ABSTRAK

Latar belakang : Mutasi gen *FMS like tyrosine kinase 3 – internal tandem duplication, tyrosine kinase domain (FLT3-ITD, -TKD(D835))* berhubungan dengan prognosis yang buruk, tingginya kekambuhan, rendahnya ketahanan hidup keseluruhan pada penderita LMA. Hubungan mutasi ini dengan aktivitas proliferasi sel *blast*, aktivitas anti-apoptosis, dan transporter transmembran obat *ara-C* penting diteliti lebih lanjut.

Tujuan : Analisis hubungan status mutasi gen *FLT3-ITD, -TKD(D835)* dengan jumlah sel *blast*, status ekspresi *CD34*, ekspresi *cyclin D1, Bcl-xL, human ezuilibrative nucleoside transporter 1 (hENT1)* pada penderita LMA.

Metode : Penelitian potong lintang dengan 35 penderita LMA *de novo* dilakukan pemeriksaan mutasi gen *FLT3-ITD, -TKD(D835)*, jumlah *blast*, status ekspresi *CD34*, ekspresi *cyclin D1, Bcl-xL,* dan *hENT1*

Hasil : Sebanyak 8 dari 35 penderita LMA (22,9%) ditemukan adanya mutasi *FLT3-ITD*, dan tidak ditemukan penderita dengan mutasi *FLT3-TKD(D835)*. Penderita LMA dengan mutasi *FLT3-ITD* memiliki jumlah *blast* lebih tinggi (71,3% vs51,5%, p=0,002), ekspresi *cyclin D1* lebih tinggi (*median fluorescent index / MFI* 68,77 vs 55,44, p = 0,036) dan ekspresi *hENT1* lebih rendah (*MFI* 30,6 vs 58,73, p = 0,0001) daripada penderita tanpa mutasi. Penderita LMA dengan dan tanpa mutasi *FLT3-ITD* tidak memiliki perbedaan status ekspresi *CD34* dan ekspresi *Bcl-xL* (p=0,97, p=0,38). Mutasi gen *FLT3-ITD* memiliki hubungan dengan jumlah *blast* (r=0,55, p=0,002), ekspresi *hENT1* (r=0,7, p=0,0001) dan ekspresi *cyclin D1* (r=0,34, p=0,048). Mutasi tersebut tidak berhubungan dengan status ekspresi *CD34* dan ekspresi *Bcl-xL*.

Kesimpulan : Mutasi gen *FLT3-ITD* pada LMA berhubungan dengan jumlah *blast*, ekspresi *cyclin D1* dan *hENT1*. Mutasi tersebut tidak berhubungan dengan ekspresi *Bcl-xL* dan status ekspresi *CD34*.

Kata Kunci : *FLT3-ITD, TKD(D835), LMA, blast, CD34, hENT1*

ABSTRACT

Background : FMS like tyrosine kinase 3 - internal tandem duplication, tyrosin kinase domain (FLT3-ITD, -TKD(D835)) gene mutation were related with poor prognosis in AML. The association of these mutation in AML with the blast's proliferation, antiapoptotic activity and ara-C membrane transporter is important to be investigated.

Aim : Analyze the association of FLT3-ITD, -TKD(D835) mutation with blast count, CD34 expression status, cyclin D1, Bcl-xL, human equilibrative nucleoside transporter 1 (hENT1) expression in AML.

Method : Thirthy five de novo AML patients had been investigated for FLT3-ITD, -TKD(D835) gene mutation, bone marrow blast count, CD34 expression status, cyclin D1, Bcl-xL and hENT1 expression in a cross sectional study.

Results : Eight of 35 AML patients (22,9%) had FLT3-ITD mutation, none of AML patients had FLT3-TKD(D835) gene mutation. AML patients with FLT3-ITD gene mutation had higher blast count (71,3% vs 51,5%, p=0,002), higher expression of cyclin D1 (median fluorescent index / MFI 68,77 vs 55,44, p=0,036) and lower expression of hENT1 (MFI 30,6 vs 58,73, p = 0,0001) than patients without mutation. AML patients with and without FLT3-ITD mutation did not have different CD34 expression status and Bcl-xL expression (p=0,97 and p=0,38). FLT3-ITD mutation had association with blast count (r=0,55, p=0,002), hENT1 expression (r= 0,7, p =0,0001) and cyclin D1 expression (r=0.34, p =0,048). It did not associate with CD34 expression status and Bcl-xL expression.

Conclusion: The FLT3-ITD mutation in AML associates with blast cell count, cyclin D1 and hENT1 expression. It doesn't associate with Bcl-xL and CD34 expression status.

Keywords : *FLT3-ITD, -TKD(D835), AML, blast, CD34, hENT1*