59% of patients) and poor risk (4 points, 17% of patients). Two-year OS rates were 81%, 47%, and 21%, respectively ($p < 0.0001$) (figure).

Conclusion: This easy-to-compute scoring index may allow the identification of groups of transformed WM patients with different outcomes and could be used for improving treatment choices.

Keywords: diffuse large B-cell lymphoma (DLBCL); prognostic indices; Waldenström's macroglobulinemia (WM).

MANTLE CELL

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SERUM BIOMARKERS ARE ASSOCIATED WITH TREATMENT RESPONSE IN RELAPSED MANTLE CELL LYMPHOMA

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Introduction: Recent advances in therapeutic strategies have provided novel treatment regimens for MCL, that until recently, was associated with dismal prognosis of 3-5 yrs median overall survival. However, strategies to guide patient stratification are still lacking in both diagnostic and relapsed setting. Non-invasive methods based on liquid biopsies would facilitate the continuous sampling of patients over time and identification of companion diagnostic biomarkers is warranted. For this purpose, we have used an antibody-based platform to identify serum proteins in relapsed patients that are homogenously treated as per the Nordic MCL6 clinical trial (Philemon). We hypothesize that, the platform can identify if the immune status at treatment start can influence the response to combinatorial immune-directed therapies. We also intend to study how treatment can influence the immune status across time.

Methods: Sequential serum samples from 44 patients treated with Lenalidomide, Ibrutinib and Rituximab (Philemon trial) were processed on the IMMRay™ platform (Immunovia). We processed serum samples from 4 time-points; at baseline and 12, 24 and 36 weeks of treatment which corresponds to cycle 4, 7 and 10, of the trial. The platform, allows the analysis of 380 different epitopes among approximately 150 unique proteins. It focuses on soluble immune-related proteins such as cytokines, chemokines and complement factors, as well as, several cancer-related markers. In brief, antibody fragments are produced and printed on a solid support. Samples are biotinylated and detected using a fluorescent marker after hybridization to the array. Spot recognition and raw data processing was performed using standard operating procedure according to the IMMRay guidelines (Immunovia). Normalization and further bioinformatic and biostatistical analysis were performed using standard tools which includes R, Qlucore and SIMCA; and several other in-house built softwares developed in conjunction to the experimental platform.

Results: Preliminary results using COX regression analysis shows that, at baseline, a signature of approximately 6-8 relevant proteins are associated with PFS. Further investigations are needed to validate this in an independent cohort of patients. Current investigations aim to identify if additional prognostic and biological information related to the treatment can be derived by comparing samples at baseline, cycle 4 and beyond.

Conclusion: We have showed that prognostic information can be derived from serum samples collected from relapsed MCL patients. To our knowledge, this is the first time that an antibody-based array is used as a tool to assess the possibility of developing serum-based signatures useful for treatment selection in relapsed MCL patients.

Keywords: B-cell lymphoma; immune system; mantle cell lymphoma (MCL).

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HIGH VIRAL LOADS OF CIRCULATING EPSTEIN-BARR VIRUS DNA COPY NUMBER IN PERIPHERAL BLOOD IS ASSOCIATED WITH INFERIOR PROGNOSIS IN PATIENTS WITH MANTLE CELL LYMPHOMA

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Introduction: Mantle cell lymphoma (MCL) is a distinct subtype of B cell non-Hodgkin lymphoma. No research has yet documented to investigate the prognostic implications of Epstein-Barr virus (EBV) infection in MCL. The objective of this study was to examine whether EBV DNA load may influence the heterogeneity in the course of the disease in MCL patients.

Methods: Eighty-eight MCL patients were retrospectively enrolled in the study. EBV DNA load was detected by real-time quantitative PCR for quantification. The univariate and multivariate Cox proportional hazards models were established for the estimation of prognostic factors.

Results: Twenty-seven patients were detected positive for EBV DNA ad the median virus titer was 1.72×104 copies/mL (range, 8.20×102 to 4.14×105 copies/mL). With a median follow-up of 39 months (range, 9 to 120 months), patients in EBV DNA-positive group

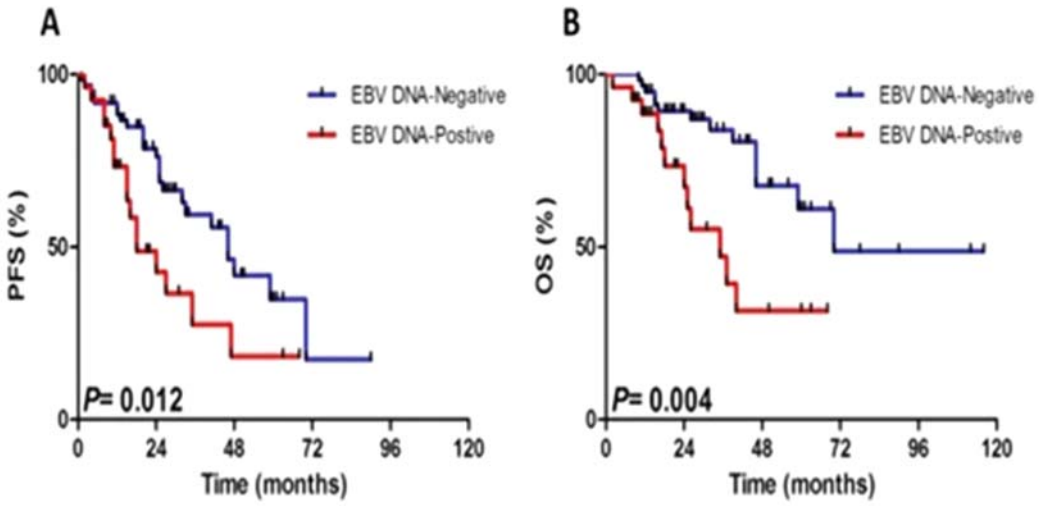

Figure 1. Progressive-free survival (PFS) and overall survival (OS) for 88 patients with the analysis of pretreatment Epstein-Barr virus (EBV) DNA status.

displayed unfavorable progression-free survival (PFS) (P=0.012) and overall survival (OS) (P=0.004) than patients in EBV DNA-negative group (Figure 1). Multivariate Cox regression analysis revealed that EBV DNA-positivity was independent risk factor for both PFS (HR, 2.04; 95% CI, 1.07 to 3.92; P=0.031) and OS (HR, 2.68; 95% CI, 1.20 to 6.00; P=0.016). Reduction in EBV copies was significantly associated with therapy-response.

Conclusion: Circulating EBV DNA load in whole blood proved to be a significant predictor of prognosis in patients with MCL, which needs further validation in large-scale clinical studies.

Keywords: Epstein-Barr virus (EBV); mantle cell lymphoma (MCL); prognostic indices.

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OBINUTUZUMAB THERAPY IN PATIENTS WITH MARGINAL ZONE AND MANTLE CELL LYMPHOMA

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Introduction: Obinutuzumab (OBI) is FDA approved in chronic lymphocytic leukemia and follicular lymphoma, with favorable efficacy profiles noted in both settings. While there was a small subpopulation of marginal zone lymphoma (MZL) and mantle cell lymphoma patients (pts) in the GAUSS trial and GADOLIN/GAUGUIN trials respectively, there is little clinical experience in using OBI in these patient populations outside the context of a clinical trial. We describe a real world experience of OBI use in MZL and MCL pts off clinical trial.

Methods: We conducted a retrospective cohort study of all adult pts who received OBI for MZL and MCL at the University of Pennsylvania between 2/2013 and 2/2019. Demographics, duration of therapy, reason for discontinuation, overall response, survival, and toxicities were examined. The primary endpoints were progression-free survival (PFS; defined as time from OBI start to disease progression or regimen change, death due to MZL/MCL or last-follow-up in remission), and overall survival using the Kaplan-Meier method. All other analyses were descriptive.

Results: We identified a total of 10 pts for the entire cohort, 6 with MZL and 4 with MCL. The median age at start of OBI was 64 years (Range 50-92). 80% of pts were stage 4, had a median of 2 prior therapies (1 MZL patient treated frontline), median ECOG status 0, and one MZL patient had an MYD88 mutation. One patient was rituximab naïve, but 70% were rituximab refractory. The median number of cycles administered of OBI was 7 (Range 1-31) respectively. 50% of pts received OBI in combination, 3 pts with bendamustine, 1 with chlorambucil, and 1 with ibrutinib. Overall response rate was 90% (10% CR). Median PFS and OS were 11.5 and 13.5 months respectively. Two pts progressed following OBI therapy; one patient with MZL who subsequently was treated with ibrutinib and one with MCL subsequently treated with venetoclax.

50% of pts experienced at least one Adverse event(AE). AEs included: Infusion related reactions (40%), thrombocytopenia (40%), diarrhea (30%), neutropenia (20%), infection (10%). Three pts were on growth factor during OBI administration. One patient discontinued therapy secondarily to an infusion related reaction.

Conclusions: OBI therapy was well tolerated in our cohort of MZL and MCL pts. We observed a high ORR and durable PFS and OS opportunity. Only two pts experienced progression following OBI therapy, both of whom are currently controlled with novel oral agents. The AE profile of OBI was well tolerated, with toxicities consistent with current package labeling. Additional clinical trials and/or pooled data from retrospective observational studies will help confirm OBI therapy's durable efficacy benefit for pts with MZL and low-risk MCL.

Keywords: mantle cell lymphoma (MCL); marginal zone lymphoma (MZL); obinutuzumab.