# 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
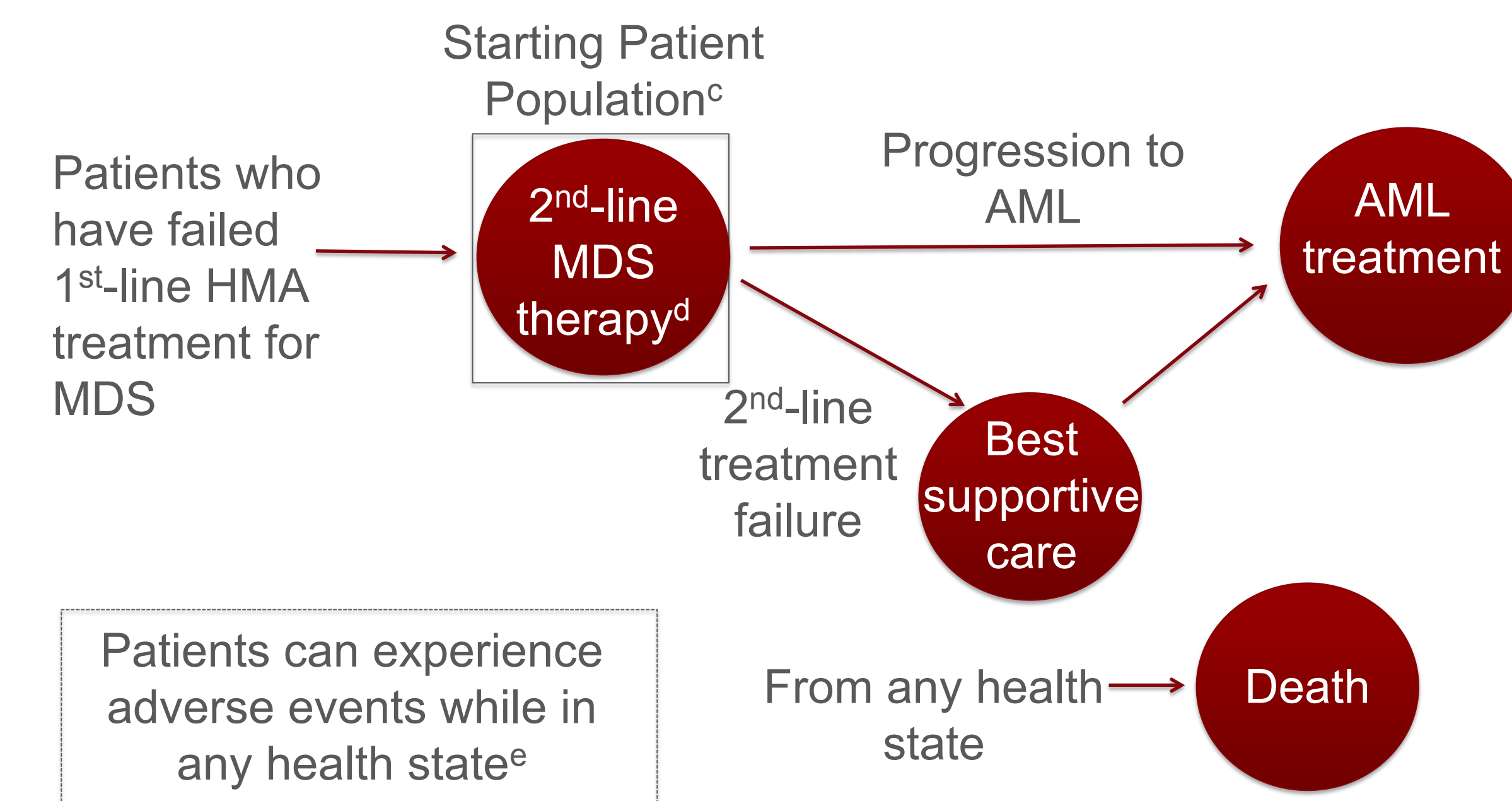
## METHODS

### 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]



Starting Patient Population[c]

Patients who have failed 1st-line HMA treatment for MDS

2nd-line MDS therapy[d]

Progression to AML

AML treatment

2nd-line treatment failure

Best supportive care

Patients can experience adverse events while in any health state[e]

From any health state

Death

[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 | |
| LIC[c] | $56 | 6-8 |
| HIC[c] | $38,554 | |
| HCT (per patient) | $161,475 | 9 |
| AML | $12,470 | 10 |

[a] Assuming 1.8m² 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 | |
| HIC | 8.9 | 11 |
| 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] | | |
| BSC | 5.2 | |
| 2nd HMA | 2.8 | |
| LIC | 5.4 | |
| HIC | 5.0 | |
| HCT | 9.0 | |
| Platelet (units per patient)[b] | | 13, Expert opinion |
| 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 | |
| Platelets (per transfusion)[d] | $633 | |
| Growth Factors (per patient, per model cycle)[d] | | 14, 15 |
| 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 ($) Absolute | Lifetime Costs ($) Difference[a] | Mean Survival (years) Absolute | Mean Survival (years) Difference[a] | ICER ($/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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