台灣婦癌醫學會會訊

2010 年 6、7 月

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壹、 會務報告

一、第七屆理監事聯席會報告

1. **99/8/14(六)假台中中山醫學大學舉辦「台灣婦癌中區研討會」**：已取得婦癌科醫學會 B 類 7 積分，及專科醫理師 2.4 積分。8/14 當日十點至十二點進行演講，十二點舉辦第七屆第三次的理監事會議，下午一點至二點許朝偉為我們講” Prophylaxis of HBV reactivation in cancer patients undergoing chemotherapy”後，接著進行 TGOG 的會議，同一時間在另一間會議室裡進行準會員口頭報告，目前計有四位準會員報名口頭訓練報告
2. **IGCS2010 將於 10/23-26 在捷克布拉格舉行：**

   (http://www2.kenes.com/igcs2010/Pages/Home.aspx)學會和旅行社連絡後，分成二個行程供本會會員選擇，請有意參與活動之會員與秘書處連絡。

   A. IGCS 2010 俄羅斯、波蘭、捷克十三日之行程：10/15 日出發，與莫斯科、聖彼得堡、波蘭華沙等該國學會進行學術交流，並

於 10/22 抵捷克，參加 10/23-26 之會議。

B. IGCS 2010 捷克開會八日之行程；10/20 出發，直接前往布拉格，10/21-22 在布拉格當地遊覽，10/23-26 參加會議。

3. **「第十六屆台灣癌症聯合學術年會」事宜報告：**2011 年舉辦的台灣癌症聯合學術年會，計畫第一天以英文演講，希望能擴大為國際研討會，以吸引更多國內外學者參加；第一次籌備會議於 8/13(五)下午 18:30 於喜來登飯店舉行。

4. 本會所頒發之專科醫師證每六年需申請更新，自本會會員領取婦科腫瘤專科醫師執照至今，已即將屆滿六年，**專科醫師換証**之申請表請詳見附件一。

5. **99 年度專科醫師甄審日期為 99/12/11(六)假台大醫院兒童醫院大樓 15 樓婦產科會議室(台北市中山南路 8 號)舉辦，即日起至 10 月 15 日截止報名**，請欲報名專科醫師甄審且符合報名資格之醫師於截止日前向秘書處報名，報名相關資料請詳見附件二。

二、近期學會活動

日期	活動名稱	活動地點	主辦單位
2010.08.14 Ｗ六	中區研討會	中山醫學大學附設醫院	TAGO
2010.11.20 Ｗ六	北區研討會	馬偕醫院淡水院區	TAGO

2010 年部分國際會議如下：

＊ 13th IGCS: Prague, Czech Republic, European Union 23-26 October 2010
http://www2.kenes.com/igcs2010/Pages/Home.aspx

三、學會網站誠徵衛教文章

歡迎各位會員踴躍賜稿，以充實學會的網站內容。來稿請e-mail至 tago.gyn@gmail.com

貳、 近期文獻選錄

莊其穆醫師

文章分享

附件三 臨床醫師如何閱讀 Meta analysis 的論文

附件四 臨床醫師研讀 randomized clinical trial (RCT) 論文應有的正確觀念

陳子健醫師

本期特選

Ref 9 Platinum-sensitive recurrence 的標準治療恐怕要改了

Pegylated liposomal Doxorubicin and Carboplatin compared with Paclitaxel and Carboplatin for patients with platinum-sensitive ovarian cancer in late relapse. J Clin Oncol. 2010 Jul 10;28(20):3323-9.

Ref 12 ASCO 曰: 化療之前宜先測 hepatitis B

American Society of Clinical Oncology provisional clinical opinion: chronic hepatitis B virus infection screening in patients receiving cytotoxic chemotherapy for treatment of malignant diseases.
J Clin Oncol. 2010 Jul 1;28(19):3199-202. Epub 2010 Jun 1.

分類選摘

子宮頸類

Ref 1 婦癌科可能的跨科合作

Human papillomavirus and survival of patients with oropharyngeal cancer. N Engl J Med. 2010 Jul 1;363(1):24-35.

Ref 2 月經週期與避孕藥對於 HPV detection 的影響

Effect of the menstrual cycle and hormonal contraceptives on human papillomavirus detection in young, unscreened women. Obstet Gynecol. 2010 Jul;116(1):67-75.

Ref 3 fertility-sparing surgery 之 review

Fertility-sparing surgery in patients with cervical cancer.
Rob L, Skapa P, Robova H. Lancet Oncol. 2010 Jul 7. [Epub ahead of print]

子宮類

Ref 4 造成手術後 leg lymphedema 的 risk factor

Risk factors for postoperative lower-extremity lymphedema in endometrial cancer survivors who had treatment including lymphadenectomy. Gynecol Oncol. 2010 Jul 15. [Epub ahead of print]

Ref 5 Cytoreductive surgery 在 endometrial cancer 之角色

Cytoreductive surgery for advanced or recurrent endometrial cancer: a meta-analysis. Gynecol Oncol. 2010 Jul;118(1):14-8.

Ref 6 子宮內膜厚度之 cutoff value

Endometrial thickness measurement for detecting endometrial cancer in women with postmenopausal bleeding: a systematic review and meta-analysis. Obstet Gynecol. 2010 Jul;116(1):160-7.

Ref 7 荷蘭 endometrial cancer 的 randomized trial: TAH vs. TLH

Safety of laparoscopy versus laparotomy in early-stage endometrial cancer: a randomised trial. Lancet Oncol. 2010 Jul 16. [Epub ahead of print]

Ref 8 澳洲 endometrial cancer 的 randomized trial: TAH vs. TLH

Quality of life after total laparoscopic hysterectomy versus total abdominal hysterectomy for stage I endometrial cancer (LACE): a randomised trial. Lancet Oncol. 2010 Jul 16. [Epub ahead of print]

卵巢類

Ref 9 Platinum-sensitive recurrence 的標準治療恐怕要改了

Pegylated liposomal Doxorubicin and Carboplatin compared with Paclitaxel and Carboplatin for patients with platinum-sensitive ovarian cancer in late relapse. J Clin Oncol. 2010 Jul 10;28(20):3323-9.

Ref 10 Early ovarian cancer 應予徹底之手術分期

Surgical staging and treatment of early ovarian cancer: long-term analysis from a randomized trial. J Natl Cancer Inst. 2010 Jul 7;102(13):982-7.

Ref 11 台灣曾參與的 Yondelis 試驗已發表

Trabectedin plus pegylated liposomal Doxorubicin in recurrent ovarian cancer. J Clin Oncol. 2010 Jul 1;28(19):3107-14. Epub 2010 Jun 1.

其他

Ref 123 ASCO 曰: 化療之前宜先測 hepatitis B

American Society of Clinical Oncology provisional clinical opinion: chronic hepatitis B virus infection screening in patients receiving cytotoxic chemotherapy for treatment of malignant diseases.
J Clin Oncol. 2010 Jul 1;28(19):3199-202. Epub 2010 Jun 1.

Ref 13 苦於 hot flash 但又不能用 estrogen 時的另一選擇

Phase III, placebo-controlled trial of three doses of citalopram for the treatment of hot flashes: NCCTG trial N05C9. J Clin Oncol. 2010 Jul 10;28(20):3278-83. Epub 2010 May 24.

Ref 14 用 modafinil 來改善 cancer-related fatigue

A phase 3 randomized, placebo-controlled, double-blind, clinical trial of the effect of modafinil on cancer-related fatigue among 631 patients receiving chemotherapy: a University of Rochester Cancer Center Community Clinical Oncology Program Research base study. Cancer.

2010 Jul 15;116(14):3513-20.

Ref 15 Vulvar cancer sentinel node metastasis 大小之影響

Size of sentinel-node metastasis and chances of non-sentinel-node involvement and survival in early stage vulvar cancer: results from GROINSS-V, a multicentre observational study. Lancet Oncol. 2010 Jul;11(7):646-52. Epub 2010 May 25.

ABSTRACTS

Ref 1 婦癌科可能要跨科合作了

Human papillomavirus and survival of patients with oropharyngeal cancer. N Engl J Med. 2010 Jul 1;363(1):24-35.

Ang KK, Harris J, Wheeler R, Weber R, Rosenthal DI, Nguyen-Tân PF, Westra WH, Chung CH, Jordan RC, Lu C, Kim H, Axelrod R, Silverman CC, Redmond KP, Gillison ML.

University of Texas M.D. Anderson Cancer Center, Houston, USA.

Comment in:

N Engl J Med. 2010 Jul 1;363(1):82-4.

Abstract

BACKGROUND: **Oropharyngeal squamous-cell carcinomas** caused by human papillomavirus (HPV) are associated with favorable survival, but the independent prognostic significance of tumor HPV status remains unknown. METHODS: We performed a retrospective analysis of the association between tumor HPV status and survival among patients with stage III or IV oropharyngeal squamous-cell carcinoma who were enrolled in a randomized trial comparing accelerated-fractionation radiotherapy (with acceleration by means of concomitant boost radiotherapy) with standard-fractionation radiotherapy, each combined with cisplatin therapy, in patients with squamous-cell carcinoma of the head and neck. Proportional-hazards models were used to compare the risk of death among patients with HPV-positive cancer and those with HPV-negative cancer. RESULTS: The median follow-up period was 4.8 years. The 3-year rate of overall survival was similar in the group receiving accelerated-fractionation radiotherapy and the group receiving standard-fractionation radiotherapy (70.3% vs. 64.3%; P=0.18; hazard ratio for death with accelerated-fractionation radiotherapy, 0.90; 95% confidence interval [CI], 0.72 to 1.13), as were the rates of high-grade acute and late toxic events. A total of **63.8%** of patients with oropharyngeal cancer (206 of 323) had **HPV-positive** tumors; these patients had **better 3-year rates of overall survival** (82.4%, vs. 57.1% among patients with HPV-negative tumors; P<0.001 by the log-rank test) and,

after adjustment for age, race, tumor and nodal stage, tobacco exposure, and treatment assignment, had a 58% reduction in the risk of death (hazard ratio, 0.42; 95% CI, 0.27 to 0.66). The risk of death significantly increased with each additional pack-year of tobacco smoking. Using recursive-partitioning analysis, we classified our patients as having a low, intermediate, or high risk of death on the basis of four factors: HPV status, pack-years of tobacco smoking, tumor stage, and nodal stage. CONCLUSIONS: **Tumor HPV** status is a strong and independent **prognostic factor for survival** among patients with oropharyngeal cancer. (ClinicalTrials.gov number, NCT00047008.)

Ref 2 在月經週期中的何時作 HPV detection

Effect of the menstrual cycle and hormonal contraceptives on human papillomavirus detection in young, unscreened women. Obstet Gynecol. 2010 Jul;116(1):67-75.

Schmeink CE, Massuger LF, Lenselink CH, Quint WG, Melchers WJ, Bekkers RL. Department of Obstetrics and Gynecology, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands. c.schmeink@obgyn.umcn.nl

Abstract

OBJECTIVE: To estimate the effect of the menstrual cycle and oral contraceptive pill (OCP) use on the prevalence, incidence, and persistence of human papillomavirus (HPV). METHODS: A longitudinal study was conducted among 2,065 women aged 18-29 years. The women returned a self-collected cervicovaginal sample and filled out a questionnaire. A total of 1,812 women participated at all three time points, month 0, month 6, and month 12. RESULTS: Low- and high-risk HPV prevalence at study entry was 8.9% and 11.8%, respectively. The annual incidence of low-risk HPV infections was 12.5% and the persistence was 2.0%. For high-risk HPV, the incidence and persistence was 12.1% and 4.5%, respectively. These results did not differ between OCP users and nonusers. A significant relationship between high-risk HPV detection and the timing of sampling was found when OCP users and nonusers were analyzed separately. In the **second half of the menstrual cycle**, high-risk HPV **detection decreased in nonusers** (P=.007) and **increased in OCP users** (P=.021). When women used OCPs continuously, high-risk HPV detection returned to the level of the first half of the menstrual cycle. CONCLUSION: High-risk HPV detection was significantly influenced by sample timing in the menstrual cycle when analyzed separately for OCP users and women with a natural menstrual cycle. This may have implications in the future, when high-risk HPV detection may become a primary screening tool in cervical cancer prevention.

Ref 3 fertility-sparing surgery 之 review

Fertility-sparing surgery in patients with cervical cancer.

Rob L, Skapa P, Robova H. Lancet Oncol. 2010 Jul 7. [Epub ahead of print]

Department of Obstetrics and Gynaecology, 2nd Medical Faculty, Charles University, Prague, Czech Republic.
Abstract
There are several types of fertility saving procedures that can be done in patients with cervical cancer, which differ in terms of surgical approach and extent of paracervical resection. This **review** assesses oncological and pregnancy results after different procedures. The oncological results of vaginal radical trachelectomies (**VRT**) and abdominal radical trachelectomies (**ART**) are similar for tumours **less than 2 cm** in size, and are now **considered safe** surgical procedures. Oncological outcomes of VRT and ART in tumours **larger than 2 cm** are also identical, but the results **cannot be considered satisfactory**. Preliminary findings of less radical procedures (ie, **deep cone and simple trachelectomy**) in patients with tumours less than 2 cm, and negative sentinel and other pelvic lymph nodes, are **comparable** with the results of VRT and ART. Downstaging tumours larger than 2 cm by **neoadjuvant chemotherapy** is still an **experimental** procedure and will need multicentre cooperation to verify its oncological safety. Pregnancy results vary statistically with the different methods.

Ref 4 造成手術後 leg lymphedema 的 risk factor

Risk factors for postoperative lower-extremity lymphedema in endometrial cancer survivors who had treatment including lymphadenectomy. Gynecol Oncol. 2010 Jul 15. [Epub ahead of print]

Todo Y, Yamamoto R, Minobe S, Suzuki Y, Takeshi U, Nakatani M, Aoyagi Y, Ohba Y, Okamoto K, Kato H.
Division of Gynecologic Oncology, National Hospital Organization, Hokkaido Cancer Center, Sapporo, Japan.
Abstract
OBJECTIVE: The aim of this study was to determine the incidence rate of lower-extremity lymphedema after systematic lymphadenectomy in patients with uterine corpus malignancies and to elucidate risk factors for this type of lymphedema.
METHODS: A retrospective chart review was carried out for all patients with uterine corpus malignant tumor managed at Hokkaido Cancer Center between 1991 and 2007. Patients who did not undergo lymphadenectomy as a treatment or died of cancer/intercurrent disease were excluded from this study. All living patients included in this study had hysterectomy, bilateral salpingo-oophorectomy and lymphadenectomy and their medical records were reviewed. We identified patients with postoperative lower-extremity lymphedema (POLEL). Logistic regression analysis was used to select the risk factors for POLEL. RESULTS: Of 286 patients evaluated, 103 (37.8%) had POLEL. Multivariate analysis confirmed that adjuvant **radiation** therapy (OR=5.2, 95% CI=2.1-12.7), resection of **more than 31 lymph nodes** (OR=2.6, 95% CI=1.4-4.9), **and removal of circumflex iliac nodes to the distal external iliac nodes** (CINDEIN)

(OR=6.1, 95% CI=1.3-28.2) were independent risk factors for POLEL. CONCLUSION: Adjuvant radiation therapy should be avoided in patients who undergo systematic lymphadenectomy if an alternative postoperative strategy is possible. Although reducing the number of resected lymph nodes is not appropriate from a therapeutical point of view, elimination of CINDEIN dissection may be helpful in reducing the incidence of POLEL. The clinical significance of CINDEIN dissection needs to be investigated by a randomized controlled trial.

Ref 5 Cytoreductive surgery 在 endometrial cancer 之角色

Cytoreductive surgery for advanced or recurrent endometrial cancer: a meta-analysis. Gynecol Oncol. 2010 Jul;118(1):14-8.

Barlin JN, Puri I, Bristow RE.

Department of Gynecology and Obstetrics, The Johns Hopkins Hospital, 600 North Wolfe St, Phipps 281, Baltimore, MD 21287, USA. jbarlin1@jhmi.edu

Abstract

OBJECTIVE: To determine the relative effect and quantify the impact of multiple prognostic variables on median overall survival time among cohorts of patients with advanced or recurrent endometrial cancer undergoing cytoreductive surgery. METHODS: Fourteen retrospective cohorts with advanced or recurrent endometrial cancer (672 patients) meeting study inclusion criteria were identified. Univariate analysis was used to assess the effect on median overall survival time of multiple variables. The limited number of studies available made multivariate analysis impractical. RESULTS: Statistically significant clinical variables associated with median overall survival time were the proportion of patients undergoing complete surgical cytoreduction, adjuvant radiation, or receiving adjuvant chemotherapy. Cohort median overall survival time was positively associated with increasing proportion of patients undergoing complete surgical cytoreduction (each 10% increase improving survival by 9.3 months, p=0.04) and receiving post-operative radiation therapy (each 10% increase improving survival by 11.0 months, p=0.004), while an increasing proportion of patients receiving chemotherapy was negatively associated with survival (each 10% increase decreasing survival by 10.4 months, p=0.007). CONCLUSIONS: The current analysis **suggests** that among patients with **advanced or recurrent endometrial cancer**, complete **cytoreduction to no gross residual disease** is associated with **superior overall survival** outcome. The unexpected correlation between treatment modality and survival may be a surrogate marker for more precise factors such as location of disease, performance status, or cytoreductive status post-operatively, which may have influenced the decision to administer adjuvant radiation versus chemotherapy and were not able to be controlled for given the limitations of the extracted data.

Ref 6 子宮內膜厚度之 cutoff value

Endometrial thickness measurement for detecting endometrial cancer in women with postmenopausal bleeding: a systematic review and meta-analysis. Obstet Gynecol. 2010 Jul;116(1):160-7.

Timmermans A, Opmeer BC, Khan KS, Bachmann LM, Epstein E, Clark TJ, Gupta JK, Bakour SH, van den Bosch T, van Doorn HC, Cameron ST, Giusa MG, Dessole S, Dijkhuizen FP, Ter Riet G, Mol BW.

Department of Obstetrics and Gynecology, Academic Medical Centre, Amsterdam, The Netherlands. anne_timmermans@hotmail.com

Abstract

OBJECTIVE: To estimate the accuracy of endometrial thickness measurement in the detection of endometrial cancer among women with postmenopausal bleeding with individual patient data using different meta-analytic strategies. DATA SOURCES: Original data sets of studies detected after reviewing the included studies of three previous reviews on this subject. An additional literature search of published articles using MEDLINE databases was preformed from January 2000 to December 2006 to identify articles reporting on endometrial carcinoma and sonographic endometrial thickness measurement in women with postmenopausal bleeding. METHODS OF STUDY SELECTION: We identified 90 studies reporting on endometrial thickness measurements and endometrial carcinoma in women with postmenopausal bleeding. TABULATION, INTEGRATION, AND RESULTS: We contacted 79 primary investigators to obtain the individual patient data of their reported studies, of which 13 could provide data. Data on 2,896 patients, of which 259 had carcinoma, were included. Several approaches were used in the analyses of the acquired data. First, we performed receiver operator characteristics (ROC) analysis per study, resulting in a summary area under the ROC curve (AUC) calculated as a weighted mean of AUCs from original studies. Second, individual patient data were pooled and analyzed with ROC analyses irrespective of study with standardization of distributional differences across studies using multiples of the median and by random effects logistic regression. Finally, we also used a two-stage procedure, calculating sensitivities and specificities for each study and using the bivariate random effects model to estimate summary estimates for diagnostic accuracy. This resulted in rather comparable ROC curves with AUCs varying between 0.82 and 0.84 and summary estimates for sensitivity and specificity located along these curves. These curves indicated a lower AUC than previously reported meta-analyses using conventional techniques. CONCLUSION: Previous meta-analyses on endometrial thickness measurement probably have overestimated its diagnostic accuracy in the detection of endometrial carcinoma. We advise the use of **cutoff level of 3 mm** for exclusion of endometrial carcinoma in women with **postmenopausal bleeding**.

Ref 7 荷蘭 endometrial cancer 的 randomized trial: TAH vs. TLH

Safety of laparoscopy versus laparotomy in early-stage endometrial cancer: a randomised trial. Lancet Oncol. 2010 Jul 16. [Epub ahead of print]

Mourits MJ, Bijen CB, Arts HJ, Ter Brugge HG, van der Sijde R, Paulsen L, Wijma J, Bongers MY, Post WJ, van der Zee AG, de Bock GH.

Department of Gynaecology, University Medical Center Groningen, University of Groningen, Netherlands.

Abstract

BACKGROUND: The standard surgery for early-stage endometrial cancer is total abdominal hysterectomy (TAH) and bilateral salpingo-oophorectomy, which is associated with substantial morbidity. Total laparoscopic hysterectomy (TLH) and bilateral salpingo-oophorectomy is less invasive and is assumed to be associated with lower morbidity, particularly in obese women. This study investigated the complication rate of TLH versus TAH in women with early-stage endometrial cancer. METHODS: This randomised trial was done in 21 hospitals in the Netherlands, and **26 gynaecologists with proven sufficient skills** in TLH participated. 283 patients with stage I endometrioid adenocarcinoma or complex atypical hyperplasia were randomly allocated (2:1) to the intervention group (TLH, n=187) or control group (TAH, n=96). Randomisation by sequential number generation was done centrally in alternate blocks of six and three participants, with stratification by trial centre. After assignment, the study coordinators, patients, gynaecologists, and members of the panel were not masked to intervention. The primary outcome was major complication rate, assessed by an independent panel. Data were analysed by a modified intention-to-treat analysis, since two patients in both groups were excluded from the main analysis. This trial is registered with the Dutch trial registry, number NTR821. FINDINGS: The proportion of **major complications** was 14.6% (27 of 185) in the TLH group versus 14.9% (14 of 94) in the TAH group, with a difference of -0.3% (95% CI -9.1 to 8.5; p=0.95). The proportion of patients with an **intraoperative** major complication (nine of 279 [**3.2%**]) was lower than the proportion with a postoperative major complication (32 of 279 [11.5%]) and did not differ between TLH (five of 185 [2.7%]) and TAH (four of 94 [4.3%]; p=0.49). The proportion of patients with a minor complication was 13.0% (24 of 185) in the TLH group and 11.7% (11 of 94) in the TAH group (p=0.76). Conversion to laparotomy occurred in 10.8% (20 of 185) of the laparoscopic procedures. TLH was associated with significantly less blood loss (p<0.0001), less use of pain medication (p<0.0001), a shorter hospital stay (p<0.0001), and a faster recovery (p=0.002), but the procedure took longer than TAH (p<0.0001). INTERPRETATION: Our results showed **no evidence of a benefit** for TLH over TAH in terms of major complications, but TLH (done by skilled surgeons) was **beneficial in terms of** a shorter hospital stay, less pain, and quicker resumption of daily activities.

Ref 8 澳洲 endometrial cancer 的 randomized trial: TAH vs. TLH

Quality of life after total laparoscopic hysterectomy versus total abdominal hysterectomy for stage I endometrial cancer (LACE): a randomised trial.

Lancet Oncol. 2010 Jul 16. [Epub ahead of print]

Janda M, Gebski V, Brand A, Hogg R, Jobling TW, Land R, Manolitsas T, McCartney A, Nascimento M, Neesham D, Nicklin JL, Oehler MK, Otton G, Perrin L, Salfinger S, Hammond I, Leung Y, Walsh T, Sykes P, Ngan H, Garrett A, Laney M, Ng TY, Tam K, Chan K, Wrede CD, Pather S, Simcock B, Farrell R, Obermair A.

Queensland University of Technology, School of Public Health, Institute of Health and Biomedical Innovation, QLD, Australia.

Abstract

BACKGROUND: This two-stage randomised controlled trial, comparing total laparoscopic hysterectomy (TLH) with total abdominal hysterectomy (TAH) for stage I endometrial cancer (LACE), began in 2005. The primary objective of stage 1 was to assess whether TLH results in equivalent or improved quality of life (QoL) up to 6 months after surgery compared with TAH. The primary objective of stage 2 was to test the hypothesis that disease-free survival at 4.5 years is equivalent for TLH and TAH. Here, we present the results of stage 1. METHODS: Between Oct 7, 2005, and April 16, 2008, 361 participants were enrolled in the QoL substudy at 19 centres across Australia, New Zealand, and Hong Kong; 332 completed the QoL analysis. Randomisation was done centrally and independently from other study procedures via a computer-generated, web-based system (providing concealment of the next assigned treatment), using stratified permuted blocks of three and six patients. Patients with histologically confirmed stage I endometrioid adenocarcinoma and Eastern Cooperative Oncology Group performance status less than 2 were randomly assigned to TLH (n=190) or TAH (n=142), stratified by histological grade and study centre. Patients and study personnel were not masked to treatment assignment. QoL was measured at baseline, 1 and 4 weeks (early), and 3 and 6 months (late) after surgery, using the Functional Assessment of Cancer Therapy-General (FACT-G) questionnaire. The primary endpoint was the difference between groups in QoL change from baseline at early and late timepoints (a 5% difference was considered clinically significant). Analysis was done according to the intention-to-treat principle. Patients for both stages of the trial have now been recruited and are being followed up for disease-specific outcomes. The LACE trial is registered with ClinicalTrials.gov, number NCT00096408. FINDINGS: Eight of 332 patients (2.4%) had treatment conversion-seven from TLH to TAH and one from TAH to TLH (patient preference). In the early phase of recovery, patients who had TLH reported significantly greater improvement in QoL from baseline compared with those who had TAH, in all subscales apart from emotional and social wellbeing. Improvements in QoL up to 6 months after surgery continued to favour TLH, except in the emotional and social wellbeing measures of FACT and the visual analogue scale of the EuroQoL five dimensions (EuroQoL-VAS). Operating time was significantly longer in the TLH group (138 min [SD 43]) than in the TAH group (109 min [34]; p=0.001). Although the

proportion of intraoperative adverse events was similar between groups (TAH eight of 142 [5.6%] vs TLH 14 of 190 [7.4%]; p=0.53); postoperatively, twice as many patients in the TAH group experienced adverse events of grade 3 or higher (33 of 142 [23.2%] vs 22 of 190 [11.6%] in the TLH group; p=0.004). Postoperative serious adverse events occurred more in the TAH group (27 of 142 [19.0%]) than in the TLH group (16 of 190 [7.9%]; p=0.002). INTERPRETATION: QoL improvements from baseline during early and later phases of recovery, and the adverse event profile, **favour TLH compared with TAH for treatment of stage I endometrial cancer**.

Ref 9 Platinum-sensitive recurrence 的標準治療恐怕要改了

Pegylated liposomal Doxorubicin and Carboplatin compared with Paclitaxel and Carboplatin for patients with platinum-sensitive ovarian cancer in late relapse.

J Clin Oncol. 2010 Jul 10;28(20):3323-9.

Pujade-Lauraine E, Wagner U, Aavall-Lundqvist E, Gebski V, Heywood M, Vasey PA, Volgger B, Vergote I, Pignata S, Ferrero A, Sehouli J, Lortholary A, Kristensen G, Jackisch C, Joly F, Brown C, Le Fur N, du Bois A.

University Paris Descartes, Assistance Publique-Hôpitaux de Paris, Hôpital Hôtel Dieu, Paris, France. epujade@arcagy.org

Abstract

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). PATIENTS AND METHODS: Patients with histologically proven ovarian cancer with **recurrence more than 6 months after** first- or second-line platinum and taxane-based therapies were randomly assigned by stratified blocks to CD (**carboplatin area under the curve [AUC] 5 plus PLD 30 mg/m(2)) every 4 weeks** or CP (carboplatin AUC 5 plus paclitaxel 175 mg/m(2)) every 3 weeks for at least 6 cycles. Primary end point was progression-free survival (PFS); secondary end points were toxicity, quality of life, and overall survival. RESULTS: Overall 976 patients were recruited. With median follow-up of 22 months, PFS for the CD arm was statistically superior to the CP arm (hazard ratio, 0.821; 95% CI, 0.72 to 0.94; P = .005); median PFS was 11.3 versus 9.4 months, respectively. Although overall survival data are immature for final analysis, we report here a total of 334 deaths. Overall severe nonhematologic toxicity (36.8% v 28.4%; P < .01) leading to early discontinuation (15% v 6%; P < .001) occurred more frequently in the CP arm. More frequent grade 2 or greater alopecia (83.6% v 7%), hypersensitivity reactions (18.8% v 5.6%), and sensory neuropathy (26.9% v 4.9%) were observed in the CP arm; more hand-foot syndrome (grade 2 to 3, 12.0% v 2.2%), nausea (35.2% v 24.2%), and mucositis (grade 2-3, 13.9% v 7%) in the CD arm. CONCLUSION: To our knowledge, this trial is the largest in recurrent ovarian cancer and has demonstrated **superiority in**

PFS and **better therapeutic index** of CD over standard CP.

Ref 10 Early ovarian cancer 應予徹底之手術分期

Surgical staging and treatment of early ovarian cancer: long-term analysis from a randomized trial. J Natl Cancer Inst. 2010 Jul 7;102(13):982-7. Epub 2010 May 5.

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Abstract

A **long-term follow-up** analysis of the randomized clinical trial Adjuvant Chemotherapy in Ovarian Neoplasm (**ACTION**) from the European Organization for Research and Treatment of Cancer was undertaken to determine whether the original results with a median follow-up of 5.5 years could be verified after longer follow-up with more events. In the ACTION trial, 448 patients with early ovarian cancer were randomly assigned, after surgery, to adjuvant chemotherapy or to observation (no further treatment). The original analysis found that adjuvant chemotherapy improved recurrence-free survival but not overall survival and found in a subgroup analysis that completeness of surgical staging was an independent prognostic factor, with better recurrence-free and overall survival among those with complete (optimal) surgical staging. After a median follow-up of 10.1 years, we analyzed the more mature data from the ACTION trial and found support for most of the main conclusions of the original analysis, except that **overall survival after optimal surgical staging was improved, even among patients who received adjuvant chemotherapy** (hazard ratio of death = 1.89, 95% confidence interval = 0.99 to 3.60; overall two-sided log-rank test P = .05). More cancer-specific deaths were observed among nonoptimally staged patients (40 [27%] of the 147 deaths in the observation arm and 11 [14%] of the 76 deaths in the adjuvant chemotherapy arm) than among optimally staged patients (seven [9%] of the 75 deaths in the observation arm and 11 [14%] of the 76 deaths in the adjuvant chemotherapy arm) (two-sided chi(2) test for heterogeneity, P = .06). Thus, **completeness of surgical staging** in patients with early ovarian cancer was found to be statistically **significantly associated with better** outcomes, and the benefit from adjuvant chemotherapy appeared to be restricted to patients with nonoptimal surgical staging.

Ref 11 台灣曾參與的 Yondelis 試驗已發表

Trabectedin plus pegylated liposomal Doxorubicin in recurrent ovarian cancer. J Clin Oncol. 2010 Jul 1;28(19):3107-14. Epub 2010 Jun 1.

Monk BJ, Herzog TJ, Kaye SB, Krasner CN, Vermorken JB, Muggia FM, Pujade-Lauraine E, Lisyanskaya AS, Makhson AN, Rolski J, Gorbounova VA, Ghatage P,

Bidzinski M, Shen K, Ngan HY, Vergote IB, Nam JH, Park YC, Lebedinsky CA, Poveda AM.
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Comment in:
J Clin Oncol. 2010 Jul 1;28(19):3101-3.
Abstract
PURPOSE: The objective of this study was to compare the efficacy and safety of trabectedin plus pegylated liposomal doxorubicin (PLD) with that of PLD alone in women with recurrent ovarian cancer after failure of first-line, platinum-based chemotherapy. PATIENTS AND METHODS: Women > or = 18 years, stratified by performance status (0 to 1 v 2) and platinum sensitivity, were randomly assigned to receive an intravenous infusion of PLD 30 mg/m(2) followed by a 3-hour infusion of trabectedin 1.1 mg/m(2) every 3 weeks or PLD 50 mg/m(2) every 4 weeks. The primary end point was progression-free survival (PFS) by independent radiology assessment. RESULTS: Patients (N = 672) were randomly assigned to trabectedin/PLD (n = 337) or PLD (n = 335). Median PFS was 7.3 months with trabectedin/PLD v 5.8 months with PLD (hazard ratio, 0.79; 95% CI, 0.65 to 0.96; P = .0190). For platinum-sensitive patients, median PFS was 9.2 months v 7.5 months, respectively (hazard ratio, 0.73; 95% CI, 0.56 to 0.95; P = .0170). Overall response rate (ORR) was 27.6% for trabectedin/PLD v 18.8% for PLD (P = .0080); for platinum-sensitive patients, it was 35.3% v 22.6% (P = .0042), respectively. ORR, PFS, and overall survival among platinum-resistant patients were not statistically different. Neutropenia was more common with trabectedin/PLD. Grade 3 to 4 transaminase elevations were also more common with the combination but were transient and noncumulative. Hand-foot syndrome and mucositis were less frequent with trabectedin/PLD than with PLD alone. CONCLUSION: **When combined with PLD, trabectedin improves PFS and ORR** over PLD alone with acceptable tolerance in the second-line treatment of recurrent ovarian cancer.

Ref 12 ASCO 曰: 化療之前宜先測 hepatitis B

American Society of Clinical Oncology provisional clinical opinion: chronic hepatitis B virus infection screening in patients receiving cytotoxic chemotherapy for treatment of malignant diseases. J Clin Oncol. 2010 Jul 1;28(19):3199-202. Epub 2010 Jun 1.

Artz AS, Somerfield MR, Feld JJ, Giusti AF, Kramer BS, Sabichi AL, Zon RT, Wong SL.
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Abstract
PURPOSE An American Society of Clinical Oncology (ASCO) provisional clinical opinion (PCO) offers timely clinical direction to ASCO's membership following publication or presentation of potentially practice-changing information. This PCO

addresses **recommendations** for chronic hepatitis B virus (**HBV) infection screening** in patients receiving **cytotoxic or immunosuppressive chemotherapy** for treatment of malignant diseases. CLINICAL CONTEXT: The Centers for Disease Control and Prevention (CDC) issued Recommendations for Identification and Public Health Management of Persons with Chronic Hepatitis B Virus Infection, recommending screening for hepatitis B infection (hepatitis B surface antigen [**HBsAg**], antihepatitis B core antigen [**anti-HBc**], and antibodies to HBsAg [**anti-HBs**]) for "persons receiving cytotoxic or immunosuppressive therapy (eg, chemotherapy for malignant diseases...)." PROVISIONAL CLINICAL OPINION: The evidence is insufficient to determine the net benefits and harms of routine screening for chronic HBV infection in individuals with cancer who are about to receive cytotoxic or immunosuppressive therapy or who are already receiving therapy. Individuals with cancer who undergo certain cytotoxic or immunosuppressive therapies and have HBV infection or prior exposure to HBV may be at **elevated risk of liver failure from HBV reactivation**. As such, HBV screening requires clinical judgment. Physicians may consider screening patients belonging to groups at heightened risk for chronic HBV infection or if highly immunosuppressive therapy is planned. Highly immunosuppressive treatments include, but are not limited to, hematopoietic cell transplantation and regimens including rituximab. Screening based on a high risk of prior HBV exposure or risk of reactivation due to planned therapeutic regimens should include testing for HBsAg as a serologic marker for HBV infection. In some populations, testing for anti-HBc should also be considered. There is no evidence to support serologic testing for anti-HBs in this context. When evidence for chronic HBV infection is found, **antiviral therapy before and throughout the course of chemotherapy** may be considered to reduce the risk of HBV reactivation, although evidence from controlled trials of this approach is limited. Screening and/or treating HBV infection should not delay the initiation of chemotherapy. NOTE: ASCO's provisional clinical opinions (PCOs) reflect expert consensus based on clinical evidence and literature available at the time they are written, and are intended to assist physicians in clinical decision-making and identify questions and settings for further research. Due to the rapid flow of scientific information in oncology, new evidence may have emerged since the time a PCO was submitted for publication. PCOs are not continually updated and may not reflect the most recent evidence. PCOs address only the topics specifically identified in the PCO and are not applicable to interventions, diseases or stages of disease not specifically identified. PCOs cannot account for individual variation among patients, and cannot be considered inclusive of all proper methods of care or exclusive of other treatments. It is the responsibility of the treating physician or other health care provider, relying on independent experience and knowledge of the patient, to determine the best course of treatment for the patient. Accordingly, adherence to any PCO is voluntary, with the ultimate determination regarding its application to be made by the physician in light of each patient's individual circumstances. ASCO PCOs describe the use of procedures and therapies in clinical practice and cannot be assumed to apply to the use of these

interventions in the context of clinical trials. ASCO assumes no responsibility for any injury or damage to persons or property arising out of or related to any use of ASCO's PCOs, or for any errors or omissions.

Ref 13 Hot flash 又不能用 estrogen 時的另一選擇

Phase III, placebo-controlled trial of three doses of citalopram for the treatment of hot flashes: NCCTG trial N05C9. J Clin Oncol. 2010 Jul 10;28(20):3278-83. Epub 2010 May 24.

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Abstract

PURPOSE: Up to 75% of women experience hot flashes, which can negatively impact quality of life. As hot flash physiology is not definitively understood, it cannot be assumed that effective agents represent class effects. Therefore, there is a continued need for rigorous evaluation to identify effective **nonhormonal options** for hot flash relief. METHODS: A randomized, double-blind trial evaluated citalopram at target doses of 10, 20, or 30 mg/d versus placebo for 6 weeks. Postmenopausal women with at least 14 bothersome hot flashes per week recorded hot flashes for 7 days before starting treatment and were then titrated to their target doses. The primary end point was the change from baseline to 6 weeks in hot flash score. RESULTS: Two hundred fifty-four women were randomly assigned onto this study. Data for hot flash scores and frequencies showed significant improvement in hot flashes with citalopram over placebo, with no significant differences among doses. **Reductions in mean hot flash scores** were 2.0 (23%), 7.0 (49%), 7.7 (**50%**), and 10.7 (55%) for placebo and 10, 20, and 30 mg of citalopram, respectively (P <or= .002). Improvement in secondary outcomes, such as the Hot Flash Related Daily Interference Scale, was statistically superior in the 20-mg arm. Citalopram was well-tolerated, with no significant negative adverse effects. CONCLUSION: Citalopram is an effective, well-tolerated agent in managing hot flashes. There does not appear to be a significant dose response above 10 mg/d, but broader helpful effects of the agent appear to be more evident at **20 mg/d**.

Ref 14 用 modafinil 來改善 cancer-related fatigue

A phase 3 randomized, placebo-controlled, double-blind, clinical trial of the effect of modafinil on cancer-related fatigue among 631 patients receiving chemotherapy: a University of Rochester Cancer Center Community Clinical Oncology Program Research base study. Cancer. 2010 Jul 15;116(14):3513-20.

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Abstract
BACKGROUND:: Cancer-related fatigue is a debilitating symptom affecting psychosocial functioning and quality of life in 70% to 100% of cancer patients during and after treatment. The authors examined the effect of 200 mg of modafinil daily on the severity of cancer-related fatigue. METHODS:: The authors conducted a multicenter, randomized, double-blind, placebo-controlled, phase 3, clinical trial to examine the effect of modafinil on patient-reported fatigue **in cancer patients undergoing chemotherapy**. A sample of 877 cancer patients beginning chemotherapy at 23 geographically separate University of Rochester Cancer Center (URCC) Community Clinical Oncology Program (CCOP) affiliates were assessed for fatigue. Patients who reported fatigue (N = 867) were randomly assigned to receive either **200 mg of oral modafinil (Provigil) daily** or a placebo. Treatment began on Day 5 of Cycle 2 and ended after Day 7 of Cycle 4. Fatigue and depression were assessed during Cycles 2 to 4 by using psychometrically valid measures. Group differences (treatment vs control) in the worst level of fatigue during the previous week at Cycle 4 were examined by using an analysis of covariance (ANCOVA) adjusting for baseline fatigue (Cycle 2). RESULTS:: There were 631 patients (315 modafinil, 316 placebo) who provided evaluable data. ANCOVA showed a significant interaction between treatment condition and baseline fatigue (P = .017), where patients with severe baseline fatigue (n = 458) benefited from modafinil, whereas patients with mild or moderate fatigue did not. Modafinil had no statistically significant effect on depression (P > .05). CONCLUSIONS:: **Modafinil may be useful** in controlling cancer-related fatigue in patients who present **with severe fatigue** but is not useful in patients with mild or moderate fatigue.

Ref 15 Vulvar cancer sentinel node metastasis 大小之影響

Size of sentinel-node metastasis and chances of non-sentinel-node involvement and survival in early stage vulvar cancer: results from GROINSS-V, a multicentre observational study. Lancet Oncol. 2010 Jul;11(7):646-52. Epub 2010 May 25.

Oonk MH, van Hemel BM, Hollema H, de Hullu JA, Ansink AC, Vergote I, Verheijen RH, Maggioni A, Gaarenstroom KN, Baldwin PJ, van Dorst EB, van der Velden J, Hermans RH, van der Putten HW, Drouin P, Runnebaum IB, Sluiter WJ, van der Zee AG.
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Comment in:
Lancet Oncol. 2010 Jul;11(7):607-8.

Abstract

BACKGROUND: Currently, all patients with vulvar cancer with a positive sentinel node undergo inguinofemoral lymphadenectomy, irrespective of the size of sentinel-node metastases. Our study aimed to assess the association between size of sentinel-node metastasis and risk of metastases in non-sentinel nodes, and risk of disease-specific survival in early stage vulvar cancer. METHODS: In the GROningen INternational Study on Sentinel nodes in Vulvar cancer (GROINSS-V), sentinel-node detection was done in patients with T1-T2 (<4 cm) squamous-cell vulvar cancer, **followed by inguinofemoral lymphadenectomy if metastatic disease was identified in the sentinel node**, either by routine examination or pathological ultrastaging. For the present study, sentinel nodes were independently reviewed by two pathologists. FINDINGS: Metastatic disease was identified in one or more sentinel nodes in 135 (33%) of 403 patients, and 115 (85%) of these patients had inguinofemoral lymphadenectomy. The risk of non-sentinel-node metastases was higher when the sentinel node was found to be positive with routine pathology than with ultrastaging (23 of 85 groins vs three of 56 groins, p=0.001). For this study, 723 sentinel nodes in 260 patients (2.8 sentinel nodes per patient) were reviewed. The **proportion of patients with non-sentinel-node metastases increased with size of sentinel-node metastasis**: one of 24 patients with individual tumour cells had a non-sentinel-node metastasis; two of 19 with metastases 2 mm or smaller; two of 15 with metastases larger than 2 mm to 5 mm; and ten of 21 with metastases larger than 5 mm. **Disease-specific survival** for patients with sentinel-node metastases larger than **2 mm** was **lower** than for those with sentinel-node metastases 2 mm or smaller (69.5%vs 94.4%, p=0.001). INTERPRETATION: Our data show that the risk of non-sentinel-node metastases increases with size of sentinel-node metastasis. No size cutoff seems to exist below which chances of non-sentinel-node metastases are close to zero. Therefore, **all patients with sentinel-node metastases should have additional groin treatment.** The prognosis for patients with sentinel-node metastasis larger than 2 mm is poor, and novel treatment regimens should be explored for these patients.