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# ORAL ABSTRACTS

## 905.OUTCOMES RESEARCH-LYMPHOID MALIGNANCIES

### Risk of Transformation By Frontline Management in Follicular Lymphoma and Marginal Zone Lymphoma: A US Population-Based Analysis

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INTRODUCTION
Follicular lymphoma (FL) and marginal zone lymphoma (MZL) are commonly characterized by an indolent nature and favorable overall survival (OS). However, patients (pts) may experience high-grade transformation (HGT) into DLBCL, with an estimated annual risk of 1%-3% and cumulative incidence of HGT are 8% for FL and 10% for MZL at 10 and 12 years, respectively. The impact of treatment and surveillance strategies on the incidence of HGT remains uncertain, with some studies indicating reduced risk in treated pts without significant OS difference post-HGT. This study uses population-based data to assess the cumulative incidence and risk factors associated with HGT, post-HGT OS and lymphoma-specific survival (LSS) across lymphoma subtypes, with either treatment or surveillance as initial strategies.
METHODS
We extracted data for pts diagnosed with grades 1-2 FL, splenic MZL (SMZL), nodal MZL (NMZL), and extranodal MZL (MALT) from SEER database (period 2000-2015 with follow-up through 2018). We only included pts with histologic confirmed lymphoma as first malignancy, complete survival and treatment data, and a minimum of 3 months from FL and MZL diagnosis to HGT. Competing risk methods were used to estimate HGT cumulative incidence rates, with time to first event (HGT or death) defined from lymphoma diagnosis to date of first event; event-free pts were censored at date of last contact. Gray's test and Fine-Gray (FG) proportional subdistribution hazard modelling was employed to identify variables associated with risk of HGT. Post-HGT OS and LSS analyses utilized Cox and FG regression models, respectively.
RESULTS
26827 pts met inclusion criteria. FL comprised 14229 pts (53%) while MZL types were SMZL 1182 (4.4%), NMZL 3916 (14.6 %) and MALT 7500 (28%). Treatment was given at diagnoses in 60.2%, 33.7%, 53.8% and 49.8% of pts with FL, SMZL, NMZL, MALT, respectively. 864 (3.2%) pts developed HGT to DLBCL, 553 (3.9%) in FL and 311 (2.5%) in MZL pts.
After a median follow-up of 84 months (range 1-227), the 10-year cumulative incidence of HGT were for FL 4.24% (95%CI 3.88%-4.62%), SMZL 6.46% (95%CI 4.98%-8.20%), NMZL 3.28% (95%CI 2.70%-3.95%) and MALT 1.73% (95%CI 1.42%-2.09%). In FL, the 10-year cumulative incidence of HGT was 3.83% (95%CI 3.40-4.31%) in treated pts and 4.88% (95%CI 4.26%-5.54%) for those under surveillance (SHR=0.80, 95%CI 0.68-0.94; p=0.009) (Figure 1). This finding was confirmed in a multivariable analysis (p=0.001) that conversely identified female gender (p<0.001) and advanced stage at diagnosis (p<0.001) with higher risk of HGT (Figure 1). In MZL, the 10-year cumulative incidence rate of HGT in treated pts versus those managed with surveillance depicted by subtypes were as follows: SMZL 6.93% (95%CI 4.40%-10.2%) vs 6.29% (95%CI 4.53%-8.43%); NMZL 3.71% (95%CI 2.87%-4.70%) vs 2.78% (95%CI 2.03%-3.71%); MALT 2.01% (95%CI 1.54%-2.57%) vs 1.45% (95%CI 1.07%-1.93%). No significant difference between treatment versus surveillance were detected in univariable and multivariable analyses for SMZL (p=0.72 and 0.54) and NMZL (p=0.07 and 0.07), whereas surveillance pts had lower risk of HGT in MALT (p=0.02 and 0.01) (Figure 2). There were 429 (49.7%) deaths, including 337 (39%) lymphoma-specific deaths recorded in 864 pts with HGT in the entire cohort; and the median OS after HGT was 3.67 years (95%CI 2.5-6.25). Frontline therapy for FL was associated with higher risk of overall and lymphoma-specific deaths post-HGT (HR=1.32, 95%CI 1.03-1.69, p=0.02; and SHR=1.33, 95%CI 1.02-1.75,

p=0.03); however, there was no significant difference in OS between frontline therapy and surveillance approach in SMZL (p=0.11), NMZL (p=0.73) and MALT (p=0.70). Interestingly, in SMZL worse LSS post-HGT was observed in those managed with frontline therapy (SHR=2.68, 95%CI 1.32-5.45, p=0.006).

CONCLUSIONS

Frontline treatment was associated to reduced HGT risk in FL, with advanced stage and female gender identified as risk factors for HGT. Contrarily, for SMZL, NMZL, and MALT, initial treatment neither diminished HGT risk nor improved overall survival post-HGT. Interestingly, in MALT initial treatment exhibits a higher HGT risk, likely due to selection bias, even though HGT cumulative incidence in MALT was lower compared to other subtypes. SMZL displayed a particularly high cumulative incidence of HGT and poorer LSS.

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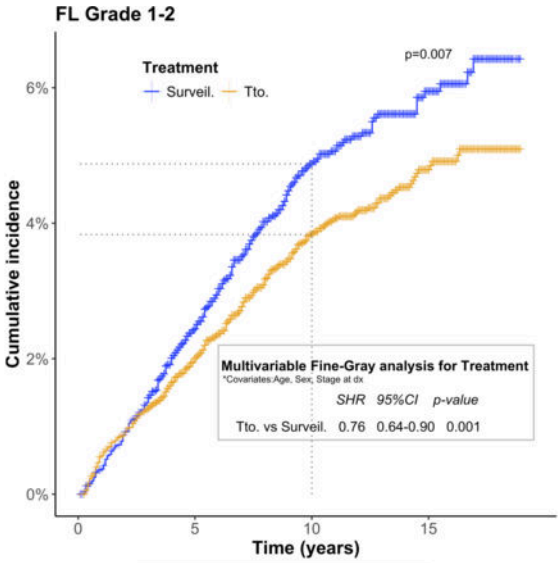


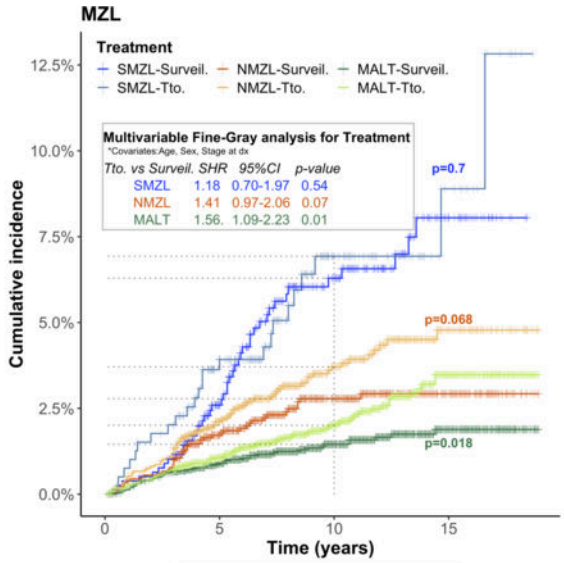


**Figures 1** and **2** describe cumulative incidence curves of high-grade transformation (HGT) across four types of lymphoma, stratified by initial management strategy (Treatment vs Surveillance). These curves, derived using the cumulative incidence function method, consider death as a competing event for HGT. Univariable Fine and Gray regression modeling was employed to compare Treatment versus Surveillance, with p-values adjacent to the curves. Multivariable Fine and Gray regression, adjusted for age, sex, and stage at diagnosis, further assesses these management strategies. Dotted lines showing 10-year cumulative incidence estimates. **Figure 1** illustrates the results for Follicular lymphoma grade 1-2, while **Figure 2** depicts findings for Splenic marginal zone lymphoma (SMZL), nodal marginal zone lymphoma (NMZL), and extranodal marginal zone lymphoma (MALT). Abbreviations; Treatment, Tto; Surveillance, Surveil.

**Figure 1**

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