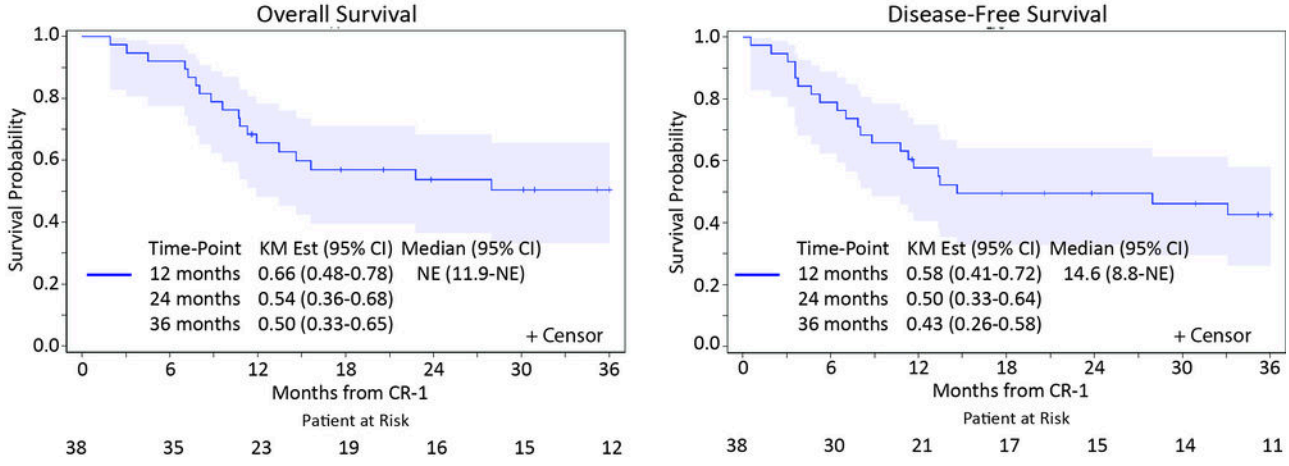

Figure 1

https://doi.org/10.1182/blood-2023-183053