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POSTER ABSTRACTS

652.MULTIPLE MYELOMA: CLINICAL AND EPIDEMIOLOGICAL

Outcomes of Triple Class Refractory Multiple Myeloma Patients: A Single Center Retrospective Study

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BACKGROUND
Despite recent advances in the treatment of multiple myeloma (MM), the disease remains incurable. Recent studies suggest that patients who are triple class refractory (TCR) to a proteasome inhibitor (PI), immunomodulatory agent (IMiD), and anti-CD38 monoclonal antibody (mAb) have especially poor outcomes with a median overall survival (OS) of less than 1 year. However, studies with these results have been conducted in large academic institutions. In this study, we retrospectively analyzed outcomes among MM patients with TCR MM in a single clinic specializing in the care of patients with MM.
METHODS
A retrospective chart review was conducted among patients with TCR MM who were treated in a single clinic specializing in the care of patients with this B-cell malignancy. From July 2003 to July 25, 2022, we determined these patients' progression-free survival (PFS), OS, cytogenetics, lines of prior therapy (LOT), and first treatment they received after they became TCR. Kaplan-Meier analysis was utilized to assess differences in PFS, OS from diagnosis, and OS from TCR status based on high-risk cytogenetics, defined as the presence of t(4;14), t(14;16), t(14;20), 1q gain, or deletion 17p, compared to those with standard-risk cytogenetics. Kaplan-Meier analysis was also used to compare PFS according to number of lines of prior LOT, time to TCR, and drug class used for the first treatment after becoming TCR.
RESULTS
TCR developed in 121 patients. The median time from diagnosis to development of TCR disease was 33.4 months (mo; range, 1.5-187 mo). Patients with a time to TCR status of > 33.4 months had a longer PFS (median 5.2 mo) compared with patients with a time to TCR status of < 33.4 mo (median 2.5 mo; p=0.0171). The median LOT these patients received was 7 (range, 3-26). The median LOT prior to becoming TCR was 3 (range: 2-12). The median PFS of patients from their first treatment following the development of TCR was 4.5 months; patients with < or > 3 LOT prior to becoming TCR had the same median PFS (4.5 mo). However, PFS was shorter for high-risk (median = 2.5 mo) than standard risk (median = 4.2 mo) TCR MM patients, but this did not reach statistical significance (p = 0.0633).
The median OS from diagnosis of MM was 94.8 mo (range, 5.8 - 320.6 mo). Cytogenetic data was available for 65 patients (54%). Of these, 35 (54%) harbored high-risk cytogenetics. The median OS of TCR patients with high-risk cytogenetics from diagnosis was 98.2 mo and was not different from those with standard risk disease (74.2 mo; p = 0.704). Notably, the median OS of patients from the time of development of TCR was 25.5 mo (range, 1.5 - 186.8 mo); OS was shorter (median 18.7 mo) among those TCR patients with high-risk cytogenetics compared with that of standard risk (38.5 mo), but this was not significant (p = 0.1109).
The first line of therapy administered following the development of TCR for the majority of patients (n= 108 [89%]) was retreatment with an IMID, PI, mAb, or a combination of agents from these drug classes. Thirteen patients (11%) were treated with a venetoclax- or alkylating agent-based combination therapy. In addition, all except 2 patients received steroids as part of their first treatment after developing TCR. The regimen with the longest PFS was the combination of a mAB and steroids (median 9.0 mo) but only 6 patients were treated with this combination. The shortest PFS was among those retreated with a PI and steroids (n = 15; median 2.4 mo). The use of an IMID with steroids was the most frequently used combination treatment (n=32) with a median PFS of 3.4 mo.
CONCLUSION
Despite being refractory to a PI, IMID, and mAb, TCR patients in our single-center retrospective study showed a median OS of more than 2 years (25.5 mo) from the development of TCR. This OS is the longest reported to date in this population of MM patients. Cytogenetic differences failed to predict both OS and PFS from the development of TCR. In addition, the number

of prior lines of therapy did not predict PFS from their first treatment after showing TCR. The time to development of TCR, however, did predict OS as patients who took longer to become TCR had a longer median OS. The results of this study show that time to becoming TCR is a prognostic factor for this group of patients. Our study shows that OS is considerably longer for patients with TCR than has been previously reported.

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