Treatment of Lower-risk MDS

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Disclosures

• CTI Biopharma, Servier Pharmaceuticals, Geron
How Recent Developments Are Changing MDS Care

Since 2020, there has been an increase in the pace of innovation, with several new MOAs established or emerging in LR- or HR-MDS\(^1\)-\(^5\) +

Newer MDS classifications and prognostic tools


**Cedazuridine + decitabine**
- FDA approval: 2020

**Luspatercept**
- FDA approval: 2020

**1L luspatercept**
- FDA approval: 2023
- BCL2? IDH?
- Telomerase inhibitor? Tamibarotene?

**Evolution of MDS classification & prognostication tools**

- 2020
- 2022
- 2023 +
Clinical Consult: Presenting with Anemia

Robert is a 75-year-old man presenting to clinic with fatigue (referred by primary care)

- Anemia (Hb: 8.5 g/dL over 6 months)
- Platelets: 250
- ANC: 5,000

What tests should be considered to confirm MDS and rule out other syndromes when assessing anemia?
Clinical Consult: Next Steps for Robert

MDS confirmed based on additional testing

- Anemia (Hb: drops to 7.5 g/dL over 3 months)
- Platelets: 250
- ANC: 5,000
- No bleeding or nutritional deficiencies
- 18% RS with erythroid dysplasia
- 2% BM blasts
- SF3B1 H662D mutation

Ring sideroblasts
LR-MDS confirmed by IPSS-M:
Transfusion burden of 6 RBC units over a 2-month period

- Anemia (Hb: now 6.5 g/dL)
- Platelets: 150,000
- ANC: 2,000
- No bleeding or nutritional deficiencies
- 18% RS with erythroid dysplasia
- 2% BM blasts
- $SF3B1$ H662D mutation

Is this patient considered to be transfusion dependent?

In 2023, what would your next step have been?
Classically, Management of Anemia in MDS Centered on ESA Therapy and Transfusion

**ESA (part of MDS anemia treatment guidelines, although not approved in the United States for MDS)**

- Larger doses may be necessary
- Loss of effect over time

**RBC transfusion**

- Iron overload risk
- Burden on patients and rare infection risk
- Transfusion dependency and increased risk of AML transformation
In LR-MDS, the Impact of Transfusion Dependence (TD) On Survival Has Been a Long-Standing Challenge

**2007 OS**

- HR = 1.91; $P < .001$

**2016 OS**

- Low- and unspecified-grade MDS, TI

Primary resistance to ESA is frequent\(^1\)

- Relapse in 70% of cases, likely due to loss of sensitivity of erythroid progenitors to ESAs
- Median DOR for ESA treatment is 18 to 24 months

**Scoring System for Prediction of Response to ESA-Based Therapy in MDS Patients\(^2\)**

<table>
<thead>
<tr>
<th>Feature</th>
<th>Range</th>
<th>Points Assigned</th>
</tr>
</thead>
<tbody>
<tr>
<td>sEPO, units/L</td>
<td>&lt;100</td>
<td>+2</td>
</tr>
<tr>
<td></td>
<td>100-500</td>
<td>+1</td>
</tr>
<tr>
<td></td>
<td>&gt;500</td>
<td>-3</td>
</tr>
<tr>
<td>Transfusion pRBC, units/mo</td>
<td>&lt;2</td>
<td>+2</td>
</tr>
<tr>
<td></td>
<td>≥2</td>
<td>-2</td>
</tr>
</tbody>
</table>

Low-risk MDS  
(add points from sEPO and PRBC together)

<table>
<thead>
<tr>
<th>Sum score</th>
<th>Good response</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;+1</td>
<td>~70%</td>
</tr>
</tbody>
</table>
| -1 to 1    | Intermediate response  
~20%            |
| <1         | Poor response   
~10%            |

Higher sEPO and transfusion burden are hallmarks of ESA failure/poor response

Clinical Consult: What if Robert Had Presented with ESA-Refractory Disease?

Assume Robert received ESA therapy for anemia after diagnosis

<table>
<thead>
<tr>
<th>Initial diagnosis of LR-MDS (RS) with anemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment:</td>
</tr>
<tr>
<td>• ESA and RBC transfusion</td>
</tr>
<tr>
<td>• After 14 months, <strong>transfusion requirement increased to 6 units/month</strong> (+ ↑ sEPO)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Is this considered ESA failure? Or is more time on therapy needed?</th>
</tr>
</thead>
<tbody>
<tr>
<td>What are the available options in the ESA-refractory setting?</td>
</tr>
<tr>
<td>• Luspatercept?</td>
</tr>
<tr>
<td>• Imetelstat?</td>
</tr>
<tr>
<td>• Lenalidomide?</td>
</tr>
<tr>
<td>• Oral cedazuridine/decitabine?</td>
</tr>
</tbody>
</table>
Enhancing Late-Stage Erythropoiesis to Alleviate Anemia

1. Luspatercept is a fusion protein that consists of a modified activin receptor (ActRIIB)—a member of the TGFβ superfamily—and the Fc of human IgG1
2. Inhibits Smad2/3 signaling and traps GDF8, GDF11, and ActB
3. Stimulates RBC production

Smad2 phosphorylation
Inhibits RBC maturation

Smad2 signaling
inhibited
Promotes RBC maturation

Ligand
Activin receptor

Ligand
Luspatercept
(ligand trap)
MEDALIST: Red Cell Transfusion Independence With Luspatercept in MDS-RS

Luspatercept (n = 153) vs Placebo (n = 76)

<table>
<thead>
<tr>
<th>No. of patients with response (% [95% CI])</th>
<th>Luspatercept</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥8 wk (Wk 1-24)</td>
<td>38 (38 [30-46])</td>
<td>13 (13 [6-23])</td>
</tr>
<tr>
<td>≥12 wk (Wk 1-24)</td>
<td>28 (28 [21-36])</td>
<td>8 (6 [3-16])</td>
</tr>
<tr>
<td>≥12 wk (Wk 1-48)</td>
<td>33 (33 [26-41])</td>
<td>12 (6 [6-21])</td>
</tr>
<tr>
<td>≥16 wk (Wk 1-24)</td>
<td>29 (19 [13-26])</td>
<td>4 (4 [1-11])</td>
</tr>
<tr>
<td>≥16 wk (Wk 1-48)</td>
<td>43 (28 [21-36])</td>
<td>7 (5 [2-15])</td>
</tr>
</tbody>
</table>

P < .001
MEDALIST: RBC-TI ≥8 Weeks$^{1,2}$

<table>
<thead>
<tr>
<th>RBC-TI ≥8 Weeks Over the Entire Treatment Period</th>
<th>Luspatercept (n = 153)</th>
<th>Placebo (n = 76)</th>
<th>Luspatercept Minus Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR (95% CI)$^a$</td>
<td>$P^a$</td>
<td></td>
</tr>
<tr>
<td>Average baseline RBC transfusion requirement, n/N (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥6 U/8 weeks</td>
<td>14/66 (21.2)</td>
<td>2/33 (6.1)</td>
<td>4.17 (.98-19.6)</td>
</tr>
<tr>
<td>≥4 to &lt;6 U/8 weeks</td>
<td>20/41 (48.8)</td>
<td>2/23 (8.7)</td>
<td>10 (2.07-48.28)</td>
</tr>
<tr>
<td>&lt;4 U/8 weeks</td>
<td>39/46 (84.8)</td>
<td>8/20 (40)</td>
<td>8.36 (2.51-27.83)</td>
</tr>
</tbody>
</table>

More luspatercept-treated patients achieved RBC-TI ≥8 weeks over the entire treatment period compared with those receiving placebo, regardless of baseline transfusion burden.

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$^a$ Determined using a Cochran-Mantel-Haenszel test.
MEDALIST: Longer-Term Evidence Confirms Substantial Reduction in Transfusion Burden With Luspatercept

Consistent benefits after median follow-up of 26 months (updated 2022 publication)

Patients stratified by: baseline sEPO level, baseline RBC transfusion burden, and RS status

Post-treatment safety follow-up
– Monitoring for other malignancies, HR-MDS or AML progression, subsequent therapies, and survival
– For 5 y from first dose or 3 y from last dose, whichever is later

Response assessment at d 169 and every 24 wk thereafter

EOT
Due to lack of clinical benefit or disease progression per IWG criteria

Luspatercept (n = 178)
1.0 mg/kg SC every 3 wk titration up to 1.75 mg/kg

Epoetin alfa (n = 178)\(^b\)
450 units/kg SC every wk titration up to 1,050 units/kg

Phase 3 COMMANDS Trial Tested Luspatercept vs Epoetin Alfa as *Upfront* Management of MDS\(^1\)

- Aged ≥18 y
- IPSS-R very low-, low-, or intermediate-risk MDS (with or without RS) by WHO 2016, with <5% blasts in BM\(^a\)
- Required RBC transfusions (2-6 pRBC units/8 wk for a minimum of 8 wk immediately prior to randomization)
- Endogenous sEPO <500 units/L
- ESA-naïve

\(^a\) MDS with del(5q) were excluded. \(^b\) Two patients randomized to the epoetin alfa arm withdrew consent prior to receiving their first dose. \(^c\) Clinical benefit defined as transfusion reduction of ≥2 pRBC units/8 wk versus baseline.

Of 301 patients included in the efficacy analysis, 86 (58.5%) patients receiving luspatercept and 48 (31.2%) receiving epoetin alfa achieved the primary endpoint. 

**COMMANDS Primary Endpoint:** Luspatercept Superior to Epoetin Alfa\(^1,2\)

- RBC-TI $\geq$12 weeks with concurrent mean Hb increase $\geq$1.5 g/dL (weeks 1-24)

**August 2023:** FDA approval of luspatercept to treat anemia in ESA-naïve adults with very low- to intermediate-risk MDS who may require regular RBC transfusions

Luspatercept and RBC-TI Across Subgroups\textsuperscript{1,2}

**Primary endpoint:** RBC-TI $\geq$12 weeks with concurrent mean Hb increase $\geq$1.5 g/dL (weeks 1-24)

$P < .0001$

<table>
<thead>
<tr>
<th>ITT Population</th>
<th>Luspatercept</th>
<th>Epoetin alfa</th>
</tr>
</thead>
<tbody>
<tr>
<td>ITT Population</td>
<td>58.5%</td>
<td>31.2%</td>
</tr>
</tbody>
</table>

Baseline sEPO Level:
- $\leq$200 units/L: 62.7%
- $>$200 units/L: 36.4%
- <4 units/8 wk: 41.4%
- 4 units/8 wk: 12.1%

Baseline RBC Transfusion Burden:
- $\leq$4 units/8 wk: 66.3%
- $>$4 units/8 wk: 45.5%

RS Status:
- RS+: 64.8%
- RS-: 41%

SF3B1 Mutation Status:
- Mutated: 69.6%
- Wild-Type: 41.5%

Prolonged Duration of RBC-TI with Luspatercept vs Epoetin Alfa

Duration, Median (95% CI), wk

<table>
<thead>
<tr>
<th></th>
<th>Luspatercept</th>
<th>Epoetin Alfa</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ITT n = 65/98</td>
<td>126.6 (108.3-NE)</td>
<td>77 (39-NE)</td>
<td>0.456 (0.26-0.798)</td>
</tr>
</tbody>
</table>

No. at Risk

<table>
<thead>
<tr>
<th></th>
<th>Luspatercept</th>
<th>Epoetin Alfa</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>98 98 91 74 61 49 42 37 31 28 21 17 11 8 6 1 1 0 0</td>
<td>71 71 63 47 33 24 23 19 15 11 9 8 7 5 5 2 2 1 0</td>
</tr>
</tbody>
</table>

**COMMANDS: DOR in RS+ and RS- Settings**

<table>
<thead>
<tr>
<th>Setting</th>
<th>Luspatercept</th>
<th>Epoetin Alfa</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RS+</td>
<td>n = 48/77</td>
<td>n = 25/48</td>
<td>0.626</td>
</tr>
<tr>
<td></td>
<td>120.9 (76.4-NE)</td>
<td>47.0 (36.6-NE)</td>
<td>(0.361-1.085)</td>
</tr>
<tr>
<td>RS-</td>
<td>n = 17/21</td>
<td>n = 15/23</td>
<td>0.492</td>
</tr>
<tr>
<td></td>
<td>NE (46-NE)</td>
<td>95.1 (35.3-NE)</td>
<td>(0.148-1.638)</td>
</tr>
</tbody>
</table>

Clinical Consult: Treatment Options for Robert

LR-MDS confirmed by IPSS-M:
Transfusion burden of 6 RBC units over a 2-month period

- Anemia (Hb: now 6.5 g/dL)
- Platelets: 150,000
- ANC: 2,000
- No bleeding or nutritional deficiencies
- 18% RS with erythroid dysplasia
- 2% BM blasts
- SF3B1 H662D mutation

Does evidence from COMMANDS support 1L luspatercept?
Clinical Consult: Practical Aspects Of Anemia Management in LR-MDS

Assume Robert is preparing to initiate luspatercept therapy

- Anemia (Hb: now 6.5 g/dL)
- Platelets: 150,000
- ANC: 2,000
- No bleeding or nutritional deficiencies
- 18% RS with erythroid dysplasia
- 2% BM blasts
- SF3B1 H662D mutation

What are the practical considerations with luspatercept for the management team?
- Safety?
- Dosing?
- Formulary?
COMMANDS: Safety Summary

Patients, n (%)

<table>
<thead>
<tr>
<th></th>
<th>Luspatercept (n = 178)</th>
<th>Epoetin Alfa (n = 176)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Any Grade</td>
<td>Grade 3/4</td>
</tr>
<tr>
<td><strong>Heme-related TEAEs</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anemia</td>
<td>17 (9.6)</td>
<td>13 (7.3)</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>11 (6.2)</td>
<td>7 (3.9)</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>9 (5.1)</td>
<td>7 (3.9)</td>
</tr>
<tr>
<td>Leukocytopenia</td>
<td>2 (1.1)</td>
<td>0</td>
</tr>
<tr>
<td><strong>TEAEs of interest</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td>26 (14.6)</td>
<td>1 (0.6)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>26 (14.6)</td>
<td>2 (1.1)</td>
</tr>
<tr>
<td>Peripheral edema</td>
<td>23 (12.9)</td>
<td>0</td>
</tr>
<tr>
<td>Asthenia</td>
<td>22 (12.4)</td>
<td>0</td>
</tr>
<tr>
<td>Nausea</td>
<td>21 (11.8)</td>
<td>0</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>21 (11.8)</td>
<td>7 (3.9)</td>
</tr>
<tr>
<td>TEE</td>
<td>8 (4.5)</td>
<td>5 (2.8)</td>
</tr>
</tbody>
</table>

**TEAEs of any grade**
- 164 (92.1%) luspatercept
- 150 (85.2%) epoetin alfa

**Median treatment duration**
- 41.6 (range, 0-165) weeks of luspatercept
- 27.0 (range, 0-171) weeks of epoetin alfa

Deaths

*Safety data are not exposure-adjusted.
Key Practical Considerations with Luspatercept

**Dosing Considerations**

- Recommended starting dose is 1 mg/kg once every 3 weeks SC in LR-MDS
- Prior to each dose, review the patient’s Hb and transfusion record
- Dose titration based on response is recommended; in COMMANDS titration was up to 1.75 mg/kg

**Recommendation for HTN management:**
- Monitor BP prior to each administration
- Manage new-onset HTN or exacerbations of pre-existing HTN using antihypertensives

Take-Homes From the COMMANDS Study\textsuperscript{1,2}

- Luspatercept shows superiority versus ESAs, with $\sim$2x patients achieving both TI and Hb increase
- Luspatercept delivers more durable responses, with nearly 2.5 years of median TI, which is $\sim$1 year longer than ESAs
- Luspatercept provides clinical benefit regardless of subgroups
- Luspatercept has a manageable and predictable safety profile that is consistent with previous clinical experience and has convenient (every 3 wk) administration
- Further evaluation of the mature dataset and longer follow-up are planned

Luspatercept is the first and only therapy to demonstrate superiority in a head-to-head study against ESAs and represents a paradigm shift in the treatment of LR-MDS–associated anemia
Clinical Consult: What if Robert Had Presented with ESA-Refractory Disease?

Assume Robert received ESA and Luspatercept therapy for anemia after diagnosis

Initial diagnosis of LR-MDS (RS) with anemia

Treatment:
- ESA, Luspatercept and RBC transfusion
- After 14 months, transfusion requirement increased to 6 units/month (+ ↑ sEPO)

Does IMerge suggest that imetelstat can be considered as a 2L/3L option?

What are the dosing and safety considerations?
**Imetelstat** is a 13-mer oligonucleotide

- Selectively targets malignant cells with continuously upregulated telomerase, inducing their apoptosis (cell death) and enabling the potential recovery of normal hematopoiesis
- Has potent activity in myeloid malignancies, as demonstrated in a study that included patients with MDS-RS

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Imetelstat: First-in-Class Telomerase Inhibitor

- Imetelstat is a direct and competitive inhibitor of telomerase activity\(^1,2\)
- Imetelstat has disease modifying potential to selectively kill malignant stem and progenitor cells enabling recovery of blood cell production\(^3,4\)

**IMerge: Higher Rates of Durable RBC-TI Observed With Imetelstat vs Placebo\(^1\)**

Phase 3 trial testing imetelstat vs placebo in 178 patients with LR-MDS relapsed/refractory to ESA or EPO

<table>
<thead>
<tr>
<th>Transfusion Independence</th>
<th>Imetelstat (n = 118)</th>
<th>Placebo (n = 60)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>8-wk TI</td>
<td>39.8 (30.9-49.3)</td>
<td>15 (7.1-26.6)</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>16-wk TI</td>
<td>31.4 (23.1-40.5)</td>
<td>6.7 (1.9-16.2)</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>24-wk TI</td>
<td>28 (20.1-37.0)</td>
<td>3.3 (0.4-11.5)</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>1-y TI</td>
<td>13.6 (8.0-21.1)</td>
<td>1 (0.0-8.9)</td>
<td>.012</td>
</tr>
</tbody>
</table>

**Dosing:**
7.5 mg/kg IV/4 wk

<table>
<thead>
<tr>
<th>Patients With Response, n (% [95% CI])</th>
</tr>
</thead>
<tbody>
<tr>
<td>Imetelstat</td>
</tr>
<tr>
<td>47 (39.8 [30.9-49.3])</td>
</tr>
<tr>
<td>37 (31.4 [23.1-40.5])</td>
</tr>
<tr>
<td>33 (28.0 [20.1-37.0])</td>
</tr>
<tr>
<td>16 (13.6 [8.0-21.1])</td>
</tr>
<tr>
<td>Placebo</td>
</tr>
<tr>
<td>9 (15.0 [7.1-26.6])</td>
</tr>
<tr>
<td>4 (6.7 [1.9-16.2])</td>
</tr>
<tr>
<td>2 (3.3 [0.4-11.5])</td>
</tr>
<tr>
<td>1 (1.7 [0.0-8.9])</td>
</tr>
</tbody>
</table>

Imetelstat 8-Week RBC-TI Responders Have Significantly Longer Duration of Transfusion Independence vs Placebo

<table>
<thead>
<tr>
<th>8-Week TI Responders</th>
<th>Imetelstat (n = 47)</th>
<th>Placebo (n = 9)</th>
<th>HR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median duration of RBC TI, wk (95% CI)</td>
<td>51.6 (26.9-83.9)</td>
<td>13.3 (8-24.9)</td>
<td>0.23 (0.09-0.57)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

No. at Risk

<table>
<thead>
<tr>
<th></th>
<th>Imetelstat</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TI Duration, wk</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>8</td>
<td>8</td>
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<td>16</td>
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<td>136</td>
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<td>1</td>
</tr>
<tr>
<td>144</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

Consistent With Prior Clinical Experience, the Most Common AEs Were Hematologic\(^1,a\)

- Grade 3-4 thrombocytopenia and neutropenia were the most frequently reported AEs and were most often reported during cycles 1-3
  - There were no fatal hematologic AEs
- Nonhematologic AEs were generally low grade
- Although \(\sim75\%\) of patients treated with imetelstat had dose modifications due to AEs, <15% of patients discontinued treatment due to TEAEs
- No cases of drug-induced liver injury were observed
  - The incidence of grade 3 liver function test laboratory abnormalities was similar in both treatment groups

<table>
<thead>
<tr>
<th>AE (≥10% of patients), n (%)</th>
<th>Imetelstat (n = 118)</th>
<th>Placebo (n = 59)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any Grade</td>
<td>Grade 3-4</td>
<td>Any Grade</td>
</tr>
<tr>
<td><strong>Hematologic</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>89 (75)</td>
<td>73 (62)</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>87 (74)</td>
<td>80 (68)</td>
</tr>
<tr>
<td>Anemia</td>
<td>24 (20)</td>
<td>23 (19)</td>
</tr>
<tr>
<td>Leukopenia</td>
<td>12 (10)</td>
<td>9 (8)</td>
</tr>
<tr>
<td><strong>Other</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asthenia</td>
<td>22 (19)</td>
<td>0</td>
</tr>
<tr>
<td>COVID-19</td>
<td>22 (19)(^b)</td>
<td>2 (2)(^c)</td>
</tr>
<tr>
<td>Headache</td>
<td>15 (13)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>14 (12)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>ALT increased</td>
<td>14 (12)</td>
<td>3 (3)</td>
</tr>
<tr>
<td>Edema peripheral</td>
<td>13 (11)</td>
<td>0</td>
</tr>
<tr>
<td>Hyperbilirubinemia</td>
<td>11 (9)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>9 (8)</td>
<td>2 (2)</td>
</tr>
<tr>
<td>Constipation</td>
<td>9 (8)</td>
<td>0</td>
</tr>
</tbody>
</table>

\(^a\) Data cutoff: October 13, 2022. \(^b\) Included COVID-19, asymptomatic COVID-19, and COVID-19 pneumonia. 
\(^c\) Only COVID-19 pneumonia events were grade 3-4 COVID-19.

DNMTi Are the Backbone of Disease-Modifying Therapy in MDS\textsuperscript{1,2}

- Median follow up is 32 mo
- mOS for 133 patients is 31.7 mo (95% CI: 28-NE)
- LFS is 29.1 mo (95% CI: 22.1-NE)

No. at Risk
Azacitidine 99 82 71 52 42 30 21 11 2 0
Observation 92 73 58 38 25 19 12 6 2 1

Azacitidine
Supportive care

Decitabine plus cedazuridine

Assessing the Role of Low-Dose Oral Decitabine/Cedazuridine in IPSS Low/Int-1 MDS

- Safety is consistent with the standard dose; AEs mostly consist of myelosuppression with no significant GI effects
- 11 of 23 patients became RBC-TI for 8 weeks; median OS was 31 months

10 mg DEC/100 mg CED daily X 5 days (Cohort B1) selected as the RP2D based on efficacy and safety

The Shape of Modern Treatment: LR-MDS

**Lower Risk**
(IPSS low, INT-1)
(IPSS-R VL, L, INT)
(IPSS-M VL, L, ML)

**Any Age**
Iron chelation
Growth factors
Luspatercept
Imetelstat?
HMAs?
Lenalidomide (5q-)
Immunomodulation
Clinical trial

**Aaged <70-75 y**
Intensive chemotherapy
HMA
(5-AZA/decitabine/oral decitabine)
Clinical trial

**Higher Risk**
(IPSS INT-2, high)
(IPSS-R INT, H, VH)
(IPSS-M MH, H, VH)

**Aaged <70-75 y**
HMA (5-AZA/decitabine/oral decitabine)
Clinical trial
Intensive chemotherapy

**AlloSCT**

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Thank You

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Our Patients!!!!

Hematology and SCT APPs, RNs and coordinators!