ABSTRACT

Primardhika, Rozah Fitria. 2017. **Expression Of *Hypoxia-Inducible Factor* 1-*Alpha* (HIF-1α) And *Vascular Endothelial Growth Factor* (VEGF) On Sprague Dawley Rat Dyslipidemic Model After Darapladib Injection.** Final Assignment, Medical Program, Faculty of Medicine, Brawijaya University. Supervisors: (1) Dr. Titin Andri Wihastuti, S.Kp, M.kes (2) dr. Agustin Iskandar, M.kes, Sp.PK

Atheroclerotic is a chronic inflammatory that leads cardiovascular diseases. Increase lipid profile in dyslipidemia as triggers to endothelial dysfunction, thus result in inflammation with monocyte, macrophage, T lymphosit, and Mast cell recruitment which secreted Lp-PLA_2 enzyme and binds with oxidized LDL,to increase inflammation process. This process lead to tissue hypoxia, and result in increase activation of HIF-α, and VEGF expression. The selective inhibitor of Lp-PLA2 in this study is Darapladib (DP). This study to know the correlation between Darapladib to decrease HIF-1α and VEGF expression in aortic tissue of mouse with dyslipidemia. Other data that are analysed in this study is daily intake, weight, and profile of lipid. True experimental laboratory with randomized post test control group design with 30 mouse, divided into 6 groups: Normal, DL and DLDP, each groups consist of 2 time serial, 8 and 16 weeks. The results of Kruskal-Wallis Test showed after darapladib administration with decreased HIF-1α expression ($p = 0,017$), and VEGF expression ($p = 0,161$). This result proves that Lp-PLA_2 inhibition will reduce inflammatory process, which decreases the amount of HIF-1α and VEGF expression. In conclusion, with the administration of Lp-PLA_2 selective inhibitors correlate with decreasing HIF-1α and VEGF expression in dyslipidemic conditions. Recommend further experiment to determine the effectiveness of darapladib decreases HIF-1α expression at time serial less than 8 week and VEGF expressions at time serial more than 16 week on pathogenesis of atherosclerosis.

Keywords: Atherosclerosis, Dyslipidemia, Darapladib, HIF-1α, VEGF