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EFFICACY AND SAFETY ANALYSIS OF DARATUMUMAB-INTEGRATED QUADRUPLE THERAPY VS TRIPLE THERAPY FOR NEWLY DIAGNOSED, TRANSPLANT-ELIGIBLE PATIENTS WITH MULTIPLE MYELOMA: A SYSTEMATIC REVIEW AND META-ANALYSIS

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OBJECTIVE

Define the optimal therapy for patients with newly diagnosed multiple myeloma (NDMM) eligible for transplant by comparing quadruple therapy (QT) with the addition of daratumumab versus triple therapy (TT).

Analyze the efficacy and safety of adding daratumumab to TT for newly diagnosed multiple myeloma transplant-eligible cases compared with TT alone.

METHODS

Following PRISMA guidelines, we searched Medline, Cochrane, Web of Science, and Embase databases for studies comparing daratumumab combined with TT versus TT alone for patients with NDMM.

The endpoints included overall response rate (ORR), stringent complete response (sCR) and complete response (CR) rates, risk of disease progression or death (DPD), progression-free survival (PFS), minimal residual disease negativity rate (MRDNR), and adverse events rate.

Hazard ratios (HR) and risk ratios (RR) were pooled with 95% confidence intervals using a random-effects model. Heterogeneity was assessed using I^2 statistics and leave-one-out analysis.

RESULTS

A total of 3268 records were assessed, and 4 studies involving 2081 patients (1045 received QT) were included in the final analysis. Three studies were randomized clinical trials (RCTs), and one was a retrospective cohort study.

Three studies with 2,001 patients reported the hazard ratio for disease progression or death. The pooled analysis found a decrease in 56% of disease progression or death in the QT group (HR = 0.44; 95%CI 0.35 - 0.56; I2=0%; P<0.01; Figure 1).

RESULTS

The implementation of the QT for NDMM transplant-elegible patients was also associated with significant higher rates of CR or better (RR= 1.34 95%CI 1.21 - 1.47; I2=35%; P<0.01; Figure 2) and a trend towards higher OR rates (RR= 1.02; 95%CI 1.00 - 1.04; I2=0%; P=0.03; Figure 3).

Regarding the MRD negativity assessment, our pooled analysis revealed that patients treated with the daratumumab based QT are more likely to achieve a minimal residual disease-negativity (RR= 1.57; 95%CI 1.39 - 1.78; I2=40%; P<0.01; Figure 4).

Furthermore, the 30 month-PFS indicates a significant improvement in patients treated with QT compared to the control group (RR 1.11; 95% CI 1.05–1.18; p < 0.01; I^2 = 0%; Figure 5).

The experimental group exhibited a significantly higher incidence of both hematological and non-hematological adverse effects.

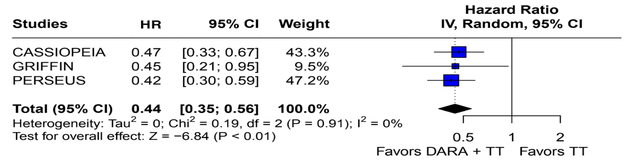


Figure 1 - Hazard Ratio for disease progression or death

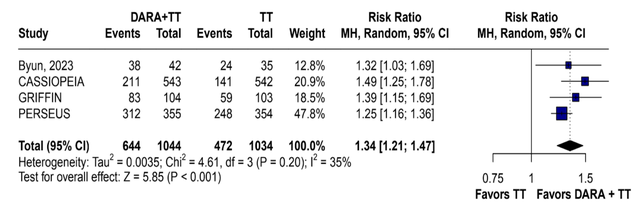


Figure 2 - Risk Ratio for complete response or better

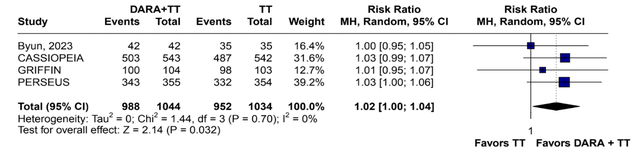


Figure 3 - Risk Ratio for overall response

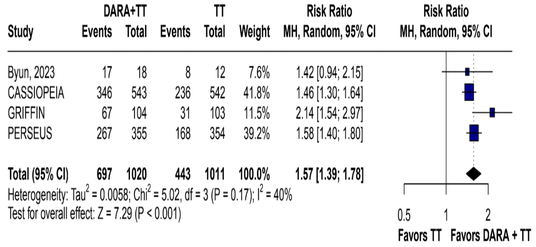


Figure 4 – Risk Ratio for the MRD negativity assessment

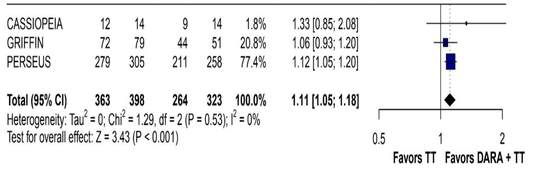


Figure 5 – Risk Ratio for the 30 month-PFS

CONCLUSIONS

The findings suggest that incorporating daratumumab into standard triple therapy for treating patients with NDMM who are transplant eligible is associated with higher response rates and reduced disease progression or mortality.

However, it is important to note that this regimen also comes with a higher incidence of adverse events.

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