Peran Mir-10b, Mir-21, supar dan pai-1 sebagai prediktor respons terapi dan progresivitas pada kanker paru jenis karsinoma bukan sel kecil kpkbsk = The role of Mir-10b, Mir-21, soluble urokinase type plasminogen activator receptor supar and plasminogen activator inhibitor pai-1 as predictors of treatment response and progressivity in non small cell lung cancer nsclc

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Abstrak

ABSTRAK
Kanker paru berkaitan dengan prognosis yang buruk. Oleh karenanya, diperlukan penanda sirkulasi untuk memprediksi respons terapi dan prognosis. Ekspresi mikroRNA 10b miR-10b dan aktivitas fibrinolitik, sebagaimana dicerminkan oleh soluble urokinase-type plasminogen activator receptor suPAR dan plasminogen activator inhibitor 1 PAI-1 , merupakan kandidat biomarker yang menjanjikan.Penelitian ini bertujuan mengevaluasi peran ekspresi miR-21, miR-10b, kadar suPAR dan PAI-1 plasma sebagai prediktor progresi dan respons terapi pada pasien kanker paru stadium lanjut.Penelitian ini merupakan studi kohort dan kesintasan di RS Kanker Dharmais RSKD , Jakarta. Subjek penelitian adalah pasien kanker paru karsinoma bukan sel kecil KPBBSK yang didiagnosis antara bulan Maret 2015 dan September 2016. Ekspresi miR-21 dan miR-10b dikuantifikasi dengan metode real-time polymerase chain reaction RT-PCR . Kadar suPAR dan PAI-1 diperiksa dengan metode enzyme-linked immunosorbent assay ELISA . Respons terapi dievaluasi berdasarkan kriteria RECIST 1.1. Pasien ditindaklanjuti sampai meninggal atau satu tahun setelah terapi.Terdapat 40 pasien yang dilibatkan dalam studi; 25 orang menyelesaikan sedikitnya4 siklus kemoterapi dan 15 lainnya meninggal selama terapi. Ekspresi miR-21 tidak berhubungan dengan progresi atau respons terapi. Kadar absolut miR-10b >592,145 copies/mL atau FC miR-10b > 0.066 bersifat protektif terhadap progresi dan respons buruk, sedangkan kadar suPAR > 4,237 pg/mL merupakan faktor risiko progresi dan respons buruk. Oleh karena dianggap penting, FC miR-10b juga dimasukkan dalam model prediksi progresi. Kadar PAI-1 > 4,6 ng/mL merupakan faktor protektif untuk respons buruk. Kadar suPAR merupakan faktor risiko independen untuk progresi dan respons buruk, sedangkan kadar PAI-1 merupakan faktor protektif independen untuk respons buruk.Simpulan: Model prediksi untuk progresi dapat dibuat dari ekspresi relatif miR-10b dan kadar suPAR, sedangkan respons terapi dapat diprediksi dari kadar suPARdan PAI-1. Dibutuhkan studi lebih lanjut untuk validiasi model-model prediksi ini.Kata kunci: kanker paru karsinoma bukan sel kecil KPKBSK , miR-10b, miR-21, overall survival, plasminogen activator inhibitor 1 PAI-1 , respons terapi, soluble urokinase-type plasminogen activator receptor suPAR
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ABSTRACT
Lung cancer is associated with poor prognosis. Circulating markers to predict treatment response and prognosis is needed. Expression of microRNA10b miR 10b and fibrinolytic activity, as reflected by soluble urokinase type plasminogen activator receptor suPAR and the plasminogen activator inhibitor 1 PAI 1 , were promising as biomarker candidates.This study aimed to evaluate the role of miR 21, miR 10b expression, suPAR and PAI 1 levels as predictors of progression during treatment and treatment response in

advanced lung cancer patients.This was cohort and survival study in Dharmais Cancer Hospital DCH . The subjects were non small cell lung cancer NSCLC patients diagnosed between March 2015 and September 2016. Expression of miRNAs were quantified using real time polymerase chain reaction RT PCR method. Levels of suPAR and PAI 1 were assayed using the enzyme linked immunosorbent assay ELISA method. Treatment response was evaluated based on RECIST 1.1. Patients were followed up until death or one year after treatment.Forty patients were enrolled 25 completed at least 4 cycles of chemotherapy and15 patients died during treatment. Absolute and FC miR 21 were not associated with progression or treatment response. Absolute MiR 10b expression 592,145 copies mL or FC miR 10b 0.066 were protective for progressive disease and poor treatment response, while suPAR levels 4,237 pg mL was a risk factor for progressive disease and poor responders. Since FC miR 10b was an important predictive factor, it was included in the prediction model of progression. PAI 1 levels 4.6 ng mL was a protective factor for poor response group of patients. suPAR level was an independent risk factors for progression and poor response, while PAI 1 level was an independent protective factor of poor response.Conclusion A model to predict progression can be developed using miR 10b expression and suPAR levels, while treatment response can be predicted by suPAR and PAI 1 levels. Further studies are needed to validate this model.Key words miR 10b, miR 21, non small cell lung cancer NSCLC , overall survival, plasminogen activator inhibitor 1 PAI 1 , soluble urokinase type plasminogen activator receptor suPAR , treatment response