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POSTER ABSTRACTS

623.MANTLE CELL, FOLLICULAR, AND OTHER INDOLENT B CELL LYMPHOMAS: CLINICAL AND EPIDEMIOLOGICAL

Six Years Follow up of Ibrutinib Plus Rituximab (IR) Followed By Short Course R-Hyper CVAD/MTX in Patients (age ≤ 65 years) with Previously Untreated Mantle Cell Lymphoma - Phase-II Window-1 Clinical Trial

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Background - We reported the efficacy and safety of using a combination of ibrutinib plus rituximab (IR) induction followed by short course (4 cycles) of R-HCVAD/MTX-ara-C as consolidation in previously untreated young (age ≤ 65 years)patients **(**pts) with mantle cell lymphoma (MCL), Wang M et al Lancet Oncology 2022. Here we report the long term follow up of this study.

Methods - We enrolled 131 previously untreated pts in this single institution, single arm, phase II clinical trial - NCT02427620. Pts received IR induction (part-A), until they achieved complete remission (CR) for up to a maximum of 12 cycles, followed by a maximum of 4 cycles of R-HCVAD/R-MTX-ara-C (part-B) as consolidation. The primary objective was to assess overall response rate (ORR), [defined as either a partial response (PR) or a complete response (CR)] after part A. Adverse events were coded as per CTCAE version 4. High risk pts received ibrutinib for 1 year and rituximab once every 2 months for 24 months after completion of part B.

Results - Among the 131 pts, the median age was 56 yrs (range - 35-65). High Ki-67 (≥30%) in 58/117 (49.5%) pts, 10 pts (8%) had high risk simplified MIPI score, 15 pts (11%) had aggressive MCL (blastoid/pleomorphic) and 114 pts (87%) had initial bone marrow involvement. Fifty percent of the patients had Ki-67 (≥30%). ORR in part-A was 98% (87% CR). After completion of part A and part B, ORR was 90% (89% CR). After a median follow up of 71 months, 43 patients progressed/died. The median progression free survival (PFS) and overall survival (OS) were not reached. Overall, 30 pts (23%) relapsed after treatment, including 5 who transformed to aggressive MCL. PFS among pts with high and low Ki-67% was 42 months vs not reached (P=0.01) while no difference was observed in OS. PFS was significantly shorter in pts with aggressive histology (p=0.001) but not the OS. PFS was similar in pts who received maintenance vs no maintenance therapy. Overall, 8 pts died (4 with progression, 2 due to disease transformation, one on study due to multiple complications including splenic hematoma, cardio-pulmonary arrest and progression and the last one expired outside and came off study due to encephalitis). 50 pts came off study for various reasons [30 disease progression (including 5 transformation), 10 pt choice, 8 intolerance, 1 second cancer and 1 lost to follow up]. Long term, grade 3-4 toxicities on part A were 6% myelosuppression and 10% each with fatigue, myalgia and rashes and 2% mucositis. Maintenance therapy did not show high toxicities.

Conclusions -Long term follow up of chemo-free induction with IR induced durable and deep responses in young MCL pts in the frontline setting. Short course R-HCVAD chemotherapy minimized toxicities and consolidated responses. IR maintenance improved survival outcomes. This combined modality treatment approach may significantly improve young MCL pts outcomes across all risk groups.

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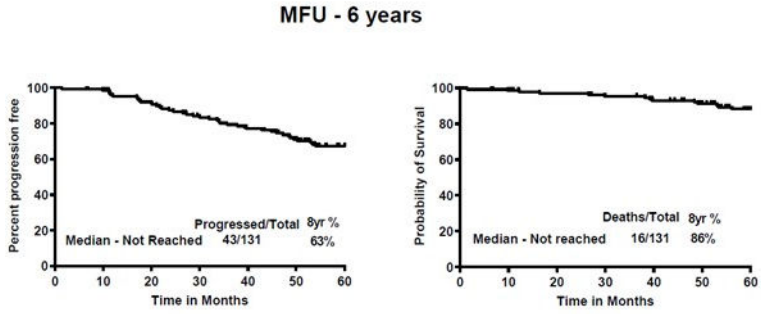

Figure 1

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