Results of real-time cell-of-origin subtype identification by gene expression profiling in patients with ABC-type diffuse large B-cell lymphoma in the phase III trial of lenalidomide plus R-CHOP vs placebo plus R-CHOP (ROBUST). First Author: Grzegorz S. Nowakowski, Mayo Clinic, Rochester, MN

Background: Gene expression profiling (GEP) is the gold standard in identification of activated B-cell-like (ABC) DLBCL, a subtype associated with inferior outcomes. The combination of lenalidomide + R-CHOP (R²-CHOP) provided efficacy based on cell-of-origin (COO) in phase II DLBCL studies. ROBUST is a global, randomized, double blind, phase III study comparing R²-CHOP vs placebo + R-CHOP in patients with previously untreated ABC-type CD20+ DLBCL (NCT02285062).

Methods: ROBUST methods were previously described (Nowakowski, Fut Oncol 2016). Formalin-fixed paraffin-embedded excisional/surgical or core needle biopsy samples were analyzed by central pathology using the NanoString Lymphoma Subtyping Test (LST), based on the Lymph2Cx GEP assay (Scott, Blood 2014). Turnaround time was defined as number of days between central pathology sample receipt and results being provided to the study site.

Results: From January 21, 2015 to August 3, 2017, 2093 patients were screened and 570 were enrolled in ROBUST. Three central pathology labs in China, USA and the UK received 2110 samples. Of 1798 successfully tested samples, COO was 788 (44%) ABC and 1010 (56%) non-ABC; 312 (15%) samples were non-processable for technical reasons (incorrect/insufficient slides or blocks, or low tissue RNA concentration and/or purity). According to geographic region of origin, the ABC-type DLBCL rate among successfully tested samples was 60% (241/404) from China/Japan/SK/Taiwan; 40% (441/1105) from Russia/Europe/Middle East; and 37% (106/289) from North America/Australia/New Zealand. Mean turnaround time was 2.4 days.

Conclusions: Real-time COO assessment was feasible from multiple regions globally with a short turnaround time in the phase III ROBUST study, which minimizes the delay in receiving treatment. The percent of ABC-type DLBCL was similar to other reported studies of subtype analysis in the literature. Our findings impact the design and size estimation of future studies in newly diagnosed DLBCL utilizing COO as a biomarker, which provides a significant advance in precision medicine in DLBCL. Clinical trial information: NCT02285062.