# NEWSLETTER

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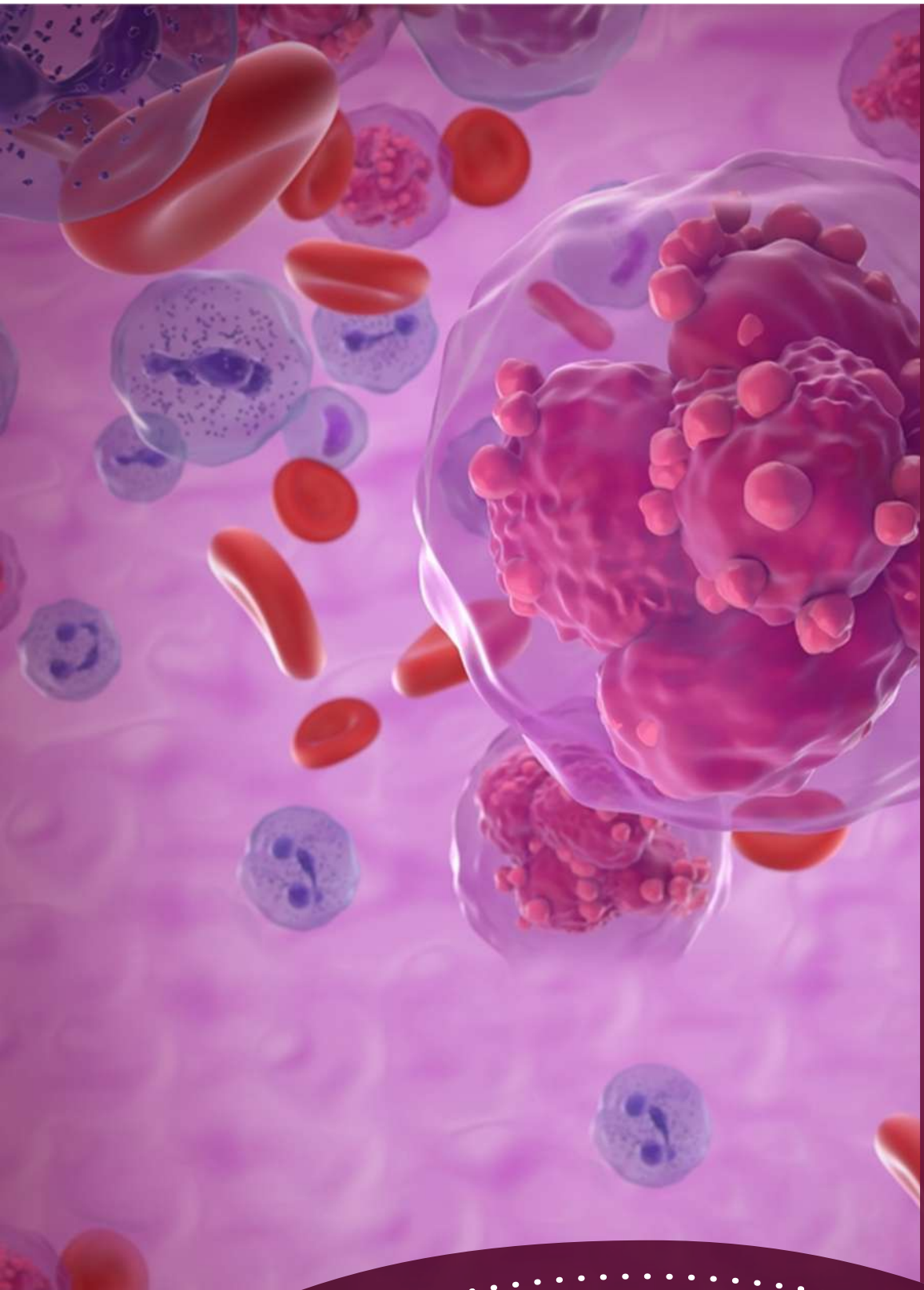
*An Indian Myeloma Academic Groupe Publication (IMAGe)*





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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

**Maj. (Dr.) Abhinav Kumar**
Asst. Professor,
Dept. of Internal Medicine,
AFMC, Pune

Facon T, Kumar SK, Plesner T, Orlowski RZ, Moreau P, Bahlis N, et al. Daratumumab, lenalidomide, and dexamethasone versus lenalidomide and dexamethasone alone in newly diagnosed multiple myeloma (MAIA): overall survival results from a randomized, open-label, phase 3 trial. The Lancet Oncology. 2021 Nov 1;22(11):1582-96.

**Background**
This article covers the updated follow-up data of the patients enrolled in the MAIA trial at 56 months.

**Methods**
MAIA trial is a randomised, open-label, active-controlled phase 3 trial. Newly diagnosed multiple myeloma patients above the age of 18 were included in the trial. These patients were ineligible for upfront toxic chemotherapy and transplant. The exposure group received intravenous daratumumab plus oral lenalidomide and oral dexamethasone whereas, the control group received lenalidomide and dexamethasone alone. PFS was taken as the primary endpoint while secondary endpoints included OS, VGPR( Very good partial remission), PR and safety.

**Findings**
A total of 737 patients were randomly allocated to the exposure(n=368) and the control group(n=369). At the end of 56 months (IQR 52·7–59·9) of follow up median PFS was not reached in the Daratumumab group while in the control group, it was documented at 34·4 months (29·6–39·2). Median OS was not reached in both groups.

**Interpretation**
Daratumumab added to Dexamethasone and Lenalidomide showed significant improvement in PFS and OS when compared to Dexamethasone and Lenalidomide alone, in transplant-ineligible newly diagnosed Multiple Myeloma patients. There was no new safety concern identified in the follow-up analysis.

**Commentaries –**

**PECOT analysis:**

- **P**articipants: 737 Patients who were transplanted ineligible Multiple myeloma patients. They were randomized and allocated to exposure and comparison groups.
- **E**xposure group: This group received Daratumumab in addition to Dexamethasone and Lenalidomide.
- **C**omparison group: This group received Dexamethasone and Lenalidomide alone.
- **O**utcome: Significant PFS and OS benefit was documented in the Exposure group.
- **T**ime duration: March 2015 to October 2021.

**Limitations:**

The open-label study design might have led to a bias for early patient withdrawals in the VD group.
The primary endpoint of PFS rather than OS was suboptimal to address the clinical question at hand.
Sample size calculation was based on PFS assumptions alone.
The trial used a control treatment which is not presently the standard of care.

**Conclusion:**

Taken together, the study data showed longer OS with Daratumumab in transplant-ineligible newly diagnosed multiple myeloma. These study conclusions are fraught with multiple caveats as discussed above.

D'Agostino M, Cairns DA, Lahuerta JJ, Wester R, Bertsch U, Waage A, Zamagni E, et al. Second Revision of the International Staging System (R2-ISS) for Overall Survival in Multiple Myeloma: A European Myeloma Network (EMN) Report Within the HARMONY Project. J Clin Oncol. 2022 Oct 10;40(29):3406-3418. doi: 10.1200/JCO.21.02614. Epub 2022 May 23. Erratum in: J Clin Oncol.2022 Dec 1;40(34):4032. PMID: 35605179.

**Dr. Stalin Chowdary Bala**
Associate Prof.
Dept. of Medical Oncology,
Nizam’s Institute of Medical Sciences(NIMS)
Hyderabad

**Summary:**

Multiple myeloma is one of the hematological diseases associated with heterogeneous outcomes and survivals ranging from months to years. Revised ISS staging was proposed in 2015 which used ISS stage, LDH and presence of high-risk chromosomal abnormalities (CAs). R2-ISS was planned to address the main drawbacks of the R-ISS that 62% of patients were classified into the intermediate-risk category (R-ISSII) and 1q+ not being classified as high risk CA. The data of the patients enrolled in 16 international multicentre trials from 2005 to 2016 was used to develop R2-ISS. del (17p), gain/amp (1q21), t (4;14), and t(14;16) were the CAs used for developing R2-ISS. The patient population was divided into a training set (7,072 patients enrolled in 15 clinical trials) and a validation set (3,771 patients treated in the UK NCRI Myeloma XI trial. The top predictors significantly affecting both OS and PFS (ISS, del (17p), LDH, t(4;14), and 1q+) were used to build an additive score. A score value was given for ISS stage and each CA so that a total additive score can be formed. Based on the total score, patients were sub grouped into 4 stages, Low (I), Low-intermediate (II), High Intermediate (III) and High (IV). In the training set, R2-ISS I, II, III, and IV patients were 19.2%, 30.8%, 41.2%, and 8.8% respectively. Median OS was NR, 109.2, 68.5, 37.9 months with a 5-year OS rate of 88%, 75%, 56%, and 37% in the R2-ISS I, II, III, and IV groups, respectively. The main aims of the study to delineate R ISS II stage and to use 1q+ for staging were met and thus R2 ISS had 4 stages for better prognostication of the newly diagnosed myeloma patients. The R2-ISS score included simple and widely used prognostic markers, and the additive nature of its calculation easily allows the future inclusion of new prognostic variables and compared with the R-ISS, it showed an improved discriminating capability, especially in the large group of patients with intermediate-risk NDMM.

**Commentary:**

This study was designed to develop a new prognostic system in multiple myeloma by incorporating newer poor prognostic markers like 1q+ and also to delineate the intermediate stage R-ISS which constitute the majority and represent heterogeneous group of patients. R2-ISS was developed by using the data of the patients enrolled in various clinical trials in Europe and impact of this staging system on outcomes in patients of other countries and in the real world are not known. Also t(14; 16) one of the poor prognostic marker in myeloma is excluded from analysis and there is good data previously to show the bad prognostic impact of t(14:16) on outcomes. Patients enrolled in clinical trials are carefully selected with good performance status and without significant comorbidities; different from real world scenario and impact of patient related factors were not addressed in this newer staging system. Though the primary end point of this analysis was met and new prognostic scoring system was developed by using high risk chromosomal abnormalities and ISS stage, the validity of such prognostic system in day to day practice is exactly not known and it needs further validation in other countries and in real world practice.

"Inshorts-Through expert's lens" Journal Club

**Dr. Annie Kanchan Baa**
MD, DM
Assistant Prof.,
Dept. of Medical Oncology,
St. John's Medical College & Hospital,
Bangalore

Chari A, Minnema MC, Berdeja JG, Oriol A, van de Donk NW, Rodríguez-Otero P, Askari E, Mateos MV, Costa LJ, Caers J, Verona R. Talquetamab, a T-Cell–Redirecting GPRC5D Bispecific Antibody for Multiple Myeloma. New England Journal of Medicine. 2022 Dec 15;387(24):2232-44.

**Summary:**

The feasibility of Talquetamab, an anti-GPRC5D x CD3 bispecific antibody in relapsed refractory multiple myeloma(RRMM) was explored in phase 1, MonumenTAL-1 study. The dose escalation phase (part-1) enrolled a total of 232 patients; testing doses 0.5-180mcg/kg and 5-1600mcg/kg in intravenous (n=102) and subcutaneous (n=130) cohorts respectively. The key objective of choosing the Recommended Phase 2 dose (RP2D) was based on the subcutaneous route's (doses: 405mcg/weekly and 800mcg/q2weekly) favourable safety, efficacy, pharmacokinetic and pharmacodynamic profile. The dose expansion phase (part-2) recruited 74 patients with 405mcg/kg/weekly (n=30) and 800mcg/kg/q2weekly(n=44) given subcutaneously as the RP2D.

The common adverse events were cytokine release syndrome ( in77% and 80%; grade 3 seen in 1 patient ); skin/nail-related toxicities (in 67% and 70%; related to on-target Talquetamab activity) and dysgeusia (in 63% and 57%). The grade 3 & 4 haematological events encountered were reversible and seen during the step-up dosing schedule. The response rates were 70% (CI:51-85) and 64% (CI:48-78) after a median follow-up of 11.7 months (405mcg) and 4.2 months (800mcg)) respectively.

**Commentary:**

GPRC5D (G-protein coupled receptor, family C, group 5, member D), an orphan receptor has emerged as an attractive target for patients with RRMM. Protein shedding which leads to the "sink effect" was comparatively lower. Talquetamab, a novel T-cell redirecting bispecific antibody, appears tolerable in heavily pretreated patients with RRMM. The 800mcg SC Q2wkly appears to have comparable efficacy and safety to the 405mcg weekly dose. The overall response rates were encouraging across all patients, including those who were triple-class and penta-drug refractory (67-70%). The responses were durable and deepened over time. It has proven to be a promising option for those who progressed on BCMA-directed therapies, due to its independent expression. However, the severity of dysgeusia resulting in weight loss is an adverse event of concern. Also, the sequencing of Talquetamab in the CART era is unanswered, further studies exploring the same are warranted.

## Awards and Accolades

**1ST TEAM:** Nizam's institute of medical sciences, Hyderabad

**Dr. G. Sindhu**
Final Year resident
D.M. Medical Oncology
Nizam's institute of
Medical Sciences, Hyderabad

INR 100000

**Dr. Susmita Sadhukhan**
Finla Year Resident
D.M. Medical Oncology
Nizam's institute of
Medical Sciences, Hyderabad

**2ND TEAM:** Madras Medical College

**Dr. Gayathri R Nair**
Final year resident
DM Medical Oncology
Madras Medical College

INR 50000

**Dr. Dinesh R**
Final year resident
DM Medical Oncology
Madras Medical College

**3RD TEAM:** Sanjay Gandhi Postgraduate Institute of Medical Sciences

**Dr. Nitin Chaudhary**
Senior Resident, 3rd Year
SGPGI, Lucknow

INR 20000

**Dr. Poorvi Kapoor**
Senior Resident
DM clinical Hematology
SGPGI, Lucknow

**1ST Prize:** STEM Talks

**Dr. Shreyasi Seth**

**2ND Prize:** STEM Talks

**Dr. Neha Shibu**

**3RD Prize:** STEM Talks

**Dr. Karthik**

"Annual Myeloma Quiz during IMC 2023"

AWARDS & ACCOLADES

"Annual Myeloma Quiz during IMC 2023"

AWARDS & ACCOLADES

## ORAL PRESENTATION


**DR. SUMEET MIRGH**
Assistant Professor,
Adult Hematolymphoid and BMT,
Tata Memorial Centre,
ACTREC (Advanced Centre for Treatment, Research and Education in Cancer),
Mumbai, India


**DR. SHELLY SINGLA**
DM Hematopathology
(Senior resident- Fifth semester)
Department of Hematology
Postgraduate Institute of Medical Education and Research,
Chandigarh


**DR. ADITYA JINDAL**
Senior Research Associate
Dept of Clinical Hematology and Medical Oncology
PGIMER Chandigarh

## E-POSTER

★★★
1ST PRIZE
INR - 50,000
Dr. Pavithra S

★★★
2ND PRIZE
INR - 30,000
Dr. Harshini Sriram

★★★
3RD PRIZE
INR - 20,000
Dr. Reshmy G S

Article - Kadam Amare P, Nikalje Khasnis S, Hande P, et al. Cytogenetic Abnormalities in Multiple Myeloma: Incidence, prognostic significance and geographic heterogeneity in Indian and western population [published online ahead of print, 2023 Feb 13]. Cytogenet Genome Res. 2023;10.1159/000529191. doi:10.1159/000529191

**Prelude:**

Multiple Myeloma (MM) is genetically complex and heterogeneous neoplasm in which cytogenetics plays an important role in the risk stratification of disease. High risk MM as per cytogenetics include primary IGH translocations t(4;14), t(14;16), t(14;20), and secondary progressive aberrations such as gain/Amp(1q), 1p deletion, del(17p) & hypodiploidy. Metaphase cytogenetics typically gives a poor yield in myeloma, while interphase FISH (iFISH) can detect >90% cytogenetic abnormalities. This study highlights the incidence of cytogenetic abnormalities in Indian population (vs western population), frequency of double-hit and triple-hit myeloma, and corelation of metaphase cytogenetics with iFISH.

**Summary:**

Data from 1104 patients over a 7-year period (2016-2022) was analysed to decipher correlation of conventional karyotyping with FISH and to seek the geographic heterogeneity in the incidence of primary as well as secondary aberrations in our Indian vs Western population. iFISH was performed on isolated plasma cells (using CD138–coated magnetic beads) and karyotype analysis (minimum 20 cells karyotyped) was done as per ISCN, 2016,2020. Hyperdiploid MM was defined as presence of trisomy of ≥2 odd number of chromosomes. Cut-off threshold for del(13q)/-13, del17p, 1qgain/Amp was 5%, while for IGH translocation t(14q32) and trisomy was 10%. For biallelic TP53 inactivation, TP53 mutation analysis was performed by Sanger sequencing in 48 cases with del(17p). Majority (85.5%) patients were beyond 50 years of age. Interestingly, conventional karyotyping was successful in 80% cases (n=65/80), it could detect MM-related aberrations in 50% cases, of which 44% revealed highly complex karyotype with common aberrations of chromosome 1q. Overall, FISH abnormalities were seen in 67.6% cases, with an incidence of hyperdiploidy of 41%. The incidence of IGH translocation was 26% vs 40%-50% in western literature. This was primarily because of low incidence of t(11;14) - 6%, in contrast to 15-20% in other series. Most common IGH translocation was t(4;14) – 9% (n=99/1104), while least common were t(6;14) and t(14;20) (both <1%). Most common cytogenetic abnormalities were gain/Amp 1q (32%) and monosomy 13 (31%). There was significant association of monosomy 13 with t(4;14), and gain/Amp (1q) with t(4;14), t(14;16), t(14;20), MYC translocations and variant IGH translocations. The incidence of double hit MM was 13.3% (n=147/1104 cases) and triple hit MM was 5% (n=55/1104). The frequencies of del(13q) (3.4%), monosomy 13 (31%), gain/Amp(1q) (32%), del(17p) (8%) observed in this cohort does not differ markedly from those that has been reported by others, except frequency of del(1p) was comparatively low - 5.7% vs 15-30% reported in literature. Amongst patients with 17p deletion, biallelic inactivation of TP53 was observed in 15% cases. Interestingly, high risk abnormalities [del(17p), gain/Amp(1q), IGH partial deletion] were associated with hyperdiploid group, which has not been reported by previous studies. These findings strongly indicate that racial disparity leads to geographic heterogeneity in disease biology.

# Depth of response at day 100 post ASCT – Response matters...

Article - Das N, Dahiya M, Gupta R, et al. Graded Depth of Response and Neoplastic Plasma Cell Index as Indicators of Survival Outcomes in Patients With Multiple Myeloma Following Autologous Stem Cell Transplant. Am J Clin Pathol. 2023;159(1):69-80. doi:10.1093/ajcp/aqac129

**Prelude:**

Multiple Myeloma (MM) is genetically complex and heterogeneous neoplasm in which cytogenetics plays an important role in the risk stratification of disease. High risk MM as per cytogenetics include primary IGH translocations t(4;14), t(14;16), t(14;20), and secondary progressive aberrations such as gain/Amp(1q), 1p deletion, del(17p) & hypodiploidy. Metaphase cytogenetics typically gives a poor yield in myeloma, while interphase FISH (iFISH) can detect >90% cytogenetic abnormalities. This study highlights the incidence of cytogenetic abnormalities in Indian population (vs western population), frequency of double-hit and triple-hit myeloma, and corelation of metaphase cytogenetics with iFISH.

**Summary:**

Data from 1104 patients over a 7-year period (2016-2022) was analysed to decipher correlation of conventional karyotyping with FISH and to seek the geographic heterogeneity in the incidence of primary as well as secondary aberrations in our Indian vs Western population. iFISH was performed on isolated plasma cells (using CD138–coated magnetic beads) and karyotype analysis (minimum 20 cells karyotyped) was done as per ISCN, 2016,2020. Hyperdiploid MM was defined as presence of trisomy of ≥2 odd number of chromosomes. Cut-off threshold for del(13q)/-13, del17p, 1qgain/Amp was 5%, while for IGH translocation t(14q32) and trisomy was 10%. For biallelic TP53 inactivation, TP53 mutation analysis was performed by Sanger sequencing in 48 cases with del(17p). Majority (85.5%) patients were beyond 50 years of age. Interestingly, conventional karyotyping was successful in 80% cases (n=65/80), it could detect MM-related aberrations in 50% cases, of which 44% revealed highly complex karyotype with common aberrations of chromosome 1q. Overall, FISH abnormalities were seen in 67.6% cases, with an incidence of hyperdiploidy of 41%. The incidence of IGH translocation was 26% vs 40%-50% in western literature. This was primarily because of low incidence of t(11;14) - 6%, in contrast to 15-20% in other series. Most common IGH translocation was t(4;14) – 9% (n=99/1104), while least common were t(6;14) and t(14;20) (both <1%). Most common cytogenetic abnormalities were gain/Amp 1q (32%) and monosomy 13 (31%). There was significant association of monosomy 13 with t(4;14), and gain/Amp (1q) with t(4;14), t(14;16), t(14;20), MYC translocations and variant IGH translocations. The incidence of double hit MM was 13.3% (n=147/1104 cases) and triple hit MM was 5% (n=55/1104). The frequencies of del(13q) (3.4%), monosomy 13 (31%), gain/Amp(1q) (32%), del(17p) (8%) observed in this cohort does not differ markedly from those that has been reported by others, except frequency of del(1p) was comparatively low - 5.7% vs 15-30% reported in literature. Amongst patients with 17p deletion, biallelic inactivation of TP53 was observed in 15% cases. Interestingly, high risk abnormalities [del(17p), gain/Amp(1q), IGH partial deletion] were associated with hyperdiploid group, which has not been reported by previous studies. These findings strongly indicate that racial disparity leads to geographic heterogeneity in disease biology.

# When fibrils deposit in heart – an underestimated entity !

Article - Mohan B, Singh S, Tandon R, et al. Clinical profile of patients with cardiac amyloidosis in India. Indian Heart J. 2023;75(1):73-76. doi:10.1016/j.ihj.2022.12.006

**Prelude:**

Cardiac amyloidosis (CA) is characterized by extracellular deposition of amyloid fibrils, leading to progressive cardiac failure. CA is associated with a uniformly poor prognosis worldwide, which is further worsened in India due to delayed diagnosis and advanced presentation. The rarity of cardiac amyloidosis in India is likely a consequence of underdiagnosis and not reduced incidence as previously understood. Earlier and non-invasive detection can be enabled by local adaptation of published guidelines and utilizing already available techniques, including novel echocardiography parameters and histopathology from noncardiac tissues

**Summary:**

Thirteen patients over a period of 4 years (January 2018 – December 2021) were retrospectively analysed. Symptomatic patients with probable suspicion of cardiac amyloidosis (based on echocardiographic parameters and ECG findings) were included. Echocardiographic findings included unexplained left ventricular (LV) wall thickness >/= 12 mm, Grade II-IV diastolic dysfunction, reduced global longitudinal strain (GLS) or speckled pattern of interventricular septum. Supportive electrocardiographic (ECG) criteria included low voltage QRS complexes (≤1.0 mV in precordial leads or ≤0.5 mV in limb leads) or conduction abnormalities. Surrogate evidence for amyloidosis was obtained from either abdominal fat pad or rectal biopsy and evaluation for plasma cell dyscrasia was performed based on current guidelines. Median age of the cohort was 65 years with symptomatic heart failure, as the most common manifestation. Five patients (39%) were diagnosed with multiple myeloma, 80% with concomitant diagnosis of AL amyloidosis. Median LVEF was 45%. Two echocardiographic parameters were abnormal in all patients – GLS (Global longitudinal strain) and E/e' ratio at mitral annulus. GLS was reduced in all patients, with a median value of -9.47% (normal >18%). E/e' ratio was elevated in all patients, with a median value of 24 (normal <8). 30% patients succumbed within 6 months, with an overall 46% mortality. Median OS of the cohort was 15 months. VCd was the most common induction regimen, and 2 patients underwent ASCT. Absence of treatment details and toxicities are important limitations. Importantly, authors conclude with an algorithm wherein they highlight screening for cardiac amyloidosis by echocardiogram (E/e' ratio and GLS) and biomarkers (NT-pro BNP) in all patients with plasma cell dyscrasias at diagnosis.

**"Original research publications from India"** Publications from Indian Faculty

# Dawn of an era of MRD from "peripheral blood" in Multiple Myeloma

ASH 2022 Abstract – 469. Tembhare PR, Sriram H, Khanka T, et al. Circulating Clonal Plasma Cells at Diagnosis and Peripheral Blood Measurable Residual Disease Assessment Provide Powerful Prognostication Biomarkers in Newly-Diagnosed Multiple Myeloma Patients Treated without Autologous Transplant. Presented on Sunday, December 11, 2022

**Prelude:**

The importance of minimal residual disease (MRD) has grown in leaps and bounds in MM. MRD has been shown to be a surrogate marker for not only PFS, but also OS. However, MRD needs to be done from bone marrow (BM), and repeated BM examinations are tedious for patients, even in a trial setting. Circulating clonal plasma cells (CCPC) reflect tumour burden in newly-diagnosed multiple myeloma (NDMM). There is a growing interest in investigating the clinical impact of CCPC quantitation due to its easy access and non-invasive nature. However, prospective data on the real-world utility of CCPC quantitation in MM patients treated without an autologous transplant due to limited resources or transplant ineligibility is extremely scarce. Additionally, there is no data on the clinical relevance of peripheral blood measurable residual disease assessment (PB-MRD) in NDMM treated without a transplant.

**Summary:**

Tembhare et al, prospectively enrolled 141 NDMM patients, and CCPC levels were studied using 10-13 color HS-MFC (high-sensitivity multicolor-flowcytometry) (sensitivity of 1x10-6) at diagnosis, end of 3-cycles, and end of 6-cycles. Additionally, at diagnosis, BM-CPC were also studied by multiparametric flow-cytometry. Of 141 patients, 70% (n=98) received VCd and 30% (n=43) received VRd. The cut-off for detectable PB-MRD was ≥ 0.0001% CPCs. BM-CPCs were detected in 95% patients, whereas CCPCs were present in 76% cases. ROC derived cut-off of ≥0.01% CCPCs were strongly associated with EFS (22 vs. 50 months; HR-2.50; p<0.0001) and OS (52 months vs. not-reached; HR-2.28; p=0.01). PB MRD for CCPCs was repeated in patients who had CCPCs at diagnosis. PB-MRD was detectable in 44% and 34.4% patients at 3-months and 6-months, respectively. Detectable PB-MRD at both 3 and 6 months were strongly prognostic of both EFS and OS. Importantly, negative PB-MRD at any follow-up timepoint (3 or 6 months) was independently associated with better EFS (22 vs. 43 months; HR-0.47; p=0.006). Moreover, PB-MRD persistence at 6 months was strongly associated with poor OS (52 months vs. not-reached; HR-3.03; p=0.008). PB-MRD and HR-cytogenetics were independently associated with EFS and OS, which was superior to conventional variables of ISS, and R-ISS on multivariate analysis. It should be remembered that this study was done in a non-transplant setting. Nonetheless, it gives us encouraging data for PB-MRD, first of its kind from India. Moreover, patchy nature of BM involvement, heterogenous nature of myeloma (not caught well in BM compartment) and given the invasive nature of BM examination, PB-MRD might soon become a reality in MM.

# "Original research publications from India"
## Publications from Indian Faculty from Dec 2022 - Feb 2023


- Kadam Amare P, Nikalje Khasnis S, Hande P, et al. Cytogenetic Abnormalities in Multiple Myeloma: Incidence, prognostic significance and geographic heterogeneity in Indian and western population [published online ahead of print, 2023 Feb 13]. Cytogenet Genome Res. 2023;10.1159/000529191. doi:10.1159/000529191
- Das N, Dahiya M, Gupta R, et al. Graded Depth of Response and Neoplastic Plasma Cell Index as Indicators of Survival Outcomes in Patients With Multiple Myeloma Following Autologous Stem Cell Transplant. Am J Clin Pathol. 2023;159(1):69-80. doi:10.1093/ajcp/aqac129
- Singh C, Panakkal V, Sreedharanunni S, et al. Clinical Features and Outcomes of Patients with Double-Hit/Triple-Hit Multiple Myeloma Detected at Relapse. Indian J Hematol Blood Transfus. 2023;39(1):151-153. doi:10.1007/s12288-022-01571-9
- Mohan B, Singh S, Tandon R, et al. Clinical profile of patients with cardiac amyloidosis in India. Indian Heart J. 2023;75(1):73-76. doi:10.1016/j.ihj.2022.12.006
- Yadav R, Nath UK, Celik I, Handu S, Jain N, Dhamija P. Identification and in-vitro analysis of potential proteasome inhibitors targeting PSMβ5 for multiple myeloma. Biomed Pharmacother. 2023;157:113963. doi:10.1016/j.biopha.2022.113963
- Kumar L, Sahoo RK, Kumar S, et al. Autologous stem cell transplant for multiple myeloma: Impact of melphalan dose on the transplant outcome. Leuk Lymphoma. 2023;64(2):378-387. doi:10.1080/10428194.2022.2148214
- Jung YY, Mohan CD, Rangappa S, et al. Brucein D imparts a growth inhibitory effect in multiple myeloma cells by abrogating the Akt-driven signaling pathway. IUBMB Life. 2023;75(2):149-160. doi:10.1002/iub.2684
- Patel H, Sheikh A, Medarametla GD, et al. Uncommon Presentation of Undiagnosed B-Cell Lymphoproliferative Disorder as Nodular Pulmonary Amyloidosis. J Med Cases. 2023;14(1):36-43. doi:10.14740/jmc4026
- Gupta A, Gehlot S, Goswami S, et al. SegPC-2021: A challenge & dataset on segmentation of Multiple Myeloma plasma cells from microscopic images. Med Image Anal. 2023;83:102677. doi:10.1016/j.media.2022.102677


*"In case of any additional publication in the last 3 months - please contact the editorial team at* **secretary@imagesociety.co.in***"*

Q1.

Which institute used Daratumumab for the first time in India?

A. AIIMS, New Delhi
B. PGIMER, Chandigarh
C. CMC, Vellore
D. Army Hospital (R&R), Delhi Cantt
E. None of the above

Q2.

All the following trials are related to Daratumumab except ?

A. POLLUX Trial
B. CASTOR Trial
C. MAIA Trial
D. CASSIOPIEA Trial
E. None of the above

Q3.

All are labeled indication for Daratumumab in NDMM patients except?

A. In combination with VTd for transplant-eligible
B. In combination with VMP for transplant-ineligible
C. In combination with Rd for transplant-ineligible
D. In combination with Vd for transplant-ineligible
E. None of the above

Q4.

The correct prescribed dose of Dara in combination with Rd in NDDM patients is :

A. 16mg/kg IV QW for 6 doses f/b Q3W for 16 doses
B. 16mg/kg IV QW for 8 doses f/b Q2W for 8 doses
C. 16mg/kg IV QW for 6 doses f/b Q2W for 4 doses
D. 16mg/kg IV QW for 8 doses f/b Q3W for 8 doses
E. None of the above

Q5.

Pick the wrong backbone in the under mentioned Daratumumab trials?

A. POLLUX: Rd
B. MAIA: Rd
C. CANDOR: Kd
D. GRIFFIN: VRd
E. CASTOR: VRd

MYELOMA QUIZ

MYELOMA QUIZ

DEC 2022

WINNER


Dr. Aditya Jandial

Sr. Research Associate, Dept. of Clinical Hematology and Medical Oncology, PGIMER, Chandigarh

Q6.

What is the R-ISS stage for this patient : 54y/ Male; ISS Stage II; Normal LDH ; No High-risk Cytogenetics ?

A. R-ISS I
B. R-ISS II
C. R-ISS III
D. Inadequate information for calculating R-IS

Q7.

Which of these personalities is associated with the first prognostic classification of myeloma in 1975?

A. 
B. 
C. 
D. 

Q8.

All the following are limitations of R2-ISS study presented today except?

A. Prognostication in newer regimens (Dara-VRD & KRD) precluded
B. Transplant Eligible < Non-Transplant Eligible patients' representation
C. R2-ISS validated only in trial patients
D. Improved discriminating capability compared to R

Q9.

Bendamustine belongs to which drug group?

A. Alkylator
B. Anti-neoplastic agent
C. Nitrogen Mustard
D. All the above

Q10.

In case of Bendamustine extravasation which one of the following is the most appropriate intervention?

A. Subcutaneous injection of Sodium thiosulphate
B. Topical DMSO
C. Warm Compresses
D. Inject Hyaluronidase

MYELOMA QUIZ

MYELOMA QUIZ

JAN 2023

WINNER

Dr. Dinesh

Sr. Resident, Medical Oncology, Madras Medical College

Q11.

Drug X was originally created by MyoGenics, a company started in 1993 by a group of Harvard professors. Dr. Julian Adams, a chemist who had worked at two big drug companies, was hired as the chief scientist and lead. The initial idea was to mitigate the muscle wasting that accompanies some cases of cancer, AIDS and other diseases. But in animals, the drug had more effect on tumors than muscles. So ProScript, as MyoGenics was renamed, began trying the drug in various cancers. It decided to focus on multiple myeloma after its first patient with that disease had a complete remission. The company had little money, so Dr. Adams appealed to the National Cancer Institute and cancer foundations for support. But with many doubting the drug would work, ProScript ran out of money in 1999 and was sold to LeukoSite, another Cambridge company for $2.4 m. Months later, LeukoSite itself was swallowed by Millennium, which was mainly interested in Campath that time. The success of drug X resulted in Takeda buying Millennium for $8.8 billion in 2008.
ID drug X which made big fortunes for both MM patients and the company in years to come once approved by FDA ?

A. Lenalidomide
B. Melflufen
C. Bortezomib
D. Selinexor

Q12.

The International Myeloma Working Group and Bone Marrow Transplant Clinical Trials Network (BMT CTN)24 have provided guidance around definitions of MRD and performance . What is the IMWG recommendation regarding optimal sensitivity of MRD assay ?

A. $10^{-5}$
B. $10^{-4}$
C. $10^{-3}$
D. $10^{-6}$

Q13.

Which of the following is an incorrect statement wrt MRD in myeloma?

A. MRD negativity in the marrow (NGF or NGS, or both) and by imaging (PET CT), confirmed minimum 2 year apart defines sustained MRD negativity
B. Disappearance of every area of increased tracer uptake found at baseline or a preceding PET CT or decrease to less than mediastinal blood pool SUV or decrease to less than that of surrounding normal tissue defines IMAGE MRD negativity
C. The concordance of post consolidation MRD by multiparametric FCM and NGS in CASSIOPEIA trial was 80 %
D. MRD progression by FCM has been shown to predict biochemical relapse by 4 months and clinical relapse by 9 to 10 months in patient receiving lenalidomide maintenance

MYELOMA QUIZ

MYELOMA QUIZ

FEB 2023

WINNER

Dr. Ankit J

Consultant, Hematology & BMT, Apollo CBCC, Ahmedabad

Q14.

Which of the following is an incorrect statement regarding adverse events with use of Talquetamab as per the results of MonumenTAL trial ?

A. The most common adverse event was cytokine release syndrome and all but one CRS event were of grade 1 or 2
B. Hematologic toxic effects were the most common grade 3 or 4 adverse events
C. The most common reason for treatment discontinuation was progressive disease and not Grade 3/4 adverse events
D. High incidence of pneumonitis in the trial correlates with GPRC5D RNA expression on lung tissue

Q15.

Which of the following statement regarding response rates to Talquetamab in specific myeloma subgroups is incorrect wrt to findings of the MonumenTAL trial ?

A. sCR @405 µg/kg QW in triple refractory group : 25%
B. ≥ VGPR in extramedullary plasmacytoma@405 µg/kg QW : 20 %
C. ≥ VGPR in penta refractory group @405 µg/kg QW : 50 %
D. ≥ VGPR @405 µg/kg QW in high risk cytogenetics group : 30 %

ANSWERS TO MYELOMA QUIZ

ANSWERS TO MYELOMA QUIZ

SEP 2022



Q1.

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?

**Answer : Lenalidomide**

*The 5th edition of National List of Essential Medicines (NLEM) was formally released on 14 Sep 22 by the Union Health Minister. NLEM plays an important role in ensuring accessibility of affordable quality medicines at all levels of healthcare. This will give boost to cost-effective, quality medicines and contribute towards reduction in Out of Pocket Expenditure on healthcare for the citizens. The Standing National Committee on Medicines (SNCM) was constituted in Jul 2018 to review and revise the NLEM in the context of contemporary knowledge of use of therapeutic products in health & hygiene of general public. The list has 27 sections covering 384 essential medicines and antimyeloma drugs bortezomib, melphalan and lenalidomide is discussed in section 7.*
*Ref: https://main.icmr.nic.in/sites/default/files/upload_documents/Report_and_NLEM_2022.pdf*

Q2.

In the MajesTEC-1 trial ; Ph1 -2 trial about Teclistamab in R/R Multiple Myeloma which of the following was not an exclusion criteria ?

**Answer : Autologous stem cell transplant ≤24 weeks before the first dose of study drug**

*Autologous stem cell transplant ≤12 weeks before the first dose of study drug was the exclusion criteria as per the study protocol.*
*Ref: Protocol for: Moreau P, Garfall AL, van de Donk NWCJ, et al. Teclistamab in relapsed or refractory multiple myeloma. N Engl J Med 2022;387:495-505. DOI: 10.1056/NEJMoa2203478*

Q3.

Which of the following statement is incorrect with respect to Teclistamab induced cytokine release syndrome (CRS) as per the MajesTEC-1 trial results ?

**Answer : Two patients discontinued teclistamab due to CRS**

*Cytokine release syndrome occurred in 119 patients (72.1%). Most events occurred after step-up and cycle 1 doses, with 6 patients (3.6%) having cytokine release syndrome in cycle 2 or later. Most events of cytokine release syndrome were grade 1 or 2 in severity and fully resolved, except for one grade 3 event, which occurred in a patient with concurrent pneumonia and resolved in 2 days No patients discontinued teclistamab owing to the development of cytokine release syndrome.*
*Ref: Moreau P, et al. Teclistamab in Relapsed or Refractory Multiple Myeloma. NEJM.2022 Aug 11;387(6):495- 505. doi: 10.1056/NEJMoa2203478.Epub 2022 Jun 5. PMID: 35661166*

ANSWERS TO MYELOMA QUIZ

ANSWERS TO MYELOMA QUIZ

SEP 2022

Q4.

In the DETERMINATION trial which of the following was not considered a time point for bone marrow aspiration for response assessment and correlative analysis ?

**Answer : D + 100 of ASCT (RVd+ASCT arm)**

*Bone marrow aspirate samples for response evaluation and correlative analyses, plus peripheral blood samples for correlative analyses, were planned to be collected at screening, at the time of response assessment or confirmation (for patients achieving a very good partial response or better) if clinically indicated, within 42 days of ASCT (RVd+ASCT arm), on day 1 of RVd cycle 4 (RVd+ASCT arm), prior to lenalidomide maintenance, and at the time of disease relapse or progression. Samples were also to be collected annually during maintenance from patients providing additional informed consent.*
*Ref: Richardson PG, et al. Triplet Therapy, Transplantation,and Maintenance until Progression in Myeloma. N Engl JMed. 2022 Jul 14;387(2):132-147. doi: 10.1056/NEJMoa2204925.Epub 2022 Jun 5. PMID: 35660812.*

Q5.

Originally the DETERMINATION trial study was planned to be conducted together with the IFM 2009 study with a planned population size of 1000. However a landmark research finding X led to protocol revision twice and the sample size was reduced to 720. What was X ?

**Answer : Favourable PFS hazards ratio with indefinite lenalidomide maintenance**

*Based on evidence supporting the benefit of lenalidomide maintenance given until disease progression, the protocol for this study, was revised in October 2012 to extend duration of lenalidomide maintenance from 1 year to until disease progression. The IFM 2009 trial protocol retained the duration of lenalidomide maintenance as 1 year. At this time, the two trials were separated, and both trials were powered independently to detect a PFS benefit. Based on assumed hazard rates at the time, the sample size for the DFCI 10-106 study was 660 patients. Subsequently, results from a meta-analysis of the benefit of lenalidomide maintenance therapy indicated a potentially lower-than-assumed hazard rate for PFS with lenalidomide maintenance. With a reduction in the failure rate, the time to the full information could be longer than expected. Therefore, the sample size was increased further, to 720 randomized patients, to account for potential reduction in hazard rates and reduce the time to full information of the primary endpoint of PFS by 5 months.*
*Ref: Richardson PG, et al. Triplet Therapy, Transplantation,and Maintenance until Progression in Myeloma. N Engl JMed. 2022 Jul 14;387(2):132-147. doi: 10.1056/NEJMoa2204925.Epub 2022 Jun 5. PMID: 35660812.*

ANSWERS TO MYELOMA QUIZ

ANSWERS TO MYELOMA QUIZ

OCT 2022

Q6.

The European Myeloma Network, within the HARMONY project have recently proposed a second revision (R2-ISS) of the current Revised International Staging System (R ISS). Which of the following was not considered a variable for risk stratification as per R2-ISS ?

**Answer : t(14;16)(q32;q23)**

*The R2-ISS staging system is a new simple prognostic algorithm. Compared with the R-ISS, it showed an improved discriminating capability, especially in the large group of patients with intermediate-risk NDMM. The R2-ISS score includes simple and widely used prognostic markers, and the additive nature of its calculation easily allows the future inclusion of new prognostic variables. The t(14;16), which was included in the R-ISS, was significant in terms of OS but not of PFS and, as a consequence, was not included in the R2-ISS calculation. Indeed, despite its biological importance, t(14;16) is rare and usually presents together with other adverse prognostic factors. Moreover, it may not be a marker of high-risk disease per se, as observed in the HARMONY project and by other groups analyzing large cohorts of patients.*
*Ref: Second Revision of the International Staging System (R2-ISS) for Overall Survival in Multiple Myeloma: A European Myeloma Network (EMN) Report Within the HARMONY Project 10.1200/JCO.21.02614 Journal of Clinical Oncology 40, no. 29 (October 10, 2022) 3406-3418*

Q7.

In the MCARH109 trial ; 10/17 patients relapsed post CART during the follow up period. What percentage of patients continued to show persistent GPRC5D expression on myeloma cells at relapse?

**Answer : 40%**

*About 40 percent of patients continued to show persistent GPRC5D expression on myeloma cells at relapse. Additional studies are needed to understand the mechanisms of relapse after GPRC5D-targeted therapies, including the role of antigen escape.*
*Ref : Mailankody S, et al. GPRC5DTargeted CAR T Cells for Myeloma. N Engl J Med. 2022 Sep 29;387(13):1196-1206. doi: 10.1056/NEJMoa2209900.*

Q8.

In the MCARH109 trial , the primary end point was to identify the the maximum tolerated dose. What was the maximum dose level planned by investigators that could never be reached due to dose limiting toxicities encountered in the trial ?

**Answer : 800 million total CAR+ cells**

*Dose escalation follows a standard 3- by-3 escalation design. Cohorts of 3-6 patients will be infused with escalating doses of MCARH109 T cells to establish the maximum tolerated dose (MTD and will proceed to the next cohort if less than 33% of patients in a cohort experience unanticipated dose-limiting toxicity (DLT). If unacceptable toxicity is seen in 1 of 3 patients in any given cohort, up to 3 additional patients will be treated in that cohort. If 2 or more patients in any given cohort experience unacceptable toxicity, the MTD of T cells will have been exceeded, and established at the previous cohort dose level. Cytokine release syndrome was seen in 15 patients (88%) and was of grade 1 or 2 in all patients except for 1 patient who had received the highest dose level (450×106 CAR T cells: dose level 4) and had a grade 4 event (Table 2). This same patient had grade 4 ICANS and grade 4 macrophage activation syndrome constituting a dose-limiting toxic effect.Hence dose level 5 ie 800 million total CAR+ cells was never reached in this trial.*
*Ref : Mailankody S, et al. GPRC5DTargeted CAR T Cells for Myeloma. N Engl J Med. 2022 Sep 29;387(13):1196-1206. doi: 10.1056/NEJMoa2209900*

ANSWERS TO MYELOMA QUIZ

ANSWERS TO MYELOMA QUIZ

OCT 2022

Q9.

In the Larocca trial, a novel primary end point@EFS was defined by the investigators to study efficacy & feasibility of dose /schedule adjusted Rd- R in NDMM. Which of these parameters contributed maximum to the EFS benefit in the study arm ?

**Answer : Incidence of ≥ grade 3 non - hematological adverse event**

*The primary end point of the study was EFS, which was defined as the occurrence of grade 4 hematologic AEs, grade 3 to 4 nonhematologic AEs (including second primary malignancy [SPM]), discontinuation of lenalidomide, PD, or death. EFS was calculated from the time of enrollment until the occurrence of any of the defining events mentioned above, whichever came first. The most frequent ≥ grade 3 toxicities were nonhematologic. At least 1 ≥ grade 3 nonhematologic AE was reported in 33% of patients receiving Rd-R and 43% of patients receiving Rd.*
*Ref: Larocca A, et al. Dose/schedule-adjusted Rd-R vs continuous Rd for elderly, intermediate-fit patients with newly diagnosed multiple myeloma. Blood. 2021 Jun 3;137(22):3027-3036. doi: 10.1182/blood.2020009507.*

Q10.

In the Larocca trial, patients could be enrolled regardless of abnormal baseline laboratory values unlike most previous trials. Which of the following parameters was not considered an exclusion criteria?

**Answer : None of the above**

*Patients could be enrolled regardless of abnormal baseline laboratory values (eg, absolute neutrophil count ANC < 1000/ µl; Platelet count < 80000 / µl ; hemoglobin <8 g/dL; creatinine clearance <30 mL/min), so those who are generally excluded from clinical trials were included.*
*Ref: Larocca A, et al. Dose/schedule-adjusted Rd-R vs continuous Rd for elderly, intermediate-fit patients with newly diagnosed multiple myeloma. Blood. 2021 Jun 3;137(22):3027-3036. doi: 10.1182/blood.2020009507.*

ANSWERS TO MYELOMA QUIZ

NOV 2022



Q11.

The ENDURANCE trial compared the combination of the drugs bortezomib, lenalidomide, and dexamethasone(VRd) against Carfilzomib, lenalidomide, and dexamethasone(KRd) when treating patients with newly diagnosed multiple myeloma. Which of the following is not true regarding the results from the trial ?

**Answer : KRd improved PFS compared with VRd**

*ENDURANCE trial directly compares two 3-drug combinations for initial treatment of NDMM standard or intermediate risk patients who are ineligible for ASCT or did not intend to have early ASCT. 1087 patients were randomly assigned to induction therapy with VRd or KRd. PFS, OS and overall response rates were also comparable between the regimens. Although VGPR or better response rate were better with KRD, but this did not translate into PFS benefit.*
*Ref: Kumar SK, et al. Carfilzomib or bortezomib in combination with lenalidomide and dexamethasone for patients with newly diagnosed multiple myeloma without intention for immediate autologous stem-cell transplantation (ENDURANCE): a multicentre, open-label, phase 3, randomized, controlled trial. Lancet Oncol. 2020 Oct;21(10):1317-1330. doi: 10.1016/S1470-2045(20)30452-6.*

Q12.

The IKEMA study was a randomized open label multicenter study assessing the clinical benefit of isatuximab combined with carfilzomib and dexamethasone vs carfilzomib with dexamethasone in R/ R Multiple Myeloma. Which of these is the incorrect statement as per data from the trial ?

**Answer : Reaching MRD-negative status was not associated with longer PFS in Isa-Kd arm.**

*Ref: Moreau, P etal. Isatuximab, carfilzomib, and dexamethasone in relapsed multiple myeloma (IKEMA): a multicentre, open-label, randomised phase 3 trial. The Lancet, 397(10292), 2361–2371. doi:10.1016/s0140-6736(21)00592-4*

Q13.

Trispecific antibodies are being evaluated in Phase I/II trials in myeloma led by Ichnos Sciences. The trispecific antibody targets two areas found on multiple myeloma cells (BCMA and CD38) and joins that with the CD3 T cells. The company's proprietary platform is called BEAT® 2.0 technology. Which of these statements is the incorrect statement with regards to the initial research work on the drug ?

**Answer : The main limitation of the drug is that the risk of keratopathy**

*Keratopathy is a dose limiting adverse effect commonly associated with antimyeloma drug belantamab mafodotin.*

ANSWERS TO MYELOMA QUIZ

ANSWERS TO MYELOMA QUIZ

NOV 2022

Q14.

A drug used in the treatment of relapsed/refractory multiple myeloma (RRMM) is in the process of being pulled off the US market by its manufacturer. The drug is belantamab mafodotin-blmf, an antibody drug conjugate that targets B-cell maturation antigen (BCMA). What is the reason for its withdrawal?

**Answer : Phase III trials did not meet its primary end point of PFS benefit**

*On November 22, 2022, GSK announced it has initiated the process for withdrawal of the U.S. marketing authorization for Blenrep (belantamab mafadotin-blmf) following the request of the U.S Food and Drug administration (FDA). This request was based upon the previously announced outcome of the DREAMM-3 phase III confirmatory trial which did not meet the requirements of the FDA Accelerated Approval regulations. The DREAMM-3 trial was an open label randomized head-head superiority trial evaluating the efficacy and safety of single agent belantamab mafadfotin-blmf compared to pomalidomide in combination with low-dose dexamethasone (PomDex) in patients with RRMM. The primary end point was progression free survival and belantamab mafadfotin-blmf did not meet the requisite superiority test which was part of the Accelerated Approval requirement*

*Ref: GSK provides update on DREAMM-3 phase III trial for Blenrep in relapsed/refractory multiple myeloma. News release. GlaxoSmithKline plc. November 7th, 2022. Accessed: November 22, 2022. https://bit.ly/3gwmjib*

Q15.

What is the colour of cancer ribbon for multiple myeloma?

**Answer : Burgundy**

*Ref: https://en.wikipedia.org/wiki/List_of_awareness_ribbons*

**Study:**

Sonneveld P, Chanan-Khan A, Weisel K, Nooka AK, Masszi T, Beksac M, et al. Overall Survival With Daratumumab, Bortezomib, and Dexamethasone in Previously Treated Multiple Myeloma (CASTOR): A Randomized, Open-Label, Phase III Trial. Journal of Clinical Oncology. 2022 Nov: JCO-21.

**Title:**

It is a triplet versus doublet again! : Not cost effective for a 11 month overall survival benefit in Resource -Constrained settings

Multiple myeloma has no cure and we have to keep switching therapies every 3 to 4 years if standard risk and earlier if high risk. Daratumumab is a wonderful addition but a costly one. It costs INR 75,500 for a 400mg vial of Daratumumab. As per Castor study, there is a 11 month gain in overall survival if Daratumumab is added to bortezomib and dexamethasone (Median OS was 49.6 months for D-Vd versus 38.5 months for Vd) [1]. So, the cost for this gain in overall survival comes at more than INR 1 crore. A collective effort to publish the cost effectiveness in our setting should be planned [2, 3]. When incorporating CASTOR study results during discussion with our patients, they would probably ask about the control arm patients on why they received a doublet regimen. In our Resource-constrained setting, we still have pomalidomide, cyclophosphamide and bendamustine as options to be added to a bortezomib and dexa doublet. Lastly, the CASTOR trial was supported by Janssen Research & Development, LLC.

**References:**


Sonneveld P, Chanan-Khan A, Weisel K, Nooka AK, Masszi T, Beksac M, et al. Overall Survival With Daratumumab, Bortezomib, and Dexamethasone in Previously Treated Multiple Myeloma (CASTOR): A Randomized, Open-Label, Phase III Trial. Journal of Clinical Oncology. 2022 Nov: JCO-21

Prinja S, Kaur G, Malhotra P, Jyani G, Ramachandran R, Bahuguna P, Varma S. Cost-Effectiveness of Autologous Stem Cell Treatment as Compared to Conventional Chemotherapy for Treatment of Multiple Myeloma in India. Indian J Hematol Blood Transfus. 2017 Mar;33(1):31-40

Suvir Singh et al. Case for More Autologous Transplants in Myeloma in Resource-Constrained Settings. Ind J Med Paediatr Oncol 2022;43:311–313


JOURNAL SCAN COMMENTARIES

Eagle Eye Competition

BEST COMMENTARY WINNER

DEC 2022


Dr. Mona Vijayan

Associate Consultant Clinical Hematology, Sahara Hospital, Lucknow

**Study:**

Ramasamy K, Iqbal G, Brouwer R, Stalker V, Akhtar S, Varghese S, Lindsay J, et al. Bortezomib, Bendamustine and Dexamethasone vs. Thalidomide, Bendamustine and Dexa randomized in myeloma patients presenting with renal failure (OPTIMAL): a multi-center randomized phase II trial. Blood Cancer J. 2022 Nov 29;12(11):162. DOI: 10.1038/s41408-022-00758-7. PMID: 36446771; PMCID: PMC9708638.

**Title:**

Renal impairment is a serious complication of multiple myeloma and upto 25% patients will have severe renal impairment at diagnosis. Though the overall survival (OS) prospects have considerably improved for patients with myeloma, the median OS is only 2–3 years in patients with renal impairment. Authors here report a randomized trial of Bendamustine- dexamethasone combination with either bortezomib or thalidomide for newly-diagnosed myeloma (MM) with renal impairment (RI). The intriguing part of the study is that they chose Bendamustine as the backbone of therapy, leaving Bortezomib which has showed superiority in previous studies in this setting. 1 Bendamustine is commonly used in relapsed/refractory settings, 2 however the authors of this study reported similar tolerability with both the regimens. 3 The other available options for this subset of patients are free light chain removal by dialysis and Daratumumab based therapy, both of which are costly affairs. 4 This study hypothesized that a significant difference in achieving a reduction in sFLC during the first two cycles of therapy in both the arms, which is a surrogate end point and not an absolute one. Though there was statistically significant difference in response in both the groups, the overall survival rates were not statistically significant. The sample size was too small to extrapolate the results on a larger population. Hence a clinically meaningful difference was not established. Moreover, the BBD arm costs almost double that of BTD arm for a no significant benefits. To conclude, this subset of patients definitely deserves a regimen to derive the maximum benefit with manageable toxicity and maintained quality of life. The OPTIMAL trial might just be a step in that uphill battle, several questions are yet to be answered.

**References:**


Dimopoulos MA, Sonneveld P, Leung N, et al. International myeloma working group recommendations for the diagnosis and management of myeloma-related renal impairment. J Clin Oncol. 2016;34:1544–57

Offidani, M., Corvatta, L., Maracci, L. et al. Efficacy and tolerability of bendamustine, bortezomib and dexamethasone in patients with relapsed-refractory multiple myeloma: a phase II study. Blood Cancer Journal 3, e162 (2013)

Ramasamy K, Iqbal G, Brouwer R, Stalker V, Akhtar S, Varghese S, Lindsay J, et al. Bortezomib, Bendamustine and Dexamethasone vs. Thalidomide, Bendamustine and Dexa randomized in myeloma patients presenting with renal failure (OPTIMAL): a multi- center randomized phase II trial. Blood Cancer J. 2022 Nov 29;12(11):162. DOI: 10.1038/s41408-022-00758-7. PMID: 36446771; PMCID: PMC9708638

Hutchison CA, Cook M, Heyne N, Weisel K, Billingham L, Bradwell A, et al. European trial of free light chain removal by extended haemodialysis in cast nephropathy (EuLITE): A randomised control trial. Trials. 2008;9:55. doi: 10.1186/1745-6215-9-55


JOURNAL SCAN COMMENTARIES

Eagle Eye Competition

BEST COMMENTARY WINNER

JAN 2023


Dr. Revanth Boddu

Consultant, Clinical Hematology, Sparsh Superspecialty Hospital, Bengaluru

**Study:**

Yee AJ, Raje N. Minimal residual disease in multiple myeloma: why, when, where. Hematology. 2021 Dec 10;2021(1):37-45

**Title:**

MRD testing in Multiple Myeloma is more prognostic then decisive: Perfection is the enemy of the good in LMIC

MRD testing in Multiple Myeloma has been standardised in the recent years at multiple institutions and NABL accredited laboratories in India. MRD testing by next generation flow cytometry (NGF) requires a first pull sample of the bone marrow. The explaining part to a patient will be, “I am doing an invasive procedure to establish whether you have a deeper response but the treatment will not change as of now”. This reminisces us “the haematologist” of a scenario much frequently debated – “Thrombophilia work up”. An Indian earning INR 25000 per month, would be placed in the top 10 per cent of the country's wage earners [1]. It’s a long road for LMIC to receive a perfect treatment

plan in any disease. This article explains that there is a lag in data with MRD based decision making and there are various clinical trials which are designed to answer them like REMNANT (NCT04513639) [2]. MRD testing in multiple myeloma till the data matures, needs to be individualised as per the patients paying capacity and wishes.

**References:**

https://www.indiatimes.com/news/india/if-you-earn-rs-25000-per-month-you-are-among- indias-top-10-income-earners-570330.html

The Relapse from MRD Negativity as Indication for Treatment. https://clinicaltrials.gov show › NCT04513639Study

JOURNAL SCAN COMMENTARIES

Eagle Eye Competition

BEST COMMENTARY WINNER

FEB 2023

Dr. Mona Vijayan

Associate Consultant Clinical Hematology, Sahara Hospital, Lucknow

# List of Institutions and No. of Registrations

The National Myeloma Registry, as part of the IMAGe group, forms the backbone of research in collecting and collating the data prospectively on patients of Multiple Myeloma and other plasma cell dyscrasias across the subcontinent. The platform provides an opportunity for the doctors to follow up with the patients, acts as an EMR, and research database with real-time information regarding the patients. At the same time, the patient mobile application component of the Hybrid application helps improve their compliance through reminders, graphs of their investigations, answers to their routine questions, reminders regarding the investigations, hospital appointments, and drug dosing, and lastly, acts as a patient diary. The various centers registered with the number of patients enrolled by each center respectively are depicted below. The salient features of statistical analysis as on 01st Jan 2023 are depicted in the pictorial form below as a ready reckoner. For those institutes who want to join hands with IMAGe can write to us at **secretary@imagesociety.co.in**

We sincerely hope that more centres get added and share their data so that a comprehensive National Myeloma Registry can be maintained to add value to the research. Those who haven't joined yet are requested to come forward and join at **https://care4myeloma.in/welcome**

PGIMER, Chandigarh

**1187**

Army Hospital (Research & Referral)

**711**

TMC Kolkata

**701**

Rajiv Gandhi Cancer Institute

**354**

SGPGI

**144**

CH(SC) & AFMC

**132**

NIMS, Hyderabad

**113**

CMC Ludhiana

**101**

JIPMER

**62**

Believers Church Medical Hospital

**46**

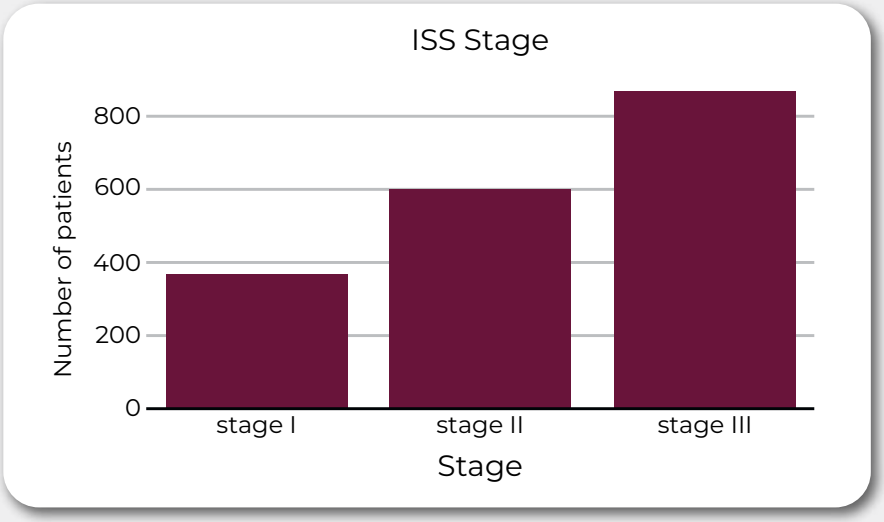
*For other institutes who are a part of the registry, please click on* **https://care4myeloma.in/welcome**

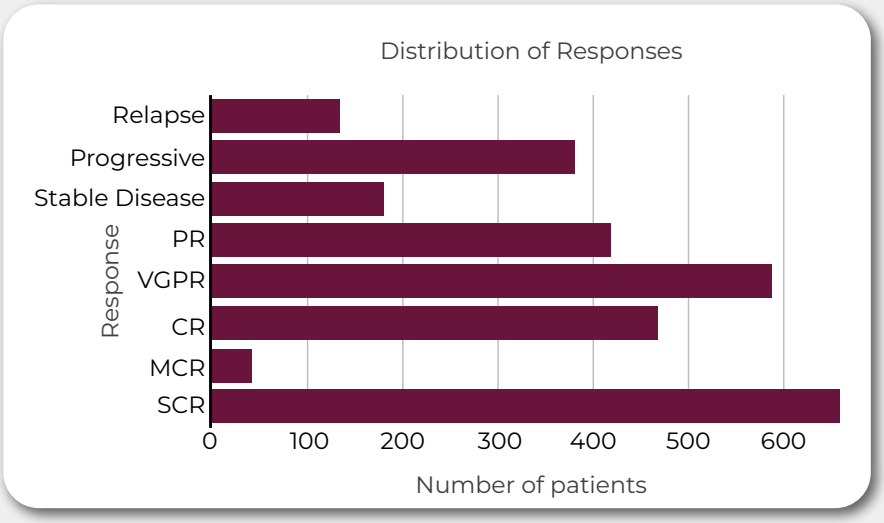
## Registry Analysis

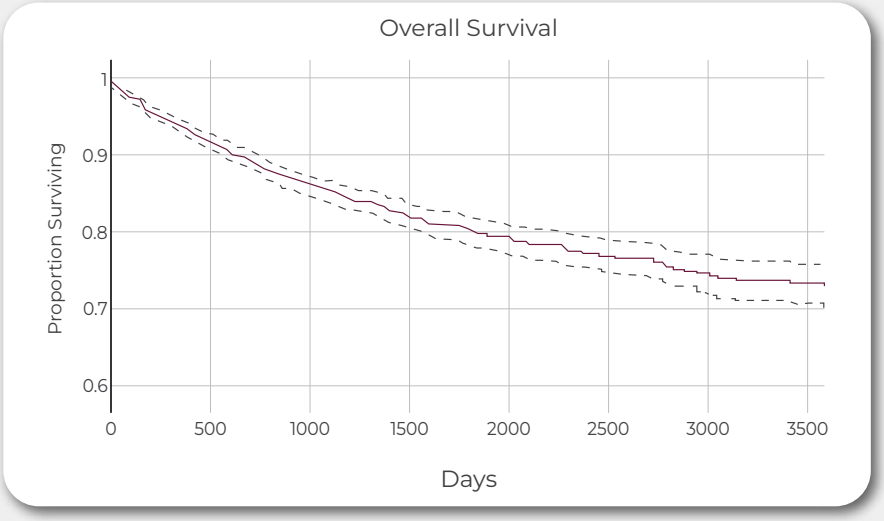
Total Number Registered **3693**

No. of Deaths Till Date **512**

**Registry Link** https://care4myeloma.in/welcome



FELLOWSHIPS


Annual award* for fellows/faculty with the largest contribution to IMAGe or the field of Plasma Cell Dyscrasias in India


Annual awards* total worth 5.1 Lakh Rupees for fellows/faculty who won in IMC 2023 under categories of

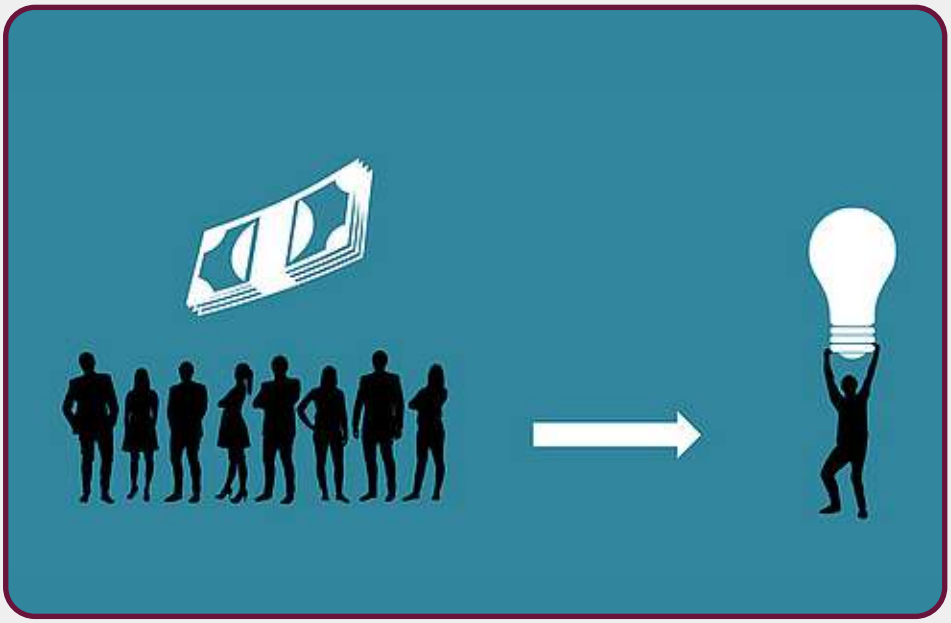
a. *Oral paper in IMC*
b. *Poster in IMC*
c. *Annual Quiz in IMC*

**Conditions Apply*

FELLOWSHIPS


Monthly awards* for fellows/ faculty who win

a. *The best commentary in Eagle Eye competition – IMAGe Certificate; IMAGe Credit hours & Amazon Voucher worth 5000/-*
b. *Monthly Quiz – IMAGe Certificate; IMAGe Credit hours & Amazon Voucher worth 1000/-*



Support to UG students maximum to an amount of ₹ **10000** who are pursuing Short term Projects in the field of plasma cell dyuscrasias*

Support for the PG students, maximum to an amount of ₹ **25000** who are pursuing thesis in the field of Plasma cell dyscrasias*

Support to PhD students maximum to an amount of ₹ **50000** who are pursuing PhD thesis in the field of plasma cell dyuscrasias*

**Conditions Apply*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An Indian Myeloma Academic Groupe (IMAGe)
INDIAN MYELOMA CONGRESS 2024
06th ANNUAL CONFERENCE OF IMAGe
12th - 14th JANUARY 2024

PATIENT GROUP MEETING

PARTICIPANTS

63

# Myeloma Patient Group Meeting - North Zone

**06th March 2023**

## Agenda

| | |
|---|---|
| 4.00 pm - 4.05 pm | Welcome and context setting<br>Speaker **: Dr. Y Uday** |
| 4.05 pm - 4.15 pm | Myeloma yoddhas experience<br>**Yoddhas** |
| 4.15 pm - 4.25 pm | Newer treatment options in Myeloma<br>Speaker : **Dr. Rayaz Ahmed** |
| 4.25 pm - 4.35 pm | Question & Answers<br>Panelists : **Dr. Rayaz Ahmed, Dr. Tapan Saikia, Dr. Joseph John, Dr. Rajeev Kumar.** |
| 4.35 pm - 4.45 pm | Relevance of ASCT in the era of newer drugs<br>Speaker : **Dr. Pankaj Malhotra** |
| 4.45 pm - 4.55 pm | **Question & Answers**<br>Panelists : **Dr. Pankaj Malhotra, Dr. Tapan Saikia, Dr. Joseph John, Dr. Rajeev Kumar.** |
| 4.55 pm - 5.05 pm | Impact of Govt schemes on Patient Outcomes<br>Speaker **: Dr. Stalin Bala C** |
| 5.05 pm - 5.15 pm | **Question & Answers**<br>Panelists : **Dr. Gayatri Bhat, Dr. Tapan Saikia, Dr. Joseph John, Dr. Rajeev Kumar.** |
| 5.15 pm - 5.20 pm | Closing remarks<br>Speaker **: Dr. Y Uday** |

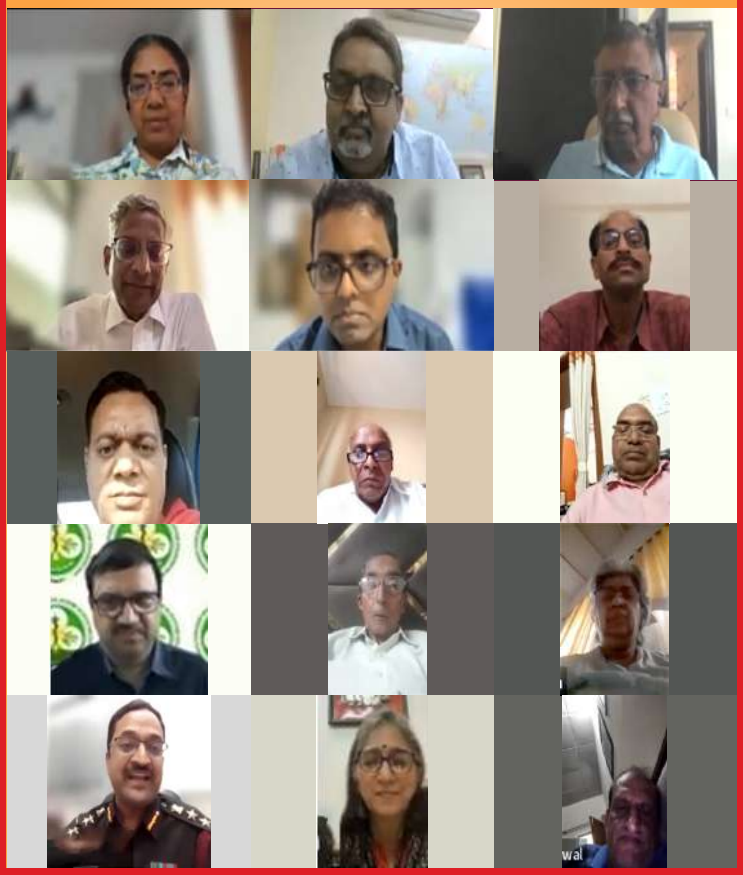
PATIENT GROUP MEETING

PARTICIPANTS

84

# Myeloma Patient Group Meeting - South Zone

**13th March 2023**



## Agenda

| | |
|---|---|
| 4.00 pm - 4.05 pm | Welcome and context setting<br>Speaker : **Dr. Y Uday** |
| 4.05 pm - 4.15 pm | Myeloma yoddhas experience<br>**Yoddhas** |
| 4.15 pm - 4.25 pm | Relevance of MRD analysis in Myeloma<br>Speaker : **Dr. Neeraj Siddharthan** |
| 4.25 pm - 4.35 pm | Question & Answers<br>Panelists : **Dr. Neeraj Siddharthan, Dr. Sadashivudu, Dr. Pankaj Malhotra** |
| 4.35 pm - 4.45 pm | CAR-T Therapy in Myeloma<br>Speaker : **Dr. Hari Menon** |
| 4.45 pm - 4.55 pm | **Question & Answers**<br>Panelists : **Dr. Hari Menon, Dr. Sadashivudu, Dr. Pankaj Malhotra** |
| 4.55 pm - 5.05 pm | Impact of Govt schemes on Patient Outcomes<br>Speaker : **Dr. Stalin Bala C** |
| 5.05 pm - 5.15 pm | **Question & Answers**<br>Panelists : **Dr. Stalin Bala C, Dr. Sadashivudu, Dr. Pankaj Malhotra** |
| 5.15 pm - 5.20 pm | Closing remarks<br>Speaker : **Dr. Y Uday** |

PATIENT GROUP MEETING

PARTICIPANTS

69

# Myeloma Patient Group Meeting - East Zone

**20th March 2023**

## Agenda

| | |
|---|---|
| 4.00 pm - 4.05 pm | Welcome and context setting<br>Speaker : **Dr. Y Uday** |
| 4.05 pm - 4.15 pm | Infections in Myeloma<br>Speaker : **Dr. Tapan Saikia** |
| 4.15 pm - 4.25 pm | Question & Answers<br>Panelists : **Dr. Neeraj Siddharthan, Dr. Sadashivudu, Dr. Pankaj Malhotra** |
| 4.25 pm - 4.35 pm | Vaccination in Myeloma<br>Speaker : **Dr. Sumeet Mirgh** |
| 4.35 pm - 4.45 pm | **Question & Answers**<br>Panelists : **Dr. Sumeet Mirgh, Dr. Prantar Chakraborthy** |
| 4.45 pm - 4.55 pm | Antimicrobial Prophylaxis in Myeloma<br>Speaker : **Dr. Prantar Chakraborthy** |
| 4.55 pm - 5.05 pm | **Question & Answers**<br>Panelists : **Dr. Prantar Chakraborthy, Dr. Sumeet Mirgh** |
| 5.05 pm - 5.15 pm | Myeloma yoddhas experience<br>**Yoddhas** |
| 5.15 pm - 5.20 pm | Closing remarks<br>Speaker : **Dr. Y Uday** |

PATIENT GROUP MEETING

PARTICIPANTS

54

# Myeloma Patient Group Meeting - West Zone

**27th March 2023**

## Agenda

| | |
|---|---|
| 4.00 pm - 4.05 pm | Welcome and context setting<br>Speaker : **Dr. Pankaj Malhotra** |
| 4.05 pm - 4.15 pm | Myeloma yoddhas experience<br>**Yoddhas** |
| 4.15 pm - 4.25 pm | Bone health in Myeloma<br>Speaker : **Dr. Reena Nair** |
| 4.25 pm - 4.35 pm | Question & Answers<br>Panelists : **Dr. Reena Nair, Dr. Navin Khattry, Dr. Pankaj Malhotra** |
| 4.35 pm - 4.45 pm | Myeloma and Neurology<br>Speaker : **Dr. Srinath Rajagopal** |
| 4.45 pm - 4.55 pm | **Question & Answers**<br>Panelists : **Dr. Srinath Rajagopal, Dr. Reena Nair, Dr. Navin Khattry, Dr. Pankaj Malhotra** |
| 4.55 pm - 5.05 pm | Kidney & Myeloma<br>Speaker : **Dr. Navin Khattry** |
| 5.05 pm - 5.15 pm | **Question & Answers**<br>Panelists : **Dr. Navin Khattry, Dr. Srinath Rajagopal, Dr. Reena Nair, Dr. Pankaj Malhotra** |
| 5.15 pm - 5.20 pm | Closing remarks<br>Speaker : **Dr. Pankaj Malhotra** |

# Indian Myeloma Congress 2023





# Indian Myeloma Congress 2023

The Indian Myeloma Academic Groupe (IMAGe) hosted its **5th Annual Indian Myeloma Congress – 2023, from 13th to 15th January 2023 at St John's Medical College and Hospital, Bengaluru.** IMAGe is a common platform for patients, caregivers, residents/fellows, and treating physicians. It was formally launched in 2018 to strengthen research and create awareness about plasma cell disorders in the Indian subcontinent. Myeloma is an incurable but controllable cancer related to the blood that is easily treated and controlled provided it is adequately diagnosed in time. With the profound improvement in survival owing to the advent of newer therapies, the theme of this year's meeting has been chosen as "Multiple Myeloma – Extending Survival"

Experts and novitiates from the national and international myeloma fraternity shared their thoughts and insights in this academic endeavor encompassing various aspects of plasma cell dyscrasias, including diagnostics, precursor screening, risk stratification, therapeutics, and future perspectives. An overarching feature of the congress was discussing myeloma research work specific to the Indian population in each of the sessions. A panoply of workshops, panel discussions, CME talks, debates, and research work presentations showcased the latest developments, innovations, challenges & opportunities in the realm of plasma cell dyscrasias.

The much-awaited Annual Quiz on plasma cell disorders was one of the highlights of the meeting, aimed primarily at encouraging post graduates get interested in myeloma work and spark the inclination to myeloma research. The congress was organized to promote academic excellence and instill in students the seeds for pursuing myeloma research in their hemato-oncology careers. Students and researchers across the country presented their work in the field of Myeloma during the much sought-after Poster and Oral presentations.

The congress saw nearly 250 registrations and participation from hematologists, hemato-oncologists, pathologists, radiologists, nephrologists statisticians and general physicians involved with myeloma care during the 3 day meeting at St. Johns Medical College and hospital. The presence of Key opinion leaders in the field of Myeloma from Dana Farber cancer Centre, (Dr. Nikhil Munshi and Dr. Noopur Raje) and from Mayo Clinic (Dr. Shaji Kumar and Dr. Vincent Rajkumar), added great value and a distinct fillip to the congress

The meeting concluded on 15th January 2023 on a successful note with excellent and positive feedback from the participants and students. The next edition is slotted for the **12th to 14th of January 2024 at Pune.**

# The Five Geeks – Editorial Team

**Dr. Uday Yanamandra**

**Dr. Sumeet Mirgh**

**Dr. Gurleen Oberoi**

**Dr. Saleem Mirza**

**Dr. Arun V A**

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