Robust Overall Survival and Sustained Efficacy Outcomes During Long Term Exposure to Momelotinib in JAK Inhibitor Naïve and Previously JAK Inhibitor Treated Intermediate/High Risk Myelofibrosis Patients

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Background: Myelofibrosis (MF)

- **Dysregulated JAK-STAT signaling**
  - Progressive anemia, splenomegaly and constitutional symptoms

- **Approved JAK inhibitors**
  - Ruxolitinib and fedratinib
  - Intrinsically myelosuppressive
  - Dose dictated by platelet count

- **OS advantage with ruxolitinib**
  - Short OS following JAK inhibitor discontinuation

Momelotinib (MMB) is a JAK1, JAK2 and ACVR1 inhibitor

- Ph3 MOMENTUM trial ongoing
- Previous Ph3 studies: SIMPLIFY-1 and SIMPLIFY-2
  - In JAK inhibitor naïve (S1) and JAK inhibitor treated (S2) patient populations
- Previously reported data suggests that momelotinib:
  - Provides similar splenic response for momelotinib vs ruxolitinib
  - Improves constitutional symptoms
  - Reduces transfusion burden and improves anemia
  - Has a favorable safety profile

<table>
<thead>
<tr>
<th>Safety Population (Randomized Period)</th>
<th>MMB (N=214)</th>
<th>RUX (N=216)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subjects with any Grade 3/4 TEAE</td>
<td>74 (34.6%)</td>
<td>94 (43.5%)</td>
</tr>
<tr>
<td>Thrombocytopenia Grade 3/4</td>
<td>15 (7.0%)</td>
<td>10 (4.6%)</td>
</tr>
<tr>
<td>Anemia Grade 3/4</td>
<td>13 (6.1%)</td>
<td>49 (22.7%)</td>
</tr>
</tbody>
</table>
Background: Completed Phase 3 Studies SIMPLIFY-1 and 2

SIMPLIFY-1: 1\textsuperscript{st}-Line Population
JAK inhibitor naïve

- JAKi-naïve
- Double-blind, N=432

**Primary Endpoint**
- Day 1
- Week 24
- Year 7
- Double-blind treatment
- Open label
- LTFU

**Goal:** Non-Inferiority

**MMB:** N=215

**RUX:** N=217

**Primary Endpoint**
- Splenic Response Rate

**Secondary Endpoints**
- Total Symptom Score
- Transfusion Independence Rate

SIMPLIFY-2: 2\textsuperscript{nd}-Line Population
Prior ruxolitinib with anemia or thrombocytopenia

- RUX-exposed
- Open label, N=156

**Primary Endpoint**
- Day 1
- Week 24
- Year 7
- Randomized treatment
- Extension
- LTFU

**Goal:** Superiority

**MMB:** N=104

**BAT:** N=52

**Primary Endpoint**
- Splenic Response Rate

**Secondary Endpoints**
- Total Symptom Score
- Transfusion Independence Rate
Momelotinib: Differentiated Heme Profile Allows High Dose Intensity

Mean Hemoglobin Levels

Crossover RUX → MMB

Mean Platelet Levels

Crossover RUX → MMB

Average Dose Intensity by Week

SIMPLIFY-1

SIMPLIFY-1: Splenic Response and Duration of Splenic Response

- 40% of patients on MMB achieved a splenic response at any time
- Duration measured from ≥ 35% reduction from baseline to return to baseline volume

**Week 24 Splenic Response Rate**

<table>
<thead>
<tr>
<th>% Responders</th>
<th>MMB</th>
<th>RUX</th>
</tr>
</thead>
<tbody>
<tr>
<td>27%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>29%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Non-inferiority p<0.001

**Median Duration of Splenic Response Not Reached on MMB**

- 40% of patients on MMB achieved a splenic response at any time.
- Duration measured from ≥ 35% reduction from baseline to return to baseline volume.
**SIMPLIFY-1: Transfusion Independence and Duration of TI**

**Landmark Week 24 TI Rate**

- **TI response at Week 24**
  - MMB: 67%
  - RUX: 49%
  - Nominal p<0.001

**Treatment**

- Median duration of TI not reached
- >3 years follow up

**Number at risk: n (%)**

<table>
<thead>
<tr>
<th>Strata</th>
<th>MMB</th>
<th>RUX</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>177</td>
<td>182</td>
</tr>
<tr>
<td>50</td>
<td>119</td>
<td>101</td>
</tr>
<tr>
<td>100</td>
<td>71</td>
<td>74</td>
</tr>
<tr>
<td>150</td>
<td>46</td>
<td>39</td>
</tr>
<tr>
<td>200</td>
<td>9</td>
<td>6</td>
</tr>
<tr>
<td>250</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

**Survival probability**

- Treatment: MMB, RUX→MMB at Week 24

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**INSIGHTS**

- Median duration of TI not reached
- >3 years follow up
**SIMPLIFY-2: Transfusion Independence and Duration of TI**

**Landmark Week 24 TI Rate**

Nominal $p=0.001$

**Treatment**

- **MMB**
- **BAT/RUX→MMB at Week 24**

<table>
<thead>
<tr>
<th>Strata</th>
<th>Number at risk: n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MMB</td>
<td>61 (100)</td>
</tr>
<tr>
<td>BAT</td>
<td>30 (100)</td>
</tr>
<tr>
<td>MMB</td>
<td>29 (48)</td>
</tr>
<tr>
<td>BAT</td>
<td>13 (43)</td>
</tr>
<tr>
<td>MMB</td>
<td>14 (23)</td>
</tr>
<tr>
<td>BAT</td>
<td>8 (27)</td>
</tr>
<tr>
<td>MMB</td>
<td>9 (15)</td>
</tr>
<tr>
<td>BAT</td>
<td>1 (3)</td>
</tr>
<tr>
<td>MMB</td>
<td>0 (0)</td>
</tr>
<tr>
<td>BAT</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>
SIMPLIFY-1: Robust Survival for JAKi-naïve Patients

Median OS 53.1 months in RUX→MMB patients
Median not reached in originally MMB-randomized patients

Treatment

- MMB
- RUX→MMB

HR = 0.99
p = 0.97

Week 24 Crossover to open-label MMB

SIMPLIFY-1

Median OS 53.1 months in RUX→MMB patients
Median not reached in originally MMB-randomized patients
SIMPLIFY-2: Robust Survival for Prior-JAKi Treated Patients

**Week 24**
Crossover to open-label MMB

- **Treatment**
  - **MMB**
  - **BAT/RUX→MMB**

**HR = 0.96**
**p = 0.86**

**Median OS**
- 37.5 months for BAT/RUX→MMB patients
- 34.3 months for originally MMB-randomized patients
Conclusions

• Robust OS in both JAKi-naïve and previously ruxolitinib treated patients
  • SIMPLIFY-1 mOS (53.1 m and not reached) consistent with OS advantage in MF provided by JAK inhibition
  • SIMPLIFY-2 mOS (34.3 and 37.5 m) represent the best reported OS in this previously ruxolitinib-treated setting
• Sustained transfusion independence and splenic response observed
• The durability of activity and survival data are consistent with momelotinib’s clinical and biologic profile:
  • JAK1, JAK2, ACVR1 inhibition
  • Potential to improve splenomegaly, constitutional symptoms and anemia
  • Low myelosuppressive potential and lack of cumulative toxicity

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