Cost Effectiveness of Treatments After Failure of a First-Line Hypomethylating Agent in Myelodysplastic Syndromes (MDS)

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BACKGROUND & OBJECTIVE

Background

- **Myelodysplastic syndromes (MDS) are a group of disorders characterized by cytopenias and multiple genetic abnormalities[1]**
- **More than 86% of patients with MDS are 60 years or older[2]**
- **High-risk elderly MDS patients are typically treated first with hypomethylating agents (HMAs)[3]; however these are not curative and require patients to consider 2nd line treatments[4]**
- **Selecting the optimal 2nd-line treatment in MDS patients is challenging due to a lack of therapeutic options and little data regarding the risks and benefits of existing disease management**

Objective

- **Evaluate the clinical outcomes, economic impact, and cost effectiveness of currently available treatment options for MDS patients who failed 1st-line HMA therapy**

METHODS

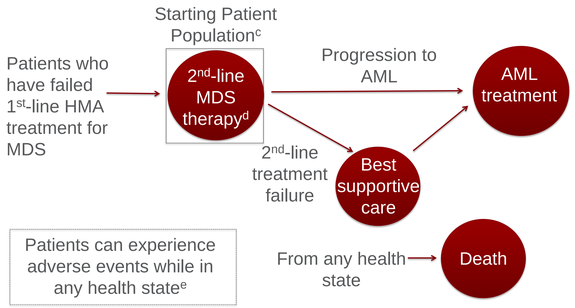
Overview

- **Study type: Markov cohort model**
- **Patient population: MDS patients who progressed on or failed previous treatment with HMAs**
- **Time-horizon: Lifetime**
- **Model cycle length: 4 weeks**
- **Perspective: Payer**
- **Model strategies:**
  - **Best supportive care (BSC)**
  - **Low-intensity chemotherapy (LIC) with BSC**
  - **High-intensity chemotherapy (HIC) with BSC**
  - **Switching HMA treatment with BSC**
  - **Hematopoietic cell transplant (HCT) with BSC**
- **Clinical and cost parameters were selected from published sources; when published data were not available, inputs were derived based on expert opinion**
- **Results were reported as:**
  - **Costs (2014 USD)**
  - **Survival in life years (LYs)**
  - **Incremental cost-effectiveness ratio (ICER)**

Model Structure

- **Hypothetical cohorts of patients who had failed a 1st-line HMA were simulated during each 4-week cycle**
- **After entering the model at the time of initiation of 2nd-line treatment, patients could:**
  - **Experience a treatment- or disease-related adverse event**
  - **Discontinue treatment**
  - **Progress to acute myeloid leukemia (AML)**
  - **Die**

Figure 1. Model Schematic[a,b]



[a] The schematic depicts a Markov model that simulates patients through 4-week cycles for their lifetime, and estimates survival and payer costs.
[b] Red circles represent model health states.
[c] Starting population represents MDS patients after failure of initial HMA therapy.
[d] 2nd-line treatment strategies/comparators are: BSC, HMA, LIC, HIC, or HCT.
[e] Adverse events include thrombocytopenia, anemia, and neutropenia.

Table 1. Treatment Cost Estimates

Treatment Costs	Cost $US 2014[a] (per 4-week cycle)	Source
BSC[b]	$1,749	5
2nd HMA[c]	$4,038	6-8
LIC[c]	$56	
HIC[c]	$38,554	
HCT (per patient)	$161,475	9
AML	$12,470	10

[a] Assuming 1.8m^2 BSA. Wastage included. The least expensive generic product was selected when identical package sizes of the same drug were available.
[b] Includes costs of hospitalization, physician visits, supportive care medication, lab tests
[c] Product administration cists added on a per-cycle basis.

Table 2. Clinical Parameters

MDS Treatment	Value	Source
Median overall survival (months)		
BSC	4.0	11
2nd HMA	6.0	12, Expert Opinion[a]
LIC	7.3	11
HIC	8.9	
HCT	19.0	
Median treatment duration (number of four-week cycles)		
HMA	4.0	12
LIC	4.0	Expert Opinion
HIC	2.5	Expert Opinion
Proportion of Patients Progressing to AML		
All Strategies	35%	Expert Opinion

[a] Estimated based on consultations with various practicing clinical oncologists.

Table 3. Adverse Event Utilization Rates and Costs

Utilization Rates	Utilization (per 4-week cycle)	Source
Red Blood Cells (units per patient)[a,b]		13, Expert opinion
BSC	5.2	
2nd HMA	2.8	
LIC	5.4	
HIC	5.0	
HCT	9.0	
Platelet (units per patient)[b]		
BSC	1.2	
2nd HMA	2.2	
LIC	3.8	
HIC	5.0	
HCT	9.0	
Growth Factors (all strategies, proportion of patients requiring a growth factor)		
Filgrastim	0.4	Data on file[c]
Epoetin	0.5	

Adverse Event Costs	Cost $2014	Source
Red Blood Cells (per transfusion)[d]	$789	14, 15
Platelets (per transfusion)[d]	$633	
Growth Factors (per patient, per model cycle)[d]		
Filgrastim	$484	
Epoetin	$300	

[a] Blood requirements and growth factor use incorporated into the model for costing purposes, to reflect resources utilized to treat thrombocytopenia, anemia, and neutropenia.
[b] Blood requirements for BSC, HMA and LIC based on Levy 2014, and doubled based on expert opinion. Values for HIC and HCT based solely on expert opinion.
[c] Burden of illness analysis of OptumInsight data to estimate healthcare utilization among 2nd-line MDS patients, conducted by PHAR, LLC, 2014.
[d] For costing, model assumed patients can receive up to 2 units in a single infusion.[14]

RESULTS

- **Treating patients who had failed 1st-line HMA with BSC was the least expensive option ($55,343 per person) but provided the shortest survival: 0.48 years.**
- **Switching patients to another HMA for 2nd-line treatment increased costs to $84,625 and extended survival only modestly.**
- **HCT patients had the highest survival (2.26 years) and lifetime costs ($492,359).**
- **Compared with BSC, the ICER for LIC was $87,343/LY gained, while HIC and HCT had ICERs of $284,303 and $291,375/LY, respectively.**
- **The strategy of switching patients to a second HMA was removed during the calculation of ICERs due to extended dominance since the next-best strategy, namely LIC, provided greater clinical benefit and had a more attractive ICER.**

Table 4. Results: All Strategies

Strategy	Lifetime Costs ($)		Mean Survival (years)		ICER
	Absolute	Difference[a]	Absolute	Difference[a]	($/LY)
BSC	$55,343	-	0.48	-	-
2nd HMA	$84,625	$29,282	0.72	0.24	Dominated[b]
LIC	$89,877	$5,252	0.88	0.15	$87,343
HIC	$146,519	$56,642	1.08	0.20	$284,303
HCT	$492,359	$345,840	2.26	1.19	$291,375

[a] Difference compared to row above.
[b] Dominated indicates there is another strategy (namely LIC) that provides greater clinical benefit with a more attractive cost effectiveness ratio.

CONCLUSION

- **For MDS patients who relapsed after, failed to respond to, or progressed during administration of a 1st-line HMA, subsequent alternative active treatments:**
  - **Provide some survival benefit**
  - **Substantially increase costs and treatment-related morbidity**
- **The significantly greater cost and accompanying increase in morbidity associated with more aggressive approaches (HIC and transplant) could be interpreted as inefficient according to current societal standards.**
- **In addition, the use of treatments such as transplant may be limited due to the risk of transplant-related adverse events, patient health status, and the availability of a suitable stem cell donor.**
- **These findings expose an unmet need among MDS patients after failure of 1st-line HMA therapy.**
- **The development of lower-cost, highly-efficacious 2nd-line MDS treatment options which do not cause an increase in cytopenia would benefit:**
  - **Clinical decision-making**
  - **Patient outcomes**
  - **Healthcare resource allocation**

Limitations

- **Further studies are needed to measure the clinical impact of 2nd-line MDS treatments as there were limited data available to inform the clinical parameters used in this analysis.**
- **This analysis did not consider the impact of treatments on quality of life. We intend to explore this in subsequent analyses.**

REFERENCES

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