**Background**
- Weekly dose-dense paclitaxel + 3-weekly carboplatin improved survival in JGOG3016 vs. standard regimen
- Delivery of ddPTX hampered by high rate of early discontinuation due to haematological toxicity
- ddPTX has not yet been evaluated in the context of neoadjuvant chemotherapy
- ICON8 is an ongoing GCIG group phase III trial investigating two dose-fractionated regimens in a largely Caucasian population
- We report results of the pre-planned safety and feasibility analysis performed after 50 pts in each arm had completed protocol therapy

**Stage IA Analysis**
- Safety & feasibility in 50 patients randomised each arm
- Pre-defined outcome measures with re-evaluation of regimens if IDMC considered conditions not satisfied
- Feasibility outcome measures:
  - (1) Treatment completion – expect >80% women in Arm 2 & 3 to complete 6 cycles; re-consider if <60% Complete cycle defined as 2 of 3 weekly doses received
  - (2) Delivered dose intensity
- Safety outcome measures:
  - (1) ≤15% increase rate Grade 3/4 toxicities in Arm 2&3 vs. Arm 1
  - (2) <10% increase febrile neutropenia & sensory neuropathy
- Analysis planned when all completed treatment or 6mths in trial

**Patient Characteristics**
- 150 patients randomised June 2011 – August 2012
- Analysis performed Mar 2013; presentation approved by IDMC
- Data available on 147 pts: 49 Arm 1, 50 Arm 2, 48 Arm 3
- Analysis performed Mar 2013; presentation approved by IDMC
- Data available on 147 pts: 49 Arm 1, 50 Arm 2, 48 Arm 3

**Feasibility (cont)**
- Treatment received
- Carboplatin
  - % total planned dose given vs. relative dose intensity
- Paclitaxel
  - % total planned dose given vs. relative dose intensity

**Feasibility**
- Chemotherapy cycles completed
  - 6 x protocol-defined
  - 5 x protocol-defined
  - 6 x platinum-based

**Safety**
- Severe adverse events
  - Any G3+ toxicity
  - % of pts experiencing any Grade 3+ adverse event

**Conclusions**
- Weekly treatment arms harder to deliver
- But increased total dose delivered & intensity
- Acceptable toxicity
- Increased GCSF use may improve compliance
- But increased total dose delivered & intensity
- No Grade 5 adverse events during Stage IA
- Higher rate of G3+ AEs in weekly arms was due to uncomplicated neutropenia; no difference between other AEs
- Difference in grade 3/4 event rates vs. Arm 1
- Arm 2 vs. Arm 1 = 24% (95% CI 4.8%, 43.2%)
- Arm 3 vs. Arm 1 = 14% (95% CI -5.4%, 33.4%)
- Lower limit confidence interval does not exclude 15%
- No significant increase in toxicity in Arm 2 or Arm 3 compared to Arm 1

**Trial Design**
- Stage IC-IV EOC/PPC/FTC
- After immediate primary surgery or planned to receive NACT plus delayed primary surgery

<table>
<thead>
<tr>
<th>Stage IC-IV EOC/PPC/FTC</th>
<th>After immediate primary surgery or planned to receive NACT plus delayed primary surgery</th>
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<tbody>
<tr>
<td>Arm 1</td>
<td>6 cycles</td>
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<tr>
<td>Arm 2</td>
<td>6 cycles</td>
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<tr>
<td>Arm 3</td>
<td>6 cycles</td>
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**Randomise 1:1:1**

**Specific Grade 3+ adverse events**
- Arm 1
  - Neutropenia: 8%
  - Anaemia: 4%
  - Thrombocytopenia: 4%
  - Febrile neutropenia: 4%
  - Sensory neuropathy (G2+): 25%

- Arm 2
  - Neutropenia: 30%
  - Anaemia: 8%
  - Thrombocytopenia: 4%
  - Febrile neutropenia: 2%
  - Sensory neuropathy (G2+): 17%

- Arm 3
  - Neutropenia: 46%
  - Anaemia: 8%
  - Thrombocytopenia: 4%
  - Febrile neutropenia: 2%
  - Sensory neuropathy (G2+): 17%

**Conclusion**
- Weekly treatment arms harder to deliver
- But increased total dose delivered & intensity
- Acceptable toxicity
- Increased GCSF use may improve compliance
- IDMC recommended treatment arms continue without modification
- Protocol amendment to recommend early GCSF
- Recruitment continues with 806/1485 enrolled

**GCIG ICON8 stage IA analysis: safety and feasibility of two dose-fractionated carboplatin-paclitaxel regimens for the first-line treatment of ovarian cancer**

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