A prospective randomized trial on the role of radical surgery and adjuvant therapy in the management of intermediate risk cervical cancer patients.

(IR: N0 but combination of risk factors: LVSI; Tu size; TFD)

CERVANTES

CERVical cancer: Adjuvant ThErapy and Surgery
Adjuvant treatment in IR risk cervical cancer patients

IR RISK GROUP (N0 AND RISK FACTORS)

- RCT; GOG 92
- Stage IB, LN neg. + 2 of: >1/3 stromal invasion OR LVI OR large tumor
  - RT (RH + PLDN → adjuvant radiotherapy) N=137
  - OBS (RH + PLDN) N=140

1988 – 1995 !!

RR for recurrence = 0.53  p=.008

RR in surgery only arm = 28 %!

Gynecol oncol 1999,73,177-183
## INTERMEDIATE RISK FACTORS

**GOG CRITERIA:**

Combinations of findings suggestive of intermediate risk stage 1B cervical cancer

<table>
<thead>
<tr>
<th>Lymphovascular space involvement</th>
<th>Depth of stromal invasion</th>
<th>Tumor size, cm</th>
</tr>
</thead>
<tbody>
<tr>
<td>yes</td>
<td>deep one-third</td>
<td>any</td>
</tr>
<tr>
<td>yes</td>
<td>middle one-third</td>
<td>2 or more</td>
</tr>
<tr>
<td>yes</td>
<td>superficial one-third</td>
<td>5 or more</td>
</tr>
<tr>
<td>no</td>
<td>deep or middle one-third</td>
<td>4 or more</td>
</tr>
</tbody>
</table>


**LIMITATIONS:**

- Not powered for survival
- Surgical part of the management was not standardized
- Selection criteria (i.e. tumor size assessed by palpation)
- Extremely poor local control in surgical arm
Intermediate risk, LN negative cases

Stage IB; LN negative

HR = 2 out of 3: LVSI + ≥ 2 cm
LVSI + DSI
≥ 4 cm

1/2000 – 12/2015

A) Surgery only group (PRG); N=136

B) Combined treatment group (MSKCC / MEL); N=104

Log-rank test: p = 0.317

Gynecol Oncol. 2018 Dec;151(3):438-443
### Recurrence rate and site of recurrence in GOG 92 and in the current study

<table>
<thead>
<tr>
<th>Study</th>
<th>GOG 92 trial</th>
<th>Current study</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Surgery only</td>
<td>Combined treatment</td>
</tr>
<tr>
<td><strong>Groups</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>28%</td>
<td>15%</td>
</tr>
<tr>
<td>Pelvic</td>
<td>19%</td>
<td>13%</td>
</tr>
<tr>
<td>Distant or combined</td>
<td>7%</td>
<td>2%</td>
</tr>
</tbody>
</table>

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**Clinical staging**
(MRI or EUS)

- T1b / T2a N0 M0, SC or AC (usual type)
  - ≥4 cm OR
  - >2 cm + (TFD<3 mm OR LVSI pos.)

**Surgery (laparotomy)**

- SLN (at least attempt) + PLND
- RH (C1 in 2-4 cm; C2 in ≥4 cm or TFD=0)

**Final histology**

- pT1b / pT2a pN0 M0
  - ≥4 cm OR
  - >2 cm + (TFD<3 mm OR LVSI pos.)

**Excluded:**
- N1 (MAC or MIC) or N0i+ (ITC)
- R1 or >pT2a
- Adequate type of surgery not performed
- Tumour type: AS or AC (unusual type)

**RANDOMIZATION**

**Adjuvant radiotherapy**

**Follow-up**
POWER ANALYSIS

Primary end-point: DFS or recurrence rate at 24 months

H0 hypothesis: adjuvant chemotherapy is non-inferior to adjuvant chemoradiation

Statistical significance: 0.05

Power: 0.8

Noninferiority margin: endpoint occurrence in reference group plus 5%

Endpoint occurrence in reference group: 10%

Endpoint occurrence in tested (experimental) group: 7%

Size of the group: 150 per group
Brainstorming meeting CERVANTES
Monday 15.30 – 16.30
Room MC 3.4