Initiating acute myeloid leukemia consolidation treatment in the outpatient setting

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Introduction

- Acute myeloid leukemia (AML), is a proliferation of immature myeloid cells in the bone marrow, primarily affecting older adults, with a median age at diagnosis of 69 years[1]
- Patients with AML who achieve complete remission with induction therapy require consolidation therapy since approximately two-thirds of patients will relapse[2]
- Consolidation therapy is typically administered in the inpatient setting, however, cancer patients are at increased risk of deleterious outcomes if exposed to SARS-CoV-2 due to their systemic immunosuppressive state [1,3]
- An outpatient program at the University of Arizona Cancer Center found that on average, patients treated with high-dose cytarabine (HiDAC) in the outpatient setting resulted in a cost savings of 198 hospital days and cost reduction of $529,650 as well as improved patient quality of life with comparable safety and efficacy[1]
- Treatment options for AML consolidation depend on patient-specific characteristics; HiDAC at a dose of 1.5g/m2 - 3g/m2 every 12 hours on days 1,3,5 or days 1,2,3, has been the standard of care regimen for younger patients with good- or intermediate-risk cytogenetics, while other regimens used less fit patients or patients unable to handle intensive chemotherapy include:
  - Vyxeos [liposomal DAUNOrubicin and cytarabine] or CPX-351
  - Hypomethylating agents (HMA) such as azaCITIDine or decitabine with or without venetoclax, along with targeted therapy as appropriate

Objective

The purpose of this study is to assess the safety and efficacy of outpatient versus inpatient consolidation treatment for AML in a community hospital.

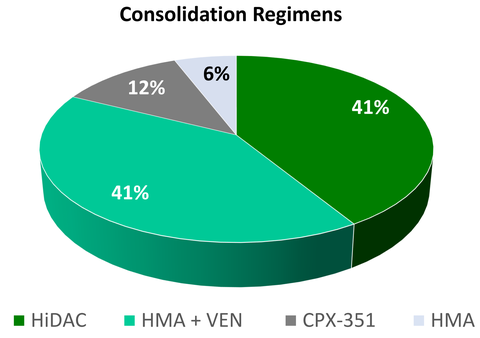
Methods

- Study Design: IRB approved single-center, retrospective chart review
- Evaluation Period:
  - Pre SARS-CoV-2: June 2019 - February 2020
  - During SARS-CoV-2: March 2020 – August 2020
- Primary outcome: Safety assessment of outpatient versus inpatient consolidation therapy through incidence of adverse drug reactions (ADR)*, infection rates and hospital re-admission within 14 days of treatment
- Secondary outcomes:
  - Pharmaceutical cost savings of outpatient versus inpatient consolidation treatment
  - Hospital readmissions within 30 days
  - Event-free survival stratified by cytogenetic risk and if received bone marrow transplant
- Exploratory outcomes:
  - Mortality rate within 30 days
  - Hospital length of stay (LOS)
- Inclusion criteria:
  - Histologically confirmed AML diagnosis
  - Received AML consolidation treatment in Baptist Hospital of Miami Oncology Inpatient Unit or Miami Cancer Institute Outpatient Infusion
  - Received an AML consolidation regimen listed above
- Exclusion criteria:
  - Pediatric patients (<18 years old)

*Toxicities graded using National Cancer Institute Common Terminology Criteria for Adverse Event [CTCAE] v. 5.0

Results

Patient Characteristics no. (%)	*Inpatient (n=8)*	*Outpatient (n=9)*
Median age, years (range)	69 (26-72)	68 (33-89)
Gender, female	5 (63)	3 (33)
Diagnoses		
• AML	7 (88)	3 (33)
• AML from MDS	1 (12)	5 (56)
• Treatment-related AML	-	1 (11)
Baseline ECOG status		
• 0	2 (25)	3 (33)
• 1	5 (63)	4 (45)
• 2	-	2 (22)
• 3	1 (12)	-



Primary Outcome	*Inpatient (n=8)*	*Outpatient (n=9)*	*P-value*
Documented Infection, no. (%)	4 (50)	3 (33)	*P*=.02
Readmission or hospitalization within 14 days, no. (%)	3 (38)	3 (33)	*P*=.55
ADR no. (%)	8 (100)	9 (100)	-

Treatment-related toxicities, no. (%)	*Inpatient (n=8)*	*Outpatient (n=9)*
Grade 3 &4 toxicities	8 (100)	9 (100)
Grade 4 neutropenia	8 (100)	8 (89)
Grade 4 thrombocytopenia	8 (100)	6 (67)
Grade 3 anemia	7 (88)	5 (56)
Grade 2 SCr increase	0	1 (11)
Febrile neutropenia	4 (50)	1 (11)

Secondary Outcome	*Inpatient (n=8)*		*Outpatient (n=9)*	
Time frame	6/19-2/20 (n=6)	3/20-8/20 (n=2)	6/19-2/20 (n=5)	3/20-8/20 (n=4)
Pharmaceutical cost, dollars	11,283.48 (14 cycles)	11,796.07 (4 cycles)	168,091.75 (22 cycles)	79,587.23 (14 cycles)
Total treatment cost, dollars	551,635.55		483,422.98	
Readmission within 30 days, no. (%)	5 (83)[a]	2 (100)[b]	3 (60)	2 (50)

a – P<.001 (Pre SARS-CoV-2 inpatient vs. outpatient setting); b – P<.001 (During SARS-CoV-2 inpatient vs. outpatient setting)

Secondary Outcome		
Median EFS based on cytogenetics, months (IQR)		
Favorable Risk	**Intermediate Risk**	**Unfavorable Risk**
14.75 (14.6-14.9)	15.2 (13.7-18.5)[a]	5.1 (3.7-12.6)[b,c]
Median EFS based on transplant status, months (IQR)		
No	**Yes**	**P-value**
5.1 (2.6-11.05)	15.2 (6.9-18.2)	0.0384

Abbreviations: EFS, event free survival; IQR, interquartile range. [a] – P=0.772 (favorable vs. intermediate); [b] – P=0.096 (intermediate vs. unfavorable); [c] – P=0.3148 (favorable versus unfavorable)

Exploratory Outcomes							
Time frame	**6/19-2/20 (n=11)**			**3/20-8/20 (n=6)**			
Regimen	CPX-351 (n=1)	HiDAC (n=6)	HMA+VEN (n=4)	CPX-351 (n=1)	HiDAC (n=1)	HMA+VEN (n=3)	HMA (n-1)
Mortality, no. (%)	0	0	0	0	1 (17)	2 (33)	0
Hospital LOS, days	0	247	0	0	39	67	0

Discussion

- Majority of patients were diagnosed with *de novo* AML or AML from myelodysplastic syndrome (MDS) and were ECOG status of 1 or greater
- Half of the patients treated in the inpatient setting had a documented infection and 38% were readmitted within 14 days of therapy; in contrast 33% of patients treated in the outpatient setting had a documented infection and were readmitted within 14 days of therapy, respectively
- Most patients received either HiDAC or an HMA combination with venetoclax for their consolidation regimen
- Outpatient administration of consolidation therapy was more cost effective than inpatient administration
- All patients experienced ADRs; 16 (94%) patients had Grade 4 neutropenia, 15 (88%) had Grade 4 thrombocytopenia, 13 (76%) had Grade 3 anemia, and 5 (29%) had febrile neutropenia
- The majority of patients (88%) required granulocyte colony-stimulating factors after administration of consolidation treatment
- The median EFS was longer, as expected, in patients with favorable and intermediate risk cytogenetics and those who proceeded to allogeneic hematopoietic stem cell transplant, although not statistically significant
- More patients were readmitted within 30 days of hospitalization in the inpatient group compared to the outpatient group
- Most readmissions were due to febrile neutropenia, transfusion support for thrombocytopenia and anemia, and infection
- Mortality occurred in 3 (18%) of 17 totally patients due to sepsis and hospice disposition

Conclusion

Patients receiving consolidation treatment at our institution in both inpatient and outpatient settings had comparable safety outcomes, median EFS, readmission at 14 days of treatment as well as a similar toxicity profile. As a result, consolidation treatment in the outpatient setting was shown to be safe, effective and led to significant cost-savings. Larger studies are necessary to further validate these findings.

Disclosures

All authors of this presentation have nothing to disclose concerning possible financial or personal relationships with commercial entities that may have direct or indirect interest in the subject matter of this presentation.

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