MDN-569 - Real-World Use of Hypomethylating Agents (HMA)/Venetoclax Combinations in Patients With Myelodysplastic Neoplasms (MDS) in the Arabian Gulf Region

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INTRODUCTION

Retrospective data thus far has supported improved responses with HMA/venetoclax combinations in both the frontline and relapsed settings. A Phase Ib trial of azacitidine and venetoclax for high-risk MDS patients demonstrated an overall response rate (ORR) of 80%. Retrospective data from the Moffitt Centre comparing HMA/venetoclax to patients who received HMA showed an ORR of 77% compared to 40% for patients who only received HMA.

AIM

Our aim was to obtain real-world evidence for use of combination HMA/venetoclax to treat myelodysplastic patients in the Arabian Gulf region.

METHOD

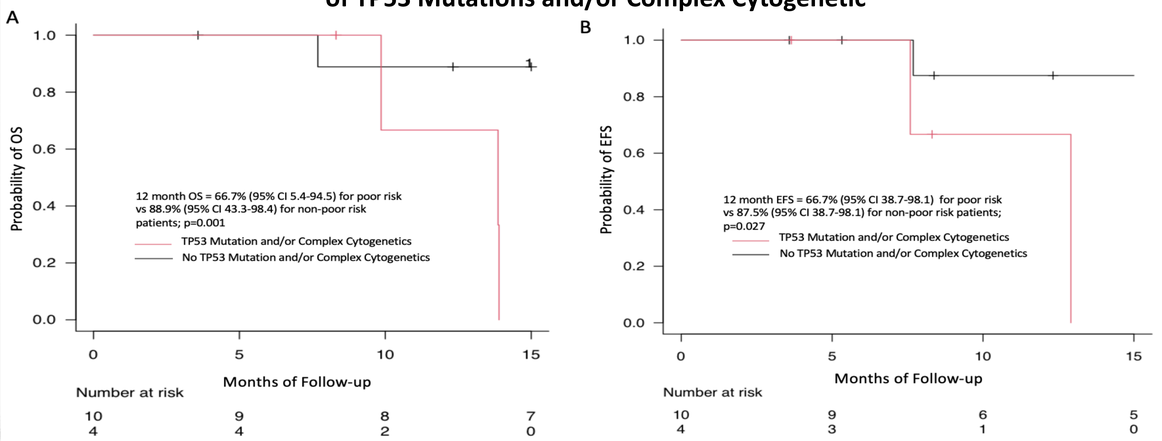
This is a retrospective study of patients with myelodysplastic neoplasm treated with a HMA/venetoclax in 4 different countries from Jan 2020 – May 2023. Cases were included if they were over the age of 18, and had a diagnosis of MDS or MDS/AML. Both frontline and relapsed/refractory patients were included. Patients were excluded if they had more than 20% blasts or received an additional agent with their regimen.

RESULTS

Table 1: Patient and Disease Demographics	
Total patients n(%)	14 (100)
Female n(%)	5 (36)
Median age (Range)	64 (51-82)
Country (KWT/QAT/SA/UAE)	8/3/2/1
Median Hb (g/L)	87
Median WBC (10^9/L)	2.3
Median ANC (10^9/L)	0.59
Median Plt (10^9/L)	47
Marrow Blasts (%)	11
Secondary MDS n(%)	3 (21)
Cytogenetics	
Diploid n(%)	6 (43)
Complex n(%)	3 (21)
Not reported/ failed n(%)	2 (14)
Gain of Ch X n(%)	1 (1)
Loss of Ch 7 n(%)	1 (1)
Deletion 5q n(%)	1 (1)
Mutations	
TP53	3
ASXL1	0
IDH1	1
IDH2	2
Others (SRSF2, STAG2, KRAS, NF1, CALR, U2AF1, CBL, SF3B1, NRAS)	10
Prognostic Score	
IPSS-R High n(%)	8 (57)
Very High n(%)	6 (43)
IPSS-M Moderate High n(%)	3 (21)
High n(%)	7 (50)
Very High n(%)	4 (39)
Treatment	
1L n(%)	13 (93)
2L n(%)	1 (1)
Azole given n(%)	10 (71)

KWT = Kuwait; QAT = Qatar; SA= Saudi Arabia; 1L = First line; 2L = Second line

Figure 1A) 12 Month OS and 1B) EFS for MDS Patients on HMA/ Venetoclax According to the Presence of TP53 Mutations and/or Complex Cytogenetic



Median follow-up was 16 months (range 4–23). A median of 6 cycles were received (range 3–14). Azacitidine was the only HMA used at a starting dose of 75mg/m^2 for 7 days. Venetoclax starting dose was 400mg (or equivalent if given with an azole) and given for a median of 28 days (0-28) Of note, most patient started treatment in 2020/21. Eleven patients achieved a CR/CRi (80%), one patient who didn't have a *TP53* mutation with complex cytogenetics, another had secondary MDS, and the third had stable disease and proceeded to transplant.

Overall survival (OS) at 12 months was 83.9% (95% CI 49.4-95.7). For patients with poor risk disease (TP53 or complex cytogenetics) OS was 66.7% (95% CI 5.4-94.5) vs 88.9% (95% CI 43.3-98.4) for non-poor risk patients; p=0.001. Median OS was 22 months (8-NR) for non-poor risk patients compared to 14 months (14-NR) for poor risk patients. Overall event-free survival (EFS) at 12 months was 81.8% (95% CI 44.7-95.1). (Fig 1A and 1B)

Four patients stopped due to failure and disease progression or transformation, 4/14 underwent stem cell transplantation, one stopped due to infectious complications, two from drug access issues, and one patient with secondary MDS had recurrence of their primary solid tumour. The most common toxicities were cytopenias and one patient died from cellulitis and COVID while on HMA/venetoclax.

CONCLUSION

The combination of HMA/ venetoclax is a feasible treatment for patients with high-risk MDS with significantly worse outcomes in patients with complex cytogenetics and/or TP53 mutations. This regimen seems to be adapted by many hematologists in our region. However, the long-term efficacy in comparison to standard of care for various subgroups of MDS needs to be explored in larger prospective studies.

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