

Randomized trial of combined chemotherapy and radiotherapy for high risk endometrial carcinoma

PORTEC – 3 / EN7



An International Intergroup Trial

PORTEC - 3: rationale

- High-risk EC: increased risk of distant metastases and cancer death
- Trials comparing RT and CT: no difference
- *RTOG phase II and NSGO/EORTC phase III trials suggest survival benefit for combination of CT and RT*
- Various schedules and sequencing used
- Toxicity and quality of life in this elderly patient group a major concern

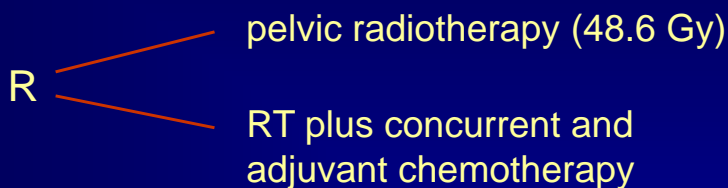


PORTEC - 3: design

- Aim: investigate OS and FFS improvement by combining chemotherapy and radiotherapy
- Primary endpoints: 5-y overall survival (OS) and failure-free survival (FFS)
- Secondary endpoints: toxicity and quality of life
- Power >0.8 for 5-yr OS difference 11.5% (HR 0.62)
 - 500 patients (670 for 5-yr OS difference 10%)
 - Intergroup trial



PORTEC-3



Concurrent: 2 cycles cisplatin 50 mg/m²

Adjuvant: 4 cycles carboplatin AUC 5 and paclitaxel 175 mg/m²

RT: 48.6 Gy (# 1.8 Gy); brachytherapy boost if cervical invasion



Eligibility

- *Endometrial carcinoma*
 - » *stage IB grade 3 and LVSI*
 - » *stage IC or IIA grade 3*
 - » *stage IIB*
 - » *stage IIIA or IIIC*
 - » *stage IB, IC, II or III and serous or clear cell*
- *WHO PS 0-2*
- *no residual macroscopic tumor after surgery*
- *Pathology review before randomization*



Pathology

- *BEFORE randomization*
- *Essential quality control*
- *Discordances in typing and grading – 8% altering patient management*
- *Confirmation of type and grade within 1 wk*
- *After informed consent: tissue sample for translational research*



Toxicity evaluation and QoL

- *Toxicity (CTCAEv3.0) at baseline, after RT and chemotherapy, at FU*
- *Investigate impact of combined treatment*
- *EORTC QLQ C-30 and CX24/part of OV28*
- *Baseline QoL, after completion of RT, at 6, 12, 24, 36 and 60 months*
- *Data and Safety Monitoring Board*
- *Interim analysis and stopping rules*



International collaboration

- **Netherlands (PORTEC/DcGOG)**
 - ✓ slow start due to new laws and regulations
 - ✓ first centres started November 2006
- **Italy (MaNGO)**
 - ✓ MaNGO Group and Ethics approval
 - ✓ accrual started April 2008
- **Australia/NZ (ANZGOG):**
 - ✓ NHMRC and Ethics approval
 - ✓ accrual started Sept 2008
- **UK (NCRI):**
 - ✓ Cancer Research UK & Ethics approval
 - ✓ UK accrual started April 2009



International collaboration

- Canada (NCIC CTG):
 - ✓ Central & Ethics approval
 - ✓ Local procedures ongoing
 - ✓ Expected start mid 2009
- Austria (Vienna):
 - ✓ Central & Ethics approval
 - ✓ Expected start mid 2009
- France (FNCLCC):
 - ✓ Central and Ethics approval procedures ongoing



Conclusions

- *Reducing indications for RT*
 - *Low risk tumors: TAH-BSO alone*
 - *Intermediate risk: vaginal brachytherapy (PORTEC-2)*
- *High risk tumors: the challenge*
 - » *Roles of pelvic RT and chemotherapy (PORTEC-3)*
 - » *Targeted therapies*
 - » *International collaboration*



PORTEC-3 international collaboration



Thank you !

www.clinicalresearch.nl/portec3