Chemotherapy-free combination of ibrutinib and obinutuzumab for untreated advanced follicular lymphoma: results of a phase II study from the German Lymphoma Alliance

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SUPPLEMENT

Primary and secondary outcomes

PFS was defined as the time from registration to lymphoma progression or death from any cause. Patients alive and without documented progression were censored at the time of last contact. OS was calculated from time of registration to death. Patients without an event were censored at the time of last contact. For patients with CR or PR at the end of induction, DoR was calculated as the time from the end of induction to progression or death from any cause. All secondary variables were evaluated on the ITT population of all registered patients. Safety was evaluated on all patients who started treatment with obinutuzumab or ibrutinib.

Response assessment was performed by the investigator according to the Revised Response Criteria for Malignant Lymphoma[8] and included physical examinations, CT/MRI scans, hematology, laboratory results and bone marrow examinations. Efficacy evaluations were performed after 6 cycles of induction treatment and every 6 months thereafter until clinical progression.

MRD was assessed on peripheral blood (PB) and/or bone marrow (BM) samples collected before treatment start and at months 3, 6, 9, 12, 18, 24 and 30. Diagnostic PB and BM samples were initially screened by consensus PCR using Biomed 2 primers[9] to detect a t(14;18) translocation and/or clonal immunoglobulin heavy chain (IgH) rearrangement. In patients with detectable t(14;18) translocation, real-time quantitative (RQ)-PCR targeting t(14;18) was used to quantify MRD at a sensitivity level of 10^{-5}. In t(14;18) negative patients, allele-specific (ASO) primers matching the junctional region of rearranged IgH genes were designed and ASO RQ-PCR was conducted to quantify MRD at a comparable sensitivity level.

In a sample, MRD status was classified as positive (including low-level positivity below

the quantifiable range) or negative. If a patient had MRD values for both peripheral blood and bone marrow, the MRD value was considered positive if any of the two values was positive, and negative if no value was positive and at least one was negative (pooled analysis). MRD analyses were continued every 6 months until clinical progression or until the end of the study.

Supplemental Figure

Supplemental Figure 1: Overall survival from progression. Kaplan-Meier estimates of OS from time of progression among 37 patients with progression of disease.