The Influence of Para-Aortic Nodal Status on Adjuvant Therapy for Endometrial Carcinoma

Dr. Steven Siu
Associate Consultant
Department of Clinical Oncology
Queen Mary Hospital

What to do if there are positive para-aortic lymph nodes?

Cochrane Database of Systematic Reviews 2014

- Adjuvant chemotherapy for advanced endometrial cancer (Galaal et al. (2014), www.cochranelibrary.com)
  - Chemotherapy increases survival time relative to radiotherapy in stage III and IV endometrial cancer
  - Further research needed
    - ?most effective and least toxic chemotherapy regimen
    - ?addition of chemotherapy further improves outcome

Recommendations by ASCO (2015)

(Meyer et al. (2015); J Clin Oncol 33: 2908-13)

- Stage IIIA and above
  - Chemotherapy +/- radiotherapy
- Unresolved issues
  - Integration of pelvic irradiation and brachytherapy
    - Prospective data lacking
    - Retrospective studies – no benefit
    - Generally not warranted unless risk factors for vaginal recurrence present
  - Integration of chemotherapy and radiotherapy
    - Clinical trials under way
    - ?Concurrent chemoradiation followed by adjuvant chemotherapy
    - ?Sequential
    - ?Sandwich type

ESMO-ESGO-ESTRO Consensus 2016

(Colombo et al. (2016); Ann Oncol 27: 16-41)

- Lymphadenectomy
  - staging procedure and allows tailoring of adjuvant therapy
  - lymphadenectomy to complete staging could be considered in previously incompletely operated high-risk patients to tailor adjuvant therapy
- In patients with high-risk, stage III endometrial cancer and no residual disease
  - EBRT is recommended to
    - Decrease pelvic recurrence
    - Improve progression free survival
    - Improve survival
  - Chemotherapy is recommended to improve progression-free and cancer-specific survivals
  - There is more evidence to give chemotherapy and EBRT in combination than either alone in stage III disease
    - Stage IIIC2: chemotherapy AND extended field EBRT to be considered

GOG 258 Trial (ASCO 2017, abstract 5505)

- Stages III-IVA (<2 cm residual disease) endometrial carcinoma or FIGO 2009 stage I/II serous or clear cell and positive cytology
  - Cisplatin and volume-directed radiation followed by carboplatin and paclitaxel for 4 cycles (C-RT, experimental arm) vs. carboplatin and paclitaxel for 6 cycles (CT, control arm)
  - Between 6/2009 and 7/2014, 813 patients enrolled and randomized (407 C-RT and 406-CT), 733 eligible (344 C-RT and 360 CT), and 680 received trial intervention (333 C-RT and 347 CT); median follow up 47 months
- 201 (58%) > grade 3 toxicity events in C-RT arm and 227 (63%) in CT arm
  - Myelosupression (40% vs. 52%)
  - Gastrointestinal (13% vs. 4%)
  - Metabolic (15% vs. 19%)
  - Neurological (7% vs. 6%)
  - Infectious (4% vs. 5%)
- Results
  - Treatment hazard ratio for RFS was 0.9 (C-RT vs. CT; CI 0.74 to 1.10)
  - C-RT reduced incidence of vaginal (3% vs. 7%, HR = 0.36, CI 0.16 to 0.82), pelvic and para-aortic recurrences (10% vs. 21%, HR=0.43, CI 02.8 to 0.66) compared to CT
  - Distant recurrences more common with C-RT vs. CT (28% vs. 21%, HR 1.36, CI 1 to 1.86)
  - Premature for OS comparison

PORTEC-3 Trial (Boer et al. (2018); Lancet Oncol 19: 295-309)

- Adjuvant chemotherapy during and after radiotherapy (chemoradiotherapy) vs. pelvic radiotherapy alone for endometrial cancer with high risk features
  - Grade 3-4 toxicities for chemoradiotherapy vs. radiotherapy alone
    - During treatment: 60% vs. 12%
    - Six months after randomization: 16% vs. 8%
  - No improvement in 5-year overall survival
  - Improvement in failure free survival
    - In particular those with stage III endometrial cancer

IMRT vs. Conventional Technique

- IMRT not associated with reduction in radiation toxicity but more costly
- Reasons
  - RT delivered to large tissue volume
  - Relative low dose (45-55Gy)

Wright et al (2013). Gynecol Oncol 130: 43-48.

Conclusion

- Endometrial carcinoma patients with para-aortic lymph node involvement may benefit from more aggressive adjuvant therapy
  - Adjuvant chemotherapy probably has a role
  - Radiotherapy may also help
  - Probably even better if both can be given
  - However we are not yet sure what’s the best way to give these and how they can actually benefit
  - Can be associated with toxicities
- Multidisciplinary approach to determine optimal management for individual patients balancing potential benefits and risks

Thank You for Your Attention