UDC 577.2 DOI: 10.25808/08697698.2018.202.6S.072

J.-Y. JEONG

Erythropoietin (EPO) receptor expression and the effects of EPO on diffuse large B cell lymphomas

Key words: erythropoiesis-stimulating agents, erythropoietin, erythropoiesis stimulating protein

Erythropoiesis-stimulating agents (ESAs), such as erythropoietin (EPO) and novel erythropoiesis stimulating protein (NESP), may alleviate anemia in diffuse large B-cell lymphoma (DLBCL) patients. However, many cancer cells express EPO receptors (EPOR), through which exogenously-administered ESAs potentially promote cancer cell growth. We conducted preclinical/phase II studies to investigate the safety and efficacy of ESAs for managing chemotherapy-related anemia in DLBCL patients. We examined EPOR expression in germinal center B-cell (GCB)- and activated B-cell (ABC)-DLBCL cell lines, and investigated the effects of ESAs on cell proliferation, and rituximab-mediated complement-dependent cytotoxicity (CDC). The clinical study enrolled 50 histologically-confirmed DLBCL patients receiving rituximab/cyclophosphamide/doxorubicin/vincristine/prednisolone (R-CHOP) who had hemoglobin levels <10.0 g/dL after a maximum of 3 R-CHOP cycles o and received ≥4 doses of fixed-dose NESP (360 μg) once every 3 weeks. The primary endpoint was hematopoietic response (a hemoglobin increase of ≥2 g/dL from baseline or a hemoglobin increase to ≥12 g/dL). EPOR mRNA was detected in all GCB-DLBCL cell lines, but little/none was detected in ABC-DLBCL cell lines. GCB-DLBCL and ABC-DLBCL cell proliferation was unaffected by EPO or NESP. Rituximab-mediated CDC of DLBCL cell lines with/without EPOR expression was not affected adversely by EPO. In the clinical study, baseline mean hemoglobin was 9.19 g/dL; the overall mean change in hemoglobin was 1.59±1.3 g/dL (16 weeks). Forty-eight percent of enrolled patients achieved a hematopoietic response. This study shows that ESAs do not affect the growth of DLBCL cells or rituximab-mediated CDC, and are effective and safe for DLBCL patients with anemia after R-CHOP.

* JEONG Jee-Yeong – PhD, Associate Professor (Department of Biochemistry and Cancer Research Institute, Kosin University College of Medicine, Busan, Korea). *E-mail: jyjeong@kosin.ac.kr