Abstract: P1137

Title: UNDETECTABLE MEASURABLE RESIDUAL DISEASE (MRD) IS ASSOCIATED WITH IMPROVED LONG-TERM OUTCOME IN PATIENTS WITH FOLLICULAR LYMPHOMA (FL) TREATED WITH CHEMO-IMMUNOTHERAPY: RESULTS FROM SWOG S0016

Abstract Type: Poster Presentation

Topic: Indolent and mantle-cell non-Hodgkin lymphoma - Clinical

Background:

Detection of MRD has demonstrated prognostic value in several hematologic malignancies. In recent years, advances in NGS methodology have enabled quantification of "molecular MRD". The ClonoSeq assay (Adaptive Biotechnology, Inc.) has been cleared by the U.S. FDA in ALL, CLL and multiple myeloma. However, the potential significance of tracking MRD in FL has not been well studied.

Aims:

To determine whether MRD status predicts clinical outcomes in a prospective cohort of patients with*de novo* FL.

Methods:

SWOG S0016 was a phase III study that randomized 531 patients with advanced-stage FL to either 6 cycles of R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone) or CHOP-RIT (CHOP + I133-tositumomab). High-throughput sequencing of the IGH and IGK/L loci (ClonoSeq assay) from pre-treatment tumor biopsy specimens* was used to define CDR3 rearrangements that tag the tumor (pre-library). One-year bone marrow specimens were screened for residual disease (post-library). Positive MRD (MRDp) was defined as a minimum Hamming distance (HD) ≤6 in a patient's post-library (in any clone also detected in a pre-library) and conserved pre-existing SHM (if HD>0). Undetectable MRD (MRDu, at <10-4) was defined as CDR3 HD>6 in a post-library with a depth >10,000 estimated number of genomes. The primary endpoint was 5-year progression-free survival (PFS; time from registration to the first observation of progression or death due to any cause). Landmark analysis was defined at 1 year after registration and used for imputing the 5-year PFS and OS. Overall survival (OS) was defined as the time from registration to date of death due to any cause or last follow-up. PFS and OS estimates and 95% CI were calculated using the Kaplan-Meier method and compared for MRDp and MRDu disease using two-sided log-rank test.

Results:

One hundred and eighty-nine patients had available pre-treatment tumor biopsy tissue; of these, 24 patients were not evaluable (16 did not consent for banking, 6 were ineligible and 4 had an early event). MRD status could not be ascertained in 47 patients due to absence of a clear trackable clone in either pre- (n=36) or post-library, a 29% failure rate. Trackable clone was detected in 116 patients, of which 83 were MRDu and 33 were MRDp. Baseline characteristics (age, sex, race, β2M, B symptoms, bulky disease, grade 3, stage, and FLIPI risk) were similar for both, but MRDp patients were more likely to exhibit baseline bone marrow involvement than MRDu patients (82% vs. 55%, p=0.01). Overall response rate was significantly higher in MRDu than MRDp patients (96% vs 79%, p=0.005), but complete responses were similar (41% vs. 30%). The estimated 5-year PFS was 72% in MRDu patients and 30% in MRDp patients (Figure); 10-year PFS was 56% and 17%; 15-year PFS was 45% and 9%, correspondingly. Patients who had MRDp status had a significantly increased risk of early disease progression (POD24) relative to MRDu patients (RR=6.5, 95% CI 3.0-14.0; p<0.0001). Five- and ten-year OS rates were similar between the two groups. Five-year PFS was superior in patients who achieved MRDu regardless of response (75% for CR and 70% for PR), compared with MRDp patients.

Summary/Conclusion: Undetectable MRD status, as assessed by Clonoseq, predicts improved 5- and 10-year

PFS in patients with FL treated with chemoimmunotherapy. MRD assessment by NGS is a promising prognostic tool in FL.

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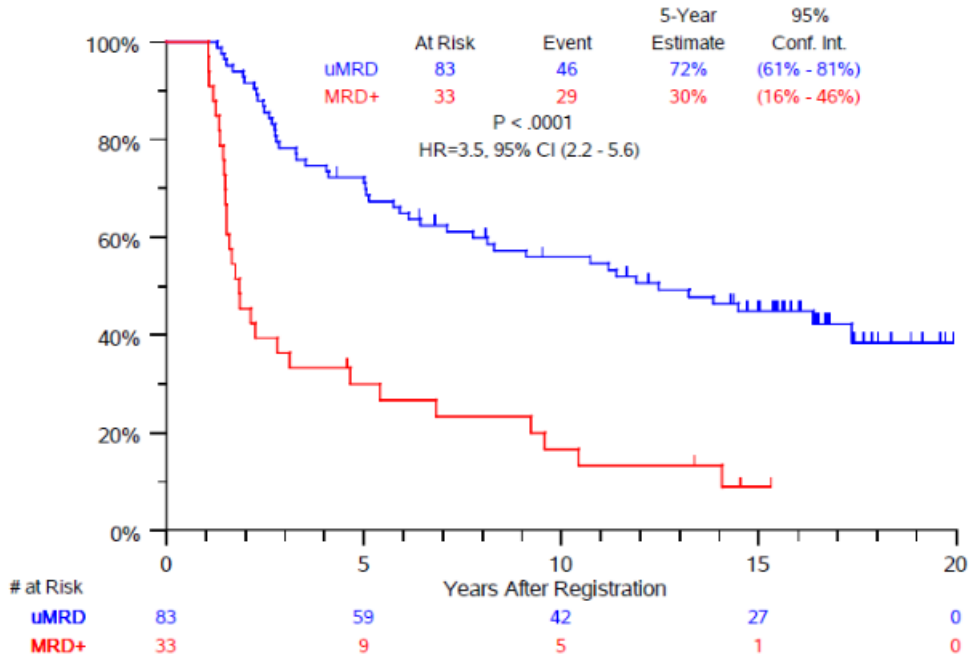
Figure. 5-year PFS in patients with FL depending on MRD status at 1 year.



Keywords: Follicular lymphoma, Survival, Minimal residual disease (MRD)