Prospective study evaluating a strategy of surgery alone and surveillance in FIGO stage I malignant ovarian germ cell tumor (KGOG 3033)

Investigators/Collaborators:

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Malignant ovarian germ cell tumor (MOGCT)

- Rare ovarian malignancy
  - 2-3% of all ovarian cancer

- Disease of children, adolescents, and young women

- 70% of MOGCT are early stage disease

- Highly curable due to high chemosensitivity

- Standard management
  - Fertility-sparing, complete staging or debulking surgery
  - Adjuvant BEP chemotherapy
Treatment of FIGO Stage I MOGCT

• Treatment guidelines were adopted based on experiences of treating malignant testicular germ cell tumor

• Fertility-sparing, complete staging surgery

• Adjuvant BEP chemotherapy
  • Except stage IA dysgerminoma & stage IA G1 immature teratoma
Surgery alone and surveillance strategy

- **Stage I malignant testicular germ cell tumors**
  - 75% of cases are cured by surgery alone
  - *Most cases of recurrent disease were salvaged by chemotherapy*
  - Overall survival is not compromised
  - 75% of stage I disease can avoid futile chemotherapy
  - Surgery alone and surveillance strategy has been accepted as standard management for all stage I testicular germ cell tumors

BEP chemotherapy

- Grade 3-4 neutropenia: 25%
- Febrile neutropenia: 10%
- Bleomycin-induced pulmonary complication: 10%
  - Sometimes fatal
- Cisplatin-induced renal impairment: 11-26%
- Cisplatin-induced ototoxicity
- Increased risk of cardiovascular disease
- Increased risk of secondary solid and hematologic malignancies

### Surgery alone and surveillance strategy in stage I MOGCT

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Journal</th>
<th>N</th>
<th>Histology</th>
<th>Outcomes</th>
</tr>
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<tbody>
<tr>
<td>Marina NM et al.</td>
<td>1999</td>
<td>JCO</td>
<td>44</td>
<td>IT</td>
<td>1 recur 1 salvaged 3Yr DFS: 97.8%</td>
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<td>Cushing B et al.</td>
<td>1999</td>
<td>AJOG</td>
<td>44</td>
<td>IT or YST</td>
<td>1 recur 1 salvaged</td>
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<tr>
<td>Baranzelli MC et al.</td>
<td>2000</td>
<td>EJC</td>
<td>12</td>
<td>MOGCT</td>
<td>6 recur 5 salvaged</td>
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<tr>
<td>Mann JR et al.</td>
<td>2000</td>
<td>JCO</td>
<td>9</td>
<td>MOGCT</td>
<td>3 recur 3 salvaged</td>
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<tr>
<td>Patterson DM et al.</td>
<td>2008</td>
<td>IJGC</td>
<td>35</td>
<td>MOGCT</td>
<td>11 recur 9 salvaged</td>
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<tr>
<td>Manglili G et al.</td>
<td>2010</td>
<td>GO</td>
<td>19</td>
<td>IT</td>
<td>2 recur 2 salvaged</td>
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<tr>
<td>Billmire DF et al.</td>
<td>2014</td>
<td>JCO</td>
<td>25</td>
<td>MOGCT</td>
<td>12 recur 11 salvaged 4yr DFS: 52% 4yr OS: 96%</td>
</tr>
</tbody>
</table>

188 cases in total, 36 recur (19%), 32 salvaged (89%)
Recent Clinical Trial

- Study period: 2003-2011
- Disease: Stage I MOGCT
- Age: 0-16 years (median, 12 years)
- Histology: YST, Embryomal Ca, ChorioCa, Mixed type
- 25 cases - YST: 11 / YST + IT (G2-3): 7 / Mixed: 7
Recent Clinical Trial

- **Surveillance**
  - ~ 9 wks: tumor marker (aFP, bHCG) q 3 wks
  - 2-6 mos: tumor marker q 1 mos
  - 6-24 mos: tumor marker q 3 mos
  - Imaging study: not defined

- **Persistence or recurrence**
  - BEP 3 cycles
  - Bleomycin 15U/m² on day 1
  - Etoposide 167mg/m² on days 1-3
  - Cisplatin 33.3 mg/m² on days 1-3
  - 12 recurrences / 11 salvaged / 1 expired
Recent Clinical Trial

Fig 2. Event-free survival (EFS) and overall survival of pediatric and adolescent female patients with stage I ovarian germ cell tumors.
Recent Clinical Trial

• Major limitation
  • Study included only children and young adolescent
  • Complete surgical staging was not defined.
Summary

- Surgery alone and surveillance strategy in stage I MOGCT
  - 81% of cases can be cured by surgery alone
  - 89% of recurrent cases can be salvaged by chemotherapy and/or surgery
  - Overall survival is not compromised in surgery alone group
  - 81% of cases can avoid futile chemotherapy

- Further clinical trial is required
  - Including old adolescent and young adult
  - Complete surgical staging should be performed
Study Scheme

Prospective study evaluating a strategy of surgery alone and surveillance in FIGO stage I malignant ovarian germ cell tumor

FIGO stage I MOGCT

Comprehensive surgical staging

Informed consent

Surveillance
- for 2 years
- Symptom, PEx, Tumor maker, Imaging study

No recur

Recur
(elevated tumor marker and/or radiologic recurrence)
: BEP chemotherapy ± Surgery

- Overall survival
- Disease free survival
- Quality of life
Eligibility

- **Inclusion**
  - FIGO stage I
  - MOGCT all histologic types
  - Complete staging
  - Age: 0-70 years

- **Exclusion**
  - Neoadjuvant chemotherapy
  - Incomplete surgical staging
  - FIGO stage II-IV
Objectives

• Primary objectives
  • 3 year overall survival

• Secondary objectives
  • 3 year disease-free survival
  • Pattern of recurrence
  • Salvage rate at recurrence
  • Quality of life
  • Ovarian function
  • Treatment related complication
Complete staging operation

- UO or USO
- Ovarian cystectomy for contralateral ovarian tumor
- Peritoneal exploration
- Peritoneal cytology
- Partial omentectomy
- Adhesiolysis and peritoneal biopsy
- LN evaluation: pelvic and paraaortic sampling or dissection
Follow-up

• Tumor marker
  • Indicated if markers elevated at initial presentation
  • 3 mos: every mos
  • 3-24 mos: every 3 mos

• Radiologic imaging (Chest X-ray, CT, MRI)
  • Not indicated unless markers normal at initial presentation
  • 1 mos and 3 mos: imaging
  • ~24 mos: every 6 mos

• Physical examination
  • ~24 mos: every 3 mos
Treatment at recurrence

• Surgery
  • Depending on the decision of surgeon

• BEP chemotherapy (no less than 3 cycles)
  • One of 2 regimen
  • 3 day regimen
    • Bleomycin 15U/m$^2$ on day 1
    • Etoposide 167mg/m$^2$ on days 1-3
    • Cisplatin 33.3 mg/m$^2$ on days 1-3
  • 5 day regimen
    • Bleomycin 15U/m$^2$ on day 1
    • Etoposide 100mg/m$^2$ on days 1-5
    • Cisplatin 20 mg/m$^2$ on days 1-5
Study duration and patients number

- Study duration
  - 4 years
- Study patients
  - 100 case
Study evaluation

- Overall survival
- Disease-free survival
- Treatment-related complication
- Quality of life
- Ovarian function
Acknowledgements

None.

Thank you for your kind attention !!!