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Tabel harus singkat dan jelas. Judul table hendaknya ditulis di atasnya dan catatan di bawahnya. Jelaskan semua singkatan yang dipergunakan. Gambar hendaknya jelas dan lebih disukai bila telah siap untuk dicetak. Judul gambar ditulis di bawahnya.

Asal rujukan table atau gambar dituliskan di bawahnya. Tabel dan gambar hendaknya dibuat dengan program Power Point, Free Hand, atau Photoshop, (menggunakan format jpeg).

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Jurnal

1. *Naskah dalam majalah/jurnal*
   Gracey M. The contaminated small-bowel syndrome: pathogenesis, diagnosis, and treatment. Am J Clin Nutr 1979; 32:234-43.
2. *Organisasi sebagai pengarang utama*
   Direktorat Jenderal PPm & PLP, Departemen Kesehatan Republik Indonesia. Pedoman pengobatan malaria. Medika 1993; 34-23-8.
3. *Tanpa nama pengarang*
   Imaging of sinusitis [editorial]. Ped Infect J 1999; 18:1019-20.
4. *Suplemen*
   Solomkim JS, Hemsel DL, Sweet R, dkk. Evaluation of new infective drugs for the treatment of intrabdominal infections. Clin Infect Dis 1992, 15 Suppl 1:S33-42.

Buku dan Monograf

1. *Penulis pribadi*
   Banister BA, Begg NT, Gillespie SH. Infectious Disease. Edisi pertama. Oxford: Blackwell Science; 1996.
2. *Penulis sebagai penyunting*
   Galvani DW, Cawley JC, Penyunting. Cytokine therapy. New York: Press Syndicate of University of Cambridge; 1992.
3. *Organisasi sebagai penulis dan penerbit*
   World Bank. World development report 1993; investing in health. New York: World Bank; 1993.
4. *Bab dalam buku*
   Loveday C. Virogoly of AIDS. Dalam: Mindel A, Miller R, penyunting. AIDS, a pocket book of diagnosis and management. Edisi kedua. London: Arnold Holder Headline Group; 1996. H. 19-41.
5. *Attention: konferensi*
   Kimura j, Shibasaki H, penyunting. Recent advanced in clinical neurophysiology. Presiding dari the 10th International 15-19 Oktober 1995.
6. *Naskah konferensi*
   Begston S, Solheim BG, Enforcement of data protection, privacy and security in medical informatics. Dalam : Lun KC, Degoultet P, Piemme TE, Reinhoff o, penyunting MEDINFO 92. Presiding the 7th World Congress on Medical Informatics: Sep 6-10, 1992; Genewa, Swiss. Amsterdam: North Holland; 1993. H. 1561-5.
7. *Laporan ilmiah*
   Akutsu T. Total heart replacement device. Bethesda: National Institute of Health, Nation Heart and Lung Institute; 1974 Apr. Report No: NHH-NHL1-69-2185-4.
8. *Disertasi*
   Suyitno RH. Pengamatan vaksinasi dalam hubungannya dengan berbagai tingkat gizi [disertasi]. Semarang: Fakultas Kedokteran Universitas Diponegoro, 1983.

Publikasi lain

1. *Naskah dalam Koran*
   Bellamy C. Gizi bayi adalah investasi masa depan. Kompas 26 Januari 2000; hal 8 kolom 7-8.
2. *Naskah dari audiovisual*
   AIDS epidemic: the physician's role [rekaman video]. Cleveland: Academy of Medicine of Cleveland, 1987.
3. *Naskah belum dipublikasi (sedang dicetak)*
   Connellv KK. Febrile neutrDpenia. J Infect Dis. In press.
4. *Naskah Jurnal dalam bentuk elektronik*
   Morse SS. Factors in the emergence of infectious disease. Emerg Infect Dis [serial online] Jan-Mar 1995 [cited 5 Jan 1996] 1910: [24 screen]. Didapat dari URL: http\\www.cdc.gov/ncidod/EID/eid.htm.
5. *Monograf dalam format elektronik*
   CDI. LliniGiil dermatology illustrated [monograph pada enROM]. Reeves JRT, Maibach H, CMEAMultimedia Lnnip, produser, edisi ke-2. Versi 2.0. San Diego: CMEA; 1995.
6. *Naskah dari file computer*
   Hemodynamics III: the ups and down of hemodynamics [program computer]. Versi 2.2. Orlando (F-L); Computerized Educational System; 1993.

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Daftar Isi

Factors Which Influenced on Two Years Recurrence of Epithelial Ovarian Cancer Patients After Surgery and Platinum Based Chemotherapy

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ABSTRACT

Ovarian cancer was the leading cause of death in gynecologic cancer which had the two years recurrence rate of 50%. We used retrospective cohort design with survival analysis technique to examine the role of post-surgery residual tumor size, cancer cell histological subtype and cancer cell grading on epithelial ovarian cancer recurrence. We also want to know the prevalence of HER-2 (Human Epidermal Receptor-2) overexpression in epithelial ovarian cancer patients. Sixty-five epithelial ovarian cancer patient (1998-2012) who had achieved remission were observed for 24 months. We reported median age of 50 years with recurrence rate of 36.9% and mean time of first recurrence was 19.15 months. Size of post-surgery residual tumor more than 1 cm increase Hazard Ratio (HR) of two years recurrence of epithelial ovarian cancer with p value 0.02 and HR of 3.31 (95% CI 1.46-7.49) but papillary serous histology subtype and poor differentiated cancer cell grading did not influence the recurrence. One of 38 patients showed cytoplasmic staining in HER-2 overexpression examination by immunohistochemistry methods. Conclusion: Size of post-surgery residual tumor more than 1 cm increase Hazard Ratio of two years recurrence of epithelial ovarian cancer while papillary serous histology subtype and poor differentiated cancer cell grading did not influence the recurrence. One sample showed cytoplasmic staining on HER-2 overexpression examination.

Keyword: *epithelial ovarian cancer, recurrence*

ABSTRAK

Kanker ovarium merupakan penyebab kematian tertinggi pada kelompok kanker ginekologik, dengan angka kekambuhan dua tahun sebesar 50%. Penelitian ini menggunakan desain kohort retrospektif dengan teknik analisis kesintasan yang bertujuan melihat peran faktor ukuran residu tumor post-operasi, jenis subtipe sel kanker, dan tingkat diferensiasi sel kanker terhadap kekambuhan dua tahun pasien kanker ovarium epitelial. Penelitian ini juga ingin melihat besarnya prevalensi overekspresi *Human Epidermal Receptor-2* (HER-2) pada pasien kanker ovarium epitelial. Sebanyak 65 pasien kanker ovarium epitelial (tahun 1998-2012) yang telah remisi diamati selama 24 bulan. Terlihat bahwa median usia pasien 50 tahun dengan proporsi kekambuhan sebesar 36,9% dengan mean waktu kekambuhan pertama 19,15 bulan. Ukuran residu tumor post-operasi lebih dari 1 cm meningkatkan rasio hazard kekambuhan dua tahun kanker ovarium epitelial dengan nilai p: 0,02 dan HR 3,31 (IK95% 1,46-7,49). Sementara, jenis subtipe histologi *papillary serosa* dan tingkat diferensiasi buruk sel kanker tidak berhubungan dengan terjadinya kekambuhan. Pada pemeriksaan overekspresi HER-2 menggunakan teknik imunohistokimia dilaporkan satu dari 38 pasien memperlihatkan adanya *cytoplasmic staining*.

Disimpulkan bahwa ukuran residu tumor post-operasi yang berukuran lebih dari 1 cm meningkatkan rasio *hazard* kekambuhan dua tahun pasien kanker ovarium epitelial, sementara jenis subtipe histologi *papillary serous* dan tingkat diferensiasi buruk sel kanker tidak berhubungan dengan terjadinya kekambuhan. Pada pemeriksaan overekspresi HER-2 menggunakan teknik imunohistokimia, dilaporkan satu sampel memperlihatkan adanya *cytoplasmic staining*.

Kata Kunci: kanker ovarium epitelial, kekambuhan

Hubungan Genotipe DNA *Human Papillomavirus* (HPV) Terhadap Respons Terapi Radiasi Pada Karsinoma Sel Skuamosa Serviks

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ABSTRACT

The importance of human papilloma virus (HPV) infection in the outcome of cervical cancer after radiotherapy remains unknown. Our study explored whether the HPV status of tumors is associated with the outcome of radiotherapy in patients with cervical cancer.

The biopsy cervix samples taken from 31 patients with squamous cell carcinoma cervix (Stage IIB-IIIB) that met in the inclusion criteria. The HPV were genotyping examination was conducted twice before and 3 month after radiation therapy. The subjects treated by radiation therapy according to standard procedures. After undergone complete radiation, response of radiation therapy was conducted by clinical assessment and repeat HPV genotyping test.

A total of 31 patients had HPV-positive tumors in 83.37% (27 cases) of patients, with the details of a single infection of 75% and 9:37% multiple infections. Based on the type of HPV type 16 was obtained (43.74%), type 18 (18.64%). Persistent infection with HPV after radiation encountered by 34.61%. Complete clinical response observed in the single infection group number of 100%, while in the group of multiple infections by 33.3% (p = 0.115). While HPV infection settled with a complete clinical response by 32% (p = 0.346).

There were no statistically relationships between clinical complete response with single or multiple HPV infection (p = 0.115). There were no statistically relationship between persistent HPV infection with complete clinical response. (p = 0.346)

Keyword: *Cervical cancer, Genotyping HPV DNA, persistent infection, clinical response*

ABSTRAK

Penelitian ini bertujuan untuk mengetahui hubungan antara tipe DNA HPV dengan terjadinya infeksi HPV menetap dan hubungan antara infeksi HPV dengan respons klinis terapi radiasi. Selain itu, penelitian ini juga bertujuan untuk mengetahui apakah infeksi HPV menetap merupakan faktor prognosis respons klinis radiasi penderita karsinoma sel skuamosa serviks.

Sebanyak 31 penderita kanker serviks stadium IIB-IIIB dengan hasil histopatologi karsinoma sel skuamosa sesuai dengan kriteria inklusi dilakukan pemeriksaan genotipe HPV DNA yang berasal dari biopsi serviks. Sampel penelitian ditata laksana dengan terapi radiasi sesuai prosedur standar. Tiga bulan setelah dinyatakan selesai radiasi, dilakukan penilaian terhadap respons klinis radiasi dan pemeriksaan genotipe DNA HPV ulang.

Dari 31 sampel penelitian didapatkan infeksi HPV sebelum radiasi sebanyak 27 sampel (83,37%) dengan rincian infeksi tunggal 75% dan multipel 9,37%. Berdasarkan tipe HPV, diperoleh tipe 16 (43,74%) dan tipe 18 (18,64%). Infeksi menetap HPV setelah radiasi ditemukan sebesar 34,61%. Respons klinis komplit ditemukan pada kelompok infeksi tunggal sebanyak 100%, sedangkan pada kelompok infeksi multipel 33,3% (p=0,115). Sedangkan infeksi HPV menetap dengan respons klinis komplit sebesar 32% (p=0,346).

Disimpulkan bahwa tipe HPV DNA yang terbanyak dijumpai pada penderita karsinoma sel skuamosa serviks adalah tipe 16, yaitu 45,16%. Infeksi HPV menetap setelah radiasi ditemukan sebanyak 34,61%. Infeksi multipel lebih banyak mengalami infeksi HPV menetap dibandingkan infeksi tunggal. Tidak terdapat perbedaan respons klinis antara infeksi tunggal dengan infeksi multipel HPV (p=0,115). Infeksi menetap HPV tidak berhubungan dengan respons terapi (p=0,346).

Kata Kunci: Kanker serviks, tipe DNA HPV, infeksi HPV menetap, respons terapi.

Profil Sel *Natural Killer* (NK) dalam Darah Perifer dan Jaringan Tumor Penderita Lesi Prakanker dan Karsinoma Sel Skuamosa Serviks

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ABSTRACT

This research was performed to investigate the profile of Natural Killer (NK) cells in peripheral blood and tumor tissues of cervical pre cancerous lesion and squamous cell carcinoma of cervix patients.

This research was an observational analysis study with cross-sectional design of 47 subjects which comprises of 17 cervical pre cancerous lesion patients, 8 early stage squamous cell carcinoma of cervix patients and 22 late stage squamous cell carcinoma of cervix patients in Dr. Soetomo Hospital-Airlangga University teaching hospital, Surabaya. After clinical and histopatologic diagnosis was established, NK cell count was perfomed on the biopsies, and both NK cell count and percentage of activated NK cells was performed on the peripheral blood of those three groups.

From this research, it was found that the average number and percentage of activated NK cells within peripheral blood of cervical pre cancerous lesion patients were lower (349.65 cell/µL; 15.13%) compared with early stage carcinoma (552 cell/µL; 18,40%) and late stage carcinoma (590.32 sel/µL; 23.29%). NK cell expression of cervical tumor tissues on three groups are very low, 0.29% on cervical pre cancerous lesion patients; 0.45% on early stage cervical cancer patients; and 0.04% on late stage cervical cancer patients.

Significant differences was found in the number of NK cells (p=0.016) and percentage of activated NK cells (p=0.041) within peripheral blood between pre cancerous lesion patients and late stage squamous cell cervical cancer patients, no significant difference was found in the number of NK cells within tumor tissue (p=0.278).

Keyword: *NK cell, pre cancerous lesion of the cervix, early stage squamous cell carcinoma of cervix, late stage squamous cell carcinoma of cervix*

ABSTRAK

Penelitian ini dilakukan untuk mengetahui profil sel *Natural Killer* (NK) dalam darah perifer dan jaringan tumor pada penderita lesi prakanker dan karsinoma sel skuamosa serviks.

Penelitian ini merupakan studi analitik observasional dengan rancangan *cross-sectional* terhadap 47 subjek yang terdiri atas 17 penderita lesi prakanker serviks, 8 penderita karsinoma sel skuamosa serviks baik stadium awal, dan 22 penderita karsinoma sel skuamosa serviks stadium lanjut di Bagian Obstetri dan Ginekologi FK Unair/ RSUD Dr. Soetomo, Surabaya. Setelah diagnosis klinik dan histopatologik ditegakkan maka terhadap ketiga kelompok tersebut dilakukan pemeriksaan jumlah sel NK dan prosentase sel NK teraktivasi dari darah tepi serta pemeriksaan jumlah sel NK dari biopsi jaringan tumor.

Hasil penelitian menunjukkan rata-rata jumlah dan prosentase sel NK teraktivasi dalam darah perifer penderita lesi prakanker serviks lebih rendah (349,65 sel/µL; 15,13%) dibandingkan dengan penderita karsinoma stadium awal (552 sel/µL; 18,40%) dan penderita karsinoma stadium lanjut (590,32 sel/µL; 23,29%). Ekspresi sel NK pada jaringan tumor serviks pada ketiga kelompok sangat rendah, yaitu 0,29% pada penderita lesi prakanker serviks; 0,45% pada penderita kanker serviks stadium awal; dan 0,04% pada penderita kanker serviks stadium lanjut.

Penelitian ini menyimpulkan bahwa terdapat perbedaan yang bermakna jumlah sel NK (p=0,016) dan sel NK teraktivasi (p=0,041) dalam darah perifer antara penderita lesi prakanker dan karsinoma sel skuamosa serviks stadium lanjut. Namun, tidak demikian halnya dengan infiltrasi sel NK dalam jaringan tumor (p=0,278).

Kata Kunci: Sel NK, lesi prakanker serviks, karsinoma sel skuamosa serviks stadium awal, karsinoma sel skuamosa serviks stadium lanjut

Batasan *Prostate Specific Antigen* (PSA) pada Pasien Kanker Prostat untuk Memprediksi Metastasis ke Tulang di Rumah Sakit Sardjito, Yogyakarta

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ABSTRACT

The object of this study to establish a serum PSA cut-off value to predict the presence of bone metastasis in prostate cancer. Methods: Consecutive patients diagnosedwith prostate cancer were retrospectively analyzed. Patients had received bone scintigraphy and had their PSA concentration measured. The proper cut-off value was established based on statistical analysis in order to predict the possibility of bone metastasis among them. Results: eighty-three consecutive patients with prostate cancer were enrolled, and 55 patients (66%) with bone metastasis confirmed by scintigraphic findings. A serum PSA concentration of 17.65 ng/ml gave the best sensitivity (78.33%) and specificity (65.21%). The PPV and NPV were 85.45% and 53.57%, respectively (p<0.05) Conclusion: a cut-off value of 17.65 ng/ml appears to be an appropriate benchmark for stratifying metastatic bone disease in prostate cancer patientssuch that if a patient with newly diagnosed prostate cancer and without any skeletal symptoms has a serum PSA concentration of less than 17.65 ng/ml,we suggest that they would not need to undergo bone scintigraphy.

Keyword: *Prostate Cancer,Prostate Specific Antigen, Bone scintigraphy*

ABSTRAK

Tujuan penelitian adalah menentukan batasan nilai PSA untuk memprediksi adanya metastasis tulang pada pasien kanker prostat. Pasien dengan kanker prostat, telah melakukan pemeriksaan sidik tulang, dan terdapat nilai PSA awal dianalisis secara retrospektif. Batasan nilai yang sesuai kemudian ditetapkan berdasarkan kemungkinan adanya metastasis tulang pada pasien kanker prostat. Pada penelitian ini, terdapat 83 pasien kanker prostat yang ikut dalam penelitian dan 55 pasien (66%) dengan metastasis tulang yang dikonfirmasi dengan sidik tulang. Nilai serum PSA 17,65 ng/ml memiliki sensitivitas (78,3%) dan spesifisitas (65,21%) terbaik. Nilai PPV dan NPV adalah 85,45% dan 53,57% (p<0,05). Kesimpulannya, nilai PSA 17,65 ng/ml tampaknya merupakan patokan yang sesuai untuk stratifikasi metastasis tulang pada pasien kanker prostat sehingga jika terdapat pasien baru didiagnosis kanker prostat tanpa gejala nyeri tulang, sebaiknya tidak dilakukan pemeriksaan sidik tulang.

Kata Kunci: Kanker prostat, *prostate Specific Antigen*, sidik tulang

Pati Resistan serta Perannya dalam Penghambatan Proliferasi dan Induksi Apoptosis Sel Kanker Kolon

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ABSTRACT

Resistant starch (RS) is starch fraction which is not digested by human starch degrading enzyme, and it will thus undergo bacterial fermentation in the colon. The main fermentation products are Short Chain Fatty Acid (SCFA): acetate, propionate and butyrate. The Fermentation products were able to inhibit the proliferation and to induce apoptosis of colon cancer cell. The apoptosis occured through mitochondrial pathway by changing the expression of pro-apoptosis related gene of Bax toward antiapoptosis related gene of Bcl-2.

Keyword: *resistant starch, fermentation, short chain fatty acid, colon cancer*

ABSTRAK

Pati resistan (*Resistant starch*: RS) merupakan fraksi pati yang tidak dicerna oleh enzim pencerna pati pada individu sehat dan ini akan difermentasi oleh bakteri di dalam kolon. Hasil fermentasi utama berupa asam lemak rantai pendek (*short chain fatty acid:* asetat, propionate, dan butirat). Produk fermentasi RS mampu menghambat proliferasi sel kanker kolon dan menginduksi apoptosis. Induksi apoptosis berlangsung melalui jalur mitokondria yang ditandai meningkatnya rasio ekspresi gen proapoptosis Bax terhadap gen antiapoptosis Bcl-2.

Kata Kunci: pati resistan, fermentasi, asam lemak rantai pendek, kanker kolon

Peran Radiologi Dalam Diagnosis *Endobronchial Carcinoid Tumor*

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ABSTRACT

Bronchial carcinoid tumors are rare neuroendocrine neoplasma consist of 1–2% of all pulmonary neoplasms and 12–15% of carcinoid tumors in United States. Recently, there is no data in Indonesia. The imaging play important role in diagnosing bronchial carcinoid tumor. This case presentation reported A 35 years old woman with chief complaint of hemoptysis. Acid fast bacilli smear was negative and mantoux test positive. From chest X ray there is a right paracardial consolidation. Chest CT Scan has been done and there was consolidation in right middle lobe with endobronchial mass in intermedius of right bronchial lung. The multidiscipline team diagnosis were endobronchial mass and pulmonary TB. Anti TB treatment had been given. The follow up CT scan after 1 month Anti TB treatment was improvement in consolidation, but the endobronchial mass was stable. She got PET CT Scan and the result was non metabolic nodule. Surgical treatment was done to remove endobronchial mass. The histopathology finding from specimen was typical bronchial carcinoid tumor.

Keyword: *endobronchial carcinoid tumor, chest x ray, chest CT.*

ABSTRAK

Tumor bronkial karsinoid merupakan neoplasma neuroendokrin yang jarang, sekitar 1–2% dari neoplasma paru dan 12–15% dari tumor karsinoid di Amerika Serikat. Sampai saat ini, belum ada data di Indonesia. Radiologi berperan penting dalam mendiagnosis tumor bronkial karsinoid. Laporan kasus ini membahas seorang wanita 35 tahun yang datang dengan keluhan utama hemoptisis. Dari hasil pemeriksaan BTA, didapatkan hasil negatif, tetapi test mantoux positif. Hasil foto toraks pasien didapatkan konsolidasi di parakardial kanan. Pasien juga dilakukan CT scan toraks. Didapatkan hasil konsolidasi di lobus tengah dengan massa endobronkial di bronkus intermedius paru kanan. Pasien ini didiagnosis oleh tim multidisiplin sebagai massa endobronkial dan tuberkulosis paru. Pasien diberikan pengobatan OAT. Hasil CT scan setelah 1 bulan terapi OAT menunjukkan ada perbaikan dalam konsolidasi, tetapi massa endobronkial menetap. Pasien menjalani PET CT Scan dengan hasil nodul non-metabolik mendukung suatu proses inflamasi. Dilakukan terapi bedah untuk mengangkat tumor endobronkial. Hasil histopatologi dari spesimen bedah sesuai dengan tumor bronkial karsinoid tipe tipikal.

Kata Kunci: tumor endobronkial karsinoid, foto toraks, CT scan toraks

Factors Which Influenced on Two Years Recurrence of Epithelial Ovarian Cancer Patients After Surgery and Platinum Based Chemotherapy

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ABSTRACT

Ovarian cancer was the leading cause of death in gynecologic cancer which had the two years recurrence rate of 50%. We used retrospective cohort design with survival analysis technique to examine the role of post-surgery residual tumor size, cancer cell histological subtype and cancer cell grading on epithelial ovarian cancer recurrence. We also want to know the prevalence of HER-2 (Human Epidermal Receptor-2) overexpression in epithelial ovarian cancer patients. Sixty-five epithelial ovarian cancer patient (1998-2012) who had achieved remission were observed for 24 months. We reported median age of 50 years with recurrence rate of 36.9% and mean time of first recurrence was 19.15 months. Size of post-surgery residual tumor more than 1 cm increase Hazard Ratio (HR) *of two years recurrence of epithelial ovarian cancer with p value 0.02 and HR of 3.31 (95% CI 1.46-7.49) but papillary serous histology subtype and poor differentiated cancer cell grading did not influence the recurrence. One of 38 patients showed cytoplasmic staining in HER-2 overexpression examination by immunohistochemistry methods.*

Conclusion: Size of post-surgery residual tumor more than 1 cm increase Hazard Ratio of two years recurrence of epithelial ovarian cancer while papillary serous histology subtype and poor differentiated cancer cell grading did not influence the recurrence. One sample showed cytoplasmic staining on HER-2 overexpression examination.

Keyword: *epithelial ovarian cancer, recurrence*

ABSTRAK

Kanker ovarium merupakan penyebab kematian tertinggi pada kelompok kanker ginekologik, dengan angka kekambuhan dua tahun sebesar 50%. Penelitian ini menggunakan desain kohort retrospektif dengan teknik analisis kesintasan yang bertujuan melihat peran faktor ukuran residu tumor post-operasi, jenis subtipe sel kanker, dan tingkat diferensiasi sel kanker terhadap kekambuhan dua tahun pasien kanker ovarium epitelial. Penelitian ini juga ingin melihat besarnya prevalensi overekspresi *Human Epidermal Receptor-2* (HER-2) pada pasien kanker ovarium epitelial. Sebanyak 65 pasien kanker ovarium epitelial (tahun 1998-2012) yang telah remisi diamati selama 24 bulan. Terlihat bahwa median usia pasien 50 tahun dengan proporsi kekambuhan sebesar 36,9% dengan mean waktu kekambuhan pertama 19,15 bulan. Ukuran residu tumor post-operasi lebih dari 1 cm meningkatkan rasio *hazard* kekambuhan dua tahun kanker ovarium epitelial dengan nilai p: 0,02 dan HR 3,31 (IK95% 1,46-7,49). Sementara, jenis subtipe histologi *papillary serous* dan tingkat diferensiasi buruk sel kanker tidak berhubungan dengan terjadinya kekambuhan. Pada pemeriksaan overekspresi HER-2 menggunakan teknik imunohistokimia dilaporkan satu dari 38 pasien memperlihatkan adanya *cytoplasmic staining*.

Disimpulkan bahwa ukuran residu tumor post-operasi yang berukuran lebih dari 1 cm meningkatkan rasio hazard kekambuhan dua tahun pasien kanker ovarium epitelial, sementara jenis subtipe histologi *papillary serosa* dan tingkat diferensiasi buruk sel kanker tidak berhubungan dengan terjadinya kekambuhan. Pada pemeriksaan overekspresi HER-2 menggunakan teknik imunohistokimia, dilaporkan satu sampel memperlihatkan adanya *cytoplasmic staining*.

Kata Kunci: kanker ovarium epitelial, kekambuhan

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INTRODUCTION

Ovarian cancer was the leading cause of death in gynecological cancer with 14.300 deaths in United States (2003).[1-2] Korea reported 3991 new cases of ovarian cancer between 1999-2001.[3] "Dharmais" Cancer Centre Hospital reported of 105 new cases in 2009, increase to 113 cases in 2010. Ranuhardy reported that most of the patients were already in advanced disease (65%).[4] The two years recurrence rate of ovarian cancer was 50% with the five year mortality rate was 75%.[5]

Surgery followed by platinum based chemotherapy was the basic management of epithelial ovarian cancer. Although almost eighty percent of patients had a good response to chemotherapy at the beginning most of the patients will get recurrent and die due to resistency.[6] Some factors which influenced on epithelial ovarian cancer recurrence include: age at diagnosis, stage of disease, cancer cell subtype, cancer cell grading, size of post-surgery residual tumor, type of surgery and resistance to platinum based chemotherapy.[7-10]

Patients who had size of post-surgery residual tumor less than 1 cm have a longer Progression Free Survival (PFS) time than patients who had size of post-surgery residual tumor more than 1 cm.[7,8] Older age, more than 60 years old and advanced stage also correlate with a higher risk of recurrency.[7] Vergote reported that cancer cell grading was the indicator of recurrence for stage I-IIA epithelial ovarian cancer with Hazard Ratio of 3.31. [9] Resistance to platinum based chemotherapy also play a role in the epithelial ovarian cancer recurrence, including overexpression of Human Epidermal Receptor 2 (HER-2).[11-12] Some studies reported of 5-66% overexpression of HER-2 in ovarian cancer patients. HER-2 overexpression will promote transduction signal which control proliferation, differentiation, migration and apoptosis process.[13-16] Angiogenesis process also play a role in the carcinogenesis process of ovarian cancer. There was increase of proangiogenic growth factor production in ovarian cancer.[17-23] Some gene/protein that play a role in the carcinogenesis of ovarian cancer include: EGFR (HER-1), HER-2, IGF, K-RAS, BRAF, PIP-3/AKT, p53, BRCA-1, BRCA-2, VEGF/VEGFR, TGF-β, C-MYC, MMPs and others, through some process: growth promotion, insensitivity to antigrowth signals, inhibition of apoptosis process and immune surveillance, limitless of replicative potential, enhanced angiogenesis and promotion of invasion and metastasis.[17]

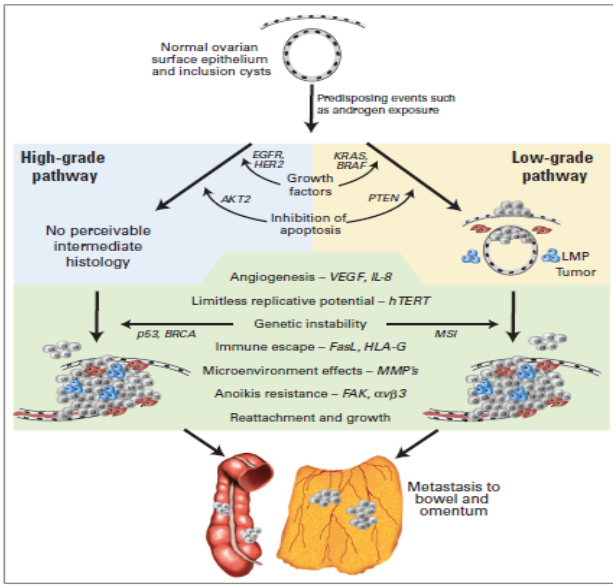

Figure 1: Carcinogenesis process of ovarian cancer

There were two kind of platinum resistance mechanism, including classical mechanism and molecular mechanism. HER-2 overexpression was one of the molecular platinum resistance mechanism. HER-2 belongs to Epidermal Growth Factor Receptors (EGFR) which involved in growth and survival cell controlling also involved in adhesion, migration, differentiation and other cellular cell process. Some studies reported 5-66% of HER-2 overexpression in ovarian cancer.[13-15,26-38] HER-2 signal increase cell proliferation through the RAS-MAPK (Mitogen Activated Kinase) pathway and also inhibit cell apoptosis process through the phosphatidylinositol 3'-kinase–AKT–mTOR (mammalian target of rapamycin).[13-15]

The mechanism how HER-2 overexpression correlate with platinum resistance in ovarian cancer still unclear. Julien reported that the main mechanism of platinum resistance was due to inhibition of intra-strand cross links that establish by platinum as cytotoxic agent.[39] Macleod reported there was an extracellular signal transduction alteration that followed by an alteration of gene expression in cisplatin resistance ovarian cancer cell lines.[40] Coquard which study was done in advanced cisplatin resistance ovarian cancer patients, reported 3 of 7 patients who had HER-2 overexpression achieved remission after addition of trastuzumab to the conventional chemotherapy.[41] Aim of this study was to know the role of post-surgery residual tumor

size, cancer cell histological subtype and cancer cell grading to epithelial ovarian cancer recurrence. We also want to know the prevalence of HER-2 overexpression in epithelial ovarian cancer.

MATERIAL AND METHODS

We used retrospective cohort design with survival analysis technique to show the role post-surgery residual tumor size, cancer cell histological subtype and cancer cell grading on time of epithelial ovarian cancer recurrence. The study was done in "Dharmais" Cancer Centre Hospital, Jakarta, Indonesia. Inclusion criteria were: patients > 18 years old with histopathology result of epithelial ovarian cancer who had done surgery by a gynecologist then followed by 6 cycles of adjuvant platinum based chemotherapy. Patients who had achieved remission after chemotherapy were followed maximal for 24 months with time of first recurrence as end point. Recurrence criteria was fixed base on NCCN 2013 and RECIST 1.1 version and time of first recurrence was counted from time of the last chemotherapy.[42]

Immunohistochemistry examination for HER-2 overexpression was done by anti HER-2 (4B5) rabbit monoclonal primary antibody, VIEW DAB and ultra-View universal DAB detection kit with Ventana automated slide stainer machine. This technique already approved by FDA for HER-2 examination for patients with trastuzumab indication.[43] In this study we use Dako Herceptest Manual Interpretation criterion and HER-2 3^+ expression (immunohistochemistry) of breast cancer as a positive control.

The data collected were processed by statistic programmed SPSS 17.0 version. Bivariate analysis by log rank test were done to examine the role of independent variable to time of recurrence. Kaplan Meier curve were done to see the survival analysis of every group with significancy level of $p<0.05$. This study already approved for ethical clearance by ethical committee of Medical Faculty Indonesia University.

RESULTS

We reported of 192 new cases of epithelial ovarian cancer patients who had done surgery at "Dharmais" Cancer Centre Hospital (1998-2012). Among of these, 100 patients should followed surgery by 6 cycles of adjuvant platinum base chemotherapy, 87 patients then finished the chemotherapy and only 65 patients achieved remission after treatment.

Table 1: Patient's characteristics

Characteristic	N (%)
Age, Median	50.0 (42-56)
Stage of disease	
Stage I	4 (6.2)
Stage II	9 (13.8)
Stage III	48 (73.8)
Stage IV	4 (6.2)
Cancer cell histology subtype	
Endometrioid	21 (32,3)
Papillary serosa	28 (43,1)
Muscinous	7 (10,8)
Clear cell	6 (9,2)
Others	3 (4,6)
Cancer cell grading	
Well differentiated	18 (27.7)
Mild differentiated	30 (46.2)
Poor differentiated	17 (26.1)
Post-surgery residual tumor size	
Residual tumor 1 cm	42 (64.6)
Residual tumor > 1 cm	23 (35.4)

Between 24 months of observation, we reported of 36.9 percent of recurrence with mean time of first recurrence was 19.15 months.

We continue HER-2 immunohistochemistry examination for 38 samples. We use anti HER-2 (4B5) rabbit monoclonal primary antibody, VIEW DAB and ultra-View universal DAB detection kit with Ventana automated slide stainer machine with 8 minutes of antigen retrieval process with no samples showed positive results. One sample showed cytoplasmic staining when we used 30 minutes of antigen retrieval process.

Table 2: Factors which influenced on ovarian cancer recurrence

	Characteristics	Recurence		Mean Recurence Time (Months)	HR (CI 95%)	p
		No	Yes			
1	Stage (n=65)					
	Stage I-II	11 (84.6	2 (15.4)		2.96	0.119
	Stage III-IV	30 (54.5)	22 (45.5)		(0.7-12.6)	
2	Post-surgery residual tumor size (n=65)					
	Residual tumor 1 cm	32 (76.2)	10 (23.8)	21.3 (19.10-23.45)	3.31	0.002
	Residual tumor > 1 cm	9 (39.1)	14 (60.9)	15.2 (11.49-18.89)	(1.46 -7.49)	
3	Cancer cell histology subtype (n=65)					
	Non papillary serosa	23 (62.2)	14 (37.8)	18.7 (15.9-21.52)	0.92	0.849
	Papillary serosa	18 (64.3)	10 (35.7)	19.7 (16.79-22.67)	(0.41-0.85)	
4	Cancer cell grading (n=65)					
	Well-mild differentiated	32 (66.7)	16 (33.3)	19.87 (17.61-22.12)	1,62	0.253
	Poor differentiated	9 (52.9)	8 (47.1)	17.04 (12.62-21.45)	(0.69-3.79)	

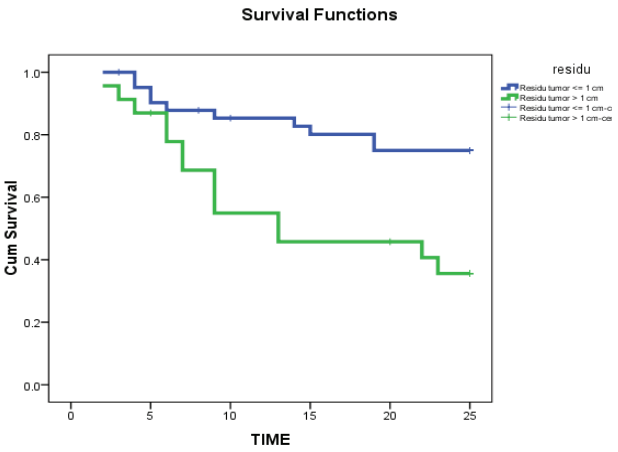

Figure 2: Kaplan Meier Curve time of epithelial ovarian cancer recurrence base on post-surgery residual tumor size

Based on figure 2, at the end of observation, 75% patients which had post residual tumor size maximal 1 cm were not suffer for recurrence, while in other group (residual tumor size more than 1 cm) 35% patients were not suffer for recurrence.

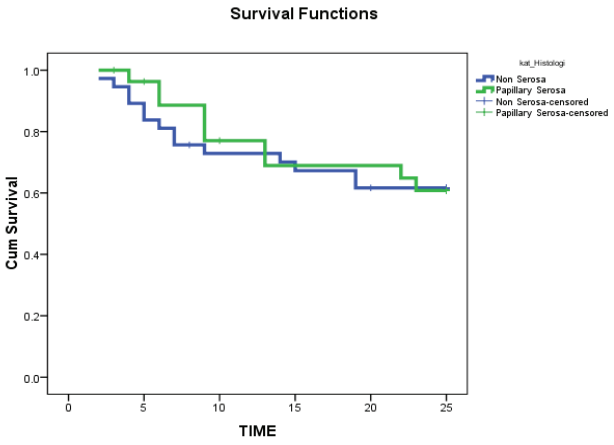

Figure 3: Kaplan Meier Curve time of epithelial ovarian cancer recurrence base on cancer cell histology subtype

Based on figure 3, at the end of observation, we reported of 62% patients which had non papillary serous histology subtype were not suffer for recurrence, while in other group (papillary histology subtype) 61% patients were not suffer for recurrence.

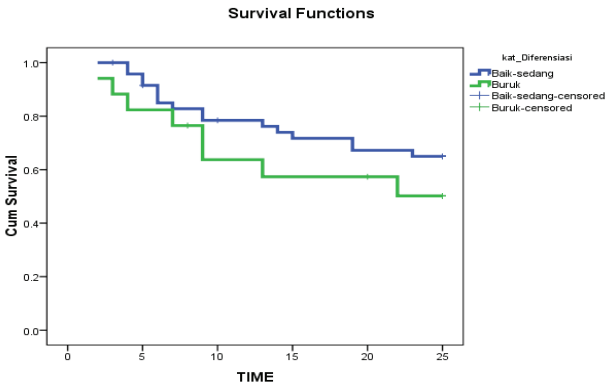

Figure 4: Kaplan Meier Curve time of epithelial ovarian cancer recurrence base on cancer cell grading

Based on figure 4, at the end of observation, we reported of 60% patients which had well-mild differentiated cell grading were not suffer for recurrence, while in other group, 50% patients were not suffer for recurrence.

DISCUSSION

We reported of 15.2 months of mean time recurrence in the group of post-surgery residual tumor size more than 1 cm while in the other group which had post-surgery residual tumor size maximal 1 cm, we reported a longer mean time of recurrence, 21.3 months (table 2), with p value of 0.002 and HR 3.31 (95% CI 1.46-7.49). Tuefferd reported that post-surgery residual tumor size more than 1 cm correlate with shorter Progression Free Survival (PFS) time, p value <0.00001 and Hazard Ratio of 2.31 and also Broet reported that post-surgery residual tumor more than 2 cm correlate with shorter Progression Free Survival (PFS) time, p value 0.05 and RR 1.31.[14, 44]

We can see in table 2 that mean recurrence time was longer in the group of papillary histology subtype than non-papillary histology subtype group (19.7 months vs 18.7 months) with p value of 0.84 and Hazard Ratio 0.92 (95% CI 0.41-0.85). Although papillary structure of cancer cell was a predictor of invasion but clear cell subtype also known as the most chemoresistance subtype so the histology subtype was not the only factor that correlate with epithelial ovarian cancer recurrence.[7,8] We also found the longer of mean recurrence time in the group of well-mild differentiated cancer cell grading than in the group of poor differentiated cancer cell grading (19.87 months vs 17.04 months) with p value of 0,253 but it was not significant statistically.

One of the platinum resistance molecular mechanism was Human Epidermal Receptor (HER-2) overexpression. Some previous studies reported of 5-66% of HER-2 overexpression in ovarian cancer. In this study we reported one of thirty-eight samples showed cytoplasmic staining by immunohistochemistry examination with 30 minutes of antigen retrieval process. There was a difference on HER-2 examination result in this study compare with some studies before. Landen showed two ovarian cancer carcinogenesis pathway, including high grade pathway and low grade pathway, that Epidermal Growth Factors Receptor (EGFR) and Human Epidermal Receptor (HER-2) expression play a role in the high grade pathway. In this study we reported that 73% patients had well-mild differentiated cancer cell grading (low grade pathway) so it is clear that we can only found one sample showed cytoplasmic staining. We also thought that the difference was due to antigen retrieval process duration that was used in previous study.

LIMITATIONS

This study was the first study in Indonesia which research HER-2 expression in epithelial ovarian cancer so the author had difficulty to establish the positive control and standard procedure of HER-2 overexpression examination in the ovarian cancer cases. Besides, the samples for HER-2 examination were not enough because the paraffin block should not be saved more than five years.

CONCLUSION

Size of post-surgery residual tumor more than 1 cm increase Hazard Ratio of two years recurrence of epithelial ovarian cancer with Hazard Ratio 3.31 while papillary serous histology subtype and poor differentiated cancer cell grading did not influence the recurrence. One sample showed cytoplasmic staining on HER-2 examination by immunohisto-chemistry.

REFFERENCE

1. Canistra SA, Gershenson DM, Recht A. Ovarian cancer, fallopian tube carcinoma and peritoneal acarcinoma. In: Devita VT, Vincent T, editors. Cancer principle and practice of oncology 8th edition.Philadelpia: Lippincot Williams & Wilkins.2008.p.674-5.
2. Jemal A, Murray T, Samuel A. Cancer Statistics. *Ca J Clin.* 2003;53: 5-26.
3. Shin HR. Nationwide cancer incidence in Korea, 1999-2001. First result using the national cancer incidence data base. *Cancer Res Treat.* 2005;37: 325-31.
4. Ranuhardy D. Karakteristik dan penatalaksanaan kanker ovarium periode Juli-Desember 2009.Analisis data rekam medik RSKD (tidak dipublikasi).
5. Colombo N, Parma G, Bocciolone L. Role of chemotherapy in relapsed ovarian cancer. *Crit Rev Oncol Haematol.* 1993;32: 221-8.
6. NCCN. Clinical Practice in Oncology Guidelines Ovarian Cancer. [cited 2013 Dec 24]. Available from: http//www.nccn.com.2013.
7. Agrawal V. Prognostic factor of ovarian cancer [cited 2012 April 24]. Available from: http//www.obgyn.net.
8. Canistra SA. Cancer of the Ovary. *N Engl J Med.* 2004;351: 2519-29.
9. Vergote J, De Brabanter, Fyles A. Prognostic importance of degree of differentiation and cyst rupture in stage I invasive epithelial ovarian carcinoma. *Lancet* 2001;357: 176-82.
10. Lonley DB, Johnson PG. Molecular mechanism of drug resistance. *J Pathol.* 2005;205: 272-92.
11. Stewart DJ. Mechanism of resistance to cisplatin and carboplatin. *Clin Rev in Oncol Haematol.* 2007;63: 12-31.
12. Surowiak P. Prediction of the response to chemotherapy in ovarian cancer. *Folia morphol.* 2006;65: 285-94.
13. Amler LC, Wang Y, Hampton G. HER-2 as therapeutic target in ovarian cancer.[cited 2013 March 3]. Available from: http// www.intechopen.com.
14. Tuefferd M, Couturier J, Llorca FP, et al. HER-2 status in ovarian cancer: a multicenter GINECO study of 320 patients. *PLoS One.* 2007;2: 1138.
15. Hudis CA. Trastuzumab mechanism of action and clinical use. *N Engl J Med.* 2007;357:39-51.
16. Ibrahim MA, Srivenugopal KS, Rasul KI. Platinum resistance: the role of molecular, genetic and epigenetic factors. *J Med Sci.* 2013;13: 160-8.
17. Landen CN, Birrer MJ, Anil K Sood. Early events in the pathogenesis of epithelial ovarian cancer. *J Clin Oncol.* 2008;26: 995-1005.
18. Jain RK, Booth MF. What bring pericytes to tumor vessels. *J Clin Invest.* 2003;112: 1134-6.
19. Martin L, Schilder R. Novel approach in advancing the treatment of epithelial ovarian cancer: the role of angiogenesis inhibition. *J Clin Oncol.* 2007;25: 2894-901.
20. Hilberg F, Roth GJ, Krsak M. Triple angiokinase inhibitor with sustained receptor blockade and good antitumor efficacy. *Cancer Res.* 2008;68: 4774-82.
21. Cao Y, Cao R. Hendlund EM. Regulation of tumor angiogenesis and metastasis by FGF and PDGF signaling pathway. *J Mol Med.* 2008;86: 785-9.
22. Presta M, Dell Era, Mitola S, et al. Fibroblast growth factor/ fibroblast growth factor system in angiogenesis. *Cytokine Growth Factor Rev.* 2005;16: 159-78.
23. Memarzadeh S, Berek JS. Gynecologic Cancer. In: Casciato DA, editor. Manual of clinical oncology 6th edition. Philadelpia: Lippincot Williams & Wilkins,2004.p.265-97.
24. Skeel RT. Antineoplastic drugs and biologic response modifiers: classification, use, and toxicity of clinically useful agents. In: Skeel RT, editor. Handbook of cancer chemotherapy 7th edition. Philadelpia: Lippincot William & Wilkins.2003.p.53-7.
25. Casciato DA. Cancer Chemotherapeutic agents. In: Casciato DA, editor. Manual of clinical oncology 6th edition. Philadelpia: Lippincot Williams & Wilkins, 2004.p.46-56.
26. Gottesman MM, Fijo T, Bates SE. Multidrug resistance in cancer: Role of ATP dependent transporters. *Macmilan Magazine.* 2002;2: 48-58.
27. Brennan PJ, Kumogai T, Berezov A, Murali R, Grene M. HER-2/Neu: mechanisms of dimerization/oligomerization. *Oncogene.* 2000;19: 6093-101.
28. Scholl S, Beuzeboc P, Pouillart P. Targetting HER-2 in other tumor types. *Ann Oncol.* 2001;12: S81-7.
29. Rubin SC, Finstad CL, Wong GY, et al. Prognostic significance of HER-2/neu expression in advanced epithelial ovarian cancer: a multivariate analysis. *Am J Obstet Gynecol.* 1993;168: 162-9.
30. Bookman MA, Darcy KM, Pearson C. Evaluation of monoclonal humanized anti HER-2 antibody, trastuzumab, in patients with recurrent or refractory ovarian or primary peritoneal carcinoma with overexpression of HER-2: a phase II trial of the Gynecologic oncology Group. *J Clin Oncol.* 2003;21: 283-90.
31. Hogdall EV, Christensen L, Kjaer SK, et al. Distribution of HER-2 overexpression in ovarian carcinoma tissue and its prognostic value in patients with carcinoma: from the Danish MALOVA ovarian cancer study. *Cancer.* 2003;98: 66–73.
32. Lassus H, Leminen A, Vayrynen A, et al. ERBB2 amplification is superior to protein expression status in predicting patient outcome in serous ovarian carcinoma. *Gynecol Oncol.* 2004;92: 31–9.
33. Kupryjanczyk J, Madry R, Halasa PJ, et al. TP53 status determines clinical significance of ERBB2 expression in ovarian cancer. *Br J Cancer.* 2004;91: 1916-23.
34. Nielsen JS, Jakobsen E, Holund B, Bertelsen K, Jakobsen A. Prognostic significance of p53, Her-2, and EGFR overexpression in borderline and epithelial ovarian cancer. *Int J Gynecol Cancer.* 2004;14: 1086-96.

35. Verri E, Guglielmini P, Puntoni M, et al. HER2/neu oncoprotein overexpression in epithelial ovarian cancer: evaluation of its prevalence and prognostic significance clinical study. *Oncology* 2005;68: 154-61.
36. Steffensen KD, Waldstrom M, Jeppesen U, et al. The prognostic importance of cyclooxygenase 2 and HER2 expression in epithelial ovarian cancer. *Int J Gynecol Cancer* 2007;17: 798-807.
37. Lee CH, Huntsman DG, Cheang MC, et al. Assestment of HER-1, HER-2, and HER-3 expression and HER-2 amplification in advanced stages ovarian carcinoma. *Int J Gynecol Pathol.* 2005;24: 147-52.
38. Cloven NG, Kyshtoobayeva A, Burger RA, et al. In vitro chemoresistance and biomarker profiles are unique for histologic subtypes of epithelial ovarian cancer. *Gynecol Oncol.* 2004;92: 160-6.
39. Julien JMB, Bhosis J, Tiby MJ, Hartley JA, Hochhauser D. Involvement of HER-2 pathway in repair of DNA damaged produced by chemotherapeutic agents. *Mol Cancer Ther.* 2009;8: 3015-23.
40. Macleod K, Mullen P, Sewell J, et al. Altered ErbB receptor signaling and gene expression in cisplatin resistant ovarian cancer. *Cancer Res.* 2005;65: 6789-800.
41. Coquard RI, Guastala JP, Allouache D, et al. HER-2 overexpression/amplification and trastuzumab treatment in advanced ovarian cancer: a GINECO study phase II study. *Clinical Ovarian Cancer* 2008;1: 54-9.
42. Eisenhauer EA, Therasse P, Bogaerts J, Schwartz LH, Sargen D, Ford R. New response evaluation criteria in solid tumors: Revised RECIST guideline (version 1.1). *Eur J Cancer* 2009;45: 228-47.
43. Seidenfeld J, Samson DJ, Rothenberg BM, et al. HER-2 testing to manage patients with breast cancer or other solid tumors evidence report/technology. [cited 2014 May 31].Available from: http//www.ncbi.nlm.nih.gov.
44. Broet SC, Bessard ACH, Tourneau AL, et al. HER-2 overexpression is an independent marker of poor prognosis of advanced primary ovarian carcinoma: a multicenter study of GINECO group. *Ann Oncol.* 2004;15: 104-12.

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