

NCI Clinical Announcement

Intraperitoneal
chemotherapy for women
with ovarian cancer

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History

- Dedrick R, Myers C, Bungay P et al. PK rationale for peritoneal drug administration in the treatment of ovarian cancer. Cancer Treat Rep 1978
 - High IP drug concentration
 - Prolonged IP drug half-life
 - Prolonged systemic drug half-life

Early lessons from clinical trials

- IP chemotherapy ineffective for women with bulky intra-abdominal disease
- PK advantages high for certain drugs (IP vs IV)
 - 10-20-fold: cisplatin, carboplatin
 - >1000: paclitxel, docetaxel

Phase III evaluation

- US, Europe, Taiwan
- Six trials for women with advanced stage ovarian cancer after primary surgery
- One consolidation trial for women NED after primary surgery and chemotherapy

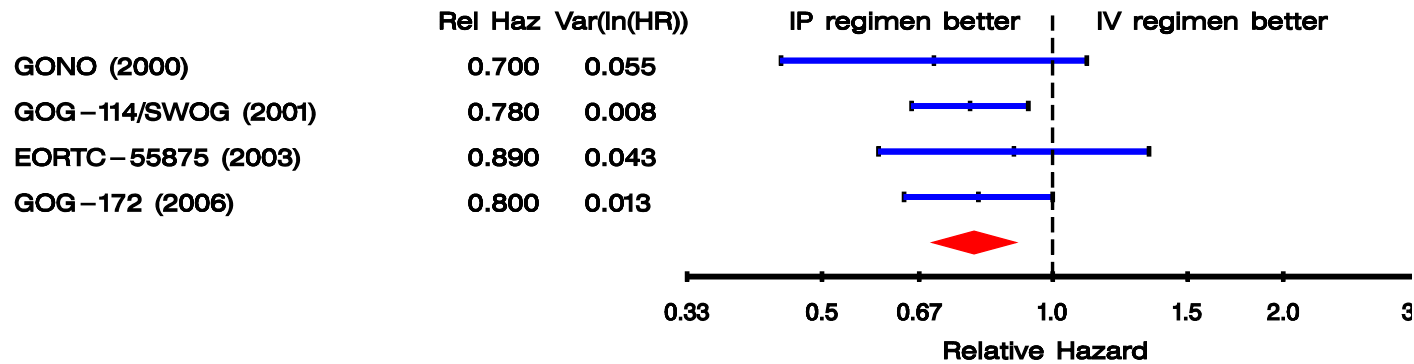
NCI sponsored phase III trials

- SWOG 8501/ GOG 104
 - Accrual: 1988-1992
 - Cisplatin/ cyclophosphamide IV vs cisplatin IP/ cyclophosphamide IV
 - NEJM 1996: Alberts et al
- GOG 114/ SWOG 9227/ECOG
 - Accrual: 1992-1993
 - Cisplatin IV/ paclitaxel IV vs carboplatin x 2 + cisplatin IP/ paclitaxel IV
 - JCO 2001: Markman et al

NCI-sponsored phase III trials

- GOG 172
 - Accrual: 1998-2001
 - Cisplatin/ paclitaxel IV vs cisplatin IP/
paclitaxel IV+IP
 - NEJM 2006: Armstrong et al

Treatment Hazard Ratios for PFS Intraperitoneal vs Intravenous Therapy



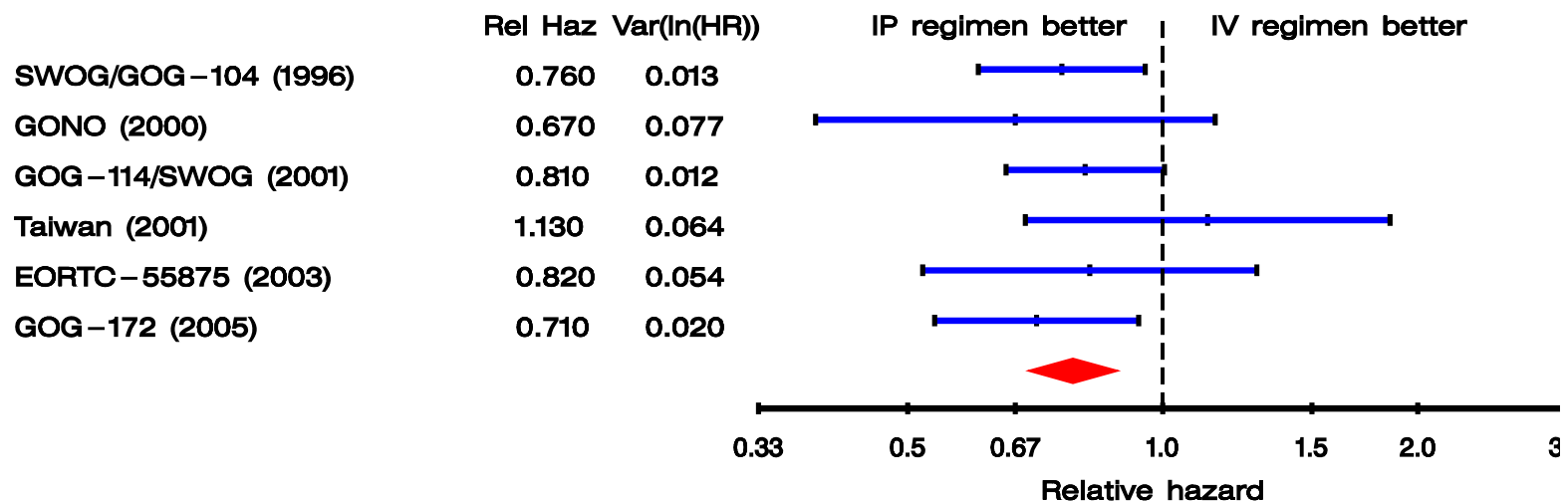
I^2 heterogeneity (3 d.f.) = 0.629, p=0.89

The red diamond shows the pooled estimate of the treatment hazard ratio for PFS: 0.79, 95% confidence interval (0.70, 0.90).

PFS hazard ratios are not available from the published report on SWOG-8501/ GOG 104 or th study of Yen et al.

PFS hazard ratio is not reported for the study of Gadducci et al but it is calculated from the available data reported.

Treatment Hazard Ratios for Death Intraperitoneal vs Intravenous Therapy



I^2 heterogeneity (5 d.f.) = 3.1, p=0.68

Hazard ratio is not reported for the GONO study but it is calculated from the available data reported.

Hazard ratio is not reported for the Greek study.

NCI Clinical Announcement

- “To bring new information of unusual importance to the attention of clinicians as rapidly as possible”
- Review of data by independent panel, nominated by investigators and NCI
- Recommendation forwarded to NCI Director
- Timed with publication of data

NCI Clinical Announcements

- Adjuvant therapy, node- breast cancer, 1988
- Levamisole & 5FU, Dukes C colon cancer, 1989
- Adjuvant therapy, rectal cancer, 1991
- Adjuvant therapy, breast cancer, tamoxifen update, 1995
- Chemoradiation for cervical cancer, 1999

Process for IP Clinical Announcement

- Proposed by GOG and SWOG investigators
- Independent panel of gyn oncs, med oncs, patient advocates, biostatisticians nominated by GOG, SWOG, EORTC, and NCI
- Panel reviewed data and voted to recommend that NCI issue a clinical announcement

Process for IP Clinical Announcement

- Proposal for clinical announcement reviewed by NCI SMT and EC
- Review of SEER and SEER/Medicare data showed <1% of women with stage III ovarian cancer received IP chemotherapy
- Focus groups of MDs, advocates, nurses

Top ten reasons not to give IP chemo

- 10. I don't believe the data.
- 9. I don't know how to give IP chemo.
- 8. I don't like to use cisplatin anymore.
- 7. There is no standard IP regimen.
- 6. It takes longer than IV chemo.

Top ten reasons not to give IP chemo (cont'd)

- 5. Giving IV carbo/ paclitaxel is so easy.
- 4. IP chemo has more toxicity.
- 3. There's no drug rep pushing IP chemo.
- 2. It's an old idea.
- 1. It requires optimal surgical cytoreduction and a IP port.

Process for IP Clinical Announcement

- Development of trans-NCI team
- Review of text of announcement
 - NIH, FDA, independent panel
 - BMS as co-sponsor of SWOG 8501 and GOG 114

NCI IP Clinical Announcement Team

- Office of the Director
 - Offices of Communication, Education & Special Initiatives, Liaison Activities, Women's Health
- Division of Cancer Control and Population Sciences
- Division of Cancer Prevention
- Division of Cancer Treatment and Diagnosis

Dissemination: publication

- Primary endpoint of GOG 172
 - Armstrong et al, NEJM 2006 (expedited)
 - Cannistra (editorial), NEJM 2006
- Secondary endpoint of GOG 172
 - IP catheter outcomes
 - Walker et al, Gynecologic Oncology 2006 (expedited, simultaneous electronic release)
 - Trimble & Christian (editorial), Gynecologic Oncology 2006
- Review articles
 - Green, Lancet (in press)

Dissemination: press

- Joint national release
 - Timed with NEJM publication
 - NCI, GOG, Society of Gynecologic Oncologists, Gynecologic Cancer Foundation, Oncology Nursing Society, Society of Gynecologic Nurse Oncologists
- Local press releases
 - NCI Cancer Centers and research sites active in IP trials

National TV coverage

- ABC: Good Morning America, World News Tonight, 17 local affiliates
- NBC News Channel->affiliates
- 14 Fox affiliates
- CBS: Morning News, 3 affiliates

National wire services

- Associated Press
- Reuters
- United Press International

National Newspaper Coverage

- USA Today
- New York Times (Jan 5 & 17)
- Boston Globe
- Los Angeles Times (Jan 5 & 23)
- Newsday
- Baltimore Sun

Local newspapers

- Seattle Post-Intelligencer, p. 1
- Columbus (Ohio) Dispatch, p. 1
- Daily Oklahoman, p. 1
- Raleigh News & Observer, p. 1
- Worcester (Mass) Telegram & Gazette, p. 1
- Cleveland Plain Dealer, p. 1

Foreign press

- Agence France
- The Australian, Perth Sunday Times
- UK Daily Mail
- Toronto Star, Montreal Gazette,
Edmonton Journal

Dissemination: advocacy groups

- Conference call organized by NCI OLA
 - Day of NEJM and IP Clinical Announcement release
 - Ovarian cancer advocacy groups in US, Canada, and UK
- Newsletters, websites, broadcast emails, presentations at annual meetings

Dissemination : web and CIS

- NCI home page
- NCI digest page on ovarian cancer
- Joint press release, FAQs
 - 9,779 page views

Dissemination: web and CIS

- PDFs of NEJM article and Clinical Announcement
- PDQ
- Listing of centers with expertise in ovarian cancer
 - Multidisciplinary, surgical cytoreduction, IP chemotherapy, clinical trials

Dissemination: web and GOG

- Educational material for doctors and nurses
 - How to place an IP port, how to give IP therapy, how to manage toxicities
- Patient educational materials

Dissemination

- Professional societies
 - ASCO, ACOG, ACOS, ONS, SGO, SGNO, SSO
- Cooperative Groups
- Local, regional and national conferences
 - Australia, Austria, Canada, UK

Plans for Evaluation

- Early adopters: NCCN, Cancer Research Network
- Later adopters: SEER 2006 Patterns of Care, SEER-Medicare, National Cancer Data Base
- Industry: IP port sales, pharmaceutical sales