NEWSLETTER

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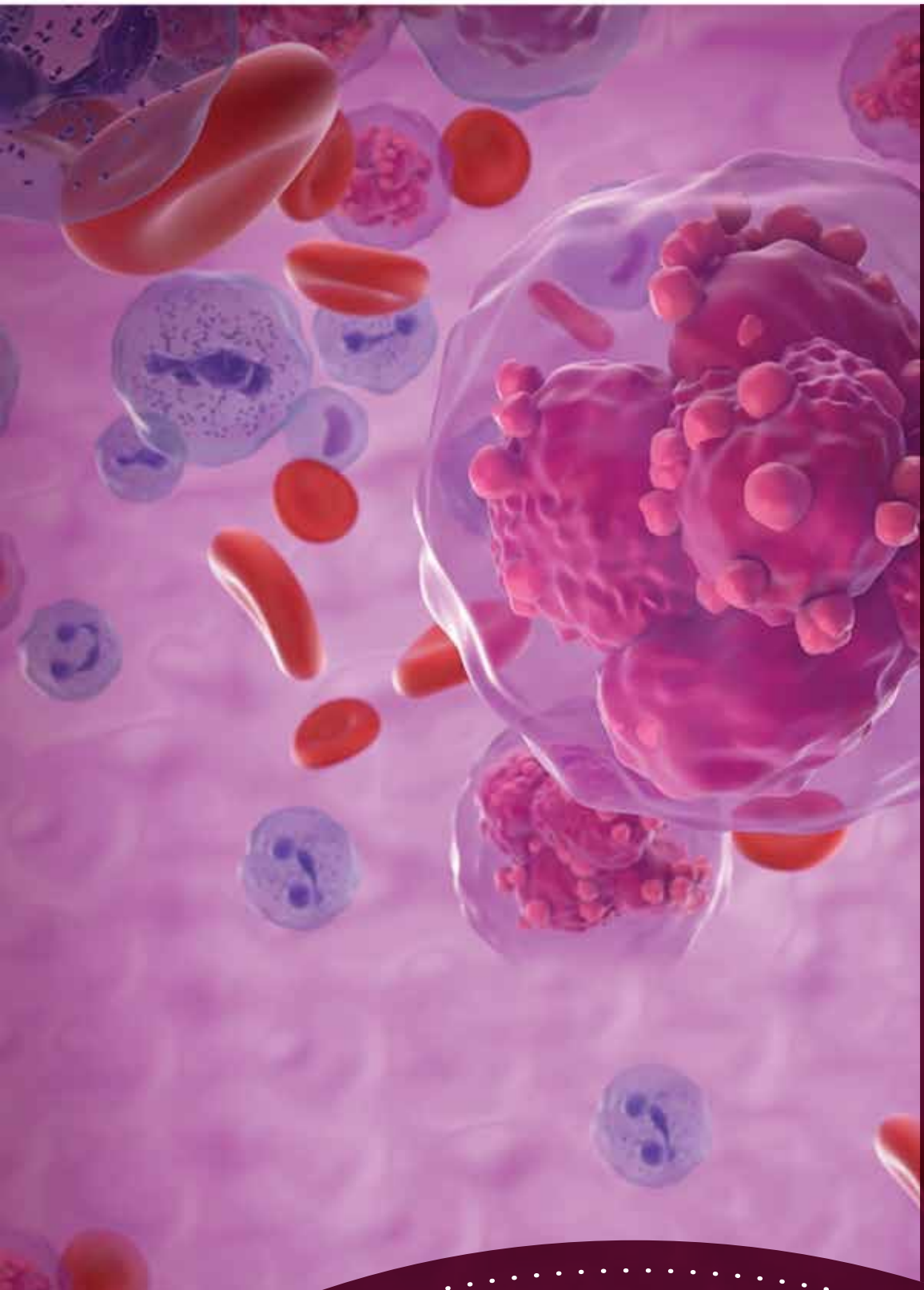

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Preface

*This newsletter was born out of sincere efforts of the **IMAGE Groupe** to serve a quarterly academic feast to all myeloma connoisseurs and novitiates with a platter of translational research work update, neuron tickling trivia, cherishable accomplishments of our members and highlights of past and upcoming academic events in the realm of myeloma. A blitzkrieg of brainstorming zoom sessions followed by pounding and grinding of intellect and prose by five geeks over weeks led to fruition of the first edition on new year eve and a greater hard work to bring forth this snippet on myeloma activities across country as second edition.*

- From Editorial Team

This bulletin will be a ready reckoner for those grappling to keep up with the progress on myeloma. As it summarizes journal clubs that paved the way for the holy grail of truth based on evidence, the eagle eye gives the synopsis of the critical thinking prowess shown by the myeloma prodigies. The rest of the sections gives us a glance at what is happening around us. The team has done a spectacular job in putting this together. Of course, not to mention the turbocharger, Dr. Uday.

- Newsletter Committee

"Inshorts-Through expert's lens" Journal Club

Dr. Sumeet Mirgh

Associate Professor, Adult Hematolymphoid & BMT, Tata Memorial Centre, ACTREC, Mumbai

Bomsztyk J, Ravichandran S, Giles HV, et al. Complete responses in AL amyloidosis are unequal: the impact of free light chain mass spectrometry in ALamyloidosis. Blood.2024;143(13):1259-1268. doi:10.1182/blood.2023022399

Summary:

Traditional sFLC assays measure all "free" light-chains i.e., both monoclonal+polyclonal. On the other hand, commercial mass-spectrometry assays (Mass-Fix/Exent), measure all "clonal" light-chains which would cover both intact+free light-chains. The FLC-MS (free-light chain mass-spectrometry by MALDI-TOF) assay described here covers both "monoclonal" and "free" light-chains, which are the epicentre of pathology in AL Amyloidosis. This was a retrospective analysis done in AL-amyloidosis patients who had serum samples stored at baseline, 6 and 12 months after diagnosis. A total of 487 patients were included; 290(59%) and 349(71.5%) had cardiac and renal involvement, respectively.

There was 100% concordance between the light-chain (LC) fibril type and LC-isotype identified by FLC-MS. At 6 and 12 months, 81(16.6%) and 101(20.7%) were FLC-MS negative. In patients who achieved a conventional hematologic CR, proportion of FLC-MS negative patients increased at 6 and 12 months to 45(27.7%) and 64(39%), respectively. At 12 months, median OS for CR+FLC-MS negative was not-reached vs 108 months in CR+FLC-MS positive (P =0.024). At 12 months, 70% of patients with FLC-MS negativity (vs 50% FLC-MS positive) achieved a cardiac response (P =0.015). In a multivariate analysis, FLC-MS negativity at 12 months was an independent predictor of better outcomes. FLC-MS assessment promises to be a new standard for response assessment in AL amyloidosis.

Commentary:

All patients were treated with a Bortezomib-based chemotherapy regimen. Whether FLC-MS would be prognostic in the era of daratumumab-based quadruplets remains to be proven. This was a landmark analysis, as only patients with baseline, and two follow-up samples at 6 months and 12months were included. This meant that patients with early mortality were ruled out, and questions the role of FLC-MS as a prognostic marker in early time-points. Difference in outcome was more apparent in those who were in ISA labelled CR, but did not achieve ANDROMEDA-labelled CR. This could be due to more stringent criteria of ANDROMEDA-labelled CR. While 40% CR patients become FLC-MS negative at 12 months, it drops down to less than 20% in patients with VGPR. This could be because FLC-MS does not detect intact M-protein, which even at a low-level may affect survival in AL amyloidosis. Lastly, it was not compared with intact-LC assays (Mass-Fix/Exent) or bone-marrow MRD.

"Inshorts- Through expert's lens" Journal Club

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Costa LJ, Chhabra S, Medvedova E, Dholaria BR, Schmidt TM, Godby KN, Silbermann R, Dhakal B, Bal S, Giri S, D'Souza A, Hall AC, Hardwick P, Omel J, Cornell RF, Hari P, Callander NS. Minimal residual disease response-adapted therapy in newly diagnosed multiple myeloma (MASTER): final report of the multicentre, single-arm, phase 2 trial. Lancet Haematol. 2023 Nov;10(11):e890-e901. doi: 10.1016/S2352-3026(23)00236-3. Epub 2023 Sep 27. PMID: 37776872; PMCID: PMC10836587.

Summary:

The MASTER trial marks a significant advancement in the treatment of newly diagnosed multiple myeloma (NDMM) by using a response-adaptive approach guided by minimal residual disease (MRD) status. This innovative design tailors treatment based on MRD negativity, allowing de-escalation for patients with sustained responses. The combination of daratumumab, carfilzomib, lenalidomide, and dexamethasone (Dara-KRd) with autologous stem cell transplantation (ASCT) shows high efficacy, reinforcing MRD as a key biomarker for risk stratification.

However, limitations include short follow-up, which restricts the assessment of long-term survival outcomes, and less favorable results in high-risk subgroups, indicating that MRD negativity may not fully mitigate poor prognoses. The aggressive treatment regimen also raises concerns about generalizability to older or frail patients. Additionally, standardizing MRD testing remains essential for broader adoption.

Opportunities for improvement involve longer follow-up to confirm durable outcomes, incorporating novel therapies for high-risk patients, and adapting strategies for less intensive regimens. Cost and accessibility challenges must also be addressed.

Overall, the MASTER trial lays the groundwork for MRD-driven precision oncology in NDMM but highlights the need for further research to refine strategies and expand applicability across diverse patient populations.

Commentary:

The MASTER trial introduces an innovative, MRD-guided treatment approach for newly diagnosed multiple myeloma (NDMM), allowing for personalized therapy de-escalation based on minimal residual disease (MRD) status. This trial demonstrates the efficacy of the Dara-KRd regimen (daratumumab, carfilzomib, lenalidomide, dexamethasone) with autologous stem cell transplantation, yielding high MRD negativity rates. The study highlights MRD as a valuable biomarker for risk stratification and treatment planning.

However, limitations include short follow-up, making long-term outcome assessments difficult, and less favorable results in high-risk cytogenetic groups. The regimen's intensity may restrict its use in older or comorbid patients. Additionally, MRD testing requires further standardization.

Future improvements involve extended follow-up, alternative therapies for high-risk patients, and evaluating MRD-guided strategies in broader populations. Addressing cost and accessibility will be crucial. Overall, the trial advances precision oncology but necessitates further research to optimize outcomes for all NDMM patients.

"Inshorts- Through expert's lens" Journal Club

Sonneveld P, Dimopoulos MA, Boccadoro M, et al. Daratumumab, Bortezomib, Lenalidomide, and Dexamethasone for Multiple Myeloma. N Engl J Med. 2024;390(4):301-313. doi:10.1056/NEJMoa2312054

Dr. Sumeet Mirgh

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Summary:

VRd induction followed by transplant, VRd consolidation, and lenalidomide maintenance is considered a standard of care for transplant-eligible patients with NDMM. This study evaluated whether addition of subcutaneous daratumumab to VRd backbone in induction and consolidation, and to lenalidomide maintenance improved PFS for NDMM patients who were transplant-eligible.

790 patients were randomly assigned to either of the two groups, and the primary end-point was PFS, while secondary end-points included CR and MRD-negativity rates. At a median follow-up of 47.5 months, the risk of disease progression or death in the D-VRd group was lower than the risk in the VRd group. The estimated 4-year PFS was 84.3% in the D-VRd group and 67.7% in the VRd group. The percentage of patients with a CR or better was higher in the D-VRd group than in the VRd group (87.9% vs. 70.1%, P<0.001), as was the percentage of patients with MRD-negative status (75.2% vs. 47.5%, P<0.001). Importantly, grade 3-4 adverse events occurred in most patients in both groups; the most common being neutropenia (62.1% with D-VRd and 51.0% with VRd) and thrombocytopenia (29.1% and 17.3%, respectively). Similar to GRIFFIN, this study re-iterates that addition of daratumumab to VRd backbone prolongs survival in NDMM.

Commentary:

Similar to many trials in MM, this trial confirms superiority of a 4-drug over a 3-drug regimen. It would be interesting to see, if another four-drug regimen, with a different PI/IMiD, would challenge Dara-VRd. Twice the number of patients in daratumumab arm needed plerixafor, with a median CD34 yield which was 1 million lower. However, there was no difference in time-to-engraftment in both the arms. Importantly, serious adverse events (AEs) were higher in quadruplet arm, with a 11% incidence of pneumonia, relevant from Indian perspective. Absence of an OS benefit for whole cohort, and PFS benefit for elderly (>65 years) coupled with increased AEs, questions the role of quadruplet for all NDMM patients. Additionally, the role of daratumumab in maintenance is still questionable, as all patients in daratumumab arm, received it in maintenance too. However, the ability to stop daratumumab after two-years of maintenance in MRD-negative patients adds credence to the value of MRD for discontinuation/de-escalation.

"Inshorts- Through expert's lens" Journal Club

Touzeau C, Perrot A, Hulin C, Manier S, Macro M, Chretien ML, Karlin L, Escoffre M, Jacquet C, Tiab M, Leleu X, Avet-Loiseau H, Jobert A, Planche L, Corre J, Moreau P. Daratumumab, carfilzomib, lenalidomide, and dexamethasone with tandem transplant for high-risk newly diagnosed myeloma. Blood. 2024 May 16;143(20):2029-2036. doi: 10.1182/blood.2023023597. PMID: 38394666.

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Summary:

The study investigates the feasibility and efficacy of a quadruplet regimen combining daratumumab, carfilzomib, lenalidomide, and dexamethasone (D-KRd), followed by tandem autologous stem cell transplantation (ASCT), in high-risk newly diagnosed multiple myeloma (NDMM). Conducted across 11 centers, this phase 2 study enrolled 50 transplant-eligible patients under 65 years, all exhibiting high-risk cytogenetic abnormalities such as del(17p), t(4;14), and t(14;16). The trial's primary endpoint was feasibility, defined by 70% of patients completing the second ASCT. Results demonstrated success, with 72% completing the procedure. The treatment achieved remarkable efficacy: 94% of patients attained minimal residual disease (MRD) negativity at a sensitivity of 10^-6 before maintenance. The overall response rate reached 100% among those completing the second transplant, with 81% achieving complete response.

Adverse events primarily included neutropenia, thrombocytopenia, and infections, though they were manageable. Notably, insufficient stem cell collection was a significant challenge, necessitating an amendment to collect cells earlier during induction. With a median follow-up of 33 months, progression-free survival (PFS) at 30 months was 80%, and overall survival was 91%. This intensive approach shows promise for addressing high-risk NDMM, underscoring the need for personalized strategies to improve outcomes.

Commentary:

He study on the quadruplet regimen of daratumumab, carfilzomib, lenalidomide, and dexamethasone (D-KRd) with tandem transplants for high-risk newly diagnosed multiple myeloma (HR NDMM) demonstrates impressive efficacy but raises critical concerns. The regimen achieved a high rate of minimal residual disease (MRD) negativity (94%) and significant progression-free survival (80% at 30 months). However, the feasibility of completing tandem transplants (72% success) highlights logistical and biological challenges, particularly insufficient stem cell collection post-cycle six. This necessitated a protocol amendment, reflecting a potential limitation in standardizing treatment timelines.

The high toxicity profile, including hematologic and infectious adverse events, and two fatalities underline the intensity of this approach. While outcomes compare favorably with standard regimens, the small sample size and lack of a control arm limit generalizability and comparative effectiveness assessment. Although promising, the regimen's intensity and resource requirements emphasize the need for refinement and further studies to validate its role in clinical practice.

"Inshorts- Through expert's lens" Journal Club

Dr. Vijay Moorthy

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Yadav U, Kumar SK, Baughn LB, Dispenzieri A, Greipp P, Ketterling R, Jevremovic D, Buadi FK, Dingli D, Lacy MQ, Fonseca R, Bergsagel PL, Ailawadhi S, Roy V, Parrondo R, Sher T, Hayman SR, Kapoor P, Leung N, Cook J, Binder M, Muchtar E, Warsame R, Kourelis TV, Go RS, Lin Y, Seth A, Lester SC, Breen WG, Kyle RA, Gertz MA, Rajkumar SV, Gonsalves WI. Impact of cytogenetic abnormalities on the risk of disease progression in solitary bone plasmacytomas. Blood. 2023 Nov 30;142(22):1871-1878. doi: 10.1182/blood.2023021187. PMID: 37494698; PMCID: PMC10731916.

Summary:

Solitary plasmacytoma defined by single mass of clonal plasma cells with or without Minimal Marrow involvement (<10%) without features of anemia, hypercalcemia/ renal insufficiency attributable to myeloma. It is unknown whether a shorter time to progression to Myeloma is linked to the presence of high-risk cytogenetic abnormalities by FISH in the clonal plasma cells.The study was carried out at the Mayo Clinic from January 2012 to July 2022. The presence of del(17p), t(14;16), t(4;14), or +1q (gain or amplification) by FISH in clonal plasma cells was defined as HR. A total of 114 patients were included in this cohort, and baseline FISH was available for 55 patients, of which 22 were classified as HR (40%). The median TTP to MM for patients with SBP and HR FISH was 8 months compared with 42 months in patients with SBP without HR FISH (P<0.001). In a multivariate analysis, only HR FISH was a significant predictor for shorter TTP to MM, independent of minimal marrow involvement and an abnormal serum free light chain ratio at diagnosis. Deletion (17p) and gain 1q abnormalities were the most common FISH abnormalities responsible for the short TTP to MM.

Commentary:

High RISK FISH in Multiple myeloma, Smoldering myeloma is well studied, not in Solitary bone plasmacytoma. This is the first study to assess the clinical value of FISH in SBP. This study has clearly shown HR FISH significantly increases the risk of progression to MM. Though the study has potential to change practice, it is a single center study, multi center studies are required to strengthen this evidence. Additional limitations include the study's lack of correlation with CR status after local therapy and m component levels, which are crucial markers of myeloma development from SBP. Though the study supports the performance of FISH assessments on the diagnostic SBP samples in those patients whose BMA do not have sufficient numbers of clonal plasma cells to perform the same FISH assessment. Validating FISH study in SBP samples at different center will be challenging. Furthermore, prospective data and clinical trials are needed to address if patients with SBP who have HR FISH could benefit from incorporating systemic adjuvant therapy after definitive radiation therapy to reduce their high risk of rapid progression to MM

"Inshorts- Through expert's lens" Journal Club

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Muchtar E, DispenzieriA, Wisniowski B, Palladini G, Milani P, Merlini G, Schönland S, Veelken K, Hegenbart U, Geyer SM, Kumar SK, Kastritis E, Dimopoulos MA, Liedtke M, Witteles R, Sanchorawala V, Szalat R, Landau H, Petrlik E, Lentzsch S, Coltoff A, Bladé J, Cibeira MT, Cohen O, Foard D, Wechalekar A, Gertz MA. Graded Cardiac Response Criteria for Patients With Systemic Light Chain Amyloidosis. J Clin Oncol. 2023 Mar 1;41(7):1393-1403. doi: 10.1200/JCO.22.00643. Epub 2022 Oct 10. PMID: 36215675; PMCID: PMC10489422.

Summary:

This was a retrospective multicenteric study which included 651 patients with light chain amyloidosis who had a hematologic response and were evaluable for cardiac response from January 2010 to December 2015. The aim was to evalutae a new graded cardiac response criteria/system (table 1) in light chain amyloidosis. Cardiac response was evaluable using NT-proBNP in 75.9%, BNP in 109 patients 16.7%, and both in 7.4%. Hematologic complete response was achieved in 38.2%, very good partial response in 38.9% and partial response in 22.9% of patients. The median follow-up was 73.5 months. Patients in cardiac stage II were more likely to achieve CarCR than patients in cardiac stage IIIA and IIIB. The median time to best cardiac response was 12 months and responses deepened with time. At 24 months, 46.9% achieved a CarCR or CarVGPR, and a significant survival advantage seen (5-year OS 93%, 79%, 65%, and 33% for CarCR, CarVGPR, CarPR, and CarNR). Two-level cardiac response measure was significantly associated with survival in multivariable models but time-dependent ROC curves and AUCs showed that four-level cardiac response criteria had greater prognostic significance especially at 24-month – the graded four-level cardiac response model had significantly widened superiority over the two-level cardiac response model and the dynamic.

Commentary:

Critical Appraisal:

This study established and validated a new cardiac response assessment tool. Application of these criteria into clinical trial end point design and routine clinical practice should be encouraged. However, this is a retrospective study with a possible selection bias. The missing information on cardiac response for fixed time point analysis was imputed for 20%-25% of patients based on adjacent measurements. There was a survivorship bias when assessing best cardiac response. Also, this is a natriuretic peptides-based response criteria which are dependent on renal function for clearance. Therefore, other more objective methods for cardiac response assessment should be explored. Radiological assessment with echocardiographic strain measurement, cardiac MRI, and functional assessment such as the 6- minute walk test may be more informative. Lastly, in current era with the availability of the novel drugs like Daratumumab and increasing use of these more targeted and organ function modifying agents, does this study hold relevant needs to be assessed.

"Inshorts-Through expert's lens" Journal Club

Zanwar S, Le-Rademacher J, Durot E, D'Sa S, Abeykoon JP, Mondello P, Kumar S, Sarosiek S, Paludo J, Chhabra S, Cook JM, Parrondo R, Dispenzieri A, Gonsalves WI, Muchtar E, Ailawadhi S, Kyle RA, Rajkumar SV, Delmer A, Fonseca R, Gertz MA, Treon SP, Ansell SM, Castillo JJ, Kapoor P. Simplified Risk Stratification Model for Patients With Waldenström Macroglobulinemia. J Clin Oncol. 2024 Jul 20;42(21):2527-2536. doi: 10.1200/JCO.23.02066. Epub 2024 May 24. PMID: 38788183; PMCID: PMC11268554.

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Summary:

Only symptomatic WM patients require treatment. IPSS-WM risk stratified WM was validated on patients diagnosed and treated prior to 2002and it did not assess the issue of nonWM-related deaths. Revised (r) IPSS-WM did not examine the impact of MYD88 L265P mutation and it could be only partially replicated in the validation cohort. Hence, a new risk stratification model has been proposed by application of rIPSS-WM model in patients evaluated with active WM between 1996 to 2017 at Mayo Clinic (Derivation Cohort). Univariate and Multivariate Cox proportional analysis was done to identify the predictors of OS. The data was validated in a cohort from 5 institutes from US and UK. Age, Beta2 microglobulin, LDH and Albumin remained as significant parameters in both univariate and multivariate analysis except Beta2 microglobulin in multivariate analysis. MYD88 mutation status did not affect OS significantly. Prognostic Model Score Calculation was done based on these parameters. Based on the composite score, 4 risk groups were made based on 3 parameters. The distinction of OS was significantly different in 4 groups both in derivation and validation cohort. The OS discrimination of intermediate risk group was better with the MSS-WM model. Non-WM related deaths were also better delineated with MSS-WM model. Being a retrospective study, only few patients on BTKi inclusion and lack of CXCR4 incorporation into the model are the few limitations. MSS-WM is a simple, externally validated risk-stratification model. With limited variables, it has better discriminative ability in OS assessment among WM patients.

Commentary:

Using limited parameters, MSS-WM model provides a comprehensive risk model for WM with better discrimination in survival of intermediate risk groups of IPSS-WM. Unlike previous risk scores like IPSS and rIPSS-WM, MSS-WM model has taken into account the MYD88 mutation status. However, the interesting point to be noted is that the MYD88 mutation status did not affect the overall survival status. This could be due to the reason that only a few patients received BTKi as primary therapy and there was only a shorter follow up of those patients. Chromosomal aberrations like del 6q was not incorporated into the model.

"Inshorts- Through expert's lens" Journal Club

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Mohan M, Monge J, Shah N, et al. Teclistamab in relapsed refractory multiple myeloma: multi-institutional real-world study. Blood Cancer J. 2024;14(1):35. Published 2024 Mar 5. doi:10.1038/s41408-024-01003-z

Summary:

The endeavour of this study was to provide data that supports better understanding of the teclistimab by assessing its safety and efficacy in real world population with multiple co-morbidities and or the ones with prior BCMA/CAR T exposure. The study was conducted across 5 US medical centres and R/R MM patients who received at least dose of teclistimab were included. Baseline patient characteristics were collected. Patients received step up doses of teclistimab as per individual institutional guidelines. Side effects like CRS/ICANS and infections were treated as per institutional guidelines. Supportive care like intravenous immunoglobulins (Ivlg) were serially infused.

At a median follow up of 3.5 months, ORR was 62%, VGPR or more was 51% and CR was 20%. The median time to best response was 1.67 months. Median PFS and OS were not reached due to the short duration of the study. At 6 months, PFS was 52% and OS 80%. No disease or prior treatment related variables were found to be predictive of response. ICANS/CRS incidences significantly increased. The only predictors of infections were found to be prior infection with previous teclistimab use and immunoglobulin levels.

The study concluded that the drug maintained its efficacy in heavily pretreated/high risk patients. Rates of VGPR or more were comparable to the MajesTEC-1 and MagnestisMM-3. There was no impact on response rate in patients with prior anti-BCMA exposure. The increased incidence of ICANS/CRS was attributed to the higher disease burden. Serial Ivlg prophylaxis significantly lowered the incidence of infections with relative risk reduced by 70%. Routine prophylaxis for PJP when BCMA bsAbs are used was beneficial.

Commentary:

This study aims to provide critical information in patient management in the real-world setting, outside of a clinical trial. The study included diverse of varied ethnicity wherein African Americans were close to 30% and 2% were Asians/Pacific islanders. Patients with prior exposure to anti-BCMA therapies/ CAR T were also included. Despite its small cohort and short duration, the role of prophylactic Ivlg in preventing serious infections, a deeper rapid response in heavily pretreated patients and the higher incidence of ICANS/CRS in real world population were highlighted. Due to short duration median PFS and OS were not reached. Lack of MRD assessment and no bone marrows being done led to reduced CR rates. Drug stepping up routine, antibiotics choice during treatment of infections and prophylactic intravenous immunoglobulin (Ivlg) dosing needed to be uniform. It has managed to provide critical information thus bridging the knowledge gap between real-world data and clinical trials.

“Inshorts-Through expert's lens” Journal Club

Noemí Puig, Cristina Agulló, Teresa Contreras, María-Teresa Cedena, Joaquín Martínez-López, Albert Oriol, María-Jesús Blanchard, Rafael Ríos, María-Belén Íñigo, Anna Sureda, Sunil Lakhwani, Javier de la Rubia, Verónica González-Calle, Valentín Cabañas, Luis Palomera, José-María Moraleda, Joan Bargay, Sergio Castro, Laura Rosiñol, Joan Bladé, Jesús F. San-Miguel, Juan-José Lahuerta, Bruno Paiva, María-Victoria Mateos; Measurable residual disease by mass spectrometry and next-generation flow to assess treatment response in myeloma. Blood 2024; 144 (23): 2432–2438.
doi: https://doi.org/10.1182/blood.2024024995

Dr. Akshaya Mandloi

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Summary:

Bone marrow MRD assessment, while crucial for multiple myeloma (MM) prognosis, has notable limitations, including invasiveness and its potential to miss spatial heterogeneity/extramedullary disease. Quantitative immunoprecipitation mass spectrometry (QIP-MS), an emerging non-invasive technique, can detect M-protein in serum, even in patients with complete response. Puig et al. evaluated the complementarity between peripheral blood (PB) MRD detection by QIP-MS (EXENT® System) and bone marrow (BM) MRD assessment using next-generation flow cytometry (NGF) in newly diagnosed transplant eligible Multiple Myeloma patients from the GEM2012MENOS65 and GEM2014MAIN trials. QIP-MS outperformed conventional serum immunofixation electrophoresis (sIFE), identifying monoclonal proteins in up to 15% of sIFE-negative patients. NGF detected MRD more frequently, with concordance between QIP-MS and NGF peaking at 85% during maintenance therapy. Despite some discordances, both methods effectively stratified patients into distinct groups based on progression-free survival (PFS). QIP-MS positivity, particularly when converted from negative to positive, strongly predicted imminent clinical progression. While NGF remains the gold standard for BM MRD assessment, QIP-MS presents a promising alternative. The study suggests that QIP-MS being less invasive could complement NGF, offering a useful tool for patient risk stratification and treatment decisions.

Commentary:

This study provides valuable insights into the potential of QIP-MS as a complementary tool for MRD assessment in MM. Its strengths include the comparison of two established methods, the analysis of longitudinal data, and the assessment of prognostic significance. However, some limitations should be considered. Firstly, the study primarily focused on transplant-eligible patients, limiting its generalizability to all MM patients. Also, the concordance between QIP-MS and NGF varied across time points, suggesting potential limitations in their absolute agreement. Furthermore, questions about the cost effectiveness, global availability and harmonization of these assays highlight crucial considerations for their broader implementation. Future research should investigate the feasability of integrating QIP-MS into routine clinical practice, particularly in resource-limited settings. Additionally, increasing the sensitivity of QIP-MS by at least 1 log and exploring the potential of QIP-MS in assessing extramedullary disease and focal lesions would further enhance its clinical utility.Overall, this study provides a foundation for further research on the role of QIP-MS in the management of MM.

Journal Scan

Article – Nørgaard JN, Abildgaard N, Lysén A, et al. Intensifying treatment in PET-positive multiple myeloma patients after upfront autologous stem cell transplantation. Leukemia. 2023;37(10):2107-2114. doi:10.1038/s41375-023-01998-7

The study aimed to evaluate the impact of post-ASCT, PET on treatment intensification with KRd and its effect on QoL in Myeloma patients. 159 MM post-ASCT patients screened, 53 were PET positive with a Deauville score ≥ 4, and 50 were included in the study. The majority (57%) of patients were MRD positive, with high-risk cytogenetics and higher stage correlating with MRD positivity. These patients received 4 cycles of KRd. Following treatment, 33% of patients converted to PET negative, 22% were PET and MRD negative, and 38% were MRD negative, although these findings were not statistically significant irrespective of pre ASCT status. Additionally, post VCD induction showed better response with KRd consolidation.

KRd consolidation was well tolerated, with a 100% completion rate. The most common SAEs were infection (36%) and DVT (4%). QoL poorly affected post 3rd cycles.

Overall, the study highlights the importance of PET in detecting residual disease after ASCT and suggests that KRd consolidation may benefit. Though small study population, Phase 2, non-randomised study requires further work for stronger evidence making.

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AIIMS, Rishikesh

Journal Scan

Pomalidomide, bortezomib, and dexamethasone for newly diagnosed multiple myeloma patients with renal impairment

Author & Affiliation

Dr. Deep Ajay Gala

SGPGIMS, Lucknow

Renal impairment(RI) is a frequent complication of Multiple Myeloma(MM) and is the second leading cause of death in MM(1). Current study is a prospective, multicentre trial where in 61 patients were enrolled. With PVD, an overall renal response of 75.7% was observed at 3 months which further improved to 78.7%. Out of 12 patients who required dialysis, 8(66.7%) became dialysis independent at a median of 26 days. Early rapid reduction of FLC (>82% at day 22) was the only factor which was significantly associated with 3-month renal-ORR in multi variate analysis. The sample size of cohort was adequate for such an analysis. 3 month hematological ORR (>Partial response) was 86.7%, however on univariate analysis, attainment of VGPR and above was not associated with renal recovery. In Indian context, a study reported by R Sharma et al conducted at PGI Chandigarh demonstrated similar overall renal response rates (73.6%) with therapies containing various combinations of bortezomib and dexamethasone with cyclophosphamide, thalidomide or lenalidomide but without pomalidomide(2). However dialysis independency rate(55%) and hematological ORR(67%) were lower compared to the current study(2). In the current study, the survival was significantly better for those who achieved a renal response.The Kaplan-Meier survival curve shows early separation and then becomes parallel suggesting likely early mortality associated with those who do not achieve a renal response, however a longer follow up is required. The study has its own limitations being a phase 2 trial with a relatively small sample size. Also the study only includes patients with Cast nephropathy while renal injury in MM also has several other etiologic factors but were excluded from this study. Also the time point at which the 4 deaths occurred has not been mentioned. ROC analysis could have been performed to determine eGFR value predicting the renal response.

Given all the strengths and limitations, the study remains relevant in Indian perspective, given the high burden of the disease in our country and availability of generic pomalidomide which could reduce the financial burden. Future direction- RCT comparing VPD with other bortezomib based regimen for MM with RI could be desirable at a consortium level.

References

1. Dimopoulos MA, Sonneveld P, Leung N, Merlini G, Ludwig H, Kastritis E, et al. International Myeloma Working Group Recommendations for the Diagnosis and Management of Myeloma-Related Renal Impairment. J Clin Oncol. 2016 May;34(13):1544-57.
2. Sharma R, Jain A, Jandial A, Lad D, Khadwal A, Prakash G, et al. Lack of Renal Recovery Predicts Poor Survival in Patients of Multiple Myeloma With Renal Impairment. Clin Lymphoma Myeloma Leuk. 2022 Aug;22(8):626-34.

Journal Scan

Article Title: Real-world data on incidence, clinical characteristics and outcome of patients with macrofocal multiple myeloma (MFMM) in the era of novel therapies: A study of the Greco-Israeli collaborative myeloma working group.

Authors: Katodritou E, Kastritis E, Gatt M, Cohen YC, Avivi I, Pouli A, Lalayianni C, Lavi N, Delimpasis S, Kyrtsonis MC, Michael M, Suriu C, Miri Z, Tzafarti K, Vadikoliou C, Maltezas D, Zikos P, Ganzel C, Vaxman Y, Aviv A, Christoforidou A, Gavriatopoulou M, Shaulov A, Verrou E, Papanota AM, Fakinos G, Gkioka AI, Palaska V, Triantafyllou T, Konstantinidou P, Anagnostopoulos A, Terpos E, Dimopoulos MA.

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Author & Affiliation

Lt Col Shikha Yadav

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The study aimed to investigate the incidence, characteristics, and outcome of patients with Macrofocal multiple myeloma (MFMM) treated with novel therapies. However, the research statement does not reflect a comparison with a control group with symptomatic MM, who did not meet the criteria of MFMM and were diagnosed and managed during the same period with similar therapies.

The exclusion criteria have not been defined & questionnaire filled by physicians for data collection is not found attached. Also, it hasn't been clearly mentioned whether MFMM was the initial diagnosis or developed after first-line therapy or as an overt relapse. The inclusion criteria for MFMM have been changed to <20% BMPCs as compared to <10% by definition. Statistically significant results obtained by this study include MFMM (i) not limited to young but also includes elderly, (ii) having less adverse prognostic features compared with typical MM, and (iii) achieving prolonged survival when treated with proteasome inhibitors. These results have not been compared to those of similar studies hence their application to patient population requires further evidence.

Journal Scan

SGLT2 Inhibitor Therapy in Patients with Transthyretin Amyloid Cardiomyopathy
(Originally by Aldostefano Porcari et al)

A CRITICAL ANALYSIS - "HEART HEISTS AND SUGAR SIEGES"

In a comprehensive study by Porcari et al., researchers delved into the potential benefits of SGLT2 inhibitors for patients with transthyretin cardiac amyloidosis (ATTR-CM). By pooling data from 14 international centers, they found that these inhibitors were generally well-tolerated and appeared to lower the risks of both all-cause mortality and heart failure hospitalizations. However, despite these encouraging results, several critical methodological concerns arise that warrant cautious interpretation.

Firstly, use of propensity score matching—though necessary to balance baseline differences—might have overstated the treatment effect. A striking 43% reduction in mortality is reported, which exceeds what has been observed in previous heart failure trials. This raises the possibility of overestimation. Secondly, an average 23-month delay between ATTR-CM diagnosis and treatment initiation may have introduced immortal time bias, skewing the survival outcomes in favor of the treatment group.

Moreover, the reasons for prescribing SGLT2i weren't clearly defined, introducing potential selection bias. Patients receiving these medications might have been healthier overall, making them more likely to experience better outcomes.

Ultimately, without randomized controlled trials, causality remains uncertain.

Author & Affiliation

Dr. Vallish Shenoy

Tata Memorial Centre
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Journal Scan

A RANDOMIZED PHASE 3 TRIAL OF ZANUBRUTINIB VS IBRUTINIB IN SYMPTOMATIC WALDENSTROM MACROGLOBULINEMIA: THE ASPEN STUDY
(Originally by Constantine S. Tam et. al, 2020)

A CRITICAL ANALYSIS -

"Zanubrutinib Takes the Crown: Safer, Smarter Choice for Waldenström's"

The ASPEN study is a pivotal phase 3 trial comparing zanubrutinib, a selective BTK inhibitor, with ibrutinib in patients with symptomatic Waldenström macroglobulinemia (WM). Zanubrutinib showed a higher rate of VGPR (28%) compared to ibrutinib (19%), although this difference was not statistically significant (P = 0.09). Both drugs had similar major response rates and 18-month PFS (approximately 85%). Zanubrutinib demonstrated a better safety profile with fewer BTK-associated toxicities, including atrial fibrillation, diarrhea, and hemorrhage, though it was linked to a higher incidence of neutropenia, which did not lead to increased severe infections. The trial's strength lies in its head-to-head comparison, providing direct evidence of zanubrutinib's efficacy and safety. A critical limitation is the relatively short median follow-up of 19.4 months, which may not fully capture long-term efficacy and safety differences. Additionally, the lack of statistical significance for the primary endpoint suggests potential limitations related to study power or sample size. Overall, zanubrutinib offers comparable efficacy with a more favorable toxicity profile, particularly cardiovascular events, making it a promising alternative for WM patients, especially those at cardiovascular risk.

Author & Affiliation

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Journal Scan

Teclistamab in relapsed or refractory AL amyloidosis: a multinational retrospective case series

Author & Affiliation

Dr. Deep Ajay Gala

SGPGIMS, Lucknow

Bortezomib, cyclophosphamide and dexamethasone with or without daratumumab forms the current standard of care for AL amyloidosis. This treatment has high response rates, however a proportion of patients will have relapse/refractory disease. The article for discussion is a letter to editor describing the efficacy of Teclistamab for relapsed/refractory AL amyloidosis. 17 patients of relapsed/refractory AL amyloidosis across 10 European centres were treated with Teclistamab. Step-up dosing was used. Median age was 67 years. Median prior lines of therapy was 4. All patients but one were daratumumab exposed. It is important to note that out of 17 patients, 10(59%) had concomitant symptomatic MM (Median baseline BM plasma cells -21%). High response rates were seen with teclistamab with 15(88%) out of 17 attaining VGPR, 7(41%) out of 17 in CR. Median time to best response was only 28 days. Time to treatment failure could not be assessed due to a short follow-up(Median-3 months). Similar response rates were reported by R Chakraborty et al in a series of 7 patients (6 out of 7 had concomitant MM). In the present study, 9 patients had CRS (all were grade 1), 1 had grade 3 ICANS and 5 had serious bacterial infections (grade3-5).

In conclusion, the current study demonstrates the efficacy of Teclistamab for R/R AL amyloidosis, however, it merits further exploration in patients with low plasma cell burden (i.e excluding the patients with concomitant MM like in the ANDROMEDA trial). High rates of infections with Teclistamab will continue to pose a challenge especially in our setup.

References

1. Chakraborty, R., Bhutani, D., Maurer, M.S. et al. Safety and efficacy of teclistamab in systemic immunoglobulin light chain amyloidosis. Blood Cancer J. 13, 172 (2023). https://doi.org/10.1038/s41408-023-00950-3

2. Kastritis E, Palladini G, et al. ANDROMEDA Trial Investigators. Daratumumab-Based Treatment for Immunoglobulin Light-Chain Amyloidosis. N Engl J Med. 2021 Jul 1;385(1):46-58. doi: 10.1056/NEJMoa2028631. PMID: 34192431.

Journal Scan

The genomic and transcriptomic landscape of primary plasma cell leukemia predicts its unique biological and clinical features.

In the April 2022 issue of Blood, Cazaubiel et al.1 gave insight into the specific genomic, transcriptional, and clinical features of pPCL, specifically the t(11;14) subentity.

In this study, genomic profiling of 90 pPCL patients revealed unique genomic profile and higher incidence of adverse secondary lesions compared with MM. About half of pPCL patients present with t(11;14), displaying a specific transcriptome and better OS.

The study was the largest series of pPCL patients. However, it excludes pPCL patients with 5-20% plasma cells2. DBQ and VRD have shown promising efficacy in pPCL patients3. None of the patients in the study received DBQ and hence the effect of Daratumumab on pPCL genomics could not be evaluated. The study does not report whether transplants can negate the impact of any adverse genomic signature. The study suggests a possible role of Venetoclax (BCL2 inhibitor) in t(11;14) pPCL. However, the study does not give an idea regarding possible therapeutic targets in non t(11;14) subgroup.

Prospective studies are necessary to confirm the role of BCL2 inhibitor in t(11;14) pPCL subentity.

Author & Affiliation

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Abbreviations:

pPCL – primary plasma cell leukemia, MM – multiple myeloma, OS – overall survival, DBQ – Daratumumab based quadruplet, VRD – Bortezomib-Lenalidomide-Dexamethasone, BCL2 – B-ell leukemia/lymphoma 2 protein

References

1. Titouan Cazaubiel, Xavier Leleu, Aurore Perrot, et al. Primary plasma cell leukemias displaying t(11;14) have specific genomic, transcriptional, and clinical features. Blood 2022; 139 (17): 2666–2672.

2. Fernández de Larrea C, Kyle R, Rosiñol L, et al. Primary plasma cell leukemia: consensus definition by the International Myeloma Working Group according to peripheral blood plasma cell percentage. Blood Cancer J. 2021;11(12):192.

3. Katodritou E, Kastritis E, Dalampira D, et al. Improved survival of patients with primary plasma cell leukemia with VRd or daratumumab-based quadruplets: A multicenter study by the Greek myeloma study group. Am J Hematol. 2023; 98(5): 730-738.

MYELOMA QUIZ : Apr 2024 - Dec 2024

Q1. The term “amyloid” was brought into the scientific literature by:

A. German botanist Matthias Schleiden

B. German pathologist Rudolf Virchow

C. German chemist Herman Bennhold

D. German psychiatrist Aloysius (Alois) Alzheimer

Q2. Which of these statements is incorrect wrt to the Joshua et al study assessing the impact of FLC-MS negativity on outcomes of AL Amyloidosis patients ?

A. In the multivariate analysis, FLC-MS negativity at 12 months was an independent predictor of better outcomes.

B. There was 100% concordance between the light chain (LC) fibril type and LC isotype identified by FLC-MS

C. At 12 months, median OS for CR + FLC-MS negative was 108 months

D. At 12 months, 70% of patients with FLC-MS negativity achieved a cardiac response.

Q3. Which of these statements is incorrect wrt to AL Amyloidosis and its association with multiple myeloma ?

A. Around 10 percent of AL patients fulfill diagnostic criteria for myeloma at the time of their diagnosis.

B. 10 to 20 percent of myeloma patients develop clinical evidence of AL, although additional patients have subclinical deposition, around 35-40%.

C. Serial bone marrow examinations show no increase in the proportion of plasma cells over time, reflecting the clonal but non-proliferative nature of plasma cells in AL

D. All are correct statements.

Q4. Which of these options is incorrectly matched with regards to the frequency of cytogenetics findings in AL amyloidosis patients ?

A. t (11,14) : 30 %

B. Del13q14 : 36%

C. Trisomies : 25%

D. Gain 1q mut : < 20%

E. t (14:16), t (4:14) and del 17p : 3%

Q5. In terms of increasing sensitivity; which is the correct sequence of tissue biopsies to detect AL amyloidosis ?

A. Salivary gland < Bone marrow < Rectal < Fat pad < Target organ

B. Rectal < Fat pad < Salivary gland < Bone marrow < Target organ

C. Bone marrow < Fat pad < Rectal < Salivary gland < Target organ

D. Bone marrow < Fat pad < Salivary gland < Rectal < Target organ

QUIZ

MYELOMA QUIZ

April 2024

WINNER

Dr. Deep Gala

Senior Resident,
SGPGI, Lucknow

MYELOMA QUIZ : Apr 2024 - Dec 2024

Q6. Which of the following statements is incorrect regarding the CONPET study ?

PET results were considered positive or negative using the Italian Myeloma Criteria for PETuse (IMPETUS)-criteria

B. PET was considered positive if the Deauville score was 4 or higher (uptake higher than liver)

C. Patients with new lesions or an increase in lesions meeting the IMWG criteria for progressive disease were included

D. One third of patients were PET positive after ASCT and one third of those PET positive became PET negative after 4 cycles of KRd consolidation

Q7. What was the target dose and schedule of Carfilzomib used in the CONPET study?

A. T36 mg/m2 twice weekly

B. 45 mg/m2 twice weekly

C. 56 mg/m2 once weekly

D. 70 mg/m2 once weekly

Q8. Which of the following statements about MASTER trial is incorrect ?

A. Study was designed to include patients with High risk cytogenetic abnormalities - t(4;14), t(14;16), del(17p)

B. Primary end point was achievement of MRD negativity which was assessed by Next generation flow-cytometry and cut off of 10^-5 were considered MRD negative

C. Patients who received upto 1 cycle of VCD were included

D. There was no upper age limit and no restriction in terms of haematological parameters

Q9. Which of the following statements regarding results of MASTER trial are incorrect ?

A. Approximately 70% participants achieved MRD of less than 10^{-5} at two consecutive assessments and 63% achieved sustained MRD negativity

B. After stopping Rx, 2-year cumulative incidence of progression was approximately 50% in patients with +2 HRCAs

C. A landmark analysis beginning at post-induction time point found that the persistence of MRD positivity (≥10^{-5}) impaired PFS and OS

D. Patients who required 8 cycles of Dara-KRd consolidation to reach MRD-SURE, the risk of progression was higher than for participants who reached MRD-SURE after autologous HSCT

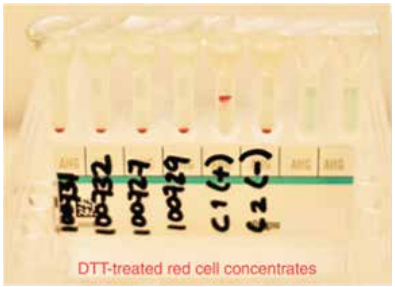
Q10. Pick the most appropriate use of the test shown below for a patient of multiple myeloma on therapy?

A. Solve cross match problem for patients on Daratumumab

B. Blood grouping problem for patients on Daratumumab

C. Solve cross match problem for patients on Elotuzumab

D. Blood grouping problem for patients on Elotuzumab



QUIZ

MYELOMA QUIZ

May 2024

WINNER

Dr. Sanjeev

SGPGI, Lucknow

Q11. Which of the following image symbolises the Greek God “PERSEUS ”?

A.

B.

C.

D.

Q12. Which of these is the incorrect statement wrt to the design of PERSEUS trial ?

A. In patients who completed at least 24 m of maintenance therapy, daratumumab was discontinued if they had a ≥ CR and had sustained MRD negative status for at least 12 months.

B. SC Dara was administered Q 4w in the maintenance phase

C. Once a week dose of dexamethasone 40mg was used during induction and consolidation arm in both groups

D. The dose of lenalidomide was escalated to 15mg/d after 2 cycles during the maintenance phase in both arms at investigator’s discretion

Q13. Which of these statements is incorrect wrt to safety signals from the PERSEUS trial ?

A. The most common grade 3 or 4 adverse events were neutropenia in both arms.

B. The most common serious adverse event was pneumonia in both the arms

C. A significantly increased number of patients in D VRD arm received plerixafor during stem cell mobilisation in comparison to VRd arm but medium time to engraftment was similar.

D. All are correct statements

Q14. Which of these statements is incorrect wrt design of the phase 2 study 2018-04 from the Intergroupe Francophone du Myelome (IFM), evaluating the feasibility and efficacy of D-KRd induction and consolidation plus tandem transplant in HR TE-NDMM ?

A. Presence of at least 1 HR cytogenetic abnormalities among del(17p), t(4;14), t(14;16) or 1 q amp by FISH was mandatory for inclusion

B. The threshold positivity for cytogenetic abnormalities were uniformly 30%

C. Stem cell harvest was planned after cycle 6 of induction for all patients

D. All patients received 2 years of maintenance therapy with lenalidomide and daratumumab post tandem transplant

Q15. In the phase 2 study 2018-04 from IFM, main cause of treatment discontinuation before second transplant was ?

A. Serious adverse events

B. Disease progression

C. Insufficient stem cell collection for tandem transplant

D. Consent withdrawal

QUIZ

MYELOMA QUIZ

June 2024

WINNER

Dr. Deep Gala

Senior Resident,
SGPGI, Lucknow

Q16.

If A is Dr. Bart Barlogie who is B ? Both pioneered the tandem transplant curative concept in myeloma.

A. 

B. 

A : Dr. Seema Singhal

B : Dr. Jennifer Gurley

C : Dr. Irene Ghobrial

D : Dr. Maria Victoria Mateos

Q17.

Which of these is the incorrect statement wrt to the design of PVD trial on NDMM with AKI by Jian Li et al ?

A. Cast nephropathy was defined by biopsy or clinical judgment by the investigators according to light chain proteinuria

B. If the proportion of urine albumin exceeded 30% of the urinary total protein, renal biopsy was required to confirm cast nephropathy.

C. Pomalidomide was used at a dose of 4mg/d x 21 days in the induction cycles

D. The primary end point was 3-month renal overall response

Q18.

Which of these statements is incorrect wrt to multiple myeloma-related renal impairment ?

A. Approx 20- 40% of patients with multiple myeloma present with renal impairment at the time of diagnosis and 2-4 % require RRT.

B. If non-selective proteinuria or involved serum FLCs < 500 mg/L is detected, then a renal biopsy should be done to identify the cause of renal impairment is mandatory .

C. There is no difference in the rates of dialysis independence between high-cut off haemodialysis and conventional high-flux haemodialysis at 3 months .

D. All are correct statements

QUIZ

MYELOMA QUIZ

July 2024

WINNER

Dr. Deep Gala

Senior Resident,
SGPGI, Lucknow

Q19. The National List of Essential Medicines (NLEM) was first compiled in 1996 and it was revised thrice earlier in 2003, 2011, and 2015. 384 drugs find place in the new list released on 14 Sep 22. Which of these myeloma drugs was added to the newly compiled list ?

A. Lenalidomide
B. Pomalidomide
C Bortezomib
D Carflizomib

Q20. In the study design by Yadav etal describing the impact of cytogenetics on solitary bone plasmacytoma (SBP) which is an incorrect statement ?

A. For FISH assessments in the bone marrow, both cytoplasmic immunoglobulin (cIg) and cell sorting to "isolate" the plasma cells before FISH staining were used
B. Probe sites with <15 metaphase nuclei were deemed insufficient for analysis
C. The level of detection required to identify fusion signals was a minimum of 3 of 50 cells (6%)
D. The level of detection required to identify enumeration probes such as TP53 or 1q was minimum of 10 of 50 cells (20%).

Q21. With respect to study results by Yadav etal describing the impact of cytogenetics on solitary bone plasmacytoma (SBP) which is an incorrect statement ?

A. All patients had a positron emission tomography–CT performed at the time of diagnosis for staging purposes.
B. All patients in the cohort received radiation therapy as part of their primary treatment for SBP
C. Information on baseline cytogenetics by FISH was available for only 30 percent patients in the cohort.
D. The median TTP to MM for patients with HR FISH was 8 months.

Q22. In the Greco – Israeli collaborative study of patients with macrofocal multiple myeloma (MFMM) which is the correct statement ?

A. Bone disease was evaluated by LDCT or PET CT in all patients in the cohort.
B. Cytogenetics by FISH showed high risk features in one third of patients
C. In the multivariate analysis; treatment with PI- based therapies was the only independent predictor for OS
D. All are incorrect statements.

Q23. In the Greco – Israeli collaborative study of patients with macrofocal multiple myeloma (MFMM) which is the correct statement ?

A. Bone marrow infiltration of 20% or more was used to define cases of MFMM
B. MFMM had less frequent advanced disease, immunoparesis, high risk cytogenetics or abnormal LDH compared with typical MM
C. Only 3 percent of total MM patients screened in the study met the case definition of MFMM
D. 40% of the diagnosed MFMM cases were ≥ 65 years of age

QUIZ

MYELOMA QUIZ

Aug 2024

WINNER

Dr. Dheeraj C.

Chandigarh

MYELOMA QUIZ : Apr 2024 - Dec 2024

Q24. Which of these was NOT a criterion of cardiac progression, if there is no infection, normal creatinine and absence of arrhythmia?

A. Rise in NT pro BNP / BNP >30% and >300 pg/mL from nadir

B. Troponin T/I increase of >33% from nadir

C. Drop in EF >=10% from best value

D. CPK-MB increase of >33% from nadir

Q25. Pick out an incorrect statement among these for the article by Muchtar et al ?

A. As the depth of hematological response increased, the proportion of patients with cardiac CR increased

B. The proportion of patients with cardiac CR and VGPR increased over time

C. In comparison with bortezomib based therapy, there was overall survival benefit with alkylator based therapy

D. At 12 and 24 month landmark, 4 level cardiac response assessment performed superior to the two level response assesment with respect to overall survival

Q26. Which of the following is incorrect regarding SGLT2 Inhibitor Therapy in Patients With ATTR Amyloid ?

A. 50% discontinuation rate over 28 months

B. Reduction in all cause and cardiovascular mortality

C. Slower decline in eGFR & fewer newer initiations of loop diuretics

D. Similar non-cardiac mortality in the two cohorts

Q27. Pick up the incorrect statement regarding SGLT2 inhibitor cohort in the study by Porcari et al ?

A. Greater drop in Systolic BP in patients treated with SGLT2 inhibitors

B. Slower rate of rise in NT-Pro BNP at 1 year

C. Less worsening of NYHA functional class

D. At diagnosis, only 20% patients received disease modifying agents (tafamidis, patisiran)

Q28. On April 12, 2024; FDA ODAC approved ----- in the field of multiple myeloma ?

A.Equivalence of peripheral blood MRD to bone marrow MRD

B. Using MRD as an accelerated approval endpoint in myeloma clinical trials

C. Using MRD for uniform risk stratification, irrespective of cytogenetics on FISH

D. Using MRD for treatment de-escalation

QUIZ

MYELOMA QUIZ

Sep 2024

WINNER

Dr. Vallish Shenoy

Senior Resident,
Medical Oncology,
TMH, Mumbai

Q29. Which of the following statements is incorrect regarding ASPEN study ?

A. None of the patients in either arm achieved a CR

B. The 18-month PFS was similar in both the arms

C. Only patients with MYD88 L265P mutation were included

D. VGPR rates were non significantly higher for zanubrutinib, while time to VGPR was similar in ND patients with both drugs

E. Sample size of 150 patients was based on superiority hypothesis of zanubrutinib over ibrutinib

Q30. Which of the following statements is incorrect regarding ASPEN study ?

All grade diarrhoea, muscle spasms, peripheral edema, bleeding were higher with ibrutinib

B. Grade >=3 AF and pneumonia was higher with ibrutinib

C. Neutropenia rates higher with Zanu, but no difference in grade>=3 infections in both arms

D. Cumulative incidence of hypertension and Atrial fibrillation decreased with time for the Ibrutinib arm

E. Higher proportion of patients in ibrutinib arm required dose reduction for adverse events

Q31. Which of these parameters of IPSS-WM was found to be significant on UVA, but not on MVA of Modified staging system for WM (MSS-WM) ?

A. B2 microglobulin >3 mcg/dL

B. Anaemia

C. Platelet<1 lac/mm3

D. IgM >7gm/dL

Q32. Which of the following statements is false regarding MSS-WM ?

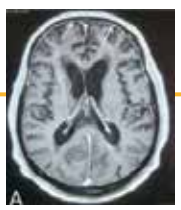
A. Rates of Richter transformation and progression to Amyloidosis was similar across all subgroups

B. Presence of MYD88 mutation favoured a significantly better survival

C. One third patients died due to non-WM related causes

D. Correlation with cytogenetic abnormalities like del 6q was not studied

Q33. A 60 yr man, past h/o WM 5 years ago, presented with confusion, progressive cognitive decline, slurred speech, and ataxia. M band – 1.5gm/dl, IgM 2.2 gm/dl. CSF flow cytometry: CD45: moderate ; CD20: moderate; CD38: moderate ; CD10: negative; CD5: negative; Surface Kappa: moderate; Surface Lambda: Negative; Likely diagnosis?



A. TEMPI syndrome

B. Hyperviscosity

C. IgM flare

D. Bing Neel syndrome

E. CANOMAD syndrome

QUIZ

MYELOMA QUIZ

Oct 2024

WINNER

Dr. Sandhya U. Maheshwari

Chidambharam Diagnostics

Q34. The term Amyloidosis is derived from the Latin word Amylum meaning ?

A. Proteinaceous
B. Gelatinaceous
C. Starch like
D. Lardaceous

Q35. Which of the following factors was a predictor of (increased/decreased) risk of infectious complications with Teclisitamab ?

A. Baseline Hypogammaglobulinemia
B. Baseline lymphopenia
C. Prior lines of therapy
D. IVIG Prophylaxis

Q36. Which of the following was NOT different in comparison between the real world study and the MajesTEC trial ?

A. Extramedullary disease
B. ORR
C. High risk cytogenetic profile
D. Median follow up

Q37. Which of the following statements is true with response to Teclisitamab in heavily treated Amyloidosis ?

A. The earliest response noted was in 14 days.
B. The median time to best hematological response was 45 days
C. Less than 60% patients achieved VGPR
D. 60% achieved an organ response.

Q38. Which of the following is not true with regard to complications and supportive care of Teclisitamab usage in AL Amyloidosis ?

A. ~ 50% developed CRS
B. ~50% developed a serious bacterial infection
C. ~30% developed a viral infection
D. Treatment discontinuation happened in ~25% for AEs/CR

QUIZ

MYELOMA QUIZ

Nov 2024

WINNER

Dr. Deep Gala

Senior Resident,
SGPGI, Lucknow

Q39. The Term Plasma cell was coined by _____ in 1875 . It is now however thought that he was possibly describing a tissue mast cell as the first accurate description of a plasma cell was by the neuroanatomist Cajal.

A. Waldeyer
B. Waldenstorm
C. Virchow
D. Bence Jones

Q40. Which of the following statements is NOT true about the genomic landscape of Primary PCL v/s MM ?

A. Higher incidence of t (11;14)
B. Higher incidence of t(4:14)
C. Lesser incidence of hyperdiploidy
D. Lesser incidence of trisomy 5

Q41. What was the overall survival in patients with PCL without a t (11:14) mutation ?

A. 10 months
B. 12 months
C. 18 months
D. 24 months

Q42. The highest concordance between the 2 methods of assessment of MRD was seen in which scenario ?

A. Post induction
B. Post ASCT
C. Post Consolidation
D. Post maintenance

Q43. What was the median PFS for those who were MRD positive post induction by either QIP/NGS ?

A. 2 years
B. 4 years
C. 6 years
D. Not reached

QUIZ

MYELOMA QUIZ

Dec 2024

WINNER

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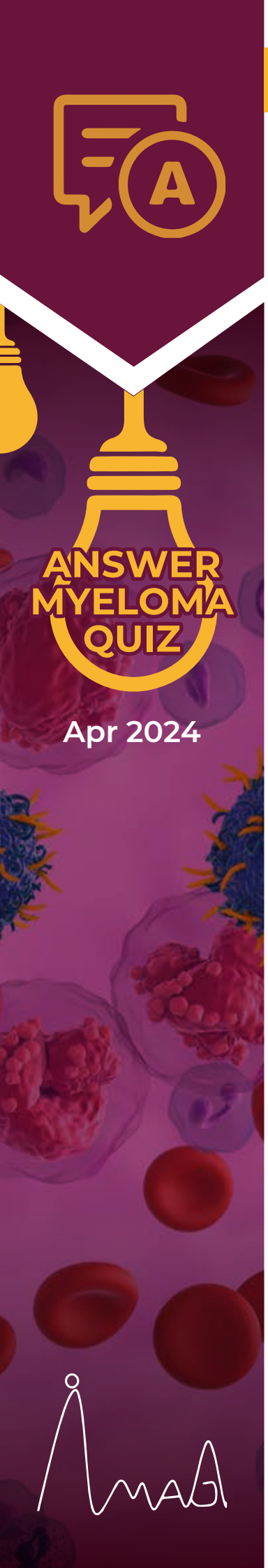
Apollo Hospital, Chennai



ANSWER MYELOMA QUIZ : Apr 2024 - Dec 2024

Q1 & Answer

The term “amyloid” was brought into the scientific literature by :

German botanist Matthias Schleiden

Explanation : German botanist Matthias Schleiden (1804-1881) coined the term "amyloid" in 1838 to describe a normal, starchy component of plants. He applied the iodine-starch test to plant preparations, which detects a blue stain when starch reacts with iodine in the presence of sulfuric acid.

Q2 & Answer

Which of these statements is incorrect wrt to the Joshua et al study assessing the impact of FLC-MS negativity on outcomes of AL Amyloidosis patients ?

At 12 months, median OS for CR + FLC-MS negative was 108 months ; It was not reached in the experimental arm and hence this statement is incorrect.

Explanation : Bomsztyk J, Ravichandran S, G, Wechalekar AD. Blood. 2024 Mar 28;143(13):1259-1268. doi: 10.1182/blood.2023022399.

Q3 & Answer

Which of these statements is incorrect wrt to AL Amyloidosis and its association with multiple myeloma ?

All are correct statements.

Explanation : Around 10 percent of AL patients fulfill diagnostic criteria for myeloma at the time of their diagnosis. 10 to 20 percent of myeloma patients develop clinical evidence of AL, although additional patients have subclinical deposition, around 35-40%. Serial bone marrow examinations show no increase in the proportion of plasma cells over time, reflecting the clonal but non-proliferative nature of plasma cells in AL

Q4 & Answer

Which of these options is incorrectly matched with regards to the frequency of cytogenetics findings in AL amyloidosis patients ?

t (11,14) : 30 %

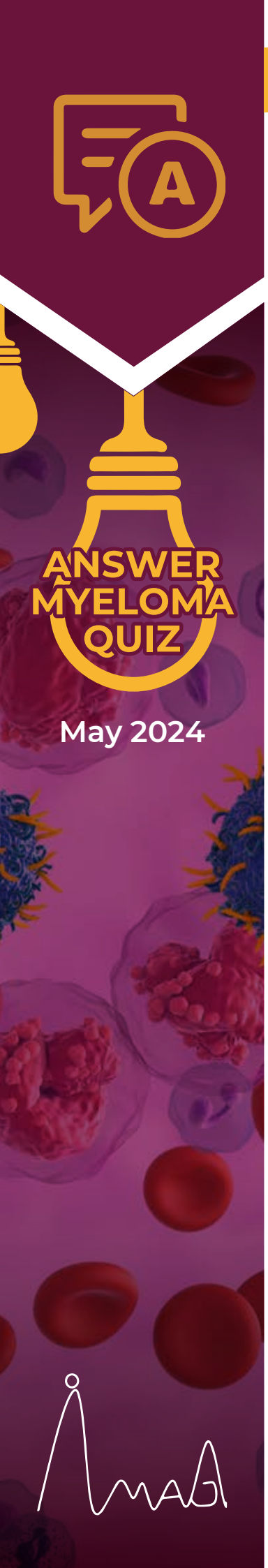
Explanation : A positive t (11,14) translocation is reported in 50 -60 % AL amyloidosis patients

Q5 & Answer

In terms of increasing sensitivity; which is the correct sequence of tissue biopsies to detect AL amyloidosis ?

Bone marrow < Fat pad < Salivary gland < Rectal < Target organ

Explanation : The most sensitive biopsy for diagnosing amyloidosis, with a sensitivity of nearly 100%. A rectal biopsy can be positive in 73–85% of cases, but it's not routinely recommended as the first-line technique. Rectal biopsies can be uncomfortable and may cause complications like bleeding and perforation. Amyloid deposits in the rectum are often found in the muscularis mucosae and submucosa, so the biopsy may miss them if it only includes mucosal tissue. A biopsy of abdominal subcutaneous fatty tissue (ASFT) can be positive in 70% of cases with AL or AA amyloidosis.



Q6 & Answer

Which of the following statements is incorrect regarding the CONPET study ?

Patients with new lesions or an increase in lesions meeting the IMWG criteria for progressive disease were included

Explanation : Ref :Nørgaard JN, Abildgaard N, F. Intensifying treatment in PET-positive multiple myeloma patients after upfront autologous stem cell transplantation. Leukemia. 2023 Oct;37(10):2107-2114. doi: 10.1038/s41375-023-01998-7.

Q7 & Answer

What was the target dose and schedule of Carfilzomib used in the CONPET study?

36 mg/m2 twice weekly

Explanation : Ref : Nørgaard JN, Abildgaard N, F. Intensifying treatment in PET-positive multiple myeloma patients after upfront autologous stem cell transplantation. Leukemia. 2023 Oct;37(10):2107-2114. doi: 10.1038/s41375-023-01998-7.

Q8 & Answer

Which of the following statements about MASTER trial is incorrect ?

B. Primary end point was achievement of MRD negativity which was assessed by Next generation flow-cytometry and cut off of 10^-5 were considered MRD negative 36 mg/m2 twice weekly

Explanation : MRD was assessed using NGS @ClonoSeq Assay and not flow cytiemetry

Q9 & Answer

Which of the following statements regarding results of MASTER trial are incorrect ?

C. A landmark analysis beginning at post-induction time point found that the persistence of MRD positivity (≥10−⁵) impaired PFS & OS

Explanation : No survival (PFS/OS) association with MRD was noticed at post induction time point in the study. Ref : Costa LJ, Chhabra S,. Minimal residual disease response-adapted therapy in newly diagnosed multiple myeloma (MASTER): final report of the multicentre, single-arm, phase 2 trial. Lancet Haematol. 2023 Nov;10(11):e890-e901. doi:10.1016/S2352-3026(23)00236-3.

Q10 & Answer

Pick the most appropriate use of the test shown below for a patient of multiple myeloma on therapy?

Solve cross match problem for patients on Daratumumab

Explanation : A DTT test, or dithiothreitol test, is a specialized technique used to detect alloantibodies in patients taking daratumumab. Daratumumab is an antibody that can interfere with routine blood bank testing by attaching to red blood cells (RBCs). The DTT test uses DTT to treat RBCs, which eliminates the interference caused by DARA. DTT is a thiol reagent that dissolves disulfide bonds between cysteine amino acids. This can potentially affect both red cell antigens and antibodies. A disadvantage of DTT is that it destroys RBC antigens, such as Cartwright (Yta), John Milton Hagen (JMH), and Knopsa (Kna, McCa, and Yka)

ANSWER MYELOMA QUIZ

June 2024

ANSWER MYELOMA QUIZ : Apr 2024 - Dec 2024

Q11 & Answer

Which of the following image symbolises the Greek God “PERSEUS”?

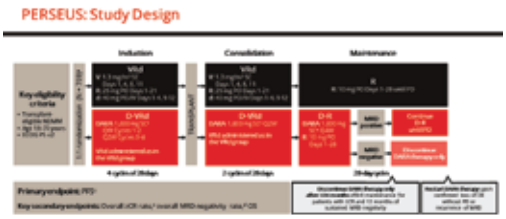
PERSEUS

Q12 & Answer

Which of these is the incorrect statement wrt to the design of PERSEUS trial ?

Once a week dose of dexamethasone 40mg was used during induction and consolidation arm in both groups

Explanation : Dexamethasone was used as weekly 4 day pulses of 40mg/d for two consecutive weeks in each cycle.



Q13 & Answer

Which of these statements is incorrect wrt to safety signals from the PERSEUS trial ?

All are correct statements

Explanation : The most common grade 3 or 4 adverse events were neutropenia in both arms (62.1% in the D-VRd group and 51.0% in the VRd group). The most common serious adverse event was pneumonia in both arms (11.4% in the D-VRd group and 6.1% in the VRd group). A significantly increased number of patients in D VRD arm received plerixafor during stem cell mobilisation in comparison to VRd arm but medium time to engraftment was similar (plerixafor @40 % vs 22.7 %)

Q14 & Answer

Which of these statements is incorrect wrt design of the phase 2 study 2018-04 from the Intergroupe Francophone du Myelome (IFM), evaluating the feasibility and efficacy of D-KRd induction and consolidation plus tandem transplant in HR TE-NDMM ?

Presence of at least 1 HR cytogenetic abnormalities among del(17p), t(4;14), t(14;16) or 1 q amp by FISH was mandatory for inclusion

Explanation : 1 q amp by FISH was not considered by the IFM group as HRMM.

Q15 & Answer

In the phase 2 study 2018-04 from IFM , main cause of treatment discontinuation before second transplant was ?

Insufficient stem cell collection for tandem transplant

Explanation : Ref Cyrille Touzeau et al ; Daratumumab, Carfilzomib, Lenalidomide, and Dexamethasone Induction and Consolidation with Tandem Transplant in High-Risk Newly Diagnosed Myeloma Patients: Final Results of the Phase 2 Study IFM 2018-04. Blood 2023; 142 (Supplement 1): 207. doi: https://doi.org/10.1182/blood-2023-174044

ANSWER MYELOMA QUIZ

July 2024

Q16 & Answer

If A is Dr Bart Barlogie who is B ? Both pioneered the tandem transplant curative concept in myeloma.

A. 

B. 

Dr. Seema Singhal

Q17 & Answer

Which of these is the incorrect statement wrt to the design of PVD trial on NDMM with AKI by Jian Li et al ?

Pomalidomide was used at a dose of 4mg/d x 21 days in the induction cycles

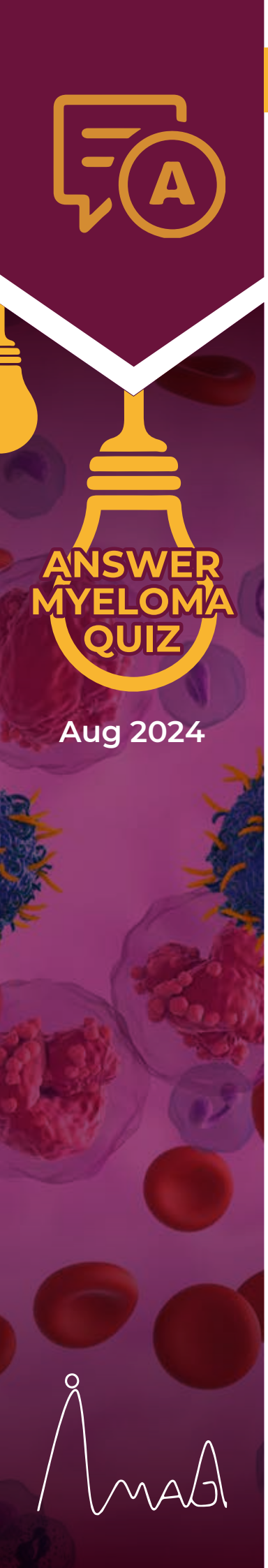
Explanation : Pomalidomide was used at a dose of 4mg/d x 14 days in the induction cycles

Q18 & Answer

Which of these statements is incorrect wrt to multiple myeloma-related renal impairment ?

All are correct statements

Explanation : Approx 20- 40% of patients with multiple myeloma present with renal impairment at the time of diagnosis and 2-4 % require RRT. If non-selective proteinuria or involved serum FLCs < 500 mg/L is detected, then a renal biopsy should be done to identify the cause of renal impairment is mandatory . There is no difference in the rates of dialysis independence between high- cut off haemodialysis and conventional high-flux haemodialysis at 3 m. Ref : Dimopoulos, Meletios A et al Management of multiple myeloma-related renal impairment: recommendations from the International Myeloma Working Group; The Lancet Oncology, Volume 24, Issue 7, e293 - e311; 2023



Q19 & Answer

The National List of Essential Medicines (NLEM) was first compiled in 1996 and it was revised thrice earlier in 2003, 2011, and 2015. 384 drugs find place in the new list released on 14 Sep 22. Which of these myeloma drugs was added to the newly compiled list ?

Lenalidomide

Explanation : Ref Ministry of Health and Family Welfare, GOI. National List of Essential Medicines (NLEM); https://main.mohfw.gov.in/newshighlights-104

Q20 & Answer

In the study design by Yadav etal describing the impact of cytogenetics on solitary bone plasmacytoma (SBP) which is an incorrect statement ?

Probe sites with <15 metaphase nuclei were deemed insufficient for analysis

Explanation : An interphase FISH was used by the investigators in the study. Ref : Yadav U et al; Impact of cytogenetic abnormalities on the risk of disease progression in solitary bone plasmacytomas. Blood. 2023 Nov 30;142(22):1871-1878. doi: 10.1182/blood.2023021187

Q21 & Answer

With respect to study results by Yadav etal describing the impact of cytogenetics on solitary bone plasmacytoma (SBP) which is an incorrect statement ?

All patients had a positron emission tomography–CT performed at the time of diagnosis for staging purposes.

Explanation : Only 89 percent patients underwent baseline PET in the trial ; Ref : Yadav U et al; Impact of cytogenetic abnormalities on the risk of disease progression in solitary bone plasmacytomas. Blood. 2023 Nov 30;142(22):1871-1878. doi: 10.1182/blood.2023021187

Q22 & Answer

In the Greco – Israeli collaborative study of patients with macrofocal multiple myeloma (MFMM) which is the correct statement ?

In the multivariate analysis; treatment with PI- based therapies was the only independent predictor for OS

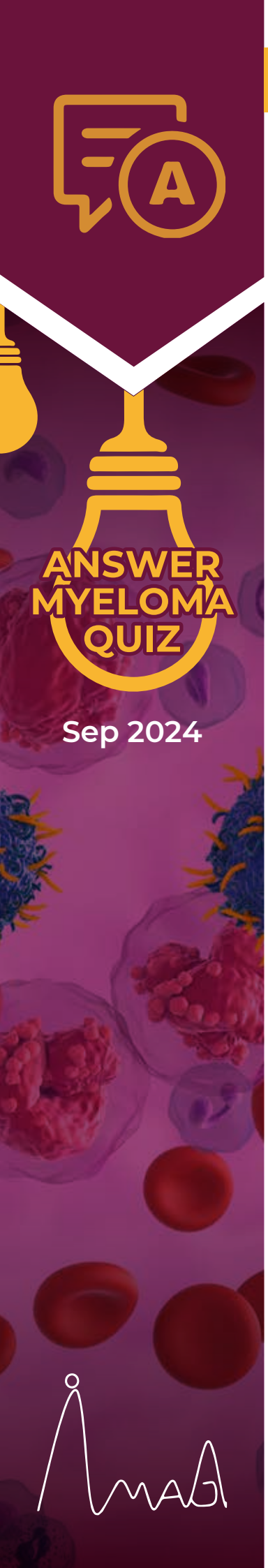
Explanation : Ref : Katodritou E et al; Real-world data on incidence, clinical characteristics and outcome of patients with macrofocal multiple myeloma (MFMM) in the era of novel therapies: A study of the Greco-Israeli collaborative myeloma working group.
Am J Hematol. 2020 May;95(5):465-471. doi: 10.1002/ajh.25755

Q23 & Answer

In the Greco – Israeli collaborative study of patients with macrofocal multiple myeloma (MFMM) which is the correct statement ?

Bone marrow infiltration of 20% or more was used to define cases of MFMM

Explanation : Bone marrow infiltration of less than 20% was used to define cases of MFMM



Q24 & Answer

Which of these was NOT a criterion of cardiac progression, if there is no infection, normal creatinine and absence of arrhythmia?

CPK-MB increase of >33% from nadir

Explanation : Rise in NT pro BNP / BNP >30% and >300 pg/mL from nadir; Troponin T/I increase of >33% from nadir; Drop in EF >=10% from best value were considered criteria for cardiac progression in the trial

Q25 & Answer

Pick out an incorrect statement among these for the article by Muchtar et al ?

In comparison with bortezomib based therapy, there was overall survival benefit with alkylator based therapy

Explanation : Ref : Muchtar E et al Graded Cardiac Response Criteria for Patients With Systemic Light Chain Amyloidosis. J Clin Oncol. 2023 Mar 1;41(7):1393-1403. doi: 10.1200/JCO.22.00643

Q26 & Answer

Which of the following is incorrect regarding SGLT2 Inhibitor Therapy in Patients With ATTR Amyloid ?

50% discontinuation rate over 28 months

Explanation : Discontinuation rate over 28 months was 5 percent in the intervention arm; Ref Porcari A et al. SGLT2 Inhibitor Therapy in Patients With Transthyretin Amyloid Cardiomyopathy. J Am Coll Cardiol. 2024 Jun 18;83(24):2411-2422. doi: 10.1016/j.jacc.2024.03.429

Q27 & Answer

Pick up the incorrect statement regarding SGLT2 inhibitor cohort in the study by Porcari et al ?

Greater drop in Systolic BP in patients treated with SGLT2 inhibitors

Explanation : There was no clinically and statistically significant drop in Systolic BP in patients treated with SGLT2 inhibitors.

Q28 & Answer

On April 12, 2024; FDA ODAC approved ----- in the field of multiple myeloma ?

Using MRD as an accelerated approval endpoint in myeloma clinical trials

Explanation : On April 12, 2024, FDA's Oncologic Drugs Advisory Committee voted 12 to 0 that the totality of available data supports the use of minimal residual disease (MRD) as an end point for accelerated approval of new treatments for patients with multiple myeloma. Ref : Oncologic Drugs Advisory Committee (ODAC) Meeting. ODAC Briefing Document. Accessed April 12, 2024. https://www.fda.gov/media/177652/download

ANSWER MYELOMA QUIZ

Oct 2024

ANSWER MYELOMA QUIZ : Apr 2024 - Dec 2024

Q29 & Answer

Which of the following statements is incorrect regarding ASPEN study ?

VGPR rates were non significantly higher for zanubrutinib, while time to VGPR was similar in ND patients with both drugs

Explanation : Ref : Tam CS et al; A randomized phase 3 trial of zanubrutinib vs ibrutinib in symptomatic Waldenström macroglobulinemia: the ASPEN study. Blood. 2020 Oct 29;136(18):2038-2050. doi: 10.1182/blood.2020006844

Q30 & Answer

Which of the following statements is incorrect regarding ASPEN study ?

Cumulative incidence of hypertension and atrial fibrillation decreased with time for the Ibrutinib arm

Explanation : Cumulative incidence of hypertension and atrial fibrillation increased with time for the Ibrutinib arm. Ref : Tam CS et al; A randomized phase 3 trial of zanubrutinib vs ibrutinib in symptomatic Waldenström macroglobulinemia: the ASPEN study. Blood. 2020 Oct 29;136(18):2038-2050. doi: 10.1182/blood.2020006844

Q31 & Answer

Which of these parameters of IPSS-WM was found to be significant on UVA, but not on MVA of Modified staging system for WM (MSS-WM) ?

B2 microglobulin >3 mcg/dL

Explanation : Ref Zanwar S et al; Simplified Risk Stratification Model for Patients With Waldenström Macroglobulinemia. J Clin Oncol. 2024 Jul 20;42(21):2527-2536. doi: 10.1200/JCO.23.02066. PMID: 38788183 10.1016/j.jacc.2024.03.429

Q32 & Answer

Which of the following statements is false regarding MSS-WM ?

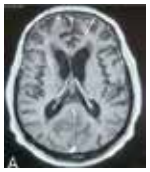
Presence of MYD88 mutation favoured a significantly better survival

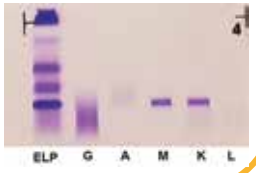
Explanation : Presence of MYD88 mutation did not impact survival outcomes in the trial.

Q33 & Answer

A 60 yr man, past h/o WM 5 years ago, presented with confusion, progressive cognitive decline, slurred speech, and ataxia. M band - 1.5gm/dl, IgM 2.2 gm/dl. CSF flow cytometry: CD45: moderate ; CD20: moderate; CD38: moderate ; CD10: negative; CD5: negative; Surface Kappa: moderate; Surface Lambda: Negative Likely diagnosis?

Bing Neel syndrome





Explanation : Leptomeneingeal enhancement in the setting of IgM paraproteinemia with a clinical profile above is diagnostic of Bing Neel syndrome syndrome

ANSWER MYELOMA QUIZ

Nov 2024

Q34 & Answer

The term Amyloidosis is derived from the Latin word Amylum meaning ?

Starch like

Explanation : German pathologist Rudolph Virchow first used the term Anyloid in 1854 to describe deposits found in tissues. He named it after starch because the earliest methods used to detect it involved treating it with an iodine solution, which turns it blue. However, amyloid initially stains deep brown with iodine, but turns blue after treatment with concentrated sulfuric acid.

Q35 & Answer

Which of the following factors was a predictor of (increased/decreased) risk of infectious

IVIG Prophylaxis

Explanation : Ref : Forgeard N, Elessa D, Carpinteiro A, et al. Teclistamab in relapsed or refractory AL amyloidosis: a multinational retrospective case series. Blood. 2024;143(8):734-737. doi:10.1182/blood.2023022937

Q36 & Answer

Which of the following was NOT different in comparison between the real world study and the MajesTEC trial ?

ORR

Explanation : ORR was approx 60 percent in both real world study with Teclistamab and the MajesTEC trial

Q37 & Answer

Which of the following statements is true with response to Teclisitamab in heavily treated Amyloidosis ?

The earliest response noted was in 14 days.

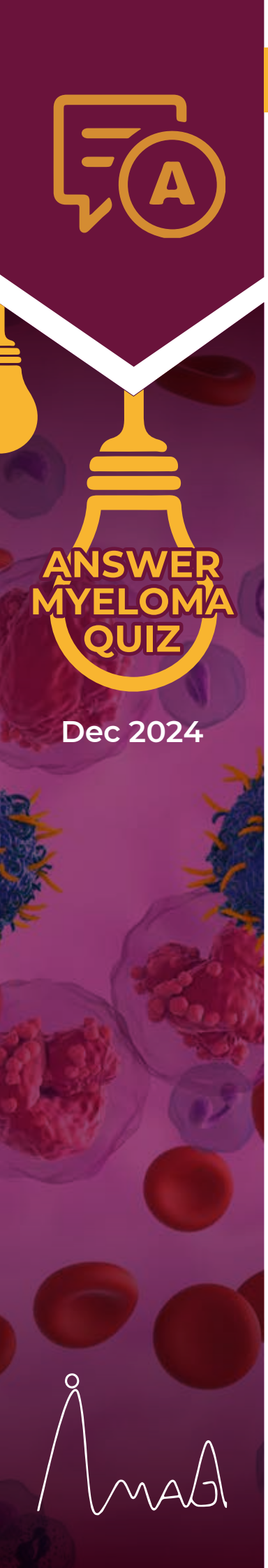
Explanation : Ref : Mohan M, Monge J, Shah N, et al. Teclistamab in relapsed refractory multiple myeloma: multi-institutional real-world study. Blood Cancer J. 2024;14(1):35. Published 2024 Mar 5. doi:10.1038/s41408-024-01003

Q38 & Answer

Which of the following is not true with regard to complications and supportive care of Teclisitamab usage in AL Amyloidosis ?

~50% developed a serious bacterial infection

Explanation : ~ 30% developed a serious bacterial infection. Ref : Mohan M, Monge J, Shah N, et al. Teclistamab in relapsed refractory multiple myeloma: multi-institutional real-world study. Blood Cancer J. 2024;14(1):35. Published 2024 Mar 5. doi:10.1038/s41408-024-01003



ANSWER MYELOMA QUIZ : Apr 2024 - Dec 2024

Q39 & Answer

The Term Plasma cell was coined by _____ in 1875 . It is now however thought that he was possibly describing a tissue mast cell as the first accurate description of a plasma cell was by the neuroanatomist Cajal.

Waldeyer

Explanation : A Waldeyer's plasma cell is a connective tissue cell with a coarse granular structure that's found close to blood vessels. The term "plasma cell" was coined in 1875 by German anatomist Heinrich Wilhelm Gottfried Waldeyer.

Q40 & Answer

Which of the following statements is NOT true about the genomic landscape of Primary PCL v/s MM ?

Higher incidence of t(4:14)

Explanation : Ref : Cazaubiel T, Leleu X, Perrot A, et al. Primary plasma cell leukemias displaying t(11;14) have specific genomic, transcriptional, and clinical features. Blood. 2022;139(17):2666-2672. doi:10.1182/blood.2021014968

Q41 & Answer

What was the overall survival in patients with PCL without a t (11:14) mutation ?

18 months

Explanation : Ref : Cazaubiel T, Leleu X, Perrot A, et al. Primary plasma cell leukemias displaying t(11;14) have specific genomic, transcriptional, and clinical features. Blood. 2022;139(17):2666-2672. doi:10.1182/blood.2021014968

Q42 & Answer

The highest concordance between the 2 methods of assessment of MRD was seen in which scenario ?

Post maintenance

Explanation : Post maintenance concordance between the 2 methods of assessment of MRD was 85 % Ref : Puig N, Agullo Roca C, Sanfeliciano TC, et al. Measurable Residual Disease by Mass Spectrometry and Next-Generation Flow to Assess Treatment Response in Myeloma. Blood. Published online September 18, 2024. doi:10.1182/blood.202402499

Q43 & Answer

What was the median PFS for those who were MRD positive post induction by either QIP/NGS ?

6 years

Explanation : Ref : Puig N, Agullo Roca C, Sanfeliciano TC, et al. Measurable Residual Disease by Mass Spectrometry and Next-Generation Flow to Assess Treatment Response in Myeloma. Blood. Published online September 18, 2024. doi:10.1182/blood.202402499

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"TP53 mutation – An Underestimated Cause of Poor Prognosis in Newly Diagnosed Multiple Myeloma in India"

Article - Sreedharanunni S, Singla S, Balakrishnan A, et al. The frequency and clinical outcome of mono-hit and multi-hit TP53 aberrations in newly diagnosed multiple myeloma. Pathology. 2024;56(4):556-564. doi:10.1016/j.pathol.2023.12.415

This study from PGIMER, Chandigarh wherein authors investigated the frequency and outcome of mono-hit and multi-hit TP53 aberrations in an Indian cohort of newly diagnosed multiple myeloma (NDMM) patients. Mono-hit TP53 aberrations included mono-allelic 17pdel or TP53mut. In contrast, multi-hit TP53 aberrations are defined as follows: (1) the presence of more than one TP53mut regardless of variant allele frequency (VAF); (2) one or more TP53mut accompanied by the deletion of 17p13 or monosomy 17; (3) TP53mut with a VAF of at least 55% (VAF≥55%). We employed fluorescence in-situ hybridisation (FISH; n=457) and targeted next-generation sequencing (NGS; n=244) on plasma cell-enriched samples. They also studied the impact of TP53mut in cases with and without 17pdeletions (17pdel).

Their cohort had a median age of 60 years. 17pdel and TP53mut were seen in 12.9% (n=59/457; 14-95% cells) and 10.2% (n=25/244; 30 variants; VAF 3.4-98.2%; median 38.2%) respectively. Mono-hit and multi-hit-TP53 aberrations were observed in 10.2% and 7.8%, respectively. In comparison to TP53wt, mono-hit and multi-hit TP53 aberrations were associated with significantly poorer PFS (22.6 vs 12.1 vs 9.5 months; p=0.004) and OS [not reached (NR) vs 13.1 vs 15.6 months respectively; p=0.024]. As expected, compared to TP53wt, PFS and OS were significantly poorer in patients with TP53mut only (9.5 vs 22.6 months and 12.1 months vs NR, respectively; p=0.020/0.004). TP53mut retained its significance even in the presence of any Revised International Staging System (HR 2.1; 95% CI 1.1-3.8; p=0.015) for OS.

This study was important with respect to various perspectives. Firstly, among the cases with 17pdel, 44% (15/34) also exhibited TP53mut. While it would be intuitive to believe that more the number of TP53 aberrations, worse the prognosis. But this study showed that multi-hit TP53 did not significantly differ in OS/PFS compared to mono-hit cases. Secondly, NGS testing aided in identifying TP53 aberrations in 10 patients (4.1%) that would have been missed by FISH testing alone. Since approximately 5% cases without 17pdel have TP53mut which contributes to poor survival, there is a merit for testing for TP53 mutation in all NDMM cases, especially those who do not have high-risk cytogenetics.

“Circulating Plasma cells at Diagnosis and MRD from Peripheral Blood – Its time to Refine Prognosis by Using Less-Invasive Methods in Newly Diagnosed Multiple Myeloma”

Article - Tembhare PR, Sriram H, Khanka T, et al. Circulating tumor plasma cells and peripheral blood measurable residual disease assessment in multiple myeloma patients not planned for upfront transplant. Hemasphere. 2024;8(4):e63. Published 2024 Apr 1. doi:10.1002/hem3.63

This study from Tata Memorial Centre, Mumbai highlighted the utility of multiparametric flow-cytometry in peripheral blood in newly diagnosed multiple myeloma. Authors prospectively studied circulating tumor plasma cells (CTPC) at diagnosis and MRD from peripheral blood in 141 NDMM patients using highly sensitive multicolor flow cytometry (HS-MFC). Patients were treated with bortezomib-based triplet induction. Amongst patients who had CTPC at diagnosis, PBMRD was monitored at the end of three cycles (PBMRD1) and six cycles (PBMRD2) of chemotherapy. Importantly, they included only patients who were not intended for upfront autologous transplant. With respect to baseline parameters, CTPC ≥ 0.01% was independently associated with poor progression-free survival (PFS) (hazard ratio [HR] = 2.77; p = 0.0047) and overall survival (OS) (HR = 2.9; p = 0.023) on multivariate analysis. In patients with detectable baseline CTPC, undetectable PBMRD at both subsequent time points was associated with longer PFS (HR = 0.46; p = 0.0037), whereas detectable PBMRD at any time point was associated with short OS (HR = 3.25; p = 0.004). Undetectable PBMRD at both time-points (PBMRD1 and PBMRD2) outperformed the conventional serological responses (serum-immunofixation-based response). On multivariate analysis, detectable PBMRD at any time point was independently associated with poor PFS (HR = 2.0; p = 0.025) and OS (HR = 3.97; p = 0.013). This study highlights that CTPC and PBMRD assessment using HS-MFC provides a robust, non-invasive biomarker for NDMM patients not planned for an upfront transplant. Importantly, there was no comparison with BM-MRD and the impact of autologous transplant could not be ascertained from this study. Nonetheless, it demonstrates that sequential PB-MRD monitoring has great potential to improve upon existing risk stratification and response assessment models.

“High-Risk Myeloma in India – Real World Outcomes Emphasizing the Role of Autologous Transplant”

Article - Soni A, Rainchwar S, Singh R, et al. Real World Outcome of High-Risk Multiple Myeloma: An Indian Tertiary Care Centre Experience. Clin Lymphoma Myeloma Leuk. Published online September 22, 2024. doi:10.1016/j.clml.2024.09.007

This study was reported from Rajiv Gandhi Cancer Institute, New Delhi, wherein authors retrospectively analysed the outcomes of patients with high-risk cytogenetic abnormalities (HRCA) in myeloma. High risk myeloma is heterogeneous with significant variation in risk stratifications. Real world outcomes differ from controlled clinical trials and affected by socioeconomical determinants. Out of 384 myeloma patients, 76(19.7%) high risk myeloma patients (median age 58 years) were analyzed. Amongst 76 patients, most common HRCA was 1q gain [n=36(47.4%)] followed by del17p [n=32(42.1%)]. 80% patients received bortezomib based triplets and 20% received daratumumab based quadruplet induction. 41% patients with HRCAs underwent ASCT. With a mfedian follow-up duration of 19.5 months, the 2-year PFS and OS was 52% and 74%, respectievly. There was a signifcant difference with respect to 3-year PFS [72.1% versus 30.3% (P = .0026)] and 3-year OS [74.7% versus 52.9% (P=0.0067)] in favour of transplant. Importantly, there was no difference in 3-year PFS [58% vs 35%; P=0.486] and 3-year OS [67.7% vs 61.9% (P=0.642)] between single-hit HRCA and multi-hit HRCA. In multivariate analysis ASCT correlated with better OS (HR 0.3, P=0.041) and PFS (HR 0.35, P=0.012). Absence of baseline renal impairment correlated with better OS (HR 4.12,P=0.004) only. Authors recommend early aggressive therapy with prompt ASCT for better survival in high risk myeloma. However, this study does not clarify the role of tandem transplant, role of MRD for prognostication in high-risk myeloma and if quadruplet induction is better than triplet induction in today’s era.

Rajiv Gandhi Cancer Institute and Research Centre
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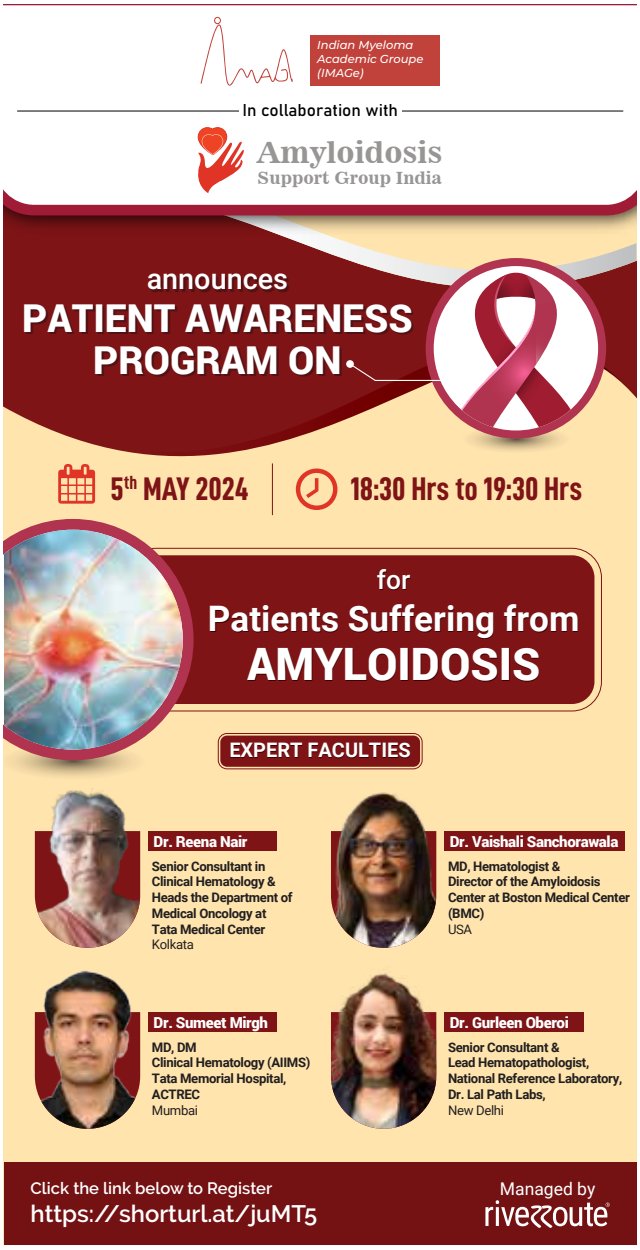
Amyloidosis Patient Awareness Program 5th May 2024

PATIENT AWARENESS PROGRAM

PARTICIPANTS

28



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Interactive Program for Patient Caregivers 12th May 2024

PATIENT AWARENESS PROGRAM

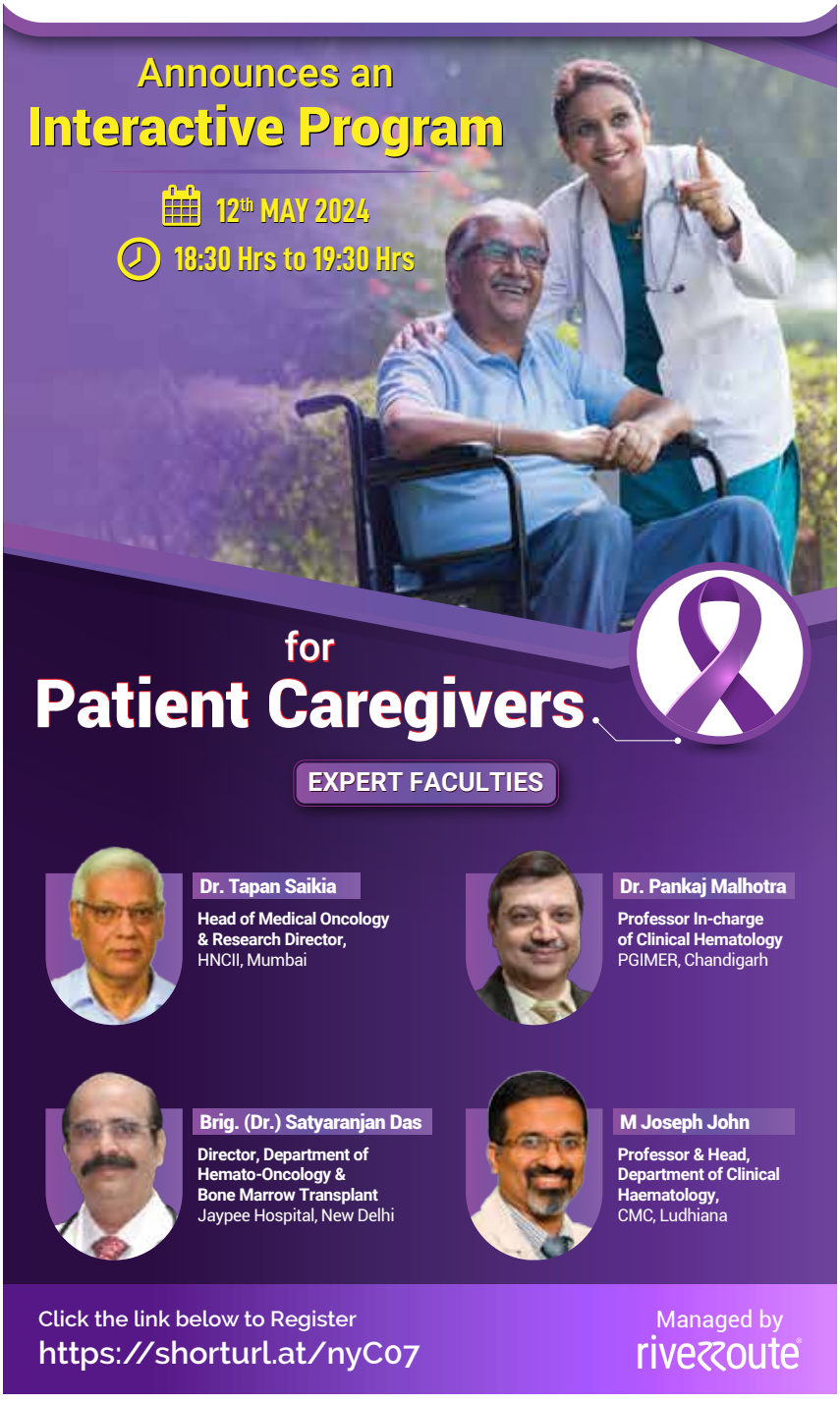
PARTICIPANTS

37

Indian Myeloma Academic Groupe (IMAGe)

In collaboration with

Caregivers ASHA Society



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Amyloidosis Patient Awareness Program 19th May 2024

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PATIENT AWARENESS PROGRAM

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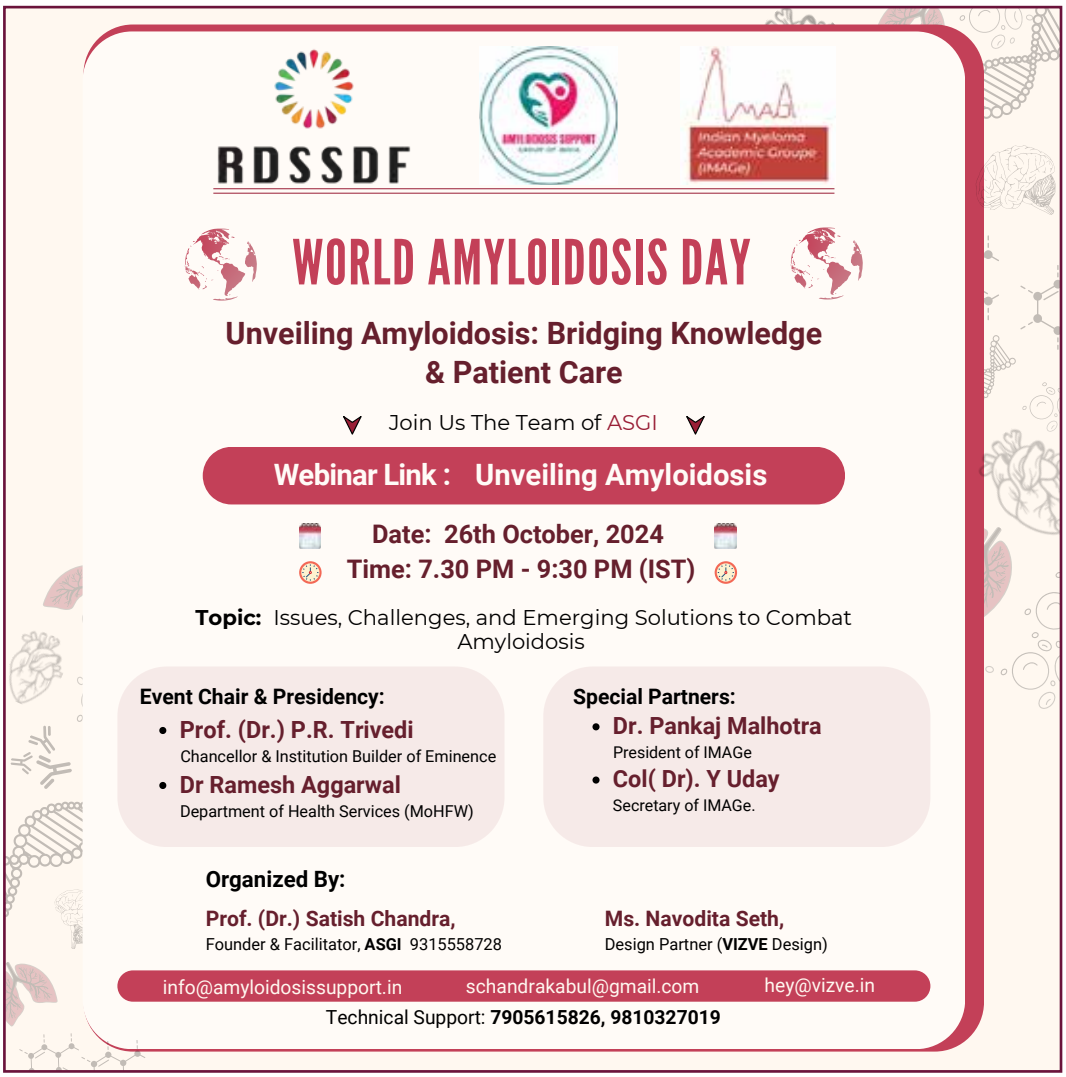
39

Unveiling Amyloidosis: Bridging Knowledge & Patient Care 26th Oct. 2024



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78

Unveiling Amyloidosis: Bihar Chapter 3rd Dec 2024

RDSSDF

In Collaboration with

UNVEILING AMYLOIDOSIS: BIHAR CHAPTER

Topic: Issues, Challenges, and Emerging Solutions to Combat Amyloidosis

WEBINAR

3 December 2024

7:00 pm - 9:30 pm (IST)

Platform: Google Meet

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Agenda

Time	Topic	Speaker
7.00 - 7.05 Pm	Opening Remarks	Prof.(Dr) Satish Chandra ASGI Founder
7.05 - 7.10 Pm	Inaugural Address	Dr. Avinash Kumar Senior Hematologist & Chairman, Bihar Chapter, ASGI
7.10 - 7.25 Pm	Introduction, ASGI	Navodita Seth & Team Vizve Design, Design Partner RDSSDF
7.25 - 7.35 Pm	Preliminary Overview	Dr. Gurleen Oberoi Senior Consultant Hematology Medanta, Gurgaon.
7.35 - 7.45 Pm	Technical Session	Dr Sanjay Kumar HoD of Neurology, PMCH, Patna, Bihar
7.45 - 7.55 Pm	Technical Session	Dr. Manjari Tripathi, Head of Neurology at AIIMS, New Delhi, India,
7.55 - 8.05 Pm	Technical Session	Dr Tulika Seth Senior Hematologist ,AIIMS - Delhi
8.05 - 8.15 Pm	Technical Session	Dr Sandeep Seth Senior Cardiologist, AIIMS ,New Delhi
8.15 - 8.25 Pm	Technical Session	Dr B. S Vivek - Senior Cardiologist at Sir Ganga Ram Hospital
8.25 - 8.35 Pm	Technical Session	Dr. Rahul Bhargav Chief Hematologist at Fortis Hospital, Gurgaon
8.35 - 8.45 Pm	Technical Session	Dr. Nikita Mehra Hematologist & Oncologist, Chennai
8.45 - 9.15 Pm	Q&A	Dr. Gurleen Oberoi & Mr. Atul Pandya
9.15 - 9.25 Pm	Patient Interaction	CS Shriya Bhargav/ Mr. CP Verma ASGI Organising Team Member
9.25 - 9.30 Pm	Concluding Remarks & Vote of Thanks	Navodita Seth Design & Research Head, Vizve Design

RSVP, ASGI

PROF. (DR.) SATISH CHANDRA
FOUNDER & FACILITATOR OF **ASGI**, 9315558728

NAVODITA SETH
DESIGN PARTNER (**VIZVE** DESIGN)

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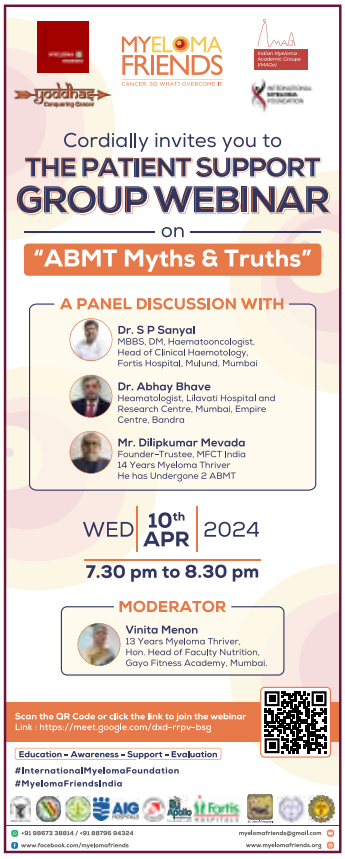
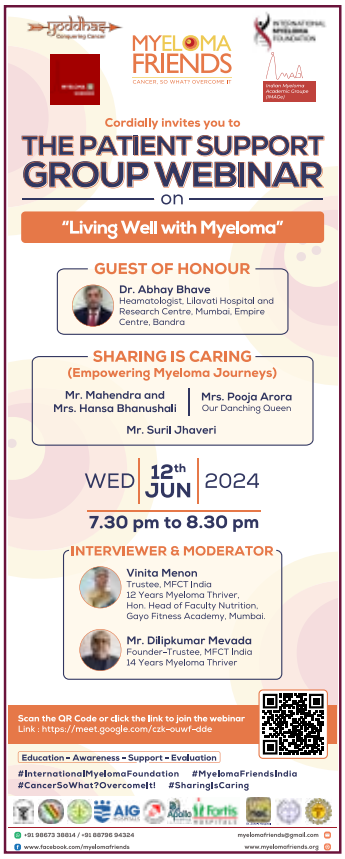
Partnership with Myeloma Friends

10th Apr, 2024



10th May, 2024

12th Jun, 2024



10th July, 2024

PATIENT AWARENESS PROGRAM

Partnership with Myeloma Friends

10th Aug, 2024

26th Aug, 2024

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10th Oct, 2024

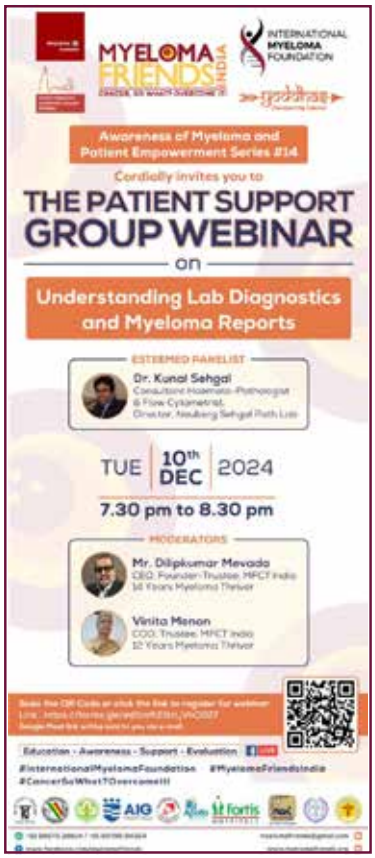
PATIENT AWARENESS PROGRAM

Partnership with Myeloma Friends

13th Nov, 2024

19th Nov, 2024

10th Dec, 2024



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Papers Presented at IMS 2023

Prevalence of MGUS in Rural Indian Population: Results of SIMPLe (IMAGe-002) Study

P-104

Uday Yanamandra, Saurabh Bobdey, Celine Raphael, Junah Hassan, Bhatti VK, Muthukrishnan Jayaraman, Pankaj Malhotra & SIMPLe study group

Introduction

MGUS Prevalence in Resource Constraint Settings

- The incidence of monoclonal gammopathies is rising across the globe.
- Prevalence of MGs has been extensively studied in Western populations, but limited data are available on the prevalence of MGs in Indian communities.
- Although the prevalence of monoclonal gammopathy of undetermined significance (MGUS) has been evaluated in two hospital-based studies in India, no data exists on its prevalence in community-based settings.

Why this study is important

- A first-of-its-kind effort from India to identify the prevalence of monoclonal gammopathies based on a door-to-door community survey.

Aim & Objectives

- To determine the prevalence of monoclonal gammopathies in a rural Indian population in a community-based setting

Methodology

Study Design:
Cross-sectional study in agrarian village of Western India

Door-to-Door community-based survey investing 12096 man-hrs
89.2% population coverage of targeted population

Study Registration: CTRI/2023/03/051220

SIMPLe: Screening Intervention for Myeloma and Prevention of Lifestyle diseases

Inclusion Criteria:
- Individuals of either gender aged >45yrs

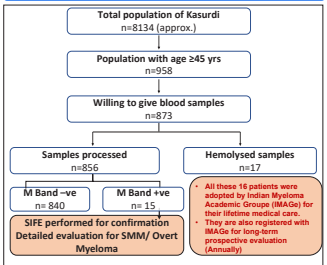
Exclusion Criteria:
- Individuals unwilling to give blood samples or consent to participate
- Individuals whose blood samples were hemolyzed or had preanalytical errors

Methodology:
- Demographic/ past medical details & blood samples collected
- Thorough Medical Examination at the doorstep (Mobile Clinic)
- Serum separated at field location (<1h) – Shipped refrigerated

Analysis: JMP ver 16.0.0

Armed Forces Medical College, India & Indian Myeloma Academic Groupe (IMAGe)

Results



- **Prevalence of MGUS:** 1.75%.
- **Mean age of individuals with MGUS:** 63.4±5.2y
- **Gender predisposition:** Male (60%).
- **Mean Hb of individuals with MGUS:** 12.39±1.8g/dL.
- **None had features of SMM/ MM (IMWG criteria)**
- **SIFE characteristics:**
  - IgG - 83.33%, IgA - 16.67%, none having IgM/ IgD paraprotein.
  - Kappa – 50%, and Lambda – 50%.
  - Two individuals only had light chain MGUS
  - IgG lambda MGUS - commonest

Discussion

Comparisons from other studies in India

– A singular hospital study on the incidence of MGUS form AIIMS New Delhi revealed 49-MGUS and 6-MM amongst 3429 patients screened. The age-wise prevalence was 0.83% (40-49y), 1% (50-59y), 2.62% (60-69y) and 1.75% (above 70y).[1]

– Limitations

– SIFE and SFLC for the entire study population could not be done owing to resource constraints.
– As India is a land of heterogeneity it would be ideal to replicate similar studies from different parts of the country[2]
– A higher sample size was preferable

Conclusion

– Our study provides a brief idea of the prevalence of MGUS in a rural community setting in India.
– The background prevalence is much less compared to the Western (both USA ~3% and European~5%) population.[3,4]

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AUTOLOGOUS STEM CELL TRANSPLANTATION FOR MULTIPLE MYELOMA - A SINGLE CENTER EXPERIENCE FROM INDIA

P-172

Sanjeev*, Madhuri smith, Manoj Singh, Ashiish Sharma, Faheema Hasan,Naresh Tripathy Manish kumar singh, Dinesh chandra,K Rahman, Ruchi Gupta, Rajesh Kashyap
Department of Hematology, Sanjay Gandhi Post Graduate Institute of Medical Sciences (SGPGIMS), Lucknow

INTRODUCTION

Autologous stem cell transplantation (ASCT) remains the standard of care for patients with newly diagnosed multiple myeloma (MM) despite the approval of novel agents. Numerous trials have demonstrated a progression-free survival (PFS) advantage with ASCT. To study the demographics, clinical profile, and outcomes of patients with MM undergoing ASCT at a tertiary care center in northern India.

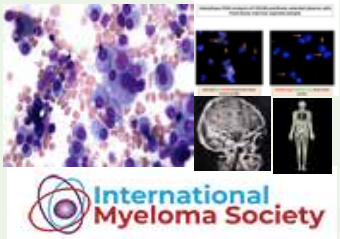
MATERIAL & METHODS

This is a medical records review of 29 patients with MM who underwent ASCT between 2007 and 2021. The demographics, clinical profile, induction regimen, details of ASCT, and outcomes were retrieved. Descriptive analysis, Progression Free Survival (PFS), and Overall Survival (OS) were determined. Data are expressed as median and interquartile range (IQR).

RESULTS

The median age of the cohort was 56 years (50-61) and 21 (72%) were males. The follow-up duration from diagnosis was 60 months (18-74). The most common immunoglobulin isotype was IgG kappa (28%) followed by IgG lambda (24%) and IgA kappa (21%). R-ISS staging was available for 26 patients and 21 of 26 (72%) had stage III disease. High-risk cytogenetics were identified in 19 patients (66%).

Nine patients (47%) had t(4;14) and four (21%) had deletion 17p. Triplet induction consisting of Bortezomib, dexamethasone, and IMiD was the most common induction regimen (18, 62%). Two patients received quadruplet induction consisting of daratumumab, bortezomib, lenalidomide, and dexamethasone. The median time from diagnosis to transplant was 12 months (8-22). Most patients (24, 79%) were transplanted in first complete remission (CR1). The most common conditioning regimen was high dose melphalan, dosed at 200mg/m2. Nine patients (31%) received a reduced dose of melphalan (140mg/m2) in view of reduced GFR, poor ECOG performance status, secondary amyloidosis, and other co-morbidities. The median stem cell dose was 5.44 x106/kg (4.98-6.01 x 106/kg). The median time to engraftment was 9 days (8-10). Mucositis was the most common complication post ASCT (26, 90%), and grade 3/4 mucositis complicated seven transplants (24%). Three patients (10.3%) died during the post-ASCT neutropenic period secondary to sepsis. Eleven patients (42%) relapsed, and the median duration of remission (PFS) post-ASCT was 34 months (30.5-40.5) (Figure 1). Of those who relapsed, five (45.5%) died of disease progression, one died (9%) of myocardial infarction and five patients (45.5%) were alive at the time of the last follow-up. The OS was 89.7% with the median survival time post-ASCT being 39 months (7-60).



International Myeloma Society

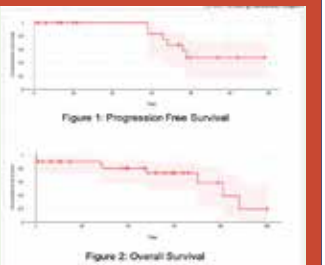


Figure 1: Progression Free Survival

Figure 2: Overall Survival

CONCLUSION

ASCT remains the standard of care for patients with multiple myeloma, especially in lower-middle income countries where access to second-line therapies is limited

Keywords: India, Melphalan, Mucositis, Progression-Free Survival, Transplantation, Autologous

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Papers Presented at IMS 2023

P-065

TITLE: WHOLE BODY LOW DOSE CT (WBLDCT), AS INITIAL IMAGING MODALITY FOR NEWLY DIAGNOSED MULTIPLE MYELOMA PATIENTS: EXPERIENCE FROM A TERTIARY CARE CENTER IN NORTH INDIA

Sanjeev*, Sauvic Saha, Raghu nandan#, Hira Lal#, Faheema Hasan, Manish kumar singh Dinesh chandraK Rahman, Ruchi Gupta, Rajesh Kashyap, Soniya Nityanand

I block, Department of Hematology, Sanjay Gandhi postgraduate institute of medical sciences, Lucknow, Uttar Pradesh, India, PIN-226014

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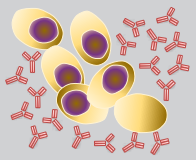
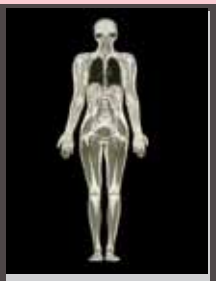
01 INTRODUCTION

For decades, the main imaging modality to detect bony lesions in multiple myeloma was whole body skeletal survey by X ray. However, X - ray had limited sensitivity and specificity. Hence, CT, MRI and PET CT came to Fore-front with better sensitivity and specificity as well as detection of extramedullary soft tissue disease. The disadvantage with CT was the high radiation dose required; hence, whole body low dose CT protocols were developed and have become the one of the investigation of choice to detect lytic lesions in multiple myeloma along with whole body MRI. We herein present Whole body low dose CT (WBLDCT) findings in Serial patients of plasma cell dyscrasia for past 1 year.

02 MATERIAL / METHODES

We retrospectively collected the data from Hospital information system (HIS) & Radiology department for our serial patients of plasma cell dyscrasia from Jan 2022 to Dec 2022. All Patients were evaluated For Myeloma related Bone diseases By WBLDC at Base line. There Myeloma related evaluation was also done as per the IMWG guidelines.



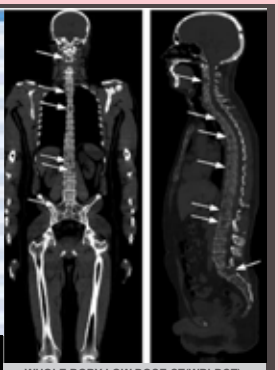


Whole Body MRI

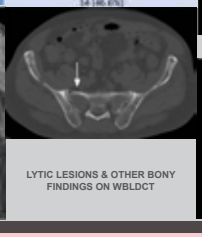
WHOLE BODY PET CT

03 RESULTS

	No. of cases (%)
Hypercalcaemia	7 (18.4%)
Kidney injury	16 (42.1%)
Anaemia	21 (55.3%)
Lytic lesions	
Skull	8 (21.1%)
Vertebra	14 (36.8%)
Ribs and sternum	10 (26.3%)
Sacrum and pelvis	11 (28.9%)
Long bone	8 (21.1%)
Lytic lesions more than 3	7 (18.4%)
Extramedullary disease	5 (13.2%)
Immunofixation	
IgG kappa	13 (34.2%)
IgG lambda	15 (39.5%)
IgA kappa	1 (2.6%)
IgA lambda	1 (2.6%)
Kappa light chain	3 (7.9%)
Lambda light chain	3 (7.9%)
R ISS stage	
1	2 (6.7%)
2	14 (46.7%)
3	14 (46.6%)



WHOLE BOBY LOW DOSE CT(WBLDCT)



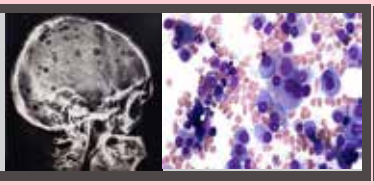
LYTIC LESIONS & OTHER BONY FINDINGS ON WBLDCT

04 DISCUSSION

The patients included were 38, out of which 29 cases of multiple myeloma, 5 cases of MGUS, 1case of smoldering multiple myeloma, 1 case of non secretory myeloma, 1 case of plasmacytoma and 1 case of plasma cell leukemia. There was presence of lytic lesions in 20 out of the 29 patients of multiple myeloma. The most commonly affected site was vertebra (36.8%) followed by sacrum and pelvis (28.9%), ribs and sternum (26.3%), skull (21.1%) and long bones (21.1%). In 7 patients (18.4%), lytic lesions were involving 3 or more sites. In 4 patients, bone lesions were the only CRAB feature present, which upgraded the diagnosis from SMM to multiple myeloma. Extramedullary disease was detected in 5 patients (13.2%). 17 out of the 20 patients (85%) with bone lesions were ISS Stage 3 whereas only 11 such patients (55%) belonged to R ISS Stage 3. We further analyzed the 7 patients who had 3 or more lytic lesions. Extramedullary disease was present in only 2 of the 7 patients. On serum immunofixation, 3 of these patients were IgG kappa, 2 were kappa light chain, 1 was IgA lambda and 1 was lambda light chain. FISH panel did not reveal any mutations in 5 patients while the rest of the 2 patients had gain 1q. All of the 7 patients belonged to ISS Stage 3. 4 patients had R ISS Stage 2 while 3 patients had R ISS Stage 3.

05 CONCLUSION

Imaging plays a very important role in the initial diagnosis and Surveillance of multiple myeloma patients. Although our study was limited by a small sample size, this is one of the first studies describing Whole body low dose whole body CT in myeloma patients in Indian Scenario.



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P-428

Clinicopathological profile and treatment outcomes in patients with Monoclonal gammopathy of renal significance (MGRS): a single centre experience

Aditya Jandial[1], Ritambhra Nada[2], Uday Yanamandra[1], Charanpreet Singh[1], Arihant Jain[1], Deepesh Lad[1], Gaurav Prakash[1], Alka Khadwal[1], Raja Ramachandran[3], Ritu Aggarwal[4], Reena Das[5], Pankaj Malhotra[1]

Departments of [1]Clinical Hematology and Medical Oncology, [2]Histopathology, [3]Nephrology, [4]Immunopathology, [5]Hematology PGIMER, Chandigarh (India)

INTRODUCTION

- A rare group of disorders characterized by abnormal monoclonal protein produced by a plasma cell or B-cell clone that results in renal dysfunction
- Do not meet the diagnostic criteria for Multiple myeloma or other plasma cell disorders
- Need renal biopsy for the confirmation of diagnosis
- One or more kidney lesions that are related to the produced monoclonal Ig
- Lack of/inadequate treatment may lead to end-stage renal disease (ESRD)
- Limited consensus on the optimal treatment strategies
- Limited literature on MGRS from India

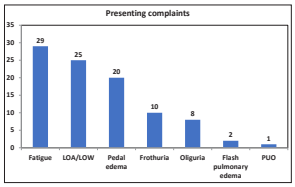
METHODS

- Study type: Retrospective, single centre
- Study duration:
  - January 2013 to December 2022
- Inclusion criteria:
  - Confirmation of MGRS on renal biopsy
- Exclusion criteria –
  - Multiple myeloma (MM)
  - Cast nephropathy and/or AL Amyloidosis on renal biopsy
- Hematologic response:
  - Complete response (CR) : normalization of FLC achieved.
  - Very good partial response (VGPR): >90% monoclonal protein reduction
  - Partial response (PR): >50% monoclonal protein reduction
- Renal response: >30% reduction of 24 h proteinuria (in the absence of renal progression)

RESULTS

Baseline Clinico-pathologic profile

Characteristic	N (%) or median [range]
Total no. of patients	31
Male gender, n (%)	17 (54.8%)
Median age, years	48 (29 – 65)
Median duration of symptoms, months	6 (1 - 24)
High BP at diagnosis	16 (51.6%)
Comorbidities	
Hypertension	9 (29.0%)
Diabetes mellitus	6 (19.3%)
Dialysis requirement at baseline	7 (22.5%)



Baseline Investigations

Characteristic (N = 25)	N (%) or median [range]
Kappa subtype	25 (80.6%)
Positive SPEP, n (%)	14 (45.2%)
Positive SIFE, n (%)	18 (58.0 %)
Serum creatinine, mg/dL	2.6 (0.8 – 7.8)
eGFR, ml/min	26.1 (7.6 – 105)
Nephrotic-range proteinuria (≥3 g urine protein/24 h)	13 (41.9 %)
BM Plasma cells, %	4 (1 - 12)
Beta-2 microglobulin	6.6 (3.9–15.6)
LDH	196 (168–216)

MGRS: Clinical Syndrome

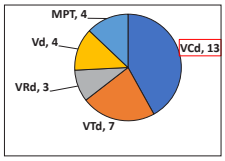
- Isolated renal insufficiency: ↓ eGFR (<60 ml/min) ± proteinuria (>1g/24h) — 17/31 (54.8%)
- Renal insufficiency + significant Proteinuria (Mixed group): ↓ eGFR + significant proteinuria — 7/31 (22.5%)
- Isolated Proteinuria: Significant proteinuria (>1g/24h) ± ↓ eGFR (<60) — 7/31 (22.5%)

77.4%

Renal pathology

Characteristic	N (%)
MIDD	20 (64.5%)
LCDD	19 (61.2%)
LHCDD	1 (3.2%)
PGNMID	4 (12.9%)
C3 glomerulopathy	3 (10.6%)
Cryoglobulinemic GN	2 (6.4%)
Crystal-storing histiocytosis	1 (3.2%)
Light chain proximal tubulopathy	1 (3.2%)

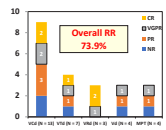
Treatment regimens

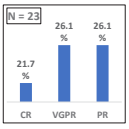


Treatment details

- Median no. of Rx lines: 1 (1 - 2)
- Median Rx duration: 8 m (2 – 24 m)
- Maintenance Rx: 11 (35.5%)
- ASCT: 3 (9.6%)
- Renal transplant: 4 (12.9%)

- Median time to best hematologic response: 6 months (4 - 12)





	N (%)	Renal Response
Isolated renal insufficiency	17 (54.8%)	7/17 (41.2%)
Renal insufficiency + Proteinuria	7 (22.5%)	3/7 (42.8%)
Isolated proteinuria	7 (22.5%)	6/7 (85%)

41.6%

- 2/7 patients became dialysis independent
- Median time to best renal response: 12 months (6 - 24)

- Median follow up: 8 months (2 – 96 months)
- Seven patients died during follow up
- OS of study cohort: 77.4%

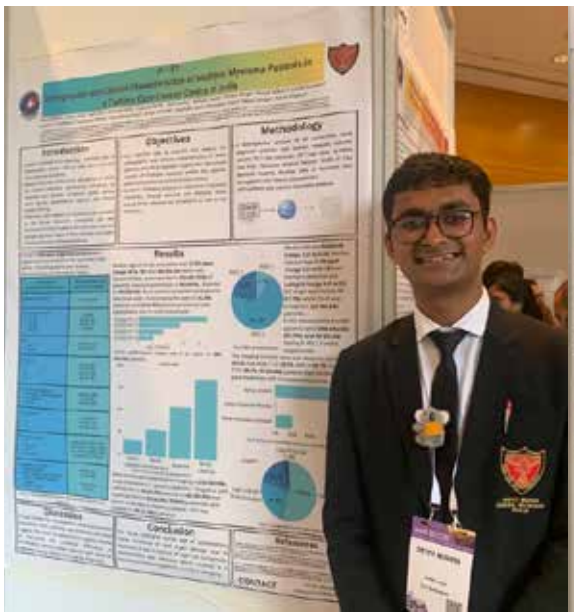
Study limitations

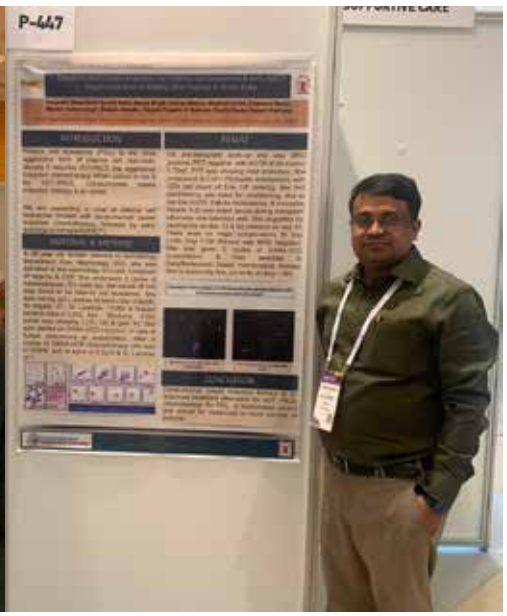
- Retrospective analysis, single center
- Small sample size

COI disclosure: None

CONCLUSIONS

- MGRS is a heterogeneous group of disorders
- Achievement of deep hematologic response possible with clone-directed therapy
- Need for uniform renal response criteria
- Low GFR at baseline is risk factor for suboptimal renal response





Awareness Meetings - March

Myeloma Awareness Month x2

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Dr. Anupam Brahma

Total Amount

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21st Annual Conference at IMS 2024

ACTIVITIES & EVENTS

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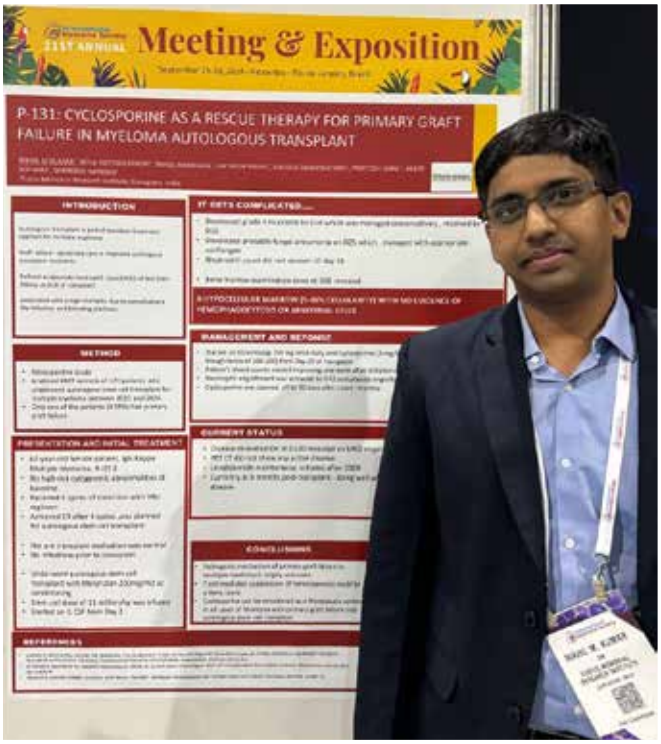
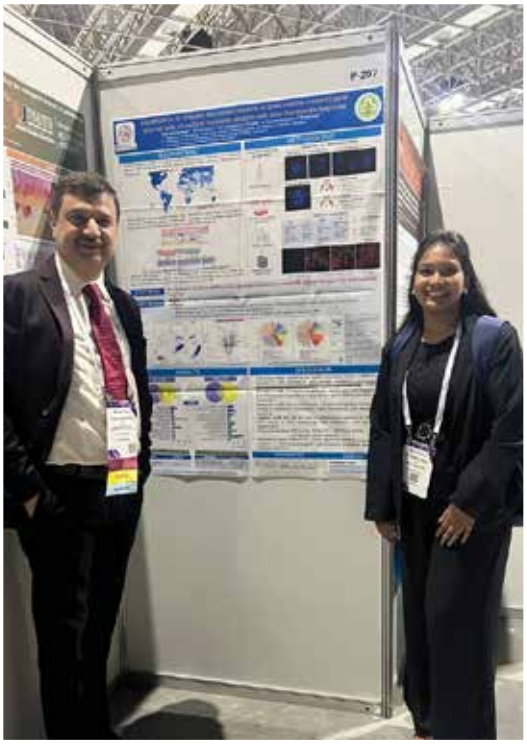
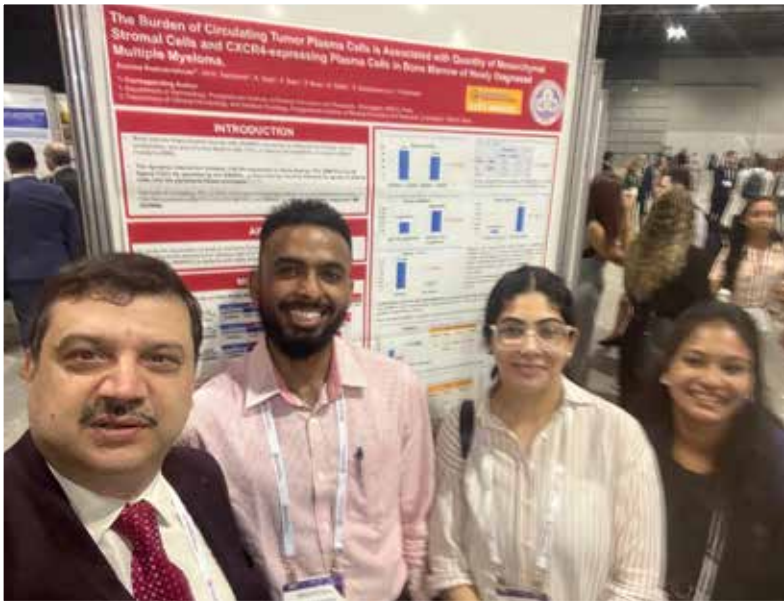
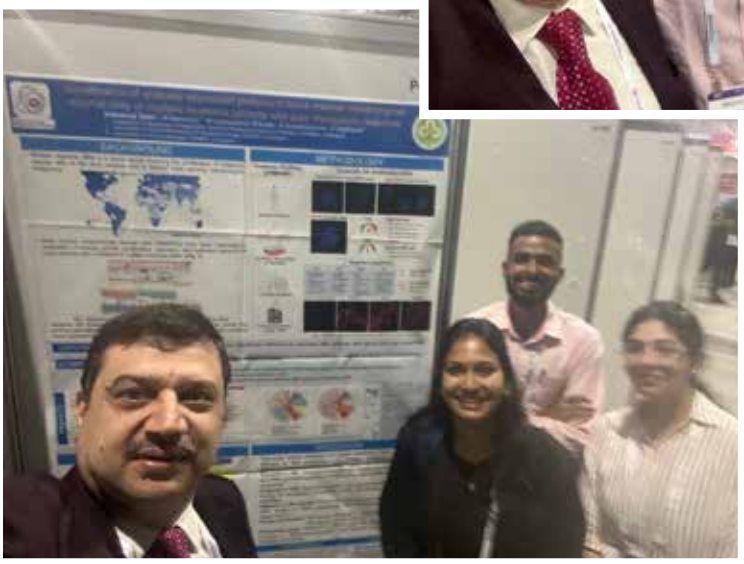








ACTIVITIES & EVENTS

Papers Presented at IMS 2024

Waldenstrom's Macroglobulinemia: Clinical presentation & treatment outcome from a tertiary care centre from India

Sanjeev, S Saha, S Kumar, M k Singh, D Chandra , K Rahman , R Gupta, R Kashyap

Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, Uttar Pradesh, India, PIN-226014

INTRODUCTION

Waldenstrom's Macroglobulinemia (WM) is a low grade, B-cell lymphoma characterized by the infiltration of the bone marrow by clonal lymphoplasmacytic cells that secrete monoclonal IgM immunoglobulin. This is a rare B NHL, which has an indolent course but remains incurable. It is characterized by MYD88 mutation, which is seen in 90% of patients. CXCR4 is the second most common mutation seen in 40% of patients. Since this is a rare malignancy, there is not much published literature in Indian settings. We herein present baseline characteristics and treatment outcomes of patients with Waldenstrom's Macroglobulinemia from a tertiary care centre in north India.

AIM

This is a single-centre retrospective study of WM patients diagnosed at our centre over a period of 86 months (Jan 2016–Jan 2024) and followed up till May 2024 (Median follow up duration 46 months). Electronic medical records and case files were analyzed for all these patients, and data was recorded. Only patients fulfilling the Mayo Clinic criteria for the diagnosis of active WM at baseline were included in the study

We retrospectively collected the data from Hospital information system (HIS) & Radiology department for patients of Waldenstrom's Macroglobulinemia from Jan 2016 to January 2024.

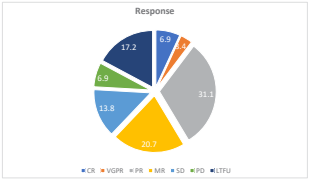
METHOD

We utilized the well-established International Prognostic Scoring System for Waldenstrom's Macroglobulinemia (IPSSWM) criteria to risk-stratify patients. Based on baseline lab and clinical parameters, all patients were risk stratified as per IPSSWM criteria, and overall survival was obtained as per risk stratification. The overall survival (OS) was calculated from the date of diagnosis to death from disease-related cause or final follow-up date. in patients with Waldenstrom's Macroglobulinemia (WM) . Overall response rates (ORR) of patients treated with 1st line chemotherapy were estimated as the best response at the end of a first-line treatment protocol. Response criteria were defined, complete remission (CR), partial response (PR) and very good PR (VGPR) as per the update of the consensus panel criteria for assessing clinical response

RESULTS

We had a total of 46 patients diagnosed with WM. The median age was 65 years with male preponderance (82.6%). Lymphadenopathy was seen in 18 patients (39.1%), splenomegaly in 11 patients (23.9%) and hepatomegaly in 7 patients (15.2%). One patient had presented with features of hyper viscosity. Mean Hb was 7.6g/dl and mean platelet count was 1.31l/dl. Mean M band on SPEP was 2.7. On IFE, majority were IgM kappa (89.1%). MYD88 mutation status was seen in 25 patients. 23 out of these 25 patients (92%) had positive MYD88. The patients were further stratified according to R IPSSWM. 2(4.3%) patients belonged to low risk, 8 (17.4%) had intermediate risk, 21 (45.7%) had high risk and 15 (32.6%) had very high risk. 29 out of the 46 patients underwent therapy at our institute. The commonly used regimens were Bortezomib, Dexa and Rituximab (BDR), Rituximab Bendamustine and Rituximab Cyclophosphamide Dexa (RCD). 5 patients were lost to follow up after initiation of therapy and hence their response could not be assessed. Out of the remaining patients, CR was observed in 2 patients, VGPR in 1 patient, PR in 9 patients and MR in 6 patients. ORR was 75%. 4 patients had stable disease and 2 patients had progressive disease. 7 patients had relapsed after frontline therapy. 3 patients received R Benda and 2 patients received BDR as 2nd line therapy. 1 patient expired and 1 patient was lost to follow up after relapse. 1 patient, who had received R Benda as 2nd line relapsed and was started on Acalabrutinib. A total of 4 patients died. 2 patients died due to disease complications in the form of hyper viscosity and sepsis with DIC. 1 patient died at relapse due to sepsis. 1 patient, in 2nd remission, died to road traffic accident.

Baseline characteristics	N=46
Median age	65 years (47-85 years)
Sex	Male- 82.6% Female- 17.4%
Lymphadenopathy	18 (39.1%)
Hepatomegaly	7 (15.2%)
Splenomegaly	11 (23.9%)
Lung lesion	1 (2.1%)
Hyperviscosity	1 (2.1%)
Mean Hb (g/dl)	7.6 (1-13.7)
Mean platelet count(x10^9/l)	131 (8-333)
Mean M band (mg/dl)	2.7 (0.3-5.4)
IFE	IgM kappa- 41 (89.1%) IgM lambda- 5 (10.9%)
MYD88	Positive- 23(50%) Not done- 23
R IPSSWM	Very low- 0 Low- 2 (4.3%) Intermediate- 8 (17.4%) High- 21 (45.7%) Very high- 15 (32.6%)



CONCLUSIONS

In this study, we report the presenting features as well as the treatment outcomes of Waldenstrom's 's Macroglobulinemia. The response rates were lower when compared to Western literature. However, this is one of the few Indian studies, till date, to report on the characteristics of the disease.

ACKNOWLEDGEMENT

Senior residents, clinical & Lab faculties, Department of hematology, SGPGI Patients & their caregivers

IMAGe Society

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Global Myeloma Action Network Summit 2024

IMF Asian Myeloma Network 8th Summit 2024

Total
₹3.34 Lakhs
awarded to Dr. Uday Yanamandra was donated to IMAGe

IMF AMN 8th Summit 2024

Travel Sponsor to Doctors

Dr. V.A. Arun

Dr. Sumeet Mirgh

Total Amount

₹93,512

spent for travel fellowships

IMS Membership for EC members

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Membership Fees

₹33,500/-

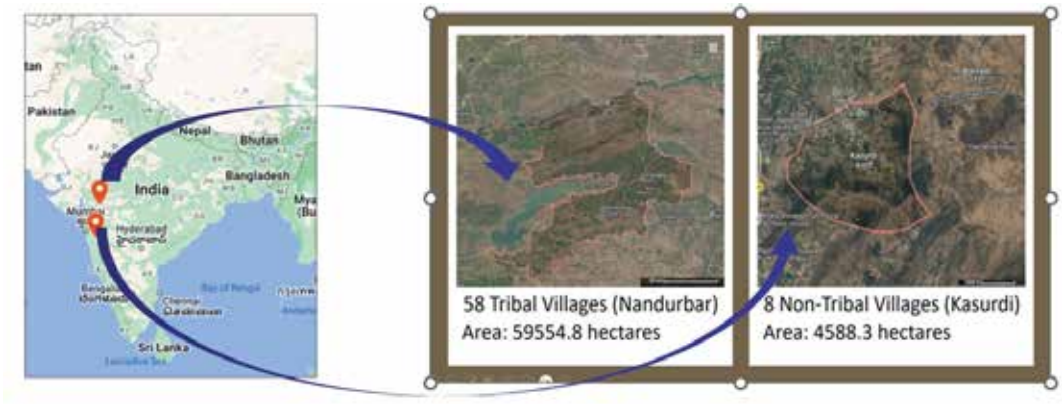
Door to Door Screening for Monoclonal Gammopathies

Screening of Tribal Population at Nandurbar Distt, Maharashtra for Monoclonal Gammopathies

In Collaboration with AFMC

9040
Individuals
From
53
Villages/ Hamlets

Google Map Location



People Supported by IMAGe

One Civilian BPL patient transplant at CHSC Pune

Mr. Somnath Ganpat Yadav

Click the link below youtube link for the video:
https://www.youtube.com/shorts/YDiq5xofzKk

Total Amount Spent

₹56,719

Number of patients helped for Investigations by IMAGe - 64

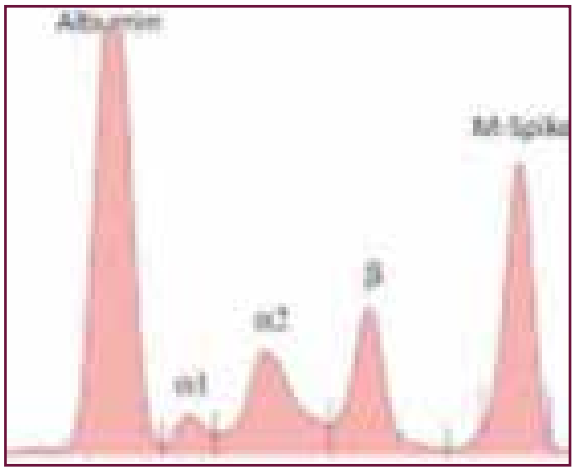
Number of Patients

64

Total Cost

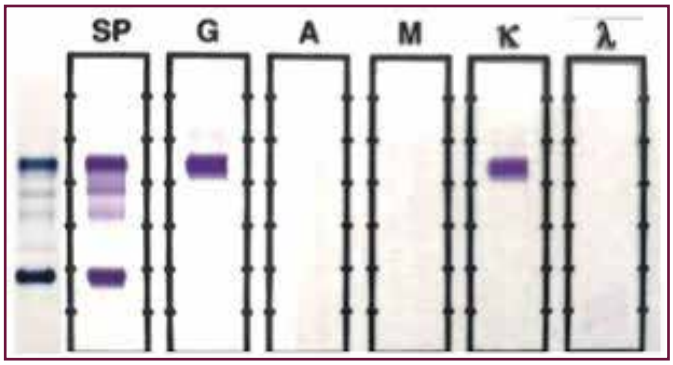
₹1,89,495/-

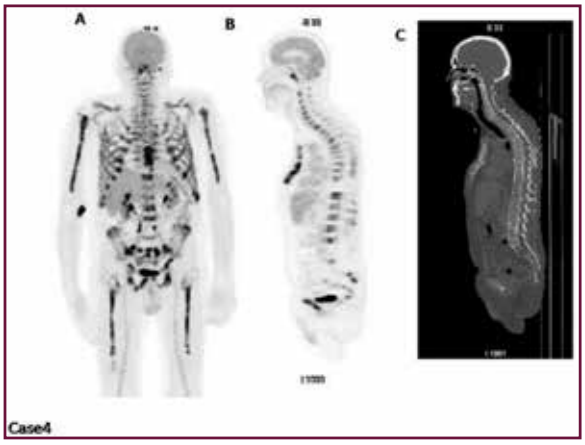
Types of Tests



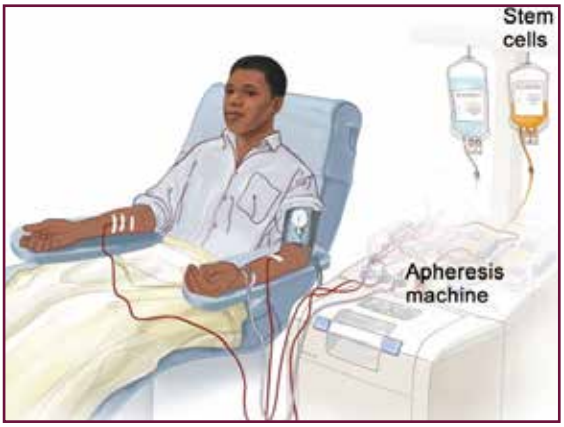
SPEP
54 Patients

SIFE
50 Patients





PET/CT Scan
09 patients



Pre-transplant Investigation -
1 patient

Representative images only and not of actual patients investigated

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Congratulations

₹15,000 Gift Vouchers

First group of Nurses trained formally for Post Diploma in HSCT in India

NURSES

Ms. C. Freeda Mobel

Ms. Reshma Vijay

Ms. Aishwarya

AWARDS & ACCOLADES

Dr. Vincent Rajkumar
Took over as Chairperson of the Board of the International Myeloma Foundation

Dr. Shaji Kumar
Bart Barlogie Award 2023, Took over as Vice President of IMS & ISA president

Dr. Sagar Lonial
Bart Barlogie Award 2024

Dr. Sundar Jagganath
Waldenström Lifetime Achievement Award 2023 & Robert Kyle Life time achievement award in IMS 2024

Reflection

Dr. Sathya P.

Ph.D. (Hematopathology)

Flow Cytometry Consultant/Scientific Officer :

Department of Laboratory Sciences at Kannappa Memorial Hospital, Chennai, India.

Recipient :

Dr. K.C. Das Memorial Award from the ISHBT Society at HAEMATOCON 2023 for paper titled "Quantification of Circulating Clonal Plasma Cells by Multiparametric Flow cytometry as a prognostic marker in patients with newly diagnosed myeloma"

Thank you very much Uday sir for your kind response and generous support. Since 2019, I have been regularly attending the Indian Myeloma Congress, which has been an invaluable experience for me. The expert insights shared during these meetings, along with your unwavering commitment to advancing myeloma research in developing countries like India, have greatly influenced my work.

Inspired by the growing focus on myeloma research across various institutions, I have dedicated myself to this field despite coming from a different background. Over the years (9 years), I have expanded my research to encompass myeloma and other hematological malignancies, including acute leukemia and lymphoma. I am proud to share that I was the first Ph.D. scholar to establish a flow cytometry laboratory in our institute, where we currently perform over 20 assays. These efforts provide free diagnostic support to clinicians and directly benefit patients.

Looking ahead, I aspire to pursue a post-doctoral fellowship, particularly in the field of myeloma research, to deepen my expertise and contribute further to this important domain. I am excited about the opportunity to meet you in person at the upcoming Congress and share more about my work and future plans.

I would like to take this opportunity to express my gratitude to my guide, co-guides, and the faculty members from my department, whose guidance and encouragement have been instrumental in my journey. Attending the Myeloma Congress in 2019 was a turning point for me, as it helped me realize the importance of aligning research outputs with the needs of patient care. It deepened my understanding of how impactful research can directly contribute to improving treatment protocols.

Since then, I have worked diligently to expand my knowledge and expertise, not just in myeloma but across various hematological malignancies. This journey has been both inspiring and fulfilling, as it has allowed me to make meaningful contributions to patient care and diagnostic advancements.

Thank you Uday sir once again for your support and for fostering an environment that inspires researchers like me to strive for excellence in this critical field.

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