Randomized phase 3 trial comparing primary cytoreductive surgery with or without hyperthermic intraperitoneal chemotherapy for stage III epithelial ovarian cancer: OVHIPEC-2

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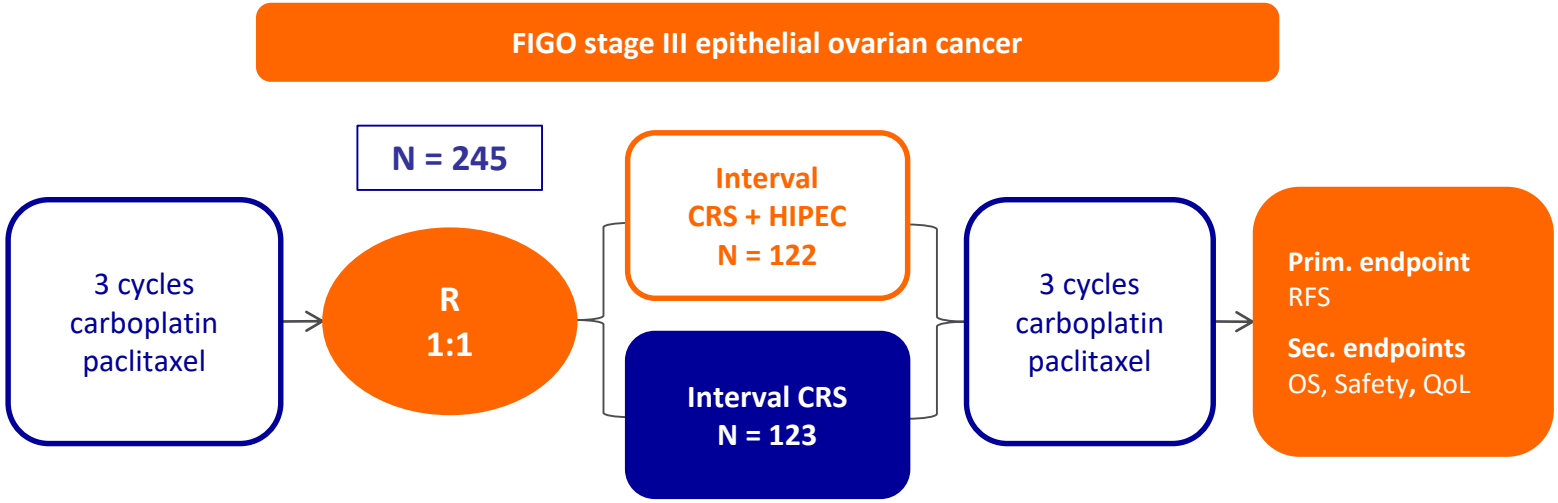
No disclosure

Rationale for hyperthermic intraperitoneal chemotherapy (HIPEC)

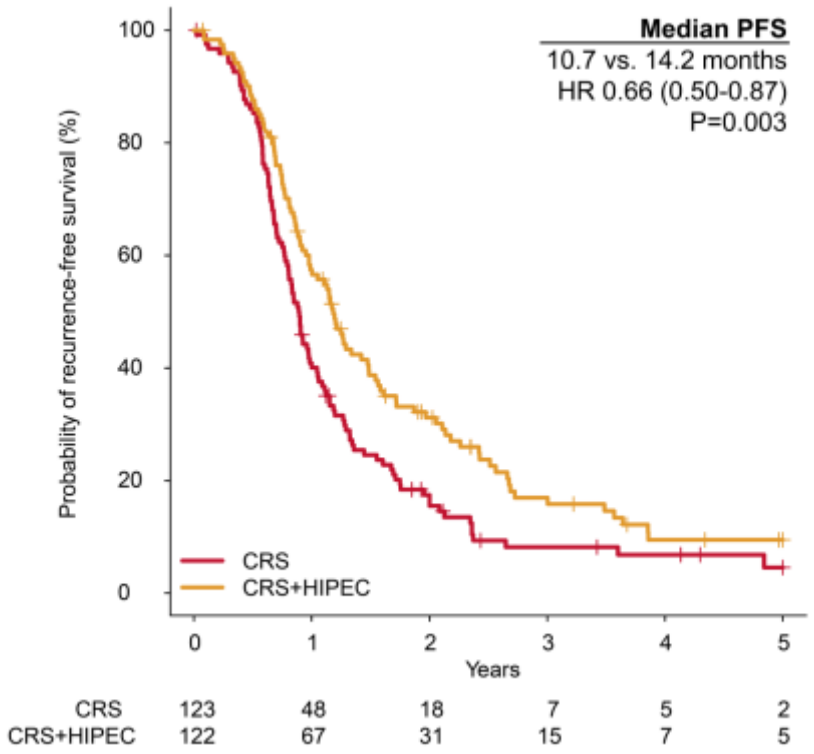
- High concentration of chemotherapy at the peritoneal surface
- Advantage in case of microscopic intra-abdominal disease
- Hyperthermia induces homologous recombination deficiency
- HIPEC improves RFS/OS after neo-adjuvant chemotherapy
- IV/IP chemotherapy improves RFS/OS after primary debulking

Study design OVHIPEC-1

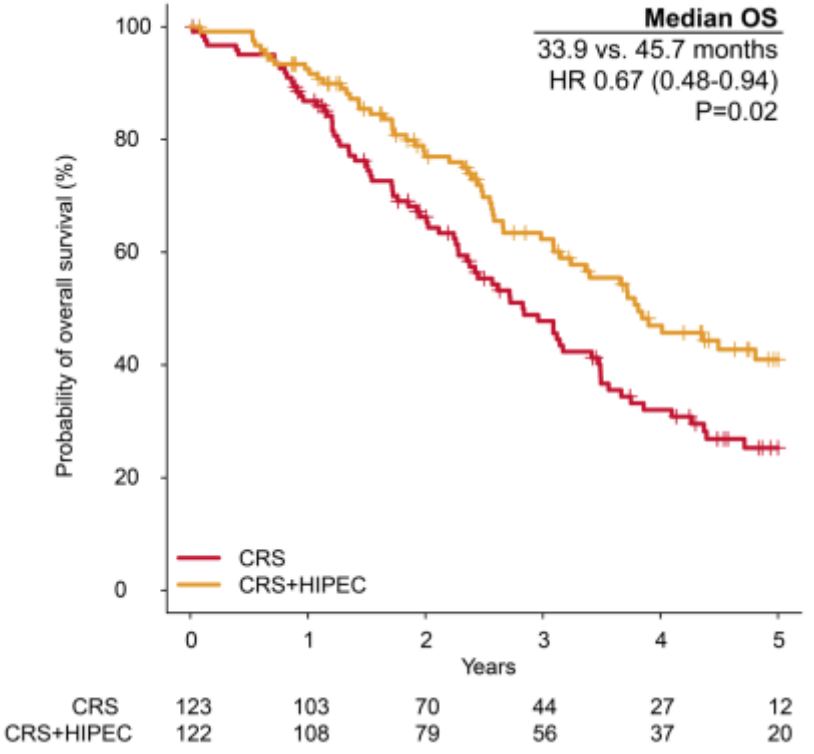


- Primary cytoreductive surgery (CRS) not possible because of extent of disease
- Follow-up visits were performed every 3 months for the first 2 years; every 6 months thereafter
- Tumor assessments with CT scans were performed 26, 52, and 104 weeks after the last chemotherapy
- The Common Terminology Criteria for Adverse Events (CTCAE) version 4.0 were used for grading toxicity

Recurrence-free survival



Overall survival



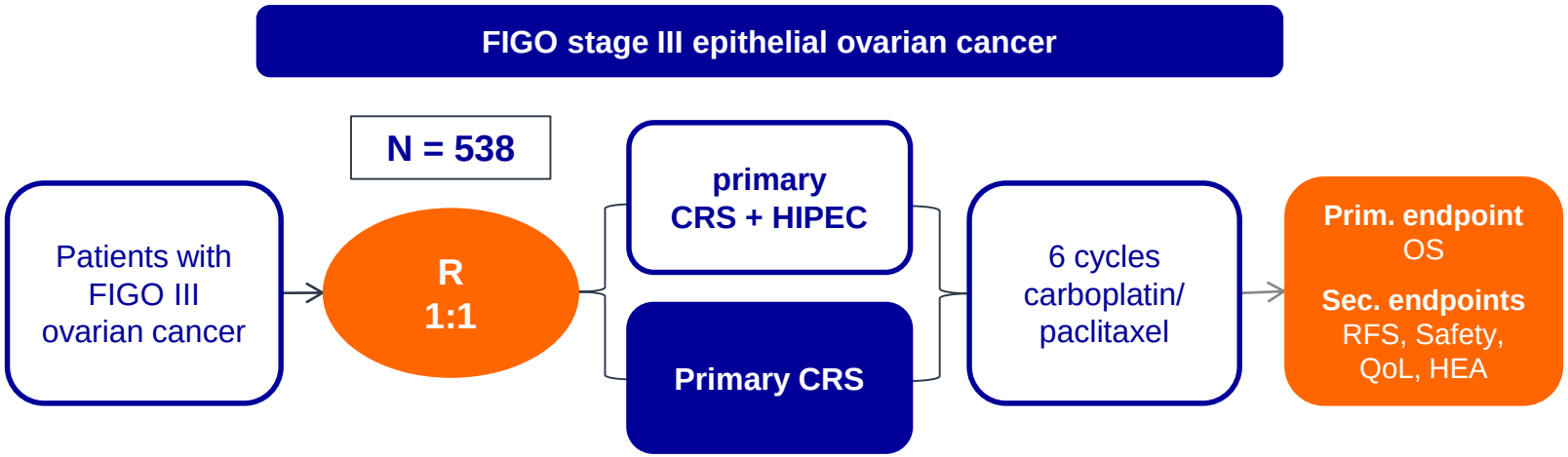
Increase of 10% in overall survival after 5 years in favour of HIPEC group

van Driel et al. NEJM 2018

Conclusion OVHIPEC-1 study

- Improves outcome of interval CRS after NACT
- FIGO stage III, primary CRS not feasible due to disease extent
- Cisplatinum 100 mg/m^2 for 90 minutes + sodium thiosulphate
- Centralized care and monitoring treatment results
- Primary cytoreductive surgery with or without HIPEC?

OVHIPEC-2



- 80% power to detect a 33% risk reduction (hazard ratio 0.67) with two-sided α=0.05
- Median survival control arm estimated to be 49.7 months (GOG 172)
- 197 events (deaths) needed
- Accrual to be completed within 60 months, additional follow-up 12 months
- Two interim analyses, after 67 and 133 OS events respectively
- Follow-up visits every 3 months for the first 2 years; every 6 months thereafter
- CT scans will be performed 6, 12 and 24 months after the last chemotherapy
- CTC Adverse Events (CTCAE) version 5.0 will be used for grading toxicity

N = 538

Inclusion criteria

- FIGO stage III epithelial ovarian cancer
- Complete CRS or residual disease <2.5 mm
- Normal renal function, liver function, blood count
- Qol baseline before randomisation
- Age >18 years
- WHO 0-1
- ASA 1-2

Exclusion criteria

- History of malignancy within 5 year prior to inclusion

- FIGO stage IV ovarian carcinoma

- Primary CRS not feasible according to pre-specified criteria
  - diffuse deep infiltration of the root of small bowel mesentery
  - diffuse carcinomatosis of the small bowel that requires resection that leads to short bowel syndrome (remaining bowel <1.5 m)
  - diffuse involvement/deep infiltration of stomach/duodenum
  - diffuse involvement/deep infiltration of head or middle part of pancreas
  - involvement of truncus coeliacus , hepatic arteries or left gastric artery
  - non-resectable enlarged lymph nodes

- Funding of the Dutch cancer foundation obtained

- Funding requested from the Dutch government to finance HIPEC procedure (decision march 2019)

- Participation in the Netherlands (10 centers)

- Additional centers in UK, France, Denmark, Sweden, Ireland, Italy and Australia

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Points raised during discussion

- Forming a steering trial involving HIPEC
- Present trial in national trial groups showing interest:
  - ANZGOG
  - MITO
  - Irish Cancer Trial Group
  - NSGO
  - NCRI