In the past 20 years there has been little change in the 1-, 3-, and 5-year survival rates for patients with ovarian cancer.

- 5-year survival is ~25% for patients diagnosed with advanced stage disease
- Recurrence is common and patients develop resistance to chemotherapy
- Platinum resistant ovarian cancer is uniformly fatal and epigenetic changes have been implicated in the development of platinum resistance

Previous experience with decitabine, a hypomethylating agent, in combination with carboplatin demonstrated activity in recurrent platinum resistant ovarian cancer patients (Matei et al. Cancer Research 2012)

Guadecitabine is a dinucleotide of decitabine and deoxyguanosine, affords increased in vivo exposure of decitabine by protecting it from dismutation due to slow release upon SQ injection

In Phase 1 studies, guadecitabine provides longer exposure and more potent hypomethylating compared to decitabine. Combining guadecitabine with carboplatin in this population may improve upon the encouraging preliminary results and an acceptable dose for phase 2 was previously established (Flaming, et al AACR 2014)

**Table 1: Demographics & prior therapies**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Guadecitabine + C (n=49)</th>
<th>TC (n=51)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>62.3 (6.9)</td>
<td>62.1 (6.9)</td>
</tr>
<tr>
<td>ECOG</td>
<td>0</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Prior Platinum</td>
<td>52 (100%)</td>
<td>48 (96%)</td>
</tr>
<tr>
<td>Prior Taxanes</td>
<td>48 (98%)</td>
<td>48 (98%)</td>
</tr>
<tr>
<td>Number of Prior Regimens</td>
<td>1-2</td>
<td>13 (25%)</td>
</tr>
<tr>
<td></td>
<td>3-4</td>
<td>23 (45%)</td>
</tr>
<tr>
<td></td>
<td>50 or more</td>
<td>12 (24%)</td>
</tr>
</tbody>
</table>

**Assessment of responses and progression**

- Progression based on RECIST, Rustin, and clinical progression as assessed by investigators
  - Subjects were encouraged to remain on treatment for 6 cycles in the absence of toxicity or clinical progression (i.e. only RECIST progression)
  - For subjects without measurable disease and detectable disease (available evaluation), progression was assessed by Rustin criteria
  - If subjects had RECIST measurable disease without a follow up scan and also had PD by CA-125 criteria, the earliest point of progression was used for both arms

**Additional subgroup analyses**

- Additional subgroup analyses were performed based on the selected TC use, comparison to topotecan or gemcitabine are presented in Figs 5 & 6.
- Because most patients crossed over to guadecitabine + carboplatin, OS is presented without censoring of crossover patients.
- Demographics showed no major differences between the groups
- Additional analyses showed excellent survival for guadecitabine + carboplatin vs. TOPO/GEM, respectively (HR=0.37)
- Unencumbered OS showed 11.0 vs 6.6 months survival for guadecitabine + carboplatin vs. TOPO/GEM, respectively (HR=0.69)

**Conclusions**

- Guadecitabine + carboplatin is tolerated at the phase 2 doses of 30 mg/m² and AUC 4 respectively
- SG11-02 Data are encouraging with a signal favoring guadecitabine + carboplatin vs. TC, particularly against TC of TOPO or GEM
- The signal seen in this randomized phase 2 study is consistent with that seen in previous non-randomized studies (1, 2) and supports the hypothesis that HMA “priming” may render platinum-resistant ovarian cancer patients more sensitive to platinum-based therapy

- Guadecitabine + carboplatin is tolerated at the phase 2 doses of 30 mg/m² and AUC 4 respectively
- SG11-02 Data are encouraging with a signal favoring guadecitabine + carboplatin vs. TC, particularly against TC of TOPO or GEM
- The signal seen in this randomized phase 2 study is consistent with that seen in previous non-randomized studies (1, 2) and supports the hypothesis that HMA “priming” may render platinum-resistant ovarian cancer patients more sensitive to platinum-based therapy