**Potential Surrogate Endpoints for Progression-free Survival (PFS) and Overall Survival (OS) in Non-Hodgkin Lymphoma: a Literature-based Meta-analysis of Phase II and Phase III Studies**

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**Objectives:** Survival-based endpoints such as progression-free survival (PFS) and overall survival (OS) are considered the gold standard in clinical trials of non-Hodgkin lymphoma (NHL) but demonstration of clinically meaningful differences in treatment regimens necessitates large and lengthy trials. The correlation between efficacy endpoints in NHL clinical trials was investigated to identify potential surrogate endpoints for PFS and OS in major histologic subtypes of NHL.

**Methods:** Phase II and Phase III studies in patients with diffuse large B cell lymphoma (DLBCL), follicular lymphoma (FL), or mantle cell lymphoma (MCL) published from 1993 to 2013 were identified. Correlations between efficacy endpoints were analyzed using weighted linear regression.

**Results:** Data used in the analysis were from 127 trials (148 trial arms), representing over 13,000 patients. In trials of newly diagnosed DLBCL, 6-month PFS was moderately correlated with 2-year OS (R2=0.81 with 95% confidence interval [CI] 0.51-0.96) and 3-year OS (R2=0.74 with 95% CI 0.45-0.95). Linear regression determined that a 10% increase in 6-month PFS would predict for a 13% +/- 1.2% increase in 2-year OS or a 14% +/- 1.4% increase in 3-year OS. For trials of FL (newly diagnosed and relapsed/refractory combined), 6-month PFS was highly correlated with 3-year PFS (R2=0.89 with 95% CI 0.62-0.96). No clear correlation was observed between complete response (CR) rate (%) and median PFS or OS or landmark PFS or OS in DLBCL, FL, and MCL patients.

**Conclusions:** Six-month PFS was moderately correlated with 2-year and 3-year OS in newly diagnosed DLBCL and highly correlated with 3-year PFS in FL patients, indicating 6-month PFS may be an appropriate surrogate endpoint. Further exploration of these correlations may facilitate future trial design and interpretation of interim data analyses.