GENETIC PROGNOSTIC MARKERS IN MANTLE CELL LYMPHOMA

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Introduction

Mantle cell lymphoma (MCL), a uncommon type of B-cell lymphoma (non-Hodgkin lymphoma), is primarily driven by the t(11;14) translocation. MCL displays significant clinical and biological diversity, often exhibiting a resistant course that can be influenced by its molecular genetic profile.

Aim

The aim was to determine the prevalence of genetic hallmarks in MCL and assess their influence on the prognosis.

Methods

The study included 24 patients with MCL stage 3–4 aged 18 to 70. Median follow-up was 29.4 months (4.8–133).All patients underwent immunochemotherapy as a first line. Karyotype was assessed in all patients. T(11;14)(q13;q32), *MYC*/8q24 rearrangement, and deletions of the *TP53*/17p13 gene were assessed by fluorescence in situ hybridization (FISH). Next-generation sequencing (NGS) with targeted lymphoid panel of 118 genes was performed in all cases.

Results

79% of patients had a normal karyotype. T(11;14) was identified in the karyotypes in 13%, *TP53*/17p13 in 8%, and a complex karyotype in 8%. FISH revealed t(11;14) in 67%, del17p in 17%, and *MYC*/8q24 in 13%. According to NGS the most frequently detected mutations were in *ATM* (36%), *RYR1* (27%), *BCR* (27%), and *KMT2D* (23%). Analysis indicated that the presence of *TP53*/17p13 significantly elevated the risk of death (HR=10.91; 95% CI: 2.36–50.50; P<0.01). Patients with *TP53*/17p13 experienced median OS of 10.6 months (95% CI: 4.8 to not reached [NR]), median PFS of 3.9 months (95% CI: 3.0–NR), while those without *TP53*/17p13 had median OS of NR and PFS of 24.8 months (95% CI: 10.5–NR; P<0.01). The presence of *MYC*/8q24 rearrangement significantly impacted median OS, which was 8.93 months (95% CI: 7.7 to not determined [ND]) compared with NR in patients lacking *MYC*/8q24 (P<0.01). The analysis revealed a significant link between an *ATM* mutation and prognosis (P=0.03). Patients with *ATM* mutation had a median OS of 12.9 months (95% CI: 10.2–ND), compared with NR in the group without *ATM* mutation. 3-year OS without *ATM* mutation was 81.1% (95% CI: 63.9–100), compared with 42.9% (95% CI: 19.2–100) in the group with *ATM* mutation.

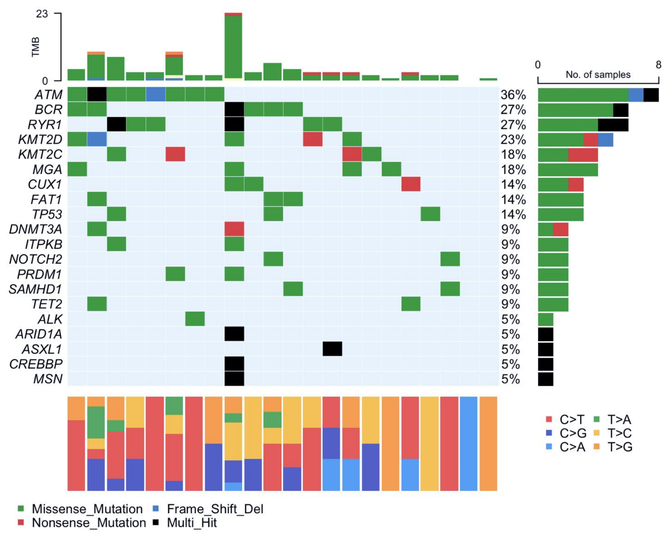


Image 1. Oncoplot (TMB - Tumor mutational burden)

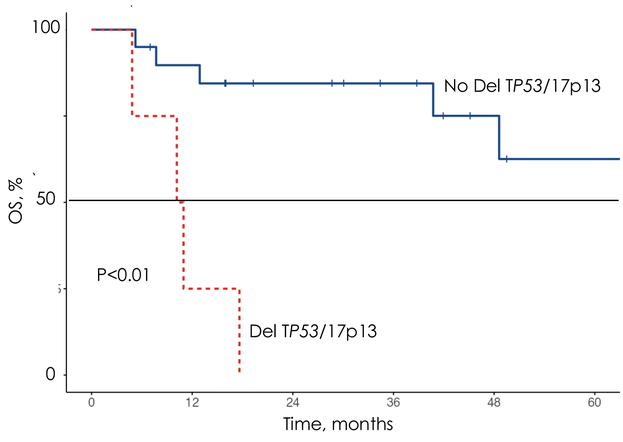


Image 2. OS depending on deletion *TP53*/17p13

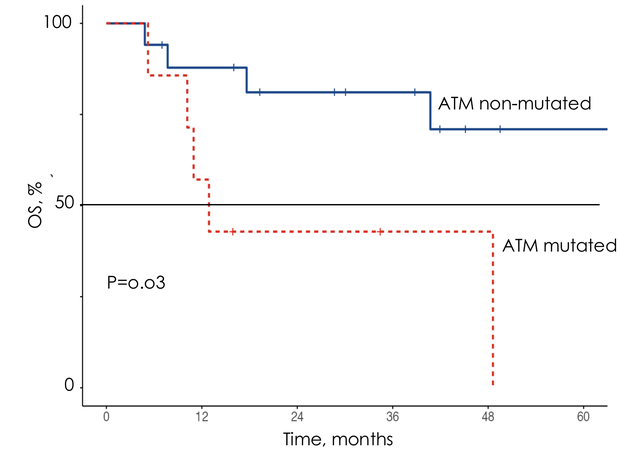


Image 3. OS depending on *ATM* mutation

Discussion

Thus, markers that influence prognosis in MCL are aberrations *TP53*/17p13, *MYC*/8q24, *ATM* mutations. Molecular profile may be a key in poor prognosis of MCL. Further investigation is needed to fully elucidate the impact of the detected markers.

References

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2. E. Silkenstedt, M. Dreyling. Mantle Cell Lymphoma-Update on Molecular Biology, Prognostication and Treatment Approaches. Hematol Oncol. 2023 Jun;41 Suppl 1:36-42. DOI: 10.1002/hon.3149.