Ovarian cancer 2010

- 22,500 cases diagnosed per year in the United States and 16,500 deaths per year1.
- Most patients are diagnosed in late stages; no screening test exists.
- Pathology: 4 different types (serous, endometrioid, clear cell and mucinous)

Jemal A, Siegel R, Ward E, et al: Cancer statistics, 2009. CA: Cancer J Clin 59(4):225-49, 2009

Unique aspects of newly diagnosed advanced ovarian cancer

- Upfront surgical management is standard of care: allows access to tissue
- OC is very chemotherapy sensitive at diagnosis;
- >80% of cancers will respond to platinum- and taxane-based chemotherapy upfront at dx.
- Cancer becomes more treatment-refractory following recurrence.
- Outcomes for newly diagnosed ovarian cancer have reached a plateau with platinum / taxane combination

1st line Tx: Dose dense or not

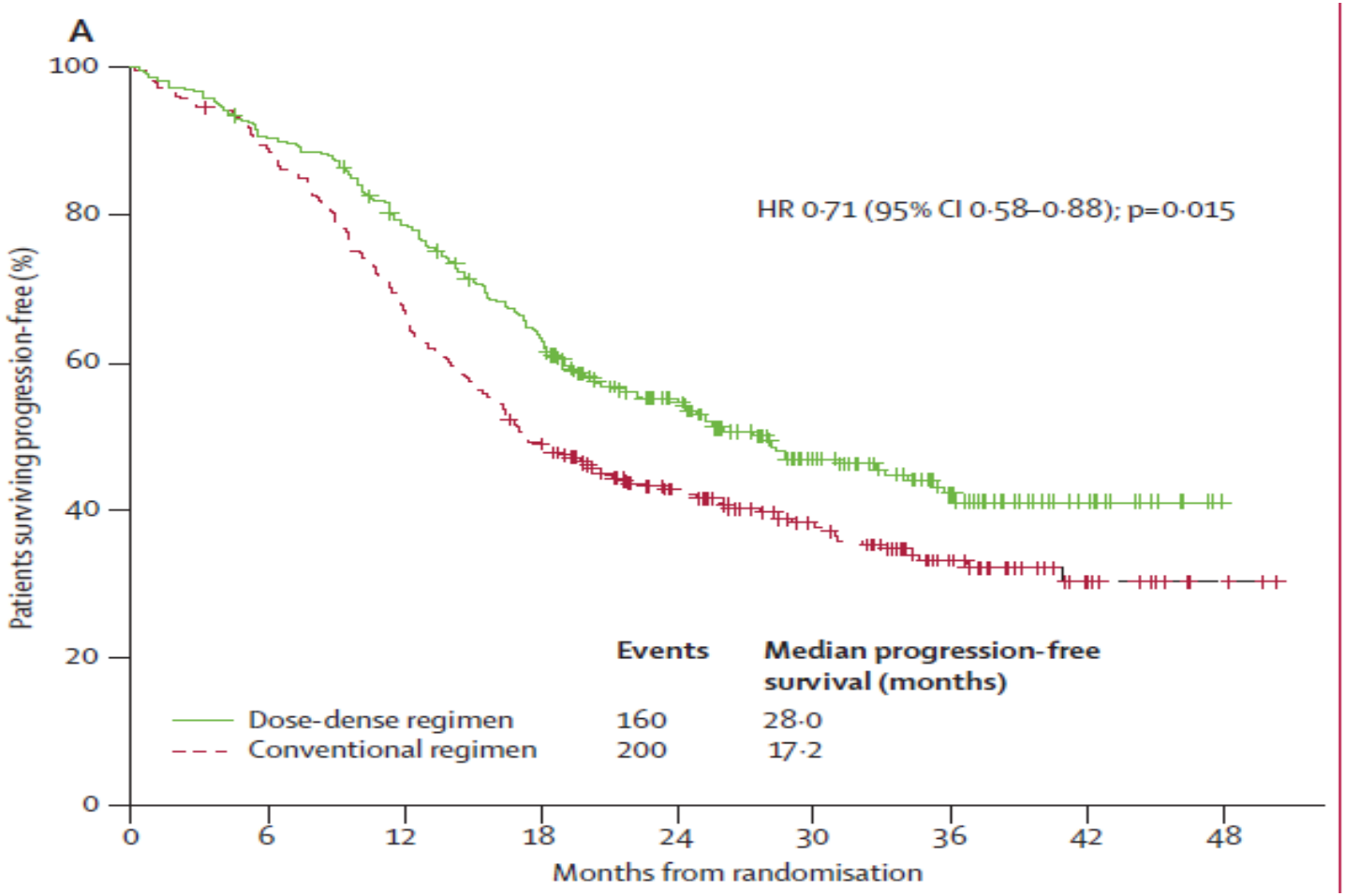
- Dose dense paclitaxel versus q 3 week paclitaxel for newly diagnosed ovarian cancer
- 631 eligible patients were enrolled
- stage II to IV epithelial ovarian cancer
- Pts could have upfront or interval debulking
- Primary endpoint was PFS
- Paclitaxel 180 mg/m2 + carboplatin AUC 6 day both day 1

  or

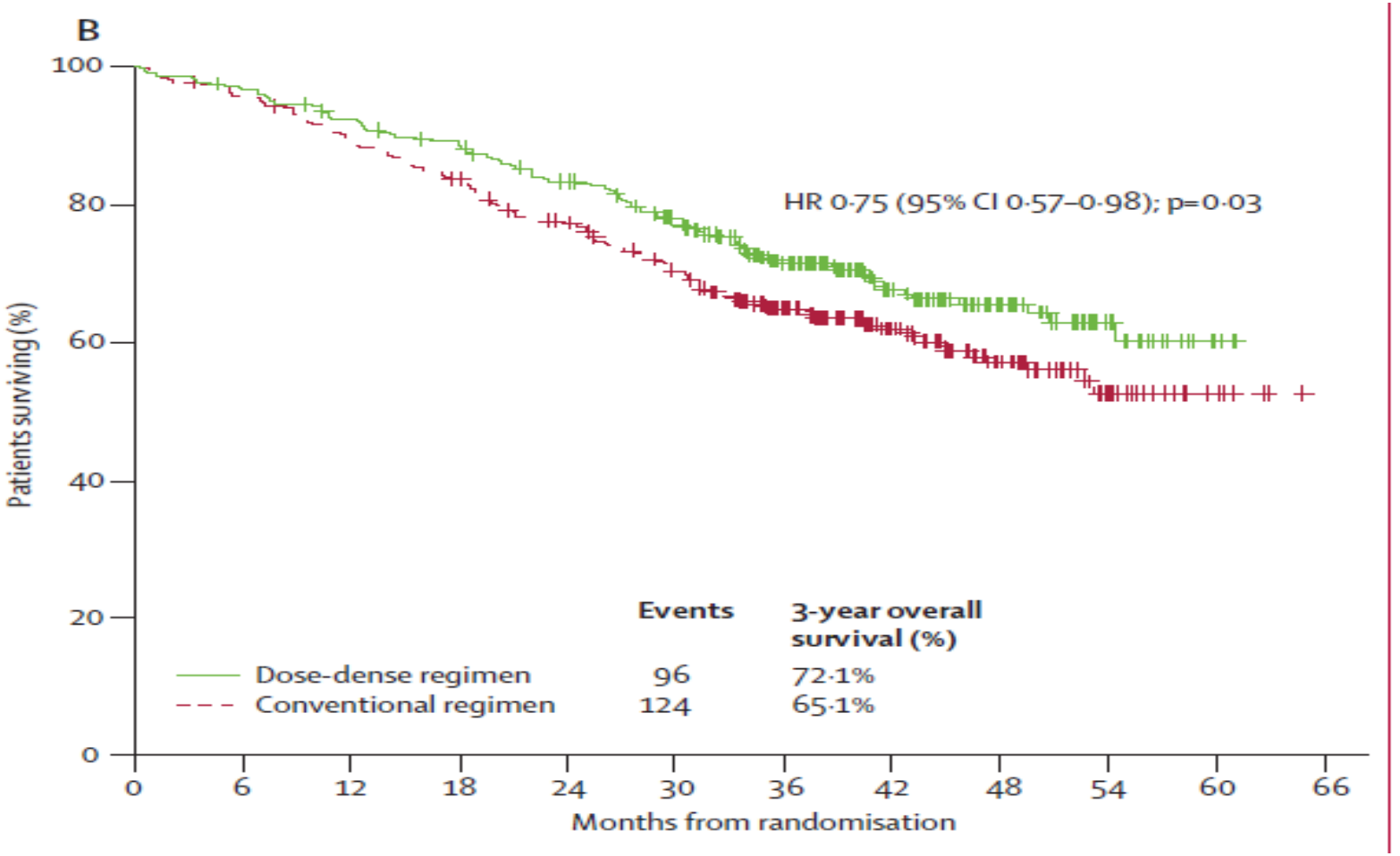
  Paclitaxel 80 mg/m2 days 1, 8, 15 + carboplatin AUC 6 day 1 (dose dense group)

Katsumata et al, Lancet 2009

Progression-free Survival



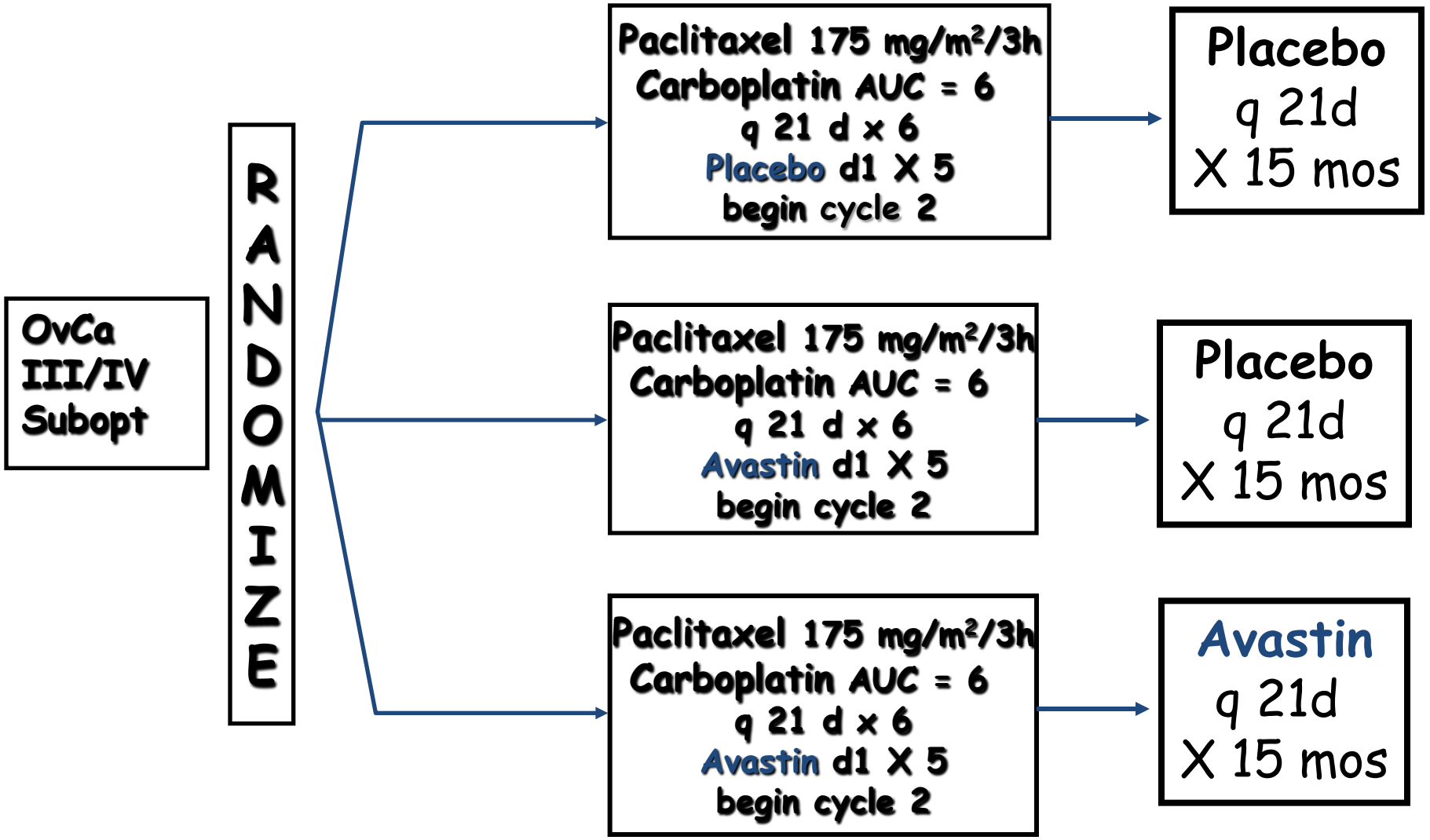
Overall Survival



Maintenance: Avastin (GOG 218)

- ASCO 2010
- Randomized phase III trial assessing standard CT versus CT+ avastin +/- avastin maintenance in stage III/IV OC
- Primary endpoint: PFS
- **Hypothesis: Avastin improves PFS when added** to standard chemotherapy for OC

Avastin: GOG 218



Burger, R. GOG 218

Avastin 15 mg/kg IV

GOG218: Conclusions

- CP + Avastin -> Avastin maintenance (Arm III) statistically superior to CP alone (Arm I)
- CP+Avastin not different than CP
- Overall survival analysis limited at this time: so far no benefit
- Toxicity profile consistent with known literature
- FIRST POSITIVE adjuvant trial since CP vs C+Cytoxan (GOG111)

IS THIS THE NEW STANDARD TREATMENT FOR OC?

GOG 218

- CP+Avastin not different than CP
- Overall survival curves do not (begin to) separate
- PFS benefit only 3.8 months

Recurrence Tx: CALYPSO

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

From the University Paris Descartes, Assistance Publique-Hôpitaux de Paris, Hôpital Hôtel-Dieu; Association de Recherche sur les Cancers dont Gynécologiques Groupe d'Investigateurs Nationaux pour l'Etude des Cancers Ovariens, Paris; Centre Catherine De Sienne, Nantes; Centre Hospitalier Universitaire-Centre François Baclesse, Caen, France; Philipps University Marburg, Marburg; University Hospital Charité/Campus Virchow-Klinikum, Berlin; Klinikum Offenbach, Offenbach; Dr Horst Schmidt Klinik, Wiesbaden, Germany; Karolinska University Hospital and Karolinska Institutet Stockholm, Sweden; NHMRC Clinical Trials Centre, Sydney, New South Wales; University of Queensland, Brisbane, Queensland, Australia; British Columbia Cancer Agency, Vancouver, British Columbia, Canada; Medical University Innsbruck, Innsbruck, Austria; University Hospital Leuven, Leuven, Belgium; National Cancer Institute, Naples; Academic Division of Gynecological Oncology, Institute for Cancer Research

Pegylated Liposomal Doxorubicin and Carboplatin Compared With Paclitaxel and Carboplatin for Patients With Platinum-Sensitive Ovarian Cancer in Late Relapse

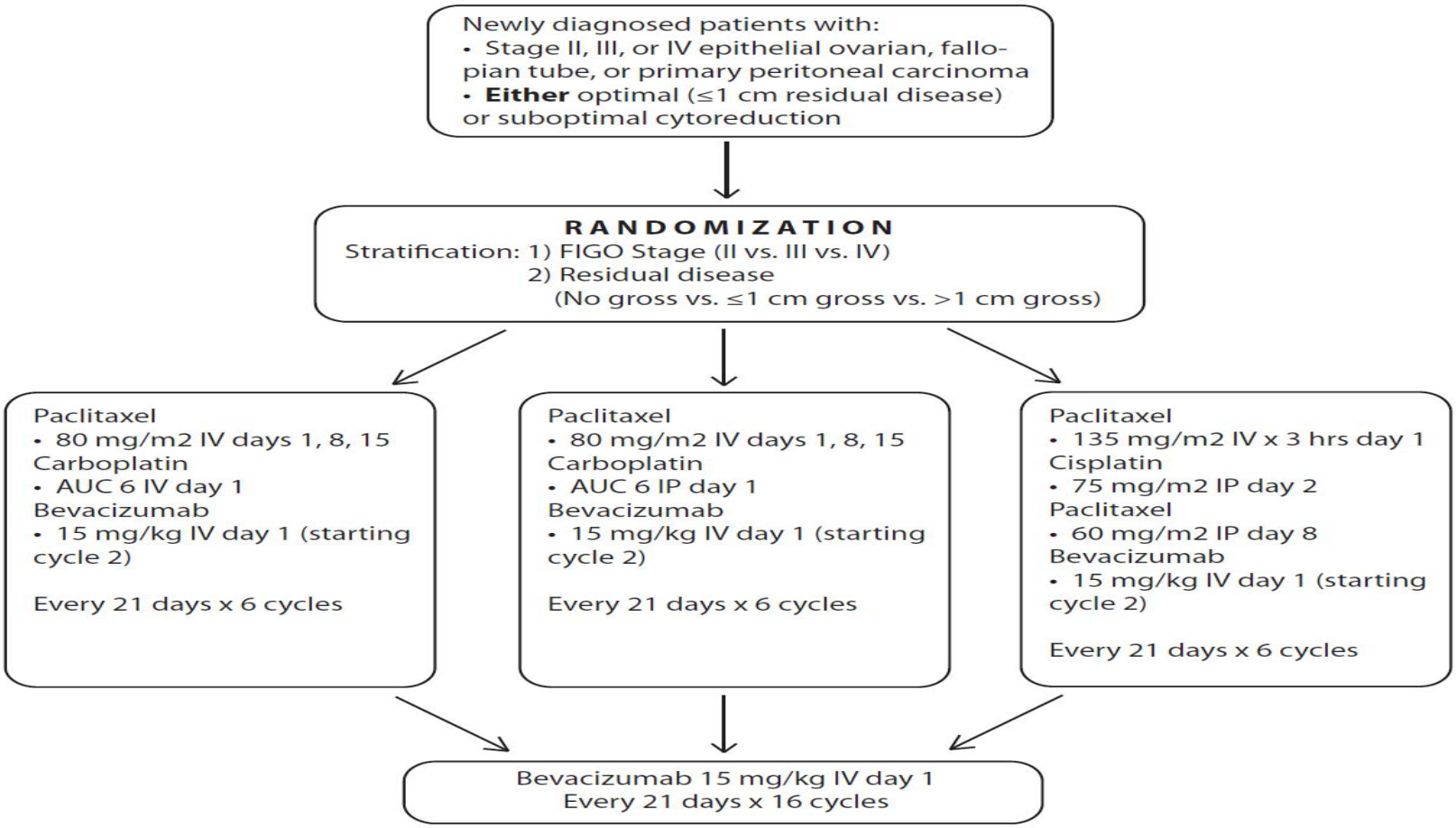
Eric Pujade-Lauraine, Uwe Wagner, Elisabeth Aavall-Lundqvist, Val Gebski, Mark Heywood, Paul A. Vasey, Birgit Volgger, Ignace Vergote, Sandro Pignata, Annamaria Ferrero, Jalid Sehouli, Alain Lortholary, Gunnar Kristensen, Christian Jackisch, Florence Joly, Chris Brown, Nathalie Le Fur, and Andreas du Bois

A B S T R A C T

Purpose

This randomized, multicenter, phase III noninferiority trial was designed to test the efficacy and safety of the combination of pegylated liposomal doxorubicin (PLD) with carboplatin (CD) compared with standard carboplatin and paclitaxel (CP) in patients with platinum-sensitive relapsed/recurrent ovarian cancer (ROC).

GOG 252: IP/dose-dense/Avastin trial ongoing



ASCO Annual '09 Meeting

GYNECOLOGIC CANCER INTERGROUP
An Organization of International Cooperative Groups for Clinical Trials in Gynecologic Cancers

EORTC European Organisation for Research and Treatment of Cancer

Early treatment of relapsed ovarian cancer based on CA125 level alone versus delayed treatment based on conventional clinical indicators

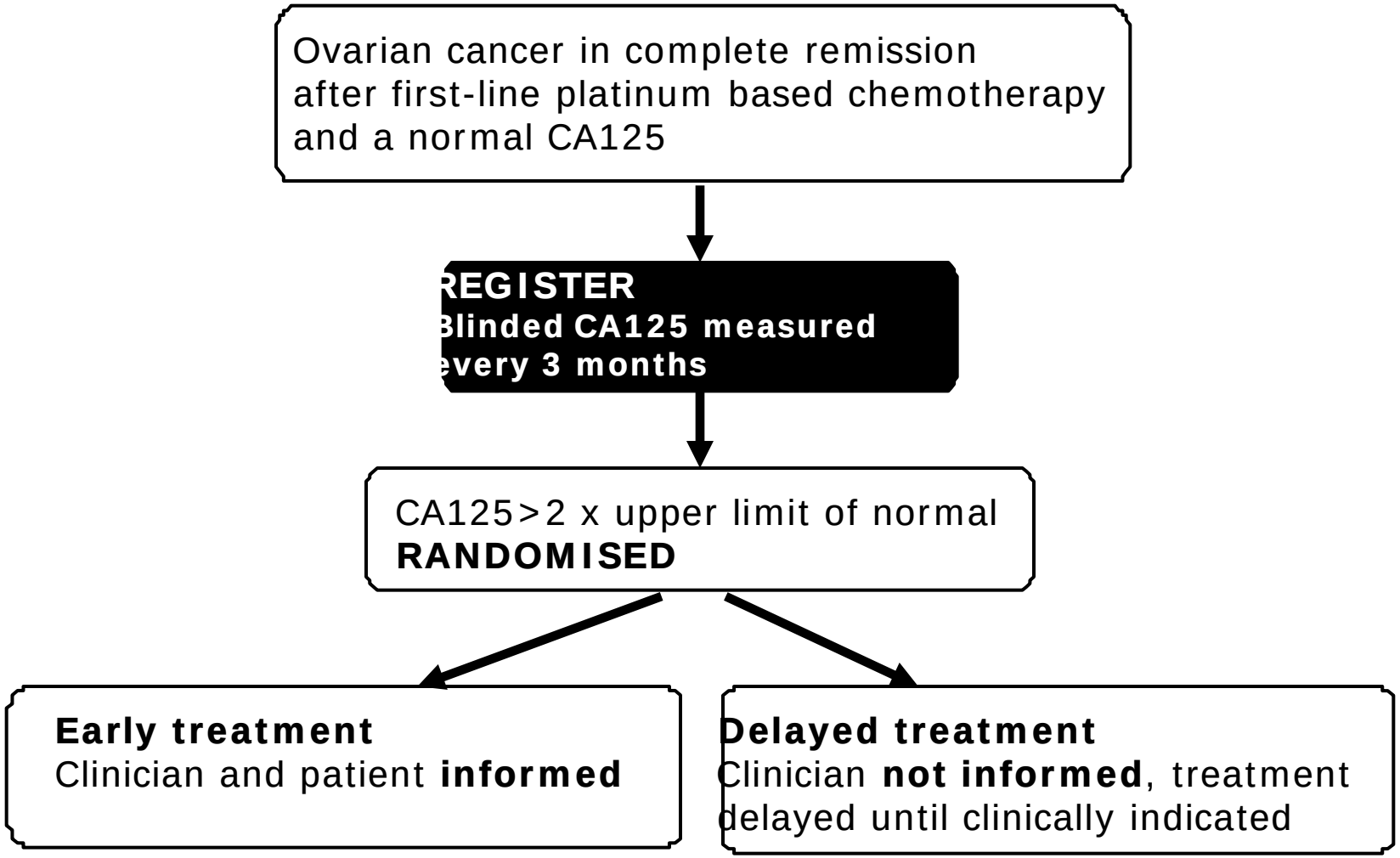
Results of the randomized MRC OV05 and EORTC 55955 trials

Gordon Rustin (Mount Vernon Cancer Centre)
and Maria van der Burg

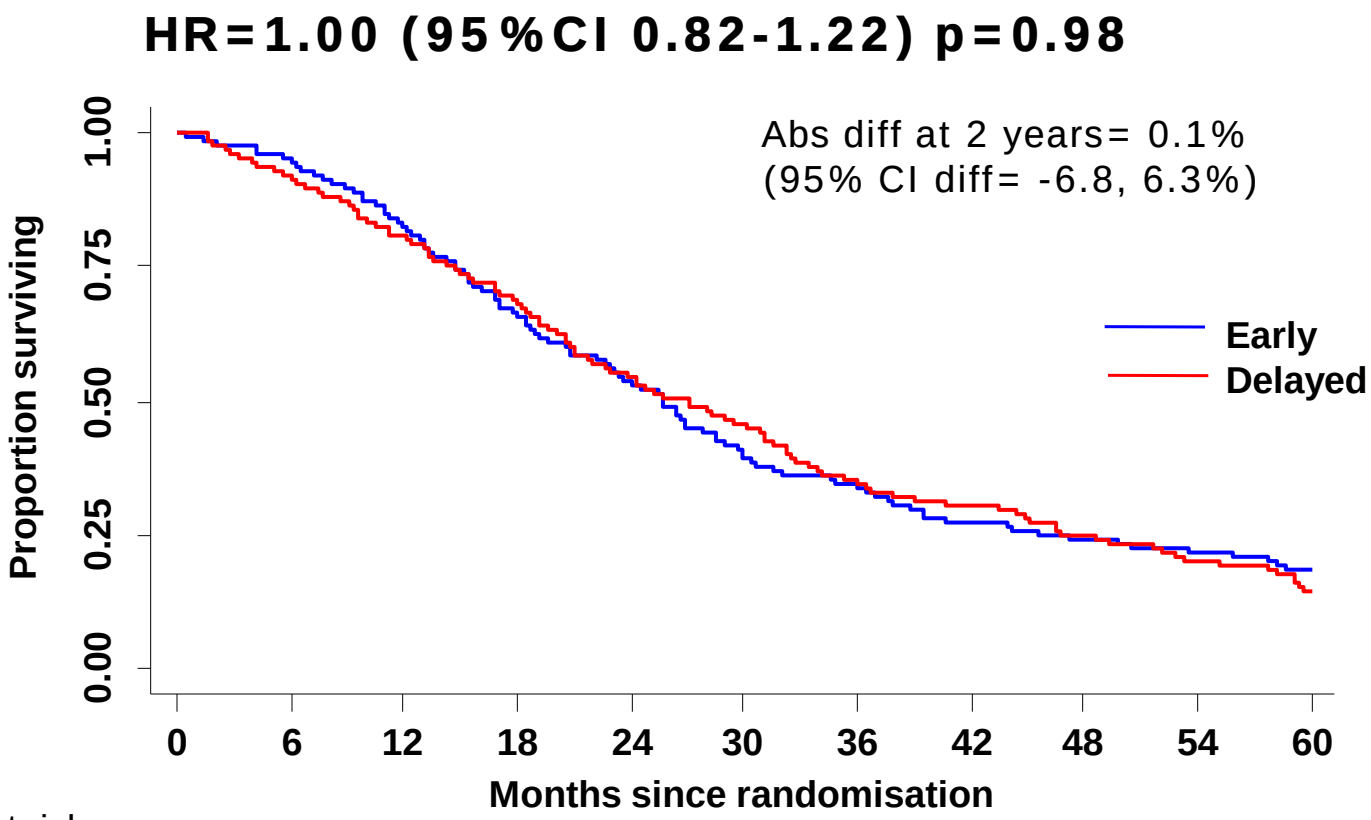
On behalf of all OV05 and 55955 Collaborators

31st May 2009

Trial Design



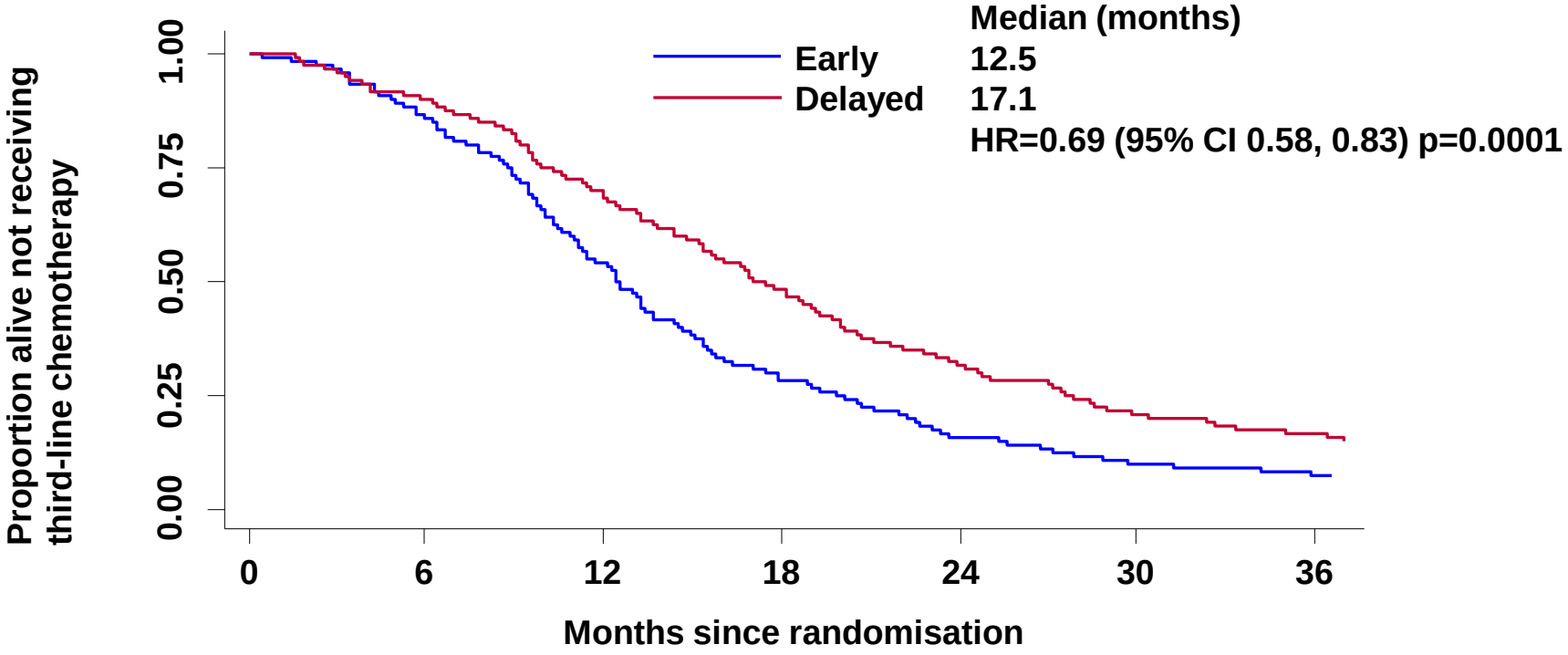
Overall Survival



Number at risk

Early	265	247	211	165	131	94	72	51	38	31	22
Delayed	264	236	203	167	129	103	69	53	38	31	19

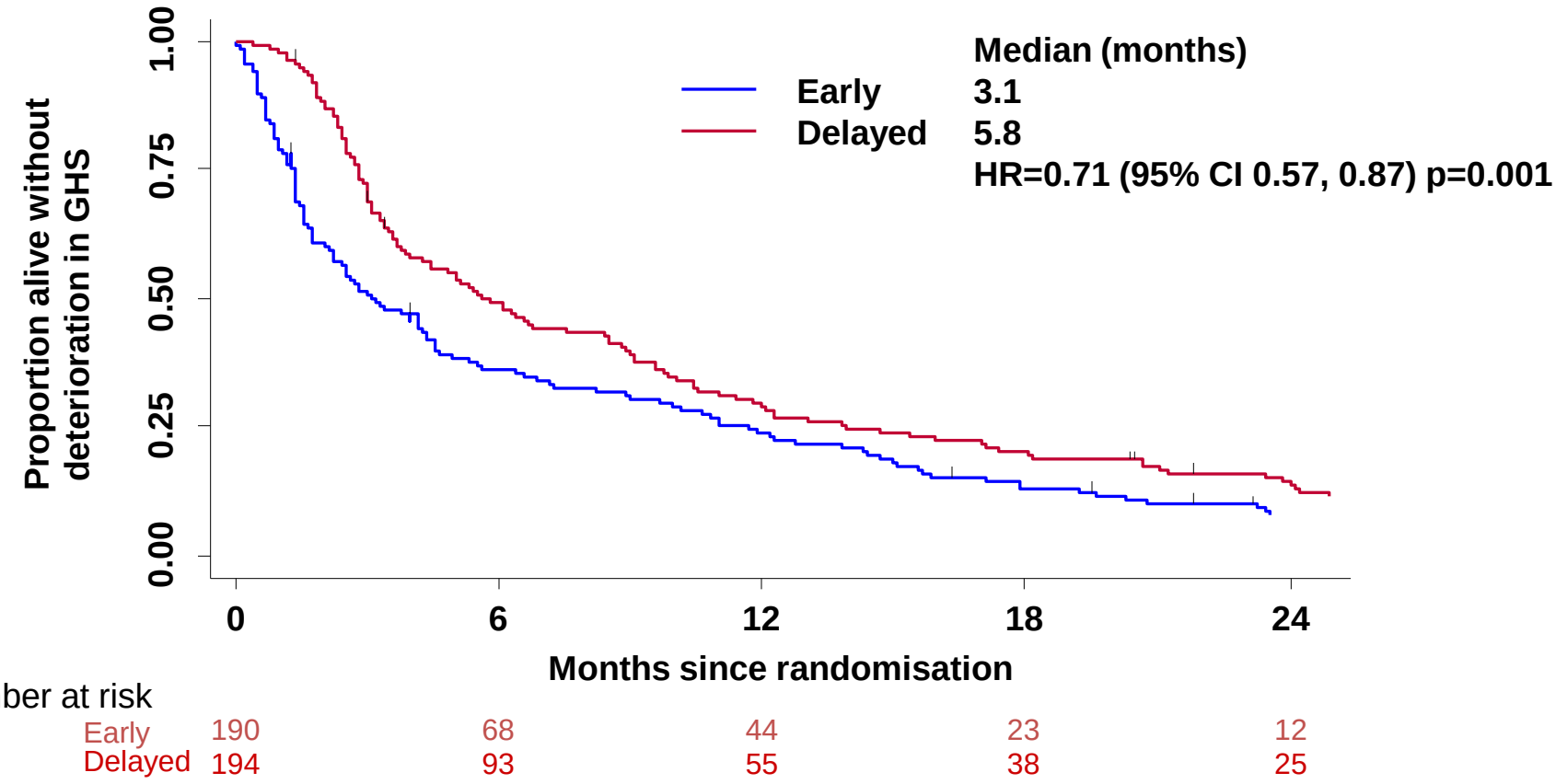
Time from randomisation to third-line treatment or death



Number at risk

Early	265	224	138	70	38	22	17
Delayed	264	232	173	117	76	48	35

Time from randomisation to first deterioration in Global Health Score (or death)



Number at risk

Early	190	68	44	23	12
Delayed	194	93	55	38	25

Conclusions

- In early treatment arm based on rise in CA125
  - Second-line chemotherapy started a median of 4.8 months earlier
  - Third-line chemotherapy started a median of 4.6 months earlier

- This early treatment did not improve overall survival
  - HR=1.00, 95% CI 0.82-1.22, p=0.98
  - Absolute difference at 2 years 0.1% (95%CI -6.8, 6.3%)

- Early chemotherapy does not improve QoL

How should this trial influence practice?

- Women can be reassured that
  - There is no benefit from early detection of relapse by routine CA125 measurements
  - Even if CA125 rises, chemotherapy can be delayed until signs or symptoms of tumor recurrence

- Women can be offered choices in follow-up
  - No routine CA125 measurements but rapid access to CA125 testing if symptoms or signs of relapse
  - Regular CA125 measurements