

# Marker cancer stem cells (CD133, CD44 dan ALDH1A1) sebagai faktor prognostik pada kanker ovarium tipe epitelial = Cancer stem cell CD133, CD44 and ALDH1A1 markers as prognostic factors on epithelial ovarian cancer

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Abstrak

<b>ABSTRAK</b><br>

Nama :Nugraha Utama PelupessyProgram Studi :S3 Ilmu KedokteranJudul :Marker Cancer Stem Cells CD133, CD44, dan ALDH1A1 Sebagai Faktor Prognostik pada Kanker Ovarium Tipe Epitelial Kanker ovarium merupakan penyakit yang bersifat heterogen dan kebanyakan pasien datang dengan stadium lanjut. Kanker ovarium epitelial tipe II mempunyai sifat pertumbuhan tumor yang cepat dan secara genetik labil dibandingkan tipe I. Keberadaan cancer stem cells CSC dianggap sebagai salah satu faktor prognostik terjadinya kemoresisten dan kesintasan hidup yang rendah.Penelitian ini bertujuan untuk membuktikan CSC sebagai faktor prognostik dengan menggunakan marker CD133, CD44, dan ALDH1A1 pada kanker ovarium tipe epitelial.Marker CD133, CD44, dan ALDH1A1 diperiksa dengan imunohistokimia dan flowcytometry. Hasil ekspresi marker CSC pasien kanker ovarium tipe I dan tipe II dimasukkan kedalam suatu tabel yang dihubungkan dengan respons kemoterapi dan kesintasan hidup. Analisis data dilakukan dengan program computer STATA 14. Analisis kesintasan dilakukan dengan analisis Kaplan-Meier dan uji asumsi cox proportional hazard. Analisis multivariat dipakai untuk model prognosis selama 10 bulan. Sistem skoring dibuat dengan menggunakan receiver operating characteristic ROC curve analyses.Data demografi kelompok terbanyak adalah usia ge; 45 tahun; 40 sampel 72,7 , stadium I, 23 sampel 41,8 , diferensiasi buruk 30 sampel 54,5 , dan tipe II 16 sampel 29,1 . Perbedaan yang bermakna antara tipe histopatologi dengan marker CSC hanya terlihat pada marker CD44. Skor Prediksi Kemoresisten SPK<sub>r</sub> 10 bulan yang dihubungkan dengan 4 variabel yaitu usia ge; 45 tahun, tipe II, stadium III minus;IV, dan CD44 tinggi dengan ROC 72,47 dan probabilitas post test 82,5 . Kurva ROC berdasarkan kombinasi marker CSC dan faktor klinikopatologi yaitu stadium III minus;IV, usia ge; 45 tahun, diferensiasi buruk, tipe II, CD133 negatif, CD44 tinggi, dan ALDH1A1 tinggi adalah 0,841. Skor Prediksi Kematian SPK<sub>m</sub> 10 bulan yang dihubungkan dengan 3 variabel yaitu stadium III minus;IV, tipe II, dan CD44 tinggi dengan AUC 80,44 dan probabilitas post test 78,7 . Kurva ROC berdasarkan kombinasi marker CSC dan faktor klinikopatologi yaitu stadium III minus;IV, usia ge; 45 tahun, diferensiasi buruk, tipe II, CD133 positif, CD44 tinggi, dan ALDH1A1 tinggi adalah 0,841.Simpulan: Marker CD44 terbukti berperan pada kanker ovarium tipe II. Skor Prediksi Kemoresisten dan Skor Prediksi Kematian dapat ditentukan selain dengan faktor klinikopatologi, juga dengan memakai marker CSC. Kata kunci: ALDH1A1, CD44, CD133, CSC, kanker ovarium epitelial, kesintasan hidup, respons kemoterapi.

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<b>ABSTRACT</b><br>

Name : Nugraha Utama PelupessyStudy Program : Doctoral Program Medical SciencesTitle :Cancer Stem Cell CD133, CD44 andALDH1A1 Markers As Prognostic Factors on Epithelial Ovarian Cancer. Ovarian cancer is a heterogeneous disease and most of the patients came with an advanced stage. Epithelial ovarian

cancer type II has the characteristic of rapid tumor growth and genetically more labile than that of type I. The presence of cancer stem cells CSC is considered as one of the prognostic factors of low mortality and survival. The aim of this study was to prove CSC as prognostic factors using CD133, CD44, and ALDH1A1 markers on epithelial ovarian cancer. Clinicopathology and demographic data were collected from medical records. CD133, CD44, and ALDH1A1 markers were examined with flow cytometry and immunohistochemistry. CSC marker expression of the patients with ovarian cancer type I and II was connected with chemotherapy and survival response. Data analysis was done by using STATA 14 software. Survival analysis was done by using Kaplan-Meier analysis and Cox proportional hazard test. Multivariate analysis is used for prognosis model for ten months. Receiver Operating Characteristic ROC curve analysis was used as the system scoring. The highest group demographic data were age  $\geq 45$  years; 40 samples 72.7%, stage I, 23 samples 41.8%, poor differentiation 30 samples 54.5%, and type II 16 samples 29.1%. A significant difference between the histopathologic type and the CSC marker was seen only in CD44 marker. Chemoresistance Prediction Score in 10 months was associated with 4 variables i.e. age  $\geq 45$  years, type II, stage III minus; IV, and CD44 high with ROC 72.47 and posttest probability 82.5%. The highest chemoresistance scoring ROC curve based on the combination of CSC marker and clinicopathology factors; stage III minus; IV, age  $\geq 45$  years, poor differentiation, type II, negative CD133, high CD44, and high ALDH1A1, was 0.841. Mortality Prediction Score in 10 months was associated with 3 variables i.e. stage III minus; IV, type II, and CD44 high with AUC 80.44 and posttest probability 78.7%. The highest mortality scoring ROC curve based on the combination of CSC marker and clinicopathology factors; stage III minus; IV, age  $\geq 45$  years, poor differentiation, type II, positive CD133, high CD44, and high ALDH1A1, was 0.841. Conclusion: The CD44 marker has a role in type II ovarian epithelial cancer. Chemoresistance Prediction Score and Mortality Prediction Score can be determined from clinicopathological factors and using CSC marker. Keywords: ALDH1A1, CD44, CD133, chemotherapy response, CSC, Epithelial Ovarian Cancer, survival