Established and Novel Agents for Myelodysplastic Syndromes

Mikkael A. Sekeres, MD, MS
Professor of Medicine
Director, Leukemia Program

- MDS Overview
- Disease Mechanisms
- Treatment of Lower-risk Disease
- Treatment of Higher-risk Disease

Calculation of prognostic score

<table>
<thead>
<tr>
<th>Score</th>
<th>0</th>
<th>0.5</th>
<th>1.0</th>
<th>1.5</th>
<th>2.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>BM Blast %</td>
<td>&lt; 5</td>
<td>5-10</td>
<td>11-20</td>
<td>21-29</td>
<td></td>
</tr>
<tr>
<td>Cytogenetics</td>
<td>Good</td>
<td>Intermediate</td>
<td>Poor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cytopenias</td>
<td>0/1</td>
<td>2/3</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Estimation of prognosis

<table>
<thead>
<tr>
<th>Overall Score</th>
<th>Low</th>
<th>Intermediate-1</th>
<th>Intermediate-2</th>
<th>High</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median Survival (Years)</td>
<td>5.7</td>
<td>3.5</td>
<td>1.2</td>
<td>0.4</td>
</tr>
</tbody>
</table>


Lower Risk

5-9% Blasts

10-19% Blasts

> 20% Blasts = AML!
MDS Prognosis Made Easy!!!

• **Lower Risk**
  - RA, RARS
  - RCMD, RCUD
  - MDS-U, MDS del (5q)
  - IPSS Low, Int-1 (0-1.0); IPSS-R V. Low, Low

• **Higher Risk**
  - RAEB (-1, -2)
  - IPSS Int-2, High (≥ 1.5); IPSS-R High, V. High

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**Clonal Hematopoiesis with Somatic Mutations is a Common, Age-Related Condition Associated with Adverse Outcomes**

Siddhartha Jaiswal, MD, PhD, Pierre Fontanillas, Jason Flannick, Alisa Manning, Peter Grauman, Brenton G. Mar, MD, PhD, R. Coleman Lindsley, MD, PhD, Craig Merril, Noel Burtt, Alexandra Chavez, John M. Higgins, MD, Vladislav Moltchanov, Leena Kinnunen, Heikki Koistinen, Clise Ladenvall, Gad Getz, Ph.D., Adolfo Correa, Stacey Gabriel, PhD, Sekar Kathiresan, Heather Shinglam, Michael Boehm on behalf of GoT2D, Brian Henderson on behalf of SIGMA T2D, Mark McCarthy on behalf of T2D-GENES, Jasko Tuomilehto, Christopher A. Haiman, Sc.D., Jeff Group, Gil Atzmon, James Wilson, Donna S. Neuberg, ScD, David Altshuler and Benjamin L Ebert, MD, PhD

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Clonal evolution

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Clonal hematopoiesis of indeterminate potential (CHIP)

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Exome sequencing of peripheral blood from > 17,000 individuals

Jaiswal et al., NEJM 2014
**DNMT3A** is frequently mutated

Most subjects had only one mutation

CHIP increases the risk of hematologic malignancy

Clonal hematopoiesis is associated with reduced overall survival

<table>
<thead>
<tr>
<th>All-cause mortality</th>
<th>HR(95% CI)</th>
<th>Events/Number at risk</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No mutation (ref)</td>
<td>1.4 (1.1-1.8)</td>
<td>65/246</td>
<td>0.018</td>
</tr>
<tr>
<td>McQatin present</td>
<td>1.8 (1.1-2.8)</td>
<td>606/4866</td>
<td></td>
</tr>
</tbody>
</table>

Cox proportional hazards models which included age, gender, and diabetes status as covariates, with results for cohorts analyzed as a fixed-effects meta-analysis

Clonal hematopoiesis is associated with higher risk of heart attack and stroke

**Regression models were adjusted for age, sex, BMI, lipids, blood pressure, and smoking**

- MDS Overview
- Disease Mechanisms
- **Treatment of Lower-risk Disease**
- **Treatment of Higher-risk Disease**
Efficacy and Safety of Lenalidomide Versus Placebo in RBC Transfusion-Dependent Patients With IPSS Low or Intermediate-1-Risk Myelodysplastic Syndromes Without del(5q) and Unresponsive or Refractory to Erythropoiesis-Stimulating Agents: Results From a Randomized Phase 3 Study (CC-5013-MDS-005)

Valeria Santini, Antonio Almeida, Antonio Lagos Giagounidis, Stefane Gripper, Anna Almeida, Norbert Vey, Giuliano J. Muthe, Reza Bukowski, Muthu Mitusam, Uwe Platzbecker, Ofer Slipperberg, Ron Ram, Consuelo del Canizo, Norbert Gattermann, Kiyoy Osewa, Alberto Mielke, Kyle J. Assuta, John Zhong, Francis Stéphy, Albert Hoanaplo, C.L. Beach, Pierre Fenaux

1) CIMG, University of Florence, Firenze, Italy; 2) Mattone, Portuguese de Ovarian Cancer, Lisbon, Portugal; 3) University Hospital, Royal Free London Foundation Trust, London, UK; 4) University Hospital, Brussels, Belgium; 5) University of Bologna, Italy; 6) University of Padua, Italy; 7) University Hospitals, Seville, Spain; 8) Hospital Vall d’Hebron, University of Barcelona, Barcelona, Spain; 9) The Institute of Hematology and Blood Transfusion, Prague, Czech Republic; 10) Natural History Collaborators, UK; 11) Laboratoire de Biologie du Cancer, INSERM U677, Hôpital Tenon, Université Paris 7, Paris, France; 12) Medical Oncology, San Francisco, CA, USA; 13) “Caritas”, Istituto di Ricerche Farmacologiche “Mario Negri”, Milan, Italy; 14) Service d’Hematologie, Hopital Saint Louis, Universite Paris 7, Paris, France

MDS-05: Study Design

Key inclusion criteria
- Central review of IPSS Low or Intermediate-1 risk MDS with karyotypes other than del(5q)
- RBC-TI
- Unresponsive or refractory to ESA

MDS-05: RBC-TI ≥ 8 Weeks

Significantly more LEN patients achieved RBC-TI ≥ 8 weeks versus placebo (P < 0.001)

MDS-05: Time to RBC-TI ≥ 8 Weeks

90% of the patients with RBC-TI ≥ 8 weeks responded within 4 cycles of treatment
Luspatercept PACE-MDS Study Overview

- Phase 2, multicenter, open-label, dose-finding study in IPSS low/inter-1 MDS
- Eligibility criteria: EPO >500 U/L or nonresponsive/refractory to ESA; no prior azacitidine or decitabine; no current lenalidomide, ESA, G-CSF
- Primary efficacy endpoints
  - Low Transfusion Burden (LTB): <4 U RBC/8 weeks, Hgb <10 g/dL
  - High Transfusion Burden (HTB): Reduction of ≥4 or ≥50% units transfused over 8 weeks
- Luspatercept administered SC every 3 weeks for 3 months

Efficacy Summary: HI-E Response Rate

<table>
<thead>
<tr>
<th>Patient Subgroup</th>
<th>0.125-0.5 mg/kg (N=9) n (%)</th>
<th>0.75-1.75 mg/kg (N=17) n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LTB patients (N=7)</td>
<td>0/2 (0%)</td>
<td>2/5 (40%)</td>
</tr>
<tr>
<td>HTB patients (N=19)</td>
<td>2/7 (29%)</td>
<td>5/12 (42%)</td>
</tr>
<tr>
<td>All patients (N=26)</td>
<td>2/9 (22%)</td>
<td>7/17 (41%)</td>
</tr>
</tbody>
</table>

**HI-E (IWG):**
- LTB: Hemoglobin increase ≥1.5 g/dL for ≥ 2 weeks
- HTB: Reduction of ≥4 units RBCs transfused over 8 weeks

Baseline Characteristics

<table>
<thead>
<tr>
<th>Category</th>
<th>N = 26</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr, median (range)</td>
<td>71 (27-88)</td>
</tr>
<tr>
<td>Sex, males (%)</td>
<td>13 (50%)</td>
</tr>
<tr>
<td>Prior ESA treatment, n (%)</td>
<td>14 (54%)</td>
</tr>
<tr>
<td>Prior lenalidomide treatment, n (%)</td>
<td>5 (19%)</td>
</tr>
<tr>
<td>Low Transfusion Burden (LTB)</td>
<td>N = 7 (27%)</td>
</tr>
<tr>
<td>Hemoglobin, g/dL, median (range)</td>
<td>9.1 (8.3-9.7)</td>
</tr>
<tr>
<td>Units RBC/8 weeks, median (range)</td>
<td>0 (0-2)</td>
</tr>
<tr>
<td>High Transfusion Burden (HTB)</td>
<td>N = 19 (73%)</td>
</tr>
<tr>
<td>Units RBC/8 weeks, median (range)</td>
<td>6 (4-13)</td>
</tr>
</tbody>
</table>

Data as of 03 Oct 2014
An Open-Label, Phase 2, Dose-Finding Study of Sotatercept (ACE-011) in Patients With Low- or Intermediate-risk Myelodysplastic Syndromes (MDS) or Non-Proliferative Chronic Myelomonocytic Leukemia (CMML) and Anemia (Receivability): Komrokji et al. 2015.

Table 2: Transfusion Response Among MDS Patients

<table>
<thead>
<tr>
<th>Soluble dose group</th>
<th>Overall (n=46)</th>
<th>Placebo (N=43)</th>
<th>Romiplostim (N=87)</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1=0.1 mg/kg</td>
<td>0.0 mg/kg</td>
<td>0.5 mg/kg</td>
<td>1.0 mg/kg</td>
</tr>
<tr>
<td>(n=7)</td>
<td>(n=6)</td>
<td>(n=17)</td>
<td>(n=15)</td>
</tr>
<tr>
<td>Transfusion burden reduction</td>
<td>6 (6/7)</td>
<td>7 (7/11)</td>
<td>8 (8/17)</td>
</tr>
<tr>
<td>Duration of longest response, median (range), days</td>
<td>NA</td>
<td>60 (60-120)</td>
<td>88 (80-106)</td>
</tr>
<tr>
<td>RBC T &lt; 50 days, n (%)</td>
<td>0 (0/7)</td>
<td>0 (0/9)</td>
<td>0 (0/17)</td>
</tr>
</tbody>
</table>

4/21/2015

Giagounides et al. 2014;120:1838.

Cleveland Clinic Taussig Cancer Institute

Lower-risk MDS: TPO Agonists

26-Week Test Treatment Period

- Romiplostim 750 mcg weekly (N = 160)
- Placebo weekly (N = 80)

24-Week Extended Treatment Period

- Romiplostim 750 mcg weekly + standard of care (N = 160)
- Placebo weekly + standard of care (N = 80)

Week 1, Week 26, Week 30, Week 54/Week 58

Cleveland Clinic Taussig Cancer Institute

Lower-risk MDS: TPO Agonists

Baseline platelets ≤ 20 x 10^9/L

<table>
<thead>
<tr>
<th>Baseline platelets ≤ 20 x 10^9/L</th>
<th>Placebo (N = 43)</th>
<th>Romiplostim (N = 87)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CSBE (rate/100 pt-yr)</td>
<td>501.2</td>
<td>514.9</td>
</tr>
<tr>
<td>PTE (rate/100 pt-yr)</td>
<td>1778.6</td>
<td>1250.5</td>
</tr>
</tbody>
</table>

Baseline platelets > 20 x 10^9/L

<table>
<thead>
<tr>
<th>Baseline platelets &gt; 20 x 10^9/L</th>
<th>Placebo (N = 45)</th>
<th>Romiplostim (N = 80)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CSBE (rate/100 pt-yr)</td>
<td>514.9</td>
<td>226.4</td>
</tr>
<tr>
<td>PTE (rate/100 pt-yr)</td>
<td>1250.5</td>
<td>251.8</td>
</tr>
</tbody>
</table>

RR = 0.71, p = 0.0001

RR = 0.35, p < 0.0001

58 weeks of follow-up

<table>
<thead>
<tr>
<th></th>
<th>Romiplostim</th>
<th>Placebo</th>
<th>HR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deaths</td>
<td>17.9% (30)</td>
<td>20.7% (17)</td>
<td>0.86</td>
<td>0.47, 1.56</td>
</tr>
<tr>
<td>AML</td>
<td>6.0% (10)</td>
<td>4.9% (4)</td>
<td>1.20</td>
<td>0.38, 3.84</td>
</tr>
<tr>
<td>AML-free survival</td>
<td>19.6% (33)</td>
<td>23.2% (19)</td>
<td>0.85</td>
<td>0.48, 1.50</td>
</tr>
</tbody>
</table>

Cleveland Clinic Taussig Cancer Institute

Lower-risk MDS: TPO Agonists

58 weeks of follow-up

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<thead>
<tr>
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<td>0.47</td>
</tr>
<tr>
<td>AML</td>
<td>1.20</td>
<td>0.38</td>
</tr>
<tr>
<td>AML-free survival</td>
<td>0.85</td>
<td>0.48</td>
</tr>
</tbody>
</table>

4/21/2015

Giagounides et al. 2014;120:1838.

HOA: MDS

- MDS Overview
- Disease Mechanisms
- Treatment of Lower-risk Disease
- Treatment of Higher-risk Disease
**MDS: Higher-risk, Treatment Algorithm**


**Higher-risk MDS: AZA**

AZA 75 mg/m²/d x 7 d q28 d [n=179]

Higher-risk MDS

Investigator CCR

Tx Selection

Randomization

Conventional care regimens

- Best Supportive Care [n=105]
- Low Dose Ara C [n=49]
- Std Chemo (7 + 3) [n=25]


**Log-Rank p=0.0001**

HR = 0.58 [95% CI: 0.43, 0.77]

Difference: 9.4 months

50.8%

15 months

26.2%

24.4 months

CCR

AZA

Proportion Surviving

Time (months) from Randomization

0.0

0.1

0.2

0.3

0.4

0.5

0.6

0.7

0.8

0.9

1.0


**Higher-risk MDS: DAC**

DAC 15 mg/m² q8° x 3 d q6w [n=119]

Higher-risk MDS

Randomization

Best Supportive Care [n=114]


**Median OS 10.1 vs. 8.5 months**

First clinical results of a randomized phase 2 study of SGI-110, a novel subcutaneous hypomethylating agent, in 102 patients with Intermediate or High Risk MDS or CMML

On Behalf of the SGI-110 Investigative Team

Mikkael A. Sekeres, MD, MS, Megan Othus, PhD, Alan F. List, MD, Alayoyosi Odenike, MD, Richard M. Stone, MD, Steven D. Gore, MD, Mark R. Eisen, MD, Rena Buckstein, MD, Mario R. Velasco, MD, Pierre Issa, MD, PhD, Scott Lunin, MD, Jesus Berdeja, MD, PhD, Hagop Kantarjian, MD, Joseph Mace, MD, PhD, Sandy Odenike, MD, and On Behalf of the SGI-110 Investigative Team

SGI-110: Patients Characteristics By MDS Status

<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>Prev. Treated (n=53)</th>
<th>Tx Naive (n=49)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median Age, (range)</td>
<td>72.5 (62-88)</td>
<td>71.7 (18-85)</td>
</tr>
<tr>
<td>Gender, M n (%)</td>
<td>32 (60)</td>
<td>35 (71)</td>
</tr>
<tr>
<td>ECOG PS % 0/1/2</td>
<td>22/18/21</td>
<td>27/60/7</td>
</tr>
<tr>
<td>Disease Category (IPSS) n (%)</td>
<td>4 (8)</td>
<td>29 (47)</td>
</tr>
<tr>
<td>Int-1</td>
<td>13(25)</td>
<td>5 (10)</td>
</tr>
<tr>
<td>Int-2</td>
<td>24(46)</td>
<td>9 (18)</td>
</tr>
<tr>
<td>CMML</td>
<td>10 (19)</td>
<td>12 (24)</td>
</tr>
<tr>
<td>Median BM Blast % (range)</td>
<td>8 (0-19)</td>
<td>3 (0-14)</td>
</tr>
<tr>
<td>Median Neutrophils (10³/µL)</td>
<td>0.81</td>
<td>1.64</td>
</tr>
<tr>
<td>Median Platelets (10¹²/µL)</td>
<td>37</td>
<td>62.5</td>
</tr>
<tr>
<td>Median Hb (g/dL)</td>
<td>9.30</td>
<td>9.10</td>
</tr>
<tr>
<td>Prior decitabine or azacitidine n (%)</td>
<td>52 (96)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Randomized Dose (n)</td>
<td>60 mg/m²</td>
<td>26</td>
</tr>
<tr>
<td>30 mg/m²</td>
<td>27</td>
<td>22</td>
</tr>
</tbody>
</table>

SGI-110: Best Response By MDS Status

<table>
<thead>
<tr>
<th>Response Category¹</th>
<th>Prev Treated (n=53)</th>
<th>Tx Naive (n=49)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall CR</td>
<td>12 (22.7)</td>
<td>19 (38.8)</td>
</tr>
<tr>
<td>HI</td>
<td>1 (1.9)</td>
<td>9 (18.4)</td>
</tr>
<tr>
<td>CR+mCR</td>
<td>11 (20.8)</td>
<td>10 (20.4)</td>
</tr>
<tr>
<td>mCR</td>
<td>9 (17.0)</td>
<td>7 (14.3)</td>
</tr>
<tr>
<td>HR</td>
<td>1 (1.9)</td>
<td>9 (18.4)</td>
</tr>
</tbody>
</table>

¹International Working Group 2006 MDS Response Criteria

SGI-110 in MDS/CMML

**Primary Endpoint:** Overall Response Rate (CR, mCR, PR, HI)

**Secondary Endpoints:** Transfusion independence, LINE-1 demethylatio to AML, overall survival

Data presented with data cutoff end of July 2014

SGI-110 – American Society of Hematology, 2015
North American Intergroup Randomized Phase 2 MDS Study S1117: Study Design

Higher-risk MDS or CML

AZA (IV/SC) 75 mg/m²/d (d1-7) N=92

AZA (IV/SC) + LEN (PO) 75 mg/m²/d (d1-7) + 10 mg/d x 21d N=93

AZA (IV/SC) + Vorin (PO) 75 mg/m²/d (d1-7) + 300mg BID (d3-9) N=91

Secondary Objectives: OS, RFS, LFS

Power 81%, alpha 0.05 for each combo arm vs. AZA

Groups: SWOG, ECOG, Alliance, NCIC

Total Sample Size: 276

Primary Objective: 20% improvement of ORR (CR/PR/HI) based on 2006 IWG Criteria

Secondary Objectives: OS, RFS, LFS

Febrile neutropenia (n) 10 13 (0.66) 13 (0.51) 36

GI (n) 4 11 (0.10) 23 (<0.001) 38

Rash (n) 2 12 (0.03) 1 (1) 15

Off Tx due to Toxicity/Side Effect/Complication 9% 23% (0.04) 24% (0.03) 19%

Non-protocol defined dose modifications 23% 41% (0.01) 36% (0.05) 33%

North American Intergroup Randomized Phase 2 MDS Study S1117: Response

Response Variable | AZA | AZA+LEN | AZA+VOR | Total n=260
--- | --- | --- | --- | ---
Median Tx Duration (Wks) | 25 | 24 | 20 | 23
Overall Response Rate (%) | 37 | 39 (1.0) | 24 (.07) | 33
CR/PR/Hi (%) | 24/0/13 | 18/1/9 (0.56) | 15/1/7 (1.2) | 19/1/13
CMLL ORR (%) | 33 (n=15) | 59 (.15) (n=19) | 13 (.41) (n=16) | 34
Relapse-free survival (median) | 7 months | 8 months (.45) | 11 months (.29) | 7 months
Relapse-free survival, on Tx >6 months (median) | 7 months | 7.5 months (.74) | 13 months (.11) | 8.5 months

North American Intergroup Randomized Phase 2 MDS Study S1117: Conclusions (I)

No differences in ORR comparing AZA + LEN or AZA + VOR to AZA monotherapy.

Some subgroups may have benefitted from AZA-based combinations.

Signal of RFS improvement with AZA + VOR; EFS/OS data maturing and analyses by cytogenetic subgroups pending.

North American Intergroup Randomized Phase 2 MDS Study S1117: Grade ≥3 Toxicities

| Toxicity Variable | AZA | AZA+LEN | AZA+VOR | Total n=260
--- | --- | --- | --- | ---
Febrile neutropenia (n) | 10 | 13 (0.66) | 13 (0.51) | 36
GI (n) | 4 | 11 (0.10) | 23 (<0.001) | 38
Rash (n) | 2 | 12 (0.03) | 1 (1) | 15
Off Tx due to Toxicity/Side Effect/Complication | 9% | 23% (0.04) | 24% (0.03) | 19%
Non-protocol defined dose modifications | 23% | 41% (0.01) | 36% (0.05) | 33%

North American Intergroup Randomized Phase 2 MDS Study S1117: Relapse-free Survival (II)

All Responders on Tx >6 Months

Overall Survival and Subgroup Analysis from a Randomized Phase III Study of Intravenous Rigosertib vs Best Supportive Care in Patients with Higher-risk Myelodysplastic Syndrome After Failure of Hypomethylation Agents (ONTIME Trial of ON 01910)

ONTIME Trial: Study Design

- Phase III, randomized, controlled, safety & efficacy study comparing rigosertib + BSC* vs BSC* alone (2:1)
  - Adult pts who had relapsed after, failed to respond to, or progressed during HMA therapy
  - 299 pts enrolled at 87 sites in US and Europe
  - Rigosertib administered as 1800 mg/24 hr for 72 hrs as a continuous IV ambulatory infusion
- Pts stratified by bone marrow blast count (5-19% vs 20-30%)
  - Additional information on the relationship between OS and BMBL is available in Poster #3259
- Primary endpoint = overall survival
- Analysis based on 242 events (deaths; ≥ 80% maturity)
- Median follow-up of >18 months

* BSC=Best supportive care: RBC & platelets; growth factors; hydroxyurea to manage blastic crises when pts transition to leukemia; pts on the BSC arm also allowed low-dose cytarabine, as medically justified.

ONTIME Trial: Primary Efficacy Results - ITT

<table>
<thead>
<tr>
<th></th>
<th>Rigosertib N = 199</th>
<th>BSC N = 100</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number (%) of deaths</td>
<td>161 (81%)</td>
<td>81 (81%)</td>
</tr>
<tr>
<td>Median follow-up (months)</td>
<td>17.6</td>
<td>19.5</td>
</tr>
<tr>
<td>Median survival (months)</td>
<td>8.2</td>
<td>5.9</td>
</tr>
<tr>
<td>95% CI</td>
<td>6.0 - 10.1</td>
<td>4.1 - 9.3</td>
</tr>
<tr>
<td>Stratified HR (rigosertib/BSC)</td>
<td>0.87</td>
<td></td>
</tr>
<tr>
<td>95% CI</td>
<td>0.67 - 1.14</td>
<td></td>
</tr>
<tr>
<td>Stratified log-rank p-value*</td>
<td>0.33</td>
<td></td>
</tr>
</tbody>
</table>

* Stratification factor: bone marrow blast at randomization (5-19% versus 20-30%)

ONTIME Trial: Median Overall Survival for Pts with Primary HMA Failure - Blinded, Centralized Assessment

ONTIME Trial: Conclusions

- Primary endpoint of OS did not reach statistical significance in the ITT population
  - 2.3-month improvement in median OS in the ITT population
- Rigosertib treatment-related improvement in OS was noted in the following well-balanced subgroups:
  - Primary HMA failure (64% of pts: HR = 0.69; p = 0.04)
  - IPSS-R Very High Risk (45% of pts: HR = 0.56; p = 0.005)
  - Cytogenetic criteria also important prognostic factors
    - Monosomy 7 (HR = 0.24; p = 0.003)
    - Trisomy 8 (HR = 0.34; p = 0.035)
- Continuous IV infusion with rigosertib had a favorable safety profile in this population of elderly pts with HR MDS

MDS: Conclusions

- The molecular landscape of MDS is becoming much more complex, and is being folded into clinical prognostic schemes.
- Therapy for lower-risk disease addresses specific cytopenias, particularly anemia.
- Standard therapy for higher-risk disease is HMA monotherapy; more data coming with combos.
- The next regulatory frontier is in the relapsed/refractory setting for lower- and higher-risk disease.