3. RELAPSED/REFRACTORY MULTIPLE MYELOMA

PROGNOSTIC ROLE OF STANDARDIZED (18)F-FDG-PET/CT AND WB-DW-MRI IN RELAPSED/REFRACTORY MULTIPLE MYELOMA PATIENTS RECEIVING T CELL-REDIRECTING THERAPIES

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Background. CAR T-cells and bispecific antibodies (BsAbs) (T cell-redirecting therapies, TCRT) have revolutionized the treatment of relapsed/refractory multiple myeloma (RRMM), with unprecedented response rates, minimal residual disease (MRD) negativity and outcome. The prognostic role of functional imaging (FDG-PET/CT and whole-body diffusion-weighted MRI, WB-DW-MRI), both at baseline and in defining imaging MRD, has been widely validated in newly diagnosed MM, but is less explored in the setting of RRMM (including TCRT). Preliminary studies have demonstrated a significant role of PET response at 3 months (mos) after CAR-T infusion.

Aims and Methods. Herein we present a single-center retrospective/prospective study aimed at assessing the prognostic role of functional imaging in the setting of TCRT. Patients (pts) underwent PET/CT and WB-DW-MRI (the latter since August 2024) prior to TCRT and every 3 mos thereafter until negative or progression. Interpretation of the two imaging techniques was based on IMPeTUs and MY-RADS criteria. Pts also underwent next generation sequencing (NGS) MRD assessment at achievement of ≥very good partial response and every 6 mos thereafter.

Results. 68 pts were enrolled until August 2025. 40 received anti-BCMA CAR-T, 13 anti-BCMA BsAbs and 15 anti-GPRC5D BsAbs. Median number of prior lines of therapy was 4; 56 pts (82%) were triple-class refractory, 24 (35%) were penta-refractory. After a median follow-up of 17 mos, median progression-free survival (mPFS) was 20 mos and median overall survival (OS) was not reached (85% alive at 24 mos). At baseline, all pts underwent PET and 35 pts underwent WB-DW-MRI. Baseline presence of paraskelatal disease (in 27 pts = 40%), extramedullary disease (in 10 pts = 15%) and >10 focal lesions by PET (in 20 pts = 29%) or WB-DW-MRI (in 13 pts = 37%) prior to TCRT were not associated with PFS (p>0.05). Among 51 pts undergoing PET after 3 mos, 28 (55%) achieved complete metabolic response (CMR), with a significant improvement of mPFS as compared to other response categories (20 vs 10 mos, p=0.029). Among 31 pts undergoing WB-DW-MRI after 3 mos, 18 (58%) achieved RAC1, with a significant improvement of mPFS as compared to other RACs (20 vs 10 mos, p=0.036). Among 27 pts repeating both imaging techniques after 3 mos, concordance was moderate in defining presence (CMR/metabolic partial response and RAC1-2) versus absence (metabolic stable/progressive disease and RAC3-5) of response (k=0.526) and fair in assessing imaging MRD (CMR and RAC1 vs other metabolic responses and RAC2-5; k=0.257). 16 pts (59%) achieved both CMR and RAC1, with a significant improvement of mPFS as compared to pts achieving CMR or RAC1 and to pts achieving neither (p=0.048). All 12 pts with evaluable and available NGS MRD data achieved MRD negativity, thus preventing correlation analyses with outcome.

Conclusions. The present study supports standardized assessment of imaging MRD by IMPeTUs and MY-RADS criteria in the setting of RRMM pts receiving TCRT. 3 mos after CAR-T infusion or BsAb initiation is a significant early time-point for assessment of imaging MRD, since a positive PET/CT or WB-DW-MRI is associated with shorter PFS predicting unfavorable outcome. Updated data with larger number of enrolled pts and extended follow-up will be presented at the meeting.