**Response by IWG: Biomarker-Positive Patients**

- Prognostically defined protocol analysis to evaluate contribution of each biomarker for patient selection demonstrates:
  - ORR = 8/11 (36%) in RARA-positive vs. 0% in RFB-negative
  - Data support using only RARA-positive biomarker status for patient selection
  - An analysis of response by RARA-positive vs. RARA-negative follows.

**Most Common Adverse Events, Regardless of Causality (≤20%)**

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>n (%)</th>
<th>Adverse Event</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhea</td>
<td>38 (75)</td>
<td>Decreased appetite</td>
<td>15 (30)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>13 (26)</td>
<td>Chemotherapy</td>
<td>13 (26)</td>
</tr>
<tr>
<td>Anemia</td>
<td>11 (22)</td>
<td>Thrombocytopenia</td>
<td>11 (22)</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>11 (22)</td>
<td>Neutropenia</td>
<td>9 (18)</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>9 (18)</td>
<td>Other (not specified)</td>
<td>9 (18)</td>
</tr>
<tr>
<td>Sepsis</td>
<td>6 (12)</td>
<td>Other (not specified)</td>
<td>5 (10)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>4 (8)</td>
<td>Other (not specified)</td>
<td>2 (4)</td>
</tr>
<tr>
<td>Nausea</td>
<td>4 (8)</td>
<td>Other (not specified)</td>
<td>2 (4)</td>
</tr>
<tr>
<td>Rash</td>
<td>8 (16)</td>
<td>Other (not specified)</td>
<td>2 (4)</td>
</tr>
</tbody>
</table>

**Safety Summary**

- AE profile of the combination is consistent with what has been previously reported for single-agent azacitidine in AML, with no evidence for increased toxicity for the combination
- Rates of myelosuppression comparable to reports of single agent azacitidine in this AML population
- The majority of non-hematologic AEs are low grade (SAEs were reported for 23 patients, the most frequent (occurring in ≥3 patients) included febrile neutropenia (7 patients), pneumonia (4 patients), and lung infection (3 patients))
- 7 patients discontinued due to AEs; none were reported in >1 patient

**Conclusions**

- **SY-1425 in combination with azacitidine showed high response rates and rapid onset of action in AML-positive patients with a 62% CR/CRI rate and 50% CR rate**
  - Most initial responses occurred at first response assessment
  - Responses were observed across risk groups
  - Treatment duration was up to 554 days and duration of response up to 344 days
- **Transfusion Independence** achieved or maintained by 82% of AML-positive patients
- **Most common adverse events** included fatigue, nausea, and diarrhea
- **Safety Summary**
  - AE profile of the combination is consistent with what has been previously reported for single-agent azacitidine in AML, with no evidence for increased toxicity for the combination
  - Rates of myelosuppression comparable to reports of single agent azacitidine in this AML population
  - The majority of non-hematologic AEs are low grade (SAEs were reported for 23 patients, the most frequent (occurring in ≥3 patients) included febrile neutropenia (7 patients), pneumonia (4 patients), and lung infection (3 patients))
  - 7 patients discontinued due to AEs; none were reported in >1 patient

**Descriptive Analysis**

- **Characteristics**
  - **Median age (years):** 63 (47-81)
  - **Sex:** Male (36), Female (24)
  - **Race:** White (76), Black (16), Other (16)

**Patient Disposition**

- **Characteristics:**
  - **Safety evaluation:** 31
  - **Treated N:** 52
- **Laboratory Abnormalities**
  - **Baseline Laboratory Values:**
    - **Prior to treatment:**
      - **Hemoglobin:** 13 (10-16)
      - **Platelets:** 169 (100-400)
      - **WBC:** 9.1 (3.8-17.2)

**Distribution of baseline characteristics**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th><em>n</em></th>
<th><em>p</em> value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>76 (63-81)</td>
<td>0.05</td>
</tr>
<tr>
<td>Sex</td>
<td>Female (24)</td>
<td>0.05</td>
</tr>
<tr>
<td>Race</td>
<td>White (76)</td>
<td>0.05</td>
</tr>
</tbody>
</table>

**Results**

- **ORR** = 8/11 (36%) in RARA-positive vs. 0% in RFB-negative
- **Data support using only RARA-positive biomarker status for patient selection**
- **Analysis of response by RARA-positive vs. RARA-negative follows**.