Gilteritinib-based combinations improve survival and enhances allogenic transplant eligibility in relapsed-refractory Acute Myeloid Leukemia(AML): Canadian Single Center Experience

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INTRODUCTION

- Outcome of relapse-refractory FLT3 mutated AML is dismal
- Use of Gilteritinib improves in EFS to 2.8 months (vs 0.7 months) and OS to 9.3 months (vs 5.6 months)
- Venetoclax –Gilteritinib and Azacytidine – Venetoclax – Gilteritinib combinations have been studied in the relapse-refractory setting in single arm studies showing high rates of CR/CRi and survival
- Despite these findings clinical equipoise exists regarding whether Gilteritinib or combination is the ideal regimen for relapse-refractory FLT3 mutated AML.

AIM

To evaluate the outcome of relapse-refractory FLT3 mutated AML treated with Gilteritinib based therapy and to compare the outcomes of monotherapy with combination therapy

METHOD

Study design

- Single center retrospective cohort study
- Included patients with relapsed-refractory *FLT3* mutated AML treated with Gilteritinib or Gilteritinib combinations between 2017 and 2024

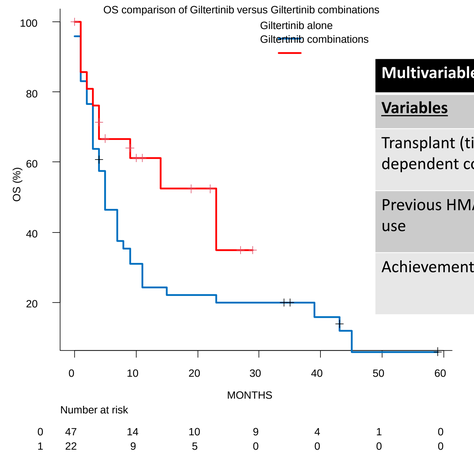
Therapy details

- Gilteritinib monotherapy
- Gilteritinib combinations included Gilteritinib + Venetoclax, Gilteritinib + azacytidine, Gilteritinib + azacytidine + Venetoclax

Endpoints:

- ***Primary endpoint***: event free survival (EFS) and overall survival(OS) of overall population
- ***Secondary endpoints***: Comparison between monotherapy and combination therapy for EFS, OS, proportion of patients proceeding to transplant

Variables (%)	Overall population (N = 69)	Gilteritinib monotherapy (N = 47)	Gilteritinib combination (N = 22)	P value (Gilteritinib monotherapy versus Gilteritinib combination)
Baseline characteristics				
Age at Gilteritinib initiation, median [range], y	65 [24 – 89]	70 [24 – 89]	58.5 [32 -71]	0.003
Setting: relapsed or refractory				1
Relapsed disease	58 (84.1)	39 (83)	19 (86.4)	
Refractory disease	11 (15.9)	8(17)	3 (13.6)	
Baseline ELN risk stratification				0.128
Favorable	5 (7.4)	2 (4.3)	3 (14.3)	
Intermediate	45 (66.2)	30 (63.8)	15 (71.4)	
Adverse	18 (26.5)	15 (31.9)	3 (1)	
FLT3 status at relapse				0.483
ITD	58 (84.1)	41 (87.2)	17 (77.3)	
TKD	8 (11.6)	4 (8.5)	4 (18.2)	
ITD + TKD	3 (4.3)	2 (4.3)	1 (4.5)	
Number of previous line of therapy, median [range]	1 [1 -3]	1 [1-3]	1 [1-3]	0.948
Previous FLT3 inhibitor use	42 (60.9)	25 (53.2)	17 (77.3)	0.068
Previous HMA-Venetoclax use	13 (18.8)	12 (25.5)	1 (4.5)	0.049
Previous allogenic stem cell transplant	18 (26.1)	13 (27.7)	5 (22.7)	0.774
Treatment details				
Gilteritinib monotherapy	47 (68.1)	47 (100)	-	
Gilteritinib + Venetoclax	8 (11.6)	-	8 (36.3)	
Gilteritinib + Azacytidine + Venetoclax	12 (17.4)	-	12 (54.5)	
Gilteritinib + Azacytidine	2 (2.9)	-	2 (9.1)	
Hematologic response				0.022
CR	6 (8.7)	2 (4.3)	4 (18.2)	
CRi/CRh	9 (13)	6 (12.8)	3 (13.6)	
MLFS	16 (23.2)	7 (14.9)	9 (40.9)	
No response	15 (21.7)	13 (27.7)	2 (9.0)	
mCRc	31 (44.9)	15 (31.9)	16 (72.7)	0.010



Multivariable cox proportional hazards model

Variables	HR (95%CI)	P value
Transplant (time dependent covariate)	0.125 (0.03 – 0.44)	0.0014
Previous HMA Venetoclax use	3.00 (1.21 – 7.44)	0.017
Achievement of mCRc	0.28 (0.13 -0.61)	0.0013

Predictors for a mCRc response

Multivariable logistic regression model

Variables	OR (95%CI)	P value
Category of therapy(Gilteritinib combination)	2.934 (0.94 – 9.14)	0.064
ELN adverse risk	0.314 (0.084 – 1.166)	0.084
Previous HMA-Venetoclax	0.237 (0.044 – 1.25)	0.091

CONCLUSIONS

- Relapsed refractory FLT3 mutated AML patients treated with gilteritinib combinations had better response rates, longer EFS, OS and transplant rates making it an effective bridge to transplant
- Use of gilteritinib combination predicts better odds of achieving mCRc making it an effective bridge to transplant

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