中文題目：瀰漫性大 B 細胞淋巴瘤臨床特色及雙重打擊對治療預後之影響

英文題目：The impact of clinical features and double hit signature on the treatment outcome of DLBCL

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Background: Diffuse large B cell lymphoma (DLBCL) with characterization of double hit (DH) or double expresser (DE) is considered to have worse outcome. CHOP-like regimen is the standard treatment for DLBCL. Several recent studies tried to evaluate the clinical feature and treatment outcome on DLBCL. However, data of double expresser or double hit is limited in Taiwan. Immunohistochemistry (IHC) stain on double expressers of MYC and BCL2 protein is standardized in our institution since January 2017. We also systemically performed Fluorescence in situ Hybridization (FISH) for double hit of MYC and BCL2 rearrangement since January 2018. Whole body PET, which provided maximum standardized uptake value (SUV), is also frequently used for staging in our daily practice. Because constitutional data is collected, we conducted this retrospective study to address the correlation of clinical features and double hit signature with treatment outcome.

Method: Medical records of 126 consecutive adult DLBCL patients diagnosed in Taichung Veterans General Hospital from January 2018 to July 2020 with double expresser profile were retrospectively reviewed. Patients who did not receive fluorescence in situ hybridization (FISH) due to inadequate sample (n = 29), primary CNS involvement (n = 3), and those without follow-up (n = 2) were excluded. Finally, a total of 92 patients were analyzed. Double hit is defined as C-MYC and BCL2/BCL6 more than 30% in FISH study. To investigate the impact of double hit, these 92 patients were further stratified into double hit group (DH, n = 14) and non-double hit group (non-DH, n = 78). The incidence of double hit in our study group is about 15% (14/92). Continuous and categorical variables between DH and non-DH groups were compared using Mann-Whitney U test and the Chi-squared tests, respectively. Numerical data are presented as means ± standard deviation. Kaplan-Meier survival curve is applied for estimate overall survival. We applied sensitivity and specificity test to evaluate the predicting accuracy of double hit. Values were considered statistically significant at $p < 0.05$.

Result: In total, we enrolled 92 DLBCL patients with complete profile of double

expresser and double hit. 14 of them have double hit (15.2%). Bulky disease in double hit and non-double hit group is 64.3% and 28.2% respectively (p=0.013). Double expresser in double hit and non-double hit group is 50.0% and 21.8% respectively (p=0.044). DLBCL patient with bulky disease and double expresser tend to have double hit (table 1). The details of the patients' clinical characteristics are listed in Table 1. In our study group, 85 patients receive CHOP-like regimen, including RCHOP, RCOP, REPOCH or hyperCVAD according to physician's evaluation. For risk of mortality on DLBCL receiving treatment, the univariate analysis revealed double hit (HR: 2.61; 95% CI: 1.26-5.41; p = 0.010), age more or equal to 65 years old (HR: 3.12; 95% CI: 1.59-6.13; p = 0.001), uric acid level (HR: 1.16; 95% CI: 1.07-1.26; p < 0.001), maximal SUV (HR: 1.07; 95% CI: 1.00-1.015; p = 0.036), performance status more than 2 (HR: 3.26; 95% CI: 1.49-7.17; p = 0.003), advance stage (HR: 7.8; 95% CI: 2.39-25.38; p = 0.001), bulky disease (HR: 2.48; 95% CI: 1.31-4.71; p = 0.005), R-IPI score (HR: 4.07; 95% CI: 1.97-8.93; p < 0.001)were associated with higher risk of mortality (table 2-1). The multivariate analysis further validated that double hit was the parameter associated with higher risk of mortality (HR: 6.19; 95% CI: 1.59-24.07; p = 0.009) under standard treatment (table 2-2). The 3 year overall survival among patients with double hit and without double hit was 49.66% and 28.57% (p = 0.008), respectively (figure 1). The specificity of non-bulky and non-double expressers on predicting double hit was 89.74% (table 3).

Conclusion: In summary, our study validated that double hit, clinical stage, R-IPI score, tumor size were critical factors for overall survival among patients with DLBCL. Clinical parameter of tumor burden including uric acid level, maximal SUValso played roles on overall survival. Double expresser didn't demonstrate significant impact on overall survival in our study. However, we could incorporate double expresser and bulky disease together to predict double hit status with high specificity.