ELSEVIER

Blood 142 (2023) 5935–5936

The 65th ASH Annual Meeting Abstracts

ONLINE PUBLICATION ONLY

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

Outcomes in Patients with Acute Myeloid Leukemia Treated with CLAG (cladribine, cytarabine, filgrastim) and/or Mitoxantrone with Venetoclax

Onyee Chan, MD[1], *Luis E. Aguirre, MD*[2], *Mary Burke, PharmD*[3], *Najla H Al Ali, MS*[1], *Zhuoer Xie, MDMS*[1], *Seongseok Yun, MDPhD*[1], *Andrew T. Kuykendall, MD*[1], *Eric Padron, MD*[1], *Alison R. Walker, MD*[1], *Jeffrey Lancet, MD*[1], *Rami S. Komrokji, MD*[1], *David A Sallman, MD*[4]

[1] Department of Malignant Hematology, Moffitt Cancer Center, Tampa, FL
[2] Dana-Farber Cancer Institute, Boston, MA
[3] Moffitt Cancer Center, Tampa, FL
[4] H. Lee Moffitt Cancer Center, Tampa, FL

Introduction: CLAG (cladribine, cytarabine, filgrastim) with or without M (mitoxantrone) has anti-leukemic activity in newly diagnosed (ND) and relapsed/refractory (R/R) AML (Wierzbowska *et al*. 2008, Jaglal *et al*. 2014, Seiter *et al*. 2016). Venetoclax (Ven) with hypomethylating agents (HMA), approved for patients (pts) who are not candidates for intensive chemotherapy (IC), is increasingly being employed even for pts who are fit for IC. R/R disease remains a major cause of mortality in fit pts with AML, and thus improved IC regimen is an area of active research. Various combination of IC with Ven are ongoing with promising early findings (DiNardo *et al*. 2021, Reville *et al*. 2022). In this study, we examined the outcomes of AML patients treated with CLAG and/or mitoxantrone with Ven, CLAG(M)/Ven.
Methods: This was a retrospective study of pts with AML who received CLAG(M)/Ven (Days 2-8) in 2022-2023. Clinical responses were reported using ELN 2022 criteria. Kaplan-Meier analyses were used to estimate overall survival (OS) from the date of CLAG(M)/Ven initiation.
Results: This cohort of 19 pts (8M/11F with median age of 60 [23-74] at diagnosis) is comprised of 68.4% (13/19) R/R and 31.6% (6/19) ND AML who had prior MDS directed therapy. There were 57.9% (11/19) with secondary/therapy-related AML and when including *de novo* AML pts who had mutations highly specific for secondary AML ontogeny, it increased to 78.9% (15/19). Most of the pts (68.4%, 13/19) had adverse risk disease by ELN 2022. Common mutations being *TP53* (26.3%, 5/19) followed by *IDH1/2* (21.1%), *ASXL1* (15.8%), and *RUNX1* (15.8%). There were 36.8% (7/19) who had received allogeneic hematopoietic cell transplant (alloHCT) (Table 1).
Similar number of pts received CLAG/Ven (47.5%) and CLAG-M/Ven (52.6%). Pts received on average 2.6 lines of treatment prior to CLAG(M)/Ven with 1 pt received 5 prior lines of treatment after AML diagnosis. Most of the pts, 78.9% (15/19), had prior HMA/Ven. The 30-day and 60-day morality was 5.3% (1/19) (disease status unknown at the time of death) and 26.3% (5/19) (disease status: 3 yes, 1 no, 1 unknown), respectively. Among these 5 early deaths within 60 days, 3 were ND AML that were heavily pretreated for prior MDS (average 3 lines of prior therapy) and 2 were R/R AML. All of them had prior HMA/Ven. Eighty percent (4/5) had adverse risk disease and received CLAG-M/Ven. Forty percent (2/5) had *TP53* mutation.
Objective response rate (ORR) of the entire cohort was 26.3% (5/19) (2 CR, 1 CRi, and 2 MLFS). Among those with evaluable response (n=10), ORR was 50%. Two CR/CRi pts achieved undetectable MRD by flow cytometry. MRD was not tested in the other 3 pts. Notably, ORR was higher in pts who received CLAG/Ven (44.4%, 4/9) compared to CLAG-M/Ven (10%, 1/10). No response in ND AML and 38.5% (5/13) ORR in R/R AML. Of the 47.4% (9/19) nonevaluable pts, 6 had aplastic marrow (2 died while getting induction, 2 transitioned to alloHCT, 1 moved onto next line of treatment, and 1 lost to follow up) and 3 had recovery marrow pending. For pts who achieved a response, 60% (3/5) underwent alloHCT (all of them alive without disease at data cutoff). The median time to count recovery was 42.5 days (27 days to never recovered). Prior HMA/Ven failure, high dose cytarabine failure, and mutations did not significantly impact response in this small cohort. The median OS from the time of CLAG(M)/Ven initiation was 5.5 months with a median follow up of 8.6 months (Figure 1). OS from the date of CLAG(M)/Ven was significantly shorter in pts with *TP53* mutation vs. wild-type (2 vs. 11.2 months, p=0.031).
Conclusions: Our findings showed the combination regimen CLAG(M)/Ven is feasible in pts with AML. It also provided better characterization in terms of early mortality and survivals in these pts, which can help inform future clinical trial design. ORR was

similar to what was previously reported with CLAG(M); however, it is encouraging that those who achieved CR/CRi and had MRD testing also achieved MRD negativity. Outcomes of *TP53*-mutated subset is dismal suggesting IC-based approach in this setting is limited. Larger cohort and longer follow up is needed to confirm the impact of factors such as specific regimen, mutations, and prior therapies on outcomes.

Disclosures Chan: *AbbVie:* Honoraria; *BMS:* Honoraria. **Kuykendall:** *CTI:* Consultancy; *AbbVie:* Consultancy; *Sierra Oncology:* Research Funding; *Protagonist Therapeutics, Inc.:* Consultancy, Research Funding; *Prelude:* Research Funding; *Morphosys:* Consultancy, Research Funding; *BMS:* Consultancy, Research Funding; *Blueprint:* Consultancy, Research Funding, Speakers Bureau; *GSK:* Consultancy; *Imago:* Consultancy; *Incyte:* Consultancy; *Novartis:* Consultancy. **Padron:** *Gilead:* Membership on an entity's Board of Directors or advisory committees; *Pharmaessentia:* Membership on an entity's Board of Directors or advisory committees; *BMS:* Research Funding; *Incyte:* Research Funding; *Kura:* Research Funding; *Abbvie:* Membership on an entity's Board of Directors or advisory committees; *CTI:* Membership on an entity's Board of Directors or advisory committees. **Lancet:** *Peer Voice:* Consultancy; *AbbVie Inc.:* Consultancy; *Novartis:* Consultancy; *Atheneum:* Consultancy; *MEDTalks:* Consultancy; *BerGenBio / DAVA Oncology:* Consultancy; *Boxer Capital:* Consultancy; *MD Anderson:* Consultancy; *Celgene:* Consultancy, Research Funding; *Jazz:* Consultancy; *Globe Life Sciences:* Consultancy; *Servier:* Consultancy; *Tegus:* Consultancy; *Jasper Therapeutics:* Consultancy; *The Dedham Group:* Consultancy. **Komrokji:** *Rigel, Taiho, DSI:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *AbbVie, CTI biopharma, Jazz, Pharma Essentia, Servio:* Honoraria, Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *BMS:* Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding; *Novartis:* Membership on an entity's Board of Directors or advisory committees; *Geron:* Consultancy. **Sallman:** *AbbVie, Affimed Gmbh, Gilead, Incyte, Intellisphere, LLC, Molecular Partners AG, PGEN Therapeutics, Inc., Takeda, Zentalis; Advisory board for AvenCell, BlueBird Bio, BMS, Intellia, Jasper Therapeutics, Kite, Magenta Therapeutics, NKARTA, Novartis, Orbita:* Consultancy; *Aprea, Jazz:* Research Funding.

Table 1. Patient characteristics and outcomes.

	N=19 (%)
Male	8 (42.1)
Female	11 (57.9)
Median age at diagnosis (range)	60 (23-74)
Type of AML	
De Novo	8 (42.1)
Secondary	7 (36.8)
Therapy-related	4 (21.1)
Hematology (median)	
WBC (k/uL)	1.7 (0.23-154.3)
Hgb (g/dL)	9.0 (5.2-12.5)
Platelets (k/uL)	43 (5-187)
Marrow blasts (%)	30 (15-81)
Cytogenetics	
Intermediate	11 (57.9)
Adverse	8 (42.1)
ELN 2022	
Intermediate	5 (26.3)
Adverse	13 (68.4)
Undetermined	1 (5.3)
Mutation burden (average)	2.1
TP53	5 (26.3)
IDH1/IDH2	4 (21.1)
ASXL1	3 (15.8)
RUNX1	3 (15.8)
Treatment	
CLAG/Ven	9 (47.4)
CLAG-M/Ven	10 (52.6)
Prior HMA/Ven failure[a]	15 (78.9)
Prior high dose cytarabine failure[a]	8 (42.1)
Prior lines of therapy[a] (average)	2.6
Allogeneic HCT[b]	7 (36.8)
Outcomes	
Response	
CR/CRi/MLFS	5 (26.3)
NR	5 (26.3)
Nonevaluable	9 (47.4)
Median OS (months)[c]	5.5

[a]If sAML, treatments from prior hematologic disease (e.g. MDS) were included.
[b]Did not count those received alloHCT for prior hematologic disease (3 patients)
[c]From the date of CLAG(M)/Ven initiation

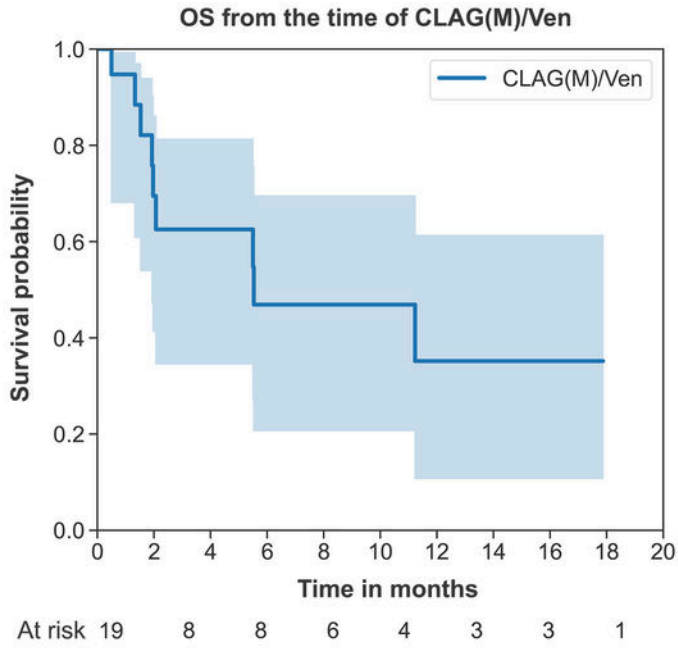

Figure 1.

Figure 1

https://doi.org/10.1182/blood-2023-173637