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**RESUMOS**

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# PO03

## COMBINATION TREATMENT WITH EXTRACORPOREAL PHOTOPHERESIS FOR ACUTE GUT GRAFT-VERSUS-HOST DISEASE WITH HIGH RISK OF MALIGNANCY RELAPSE

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**Background**

Treatment options for acute graft-versus-host disease (aGvHD) are still limited beyond the use of steroids, and no consensual timing for initiation of second-line therapy in steroid-refractory disease is currently defined. Extracorporeal photopheresis (ECP) is a non-pharmacological approach that has been gaining support for the treatment of aGvHD, and its use in combination regimens shows promising results.

**Case report**

We report the case of a 58-year old gentleman with a double diagnosis of *CALR*-mutated primary myelofibrosis on treatment with ruxolitinib, and chronic lymphocytic leukaemia (CLL) refractory to ibrutinib and the rituximab/venetoclax regimen. The patient underwent haematopoietic transplant with active disease and received a 12/12-matched sibling allograft after myeloablative conditioning with fludarabine and busulphan, with GvHD prophylaxis given through ATG and cyclosporine. His bone marrow assessment at D+28 showed a small population of 0.88% residual CLL cells by flow cytometry and 67% mixed-donor chimerism in the CD3 subset. Following initial clinical recovery, he was admitted as inpatient at D+51 due to the development of frequent episodes of watery diarrhoea, severe nausea precluding any oral intake and acute kidney injury. Cyclosporine was held and replaced by mycophenolate mofetil (MMF) 1 g 3id, while methylprednisolone 1 mg/kg and budesonide 3 mg 3id were given for empirical treatment of gut aGvHD. Stool cultures and microbiology assays were negative, while colonic biopsies obtained by flexible sigmoidoscopy showed no viral inclusions but rather large apoptotic bodies within crypts associated with crypt drop-out, confirming grade 3 aGvHD. Despite initial improvements in bowel habits, diarrhoea worsened to an output of 2 litres/24h after methylprednisolone was weaned to 0,5 mg/kg, which was alarming for steroid dependent/refractory aGvHD. ECP was chosen as second-line treatment due to the high risk of disease relapse with further immunosuppression, and treatment was started 10 days after admission alongside reintroduction of cyclosporine and increase in steroid dose, with a maximum of 2 mg/kg. Clinical recovery was progressive and he was eventually discharged 1 month after hospital admission on ECP weekly, cyclosporine 175 mg 2id, MMF 1 g 3id, budesonide 3 mg 3id and prednisolone 40 mg 1id, reporting no diarrhoea. After 20 days of ambulatory treatment, at D+104 post-transplant, the patient fully stopped prednisolone and remained asymptomatic from his gut aGvHD, while his bone marrow assessment showed 0.11% of CLL cells, with a full donor chimerism.

**Discussion**

Recurrence of symptoms after initial steroid dose reduction is one of the defining characteristics of refractory aGvHD, as was experienced by this patient. ECP has a favourable profile of adverse effects in the second-line setting because it induces immune tolerance rather than immunosuppression, and when combined with other drugs may be regarded as a steroid sparing agent. The double haematological diagnosis, previous mixed donor chimerism and MRD positivity placed this patient at high-risk of disease relapse, and ECP might have contributed to a faster prednisolone wean and improved disease and chimerism kinetics. If promptly initiated as adjuvant therapy, ECP may spare patients from additional immunosuppression during a critical period after allogeneic transplant.

# PO05

## ASSESSMENT OF MULTIPLE MYELOMA-RELATED BURDEN ON CAREGIVERS – A PORTUGUESE NATIONAL STUDY

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### Introduction

Multiple Myeloma (MM) is an incurable hematological cancer that decreases the quality of life of patients but also that of their providers. The disease course is linked with psychological stress of caregivers, but the data on the association between MM characteristics, the management of the disease, and the caregivers' burden is very scarce.

### Objective

CarMMa ("Characterization of patients with Multiple Myeloma treated in Portuguese Hospitals and of their caregivers") is an ongoing multicentric, national, cross-sectional study aiming to provide a descriptive analysis of MM patients, their disease, and their caregivers.

### Methods

QASCI, a Portuguese questionnaire for the evaluation burden of caregiving, was used to assess caregivers of patients with MM. The seven dimensions of burden (Emotional Burden; Personal Life Implications; Financial Overload; Reactions to Demands; Mechanisms of Efficacy and Control; Familiar Support; and Satisfaction with the Role) were graded on a 5-point Linkert scale. The overall burden for each caregiver was obtained and further categorized into "Low" (0-25 points), "Moderate" (26-50 points), "High" (51-75 points), and "Extreme" (≥76 points), according to the pre-set physicians' perception of burden. Pearson's chi-square test was used to assess the existence of an association between each of the variables of interest and each of the QASCI scales. The significance level is 0.050. The significance values were adjusted by Bonferroni correction for various tests.

**Results**

From July 2022 until March 2023, we enrolled 313 MM patients from 11 Portuguese centers: 63.2% were newly diagnosed, 23.9% had 2 lines of treatment and 12.7% had 3 or more lines of therapy. The patients' median age was 70 years, PS was 0-1 in 56.5%; ISS 2-3 in 64.8%. Patients with lytic lesions and extramedullary disease were 72.8% and 15.6%, respectively.

Fifty four percent of the patients identified one significant caregiver, with a median age of 59.4 years; 74% were women. The median overall score for burden of caregiving was 23: 100 (59,2%) caregivers reported a low burden, 60 (35,5%) moderate burden and 7 (4,1%) high burden. Women tended to report a higher burden than men (median 23.59 vs 18.8, P=0.057 ). Among the 7 dimensions evaluated, the rate of "High" or "Extreme" burden was higher for Personal Life Implications (19.9%), Familial Support (15.8%) and Mechanisms of Efficacy and Control (14.4%); it was lower for Reaction to Demands (3.6%). The burden was significantly higher in caregivers of patients with 2 or more lines of treatment for the dimension of Personal Life Implications (P=0.042). Financial Overload was significantly higher for caregivers of patients < 60 years of age (P=0.02), and the score for Mechanisms for Efficacy and Control was higher in patients with ISS II-II (P=0.05).

**Conclusions**

Despite most caregivers reporting an overall low burden, this study shows a higher score for women and a significant relation between higher burden of caregiving and later lines of treatment and higher disease risk scores. Specific dimensions, such as personal life and familial dynamics, as well as the financial aspect in professionally active caregivers, display a higher impact and should be addressed specifically when dealing with MM patients and their caregivers. This Portuguese multicenter national study contributes to the understanding of the social and economic impact of MM in caregivers.

Both first and second authors contributed equally for this publication.

# PO06

## VALOR PROGNÓSTICO DE VARIANTES ESTRUTURAIS DO MYC IDENTIFICADAS POR FISH NO MIELOMA MÚLTIPLO NA RECAÍDA APÓS TRANSPLANTE DE PROGENITORES HEMATOPOIÉTICOS DE SANGUE PERIFÉRICO

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### Introdução

O mieloma múlplo (MM) caracteriza-se pela proliferação neoplásica de plasmócitos produtores de imunoglobulina (Ig) monoclonal na medula óssea (MO). Em fases precoces do MM, são características variantes estruturais (VE) recorrentes de cadeia pesada de Ig e/ou hiperdiploidia, enquanto que o ganho 1q, deleção 17p e VE envolvendo o proto-oncogene MYC surgem no contexto de progressão do MM. Estas alterações genéticas contribuem para a sua heterogeneidade e têm impacto na resposta à terapêutica e prognóstico do MM.

### Objetivo

Análise do impacto de VE no gene MYC nos doentes com MM.

### Material e Métodos

Avaliação por fluorescence in situ hybridization (FISH) utilizando sondas break apart para o gene MYC em doentes adultos com diagnóstico de MM, entre 01/2007 e 12/2020, elegíveis para transplante autólogo de progenitores hematopoiéticos (TAPH) e seguidos num hospital terciário. A análise dos dados clínicos e demográficos foi efetuada através do programa IBMSPSS Statistics 26®.

### Resultados

Foram incluídos 124 doentes [54.8% homens (n=68), 45.2% mulheres (n=56)], com idade mediana ao diagnóstico de 59 anos (37-69). O subtipo mais comum foi IgG/kappa(35.5%, n=44). Ao diagnóstico, os sintomas "CRAB" mais frequentes foram a doença óssea (63.7%, n=79) e a anemia (52.4%, n=65), seguidos por LRA (21.0%, n=26) e hipercalcemia (20.2%, n=25). O revised MM International Staging System (R-ISS) foi determinado em 72.6% (n=90) doentes [I 13.3% (n=12), II 60.0% (n=54), III 26.7% (n=24)]. Ao diagnóstico, a avaliação do gene MYC por FISH revelou ausência de rearranjo em 83.9% (n=104), presença de rearranjo em 10.5% (n=13), aumento do número de cópias em 3.2% (n=4) e deleção do gene MYC em 2.4% (n=3). A análise por regressão logística multivariada não demonstrou associação entre a presença de rearranjo, deleção ou aumento do número de cópias do gene MYC com a presença de anemia, doença óssea, hipercalcemia ou LRA (p=0.227). Adicionalmente, também não foi encontrada associação com outras alterações citogenéticas, nomeadamente t(4;14), t(11;14), t(14;16), ganho 1q, deleção 13p ou 17p (p=0.906). Não foi encontrada associação entre a presença de rearranjo, deleção ou aumento do número de cópias do gene MYC com a resposta à terapêutica de indução. A recaída após TAPH foi mais frequente nos doentes que apresentavam rearranjo, deleção ou aumento do número de cópias do gene MYC, comparativamente aos doentes sem alterações no gene MYC, sendo este resultado estatisticamente significativo [p=0.019, Intervalo de confiança (IC) 95% 1.284-16.873)]. O tempo estimado até progressão foi de 23 meses nos doentes com alterações citogenéticas no gene MYC (IC 95% 7.661-38.339) e 43 meses nos doentes sem a presença destas alterações (IC 95% 35.603-50.397), sendo esta diferença estatiscamente significativa (p=0.001). Adicionalmente, apesar dos doentes que realizaram terapêutica de manutenção após TAPH apresentarem, de forma global, maior tempo até progressão (69 meses, IC 95% 32.031-105.969), os doentes com alterações citogenéticas no gene MYC progridem mais precocemente (39 meses, IC 95% 20.539-57.461), sendo esta diferença estatisticamente significativa (p=0.002).

**Discussão**

Apesar das alterações citogenéticas envolvendo o gene MYC, ao diagnóstico, terem já sido associadas a sintomas "CRAB" e a alterações citogenéticas de alto risco no MM, nesta população essa associação não se verificou. No entanto, a sua presença parece contribuir para uma recaída precoce do MM, apesar da e manutenção com lenalidomida após TAPH, sugerindo que estes doentes terão um comportamento mais agressivo do MM.

**Conclusão**

Apesar de as alterações citogenéticas envolvendo o gene MYC estarem sobretudo estudadas no contexto de progressão do MM, este estudo demonstra que a sua presença ao diagnóstico poderá ter elevado valor de prognóstico, sendo por isso importante a sua avaliação por FISH no momento do diagnóstico.

# PO07

## EVALUATION OF IMMUNE RECONSTITUTION IN MULTIPLE MYELOMA PATIENTS ON MAINTENANCE THERAPY WITH LENALIDOMIDE - THE ROLE OF HEAVYLITE CHAINS

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### Introduction

Multiple Myeloma (MM) has been the focus of major advances and developments, both in therapy and in innovative methods of diagnosis and response evaluation. One of the pillars of current MM therapy are immunomodulatory drugs such as lenalidomide, used in first-line treatment and maintenance after auto-transplantation. These drugs have an excellent anti-tumor activity by inhibiting the growth of MM cells in the bone marrow, but also by promoting the function of immune effector cells. Thus, it becomes relevant to use disease assessment methods to characterize the patient's immune status and understand the impact of disease and treatment on immunosuppression and immune reconstitution. The evaluation of HeavyLite chains (HLC) could be an important marker to assess the immune reconstitution of MM patients. The suppression of the uninvolved HLC pair (uHLC) is believed to have prognostic value and to reflect the patient's immune reconstitution.

### Objective

Analyze the evolution of involved and uninvolved HLC of patients diagnosed with MM under maintenance therapy with lenalidomide for 12 months.

### Materials and Methods

Serum samples from 18 patients diagnosed with MM (11 male and 7 female) were evaluated at day 100 after autologous transplantation (D100) and after 1 year of maintenance with lenalidomide. Involved (iHLC) and uninvolved (uHLC) HLC levels were assessed. Immunoparesis (IP) was defined when uHLC values were lower than the assay reference values. SPSS version 28 software was used for statistical analysis of the data.

### Results

The isotypes of the patients evaluated were the following: IgG Kappa (n=8), IgG Lambda (n=6), IgA kappa (n=3) and IgA Lambda (n=1). 15 were in complete response (CR) and 3 were in very good partial response (VGPR) at D100. iHLC levels at D100 and after 1 year of treatment were higher in VGPR patients compared to CR patients, without statistical significance (D100 - median iHLC: 5.02 vs 3.11 g/L respectively; 12 months - median iHLC 8.45 vs 5.02 g/L). The uHLC values were similar in both groups and in both measurements (D100 – median uHLC: 3.68 vs 3.5 g/L; 12 months - median uHLC 4.78 vs 4.4 g/L). At D100 only 2 patients had PI. After 1 year of lenalidomide maintenance, 1 of these patients recovered from IP. There were no relevant infectious intercurrences during the evaluated period.

### Discussion and Conclusions

This is an important result that confirms the efficacy of maintenance therapy with lenalidomide since the patients did not lose response and in one case there was even immunological recovery. Furthermore, it reflects the importance of controlling not only the involved but also the uninvolved HLC for a better distinction between patients with more immune dysregulation and with a potential worse prognosis. We must keep in mind that severe immunoparesis is an independent risk factor for bacteremia and early death, reinforcing the importance of selecting and evaluating HLC chain values in these specific patients.

# PO09

## IBRUTINIB AND VENETOCLAX COMBINATION AS BRIDGE FOR CHIMERIC ANTIGEN RECEPTOR T-CELL THERAPY IN RELAPSED/REFRACTORY MANTLE CELL LYMPHOMA

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### Introduction

Mantle cell lymphoma (MCL) has a heterogeneous clinical course, and an aggressive presentation has a dismal prognosis. In relapsed/refractory (R/R) MCL, treatment strategies include Bruton tyrosine kinase inhibitors (BTKi), the selective BCL2 inhibitor (BCL2i) venetoclax and chimeric antigen receptor (CAR) T-cell therapy. Dual treatment with BTKi/BCL2i seems to improve outcomes in R/R MCL. Herein, we present two cases of R/R MCL patients treated with ibrutinib/venetoclax combination (V-I), as bridge for CAR T-cell therapy.

### Case-1

Male, 75-year-old, diagnosed with MCL, stage IV-B, high-risk MCL International Prognostic Index (MIPI), submitted to therapy with rituximab/cyclophosphamide/doxorubicin/vincristine/prednisone (R-CHOP), with early progression. He started a second-line treatment with ibrutinib 560mg, initially with symptomatic improvement and reduction of lymphomatous masses. However, two months later, the patient presented progressive lymphocytosis. Disease molecular characterization showed mutated TP53, without 17p deletion. Progressive disease (PD) was documented by PET/CT scan. He started V-I as bridge for CAR T-cell therapy. However, severe febrile neutropenia led to treatment suspension, and consequently death.

### Case-2

Male, 70-year-old, diagnosed with leukemic MCL stage IV-AX, with bulky neck and abdominal masses, intermediate risk MIPI, without 17p deletion. He started on R-CHOP, with PD one month after the first cycle. He initiated a second line treatment with rituximab and high-dose cytarabine, with complete metabolic response (CMR), followed by rituximab maintenance. Nine months later, he had PD documented on PET/CT, showing supra and infradiaphragmatic lymph node involvement. He started on ibrutinib 560mg, achieving CMR, six months later. After 12 months on ibrutinib, he complained of headache and thoracic, neck and lumbar pain, and was admitted for investigation. Progressive lymphocytosis was verified and immunophenotyping of peripheral blood showed 43% of large B cells with a phenotype of MCL and a very complex karyotype, with severe hyperdiploidy and structural alterations associated with poor prognosis. PET/CT showed hepatosplenic, bone marrow lymphomatous involvement and a right submandibular hypermetabolic adenopathy. He was proposed for CAR-T cell therapy, and association of V-I was intended, after lymphocyte apheresis, for disease control. However, the patient was admitted to the Intensive Care Unit due to nosocomial pneumonia. After recovering, an MRI of the cervical segment showed diffuse lymphomatous bone infiltration involving all vertebral bodies and clivus, associated with edema/infiltration of the posterior paraspinal soft tissues of the neck. He was treated with external radiotherapy with pain relief, and V-I was started. The patient presented altered mental status 14 days after V-I start and a brain CT was done, showing a new parietal subcortical hypodense area on the left hemisphere, compatible with PD. Venetoclax was suspended 28 days after its start due to severe thrombocytopenia and septic shock after Pseudomonas aeruginosa pneumonia, which led to the patient's death.

### Conclusion

Ibrutinib and venetoclax have different, but complementary mechanisms of action, and have demonstrated synergistic antitumor activities in MCL. Some studies support the safety and efficacy of this combined therapy in patients with R/R MCL. However, the management of Ibrutinib/Venetoclax combination induced cytopenia (such as thrombocytopenia and neutropenia and the consequent infectious complications) is still challenging.

# PO10

## MATRIX INDUCTION FOLLOWED BY AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION CONSOLIDATION IN PRIMARY CENTRAL NERVOUS SYSTEM B-CELL LYMPHOMA -- REAL-WORLD SERIES

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**Introduction**

Chemoimmunotherapy with high-dose methotrexate, cytarabine, thiotepa and rituximab (MATRix) increased response rates and progression free survival in primary central nervous system diffuse large B cell lymphoma (PCNSL). Consolidation with autologous hematopoietic stem cell transplantation (aHSCT) improves outcomes in eligible patients, with less cognitive impairment when compared to consolidation with whole-brain irradiation. However, conditioning regimens are still under debate. Some studies have shown that thiotepa-based conditioning is associated with higher survival rates, compared to other regimens. Herein, the authors report four cases of patients with PCNSL treated with MATRix followed by consolidation with aHSCT after thiotepa-carmustine (TT-BCNU) conditioning.

**Case-1**

Male, 47-year-old, diagnosed with PCNSL (primary bilateral vitreoretinal involvement) and submitted to MATRix (4 cycles), with complete response, followed by TT-BCNU conditioning and aHSCT. Treatment was complicated by grade 2 oral mucositis (OM) and febrile neutropenia (FN). The patient remains in complete remission (CR) twenty-two months after transplant.

**Case-2**

Male, 64-year-old, HIV infected with undetectable viral load and PCNSL diagnosis, submitted to MATRix (4 cycles), followed by TT-BCNU conditioning and aHSCT consolidation. As treatment-related complications, he developed grade 1 OM and FN. Eight months after aHSCT, upon *de novo* complaints of dizziness, PCNSL relapse was documented. Salvage chemotherapy with ifosfamide, carboplatin, etoposide, and dexamethasone (ICE-D) resulted in disease progression. He then started palliative holocranial radiotherapy but died due to bilateral *Pneumocystis jirovecci* pneumonia.

**Case-3**

Female, 51-year-old, diagnosed with PCNSL involving the cervical cord (C1-2). She was submitted to MATRix (4 cycles) followed by TT-BCNU conditioning and aHSCT. As treatment-related complications, she developed grade 1 OM, urinary tract infection and grade 2 peripheral neuropathy, with pain. She remains in CR forty-seven months after aHSCT.

**Case-4**

Female, 48-year-old, with PCNSL diagnosis and submitted to MATRix (4 cycles), with CR. She proceeded to TT-BCNU conditioning followed by aHSCT consolidation. The process was complicated by grade 3 OM, grade 4 gastrointestinal mucositis, and septic shock due to bacteremia by *Klebsiella pneumoniae* and fungemia by *Candida kruzei.* She was admitted to Intensive Care Unit on day+9 post-aHSCT, complicated by ventilator-associated pneumonia. The patient was discharged home at day 68. CR at day+100.

**Discussion and Conclusions**

There are several challenges in dealing with PCNSL and its primary treatment and consolidation alternatives. In this real-world case series, the authors show four case reports of patients first-line treated with MATRix protocol followed by consolidation with TT-BCNU conditioning and aHSCT, with good efficacy and manageable tolerability in most cases. Despite the small sample size, intensive therapy with thiotepa-based induction and pre-aHSCT thiotepa-based conditioning appears to be an adequate protocol in fit PCNSL patients.

# PO11

## WHEN BONES HAVE THE ANSWER -- SILENT MULTIPLE MYELOMA RELAPSE AS PURELY LYTIC LESIONS

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### Introduction

Lytic bone lesions are one of the main characteristics of multiple myeloma (MM) and are present in up to 80% of patients at diagnosis. They lead to pain, hypercalcemia and bone complications, namely pathologic fractures, and spinal cord compression. Almost all patients with MM will eventually relapse. At relapse, patients may present with increasing serum and/or urine monoclonal protein alone (biochemical progression) or may present with clinical features suggestive of progression (CRAB symptoms – present in 40% of patients). Although in the majority of the patients, the clinical progression is preceded by a biochemical progression (median interval time 5.1 months), end-organ damage can appear in the absence of biochemical or bone marrow progression.

### Objective

We present the case of two patients who developed clinical progression as isolated lytic lesions.

### Case Reports

Male, 65 years old, diagnosed with IgA kappa MM, International Staging System (ISS) II, with anaemia and lytic dorsal and lumbar bone lesions at diagnosis. He was treated according to CyBorD (bortezomib, cyclophosphamide, and dexamethasone) protocol for 4 cycles plus bone radiotherapy, achieving a very good partial response (VGPR), and received consolidation with melphalan 200 mg/m2 followed by autologous stem cell transplant (ASCT). At day +100, he presented normal blood count and biochemistry evaluation, complete response (CR) criteria in serum and urine, and a negative mensurable residual disease by flow cytometry (sensitivity 10^-5) in bone marrow. Before maintenance the patient remained asymptomatic, except for a slight lumbar pain that remained since day + 89. A computed tomography (CT) scan of the spine and a positron emission tomography/CT (PET/CT) were performed (per protocol for post-ASCT evaluation) and revealed multiple lytic lesions in the right humerus, several ribs, 12th dorsal and 3rd lumbar vertebras and right iliac (maximal SUV 10.4-15.1). A clinical progression was established, and the patient started treatment with daratumumab/lenalidomide/dexamethasone (DRd). Male, 66 years old, diagnosed with IgG kappa MM, R-ISS II, with hyperviscosity syndrome, kidney failure, anemia, and lytic bone lesions (cranial and in both humerus) at diagnosis. He was treated according to CyBorD protocol for 6 cycles, achieving VGPR. Before the admission for ASCT, he was asymptomatic but presented mild thrombocytopenia (102x10^6/L) and elevated lactate dehydrogenase(301 U/L; N<240). Serum and urine studies maintained VGPR criteria. Bone marrow morphology showed 1% plasma cells and flow cytometry 0.03% clonal plasma cells. A PET/CT revealed large lytic lesions in the 2nd dorsal and 2nd lumbar vertebras (maximal SUV 8.8-19.3). A week later, he developed paraparesis, with spine magnetic resonance confirming medullary spinal cord compression by these lesions. The patient underwent decompressive surgery with complete recovery of symptoms, and he will start treatment according to DRd protocol.

### Conclusion

These cases reinforce the need to maintain a high suspicion of bone progression even in the absence of biochemical/bone marrow progression or exuberant symptoms, allowing a timely and appropriate treatment.

# PO12

## IGD MULTIPLE MYELOMA – A RARE (AND PROBABLY UNRECOGNISED) ISOTYPE OF MULTIPLE MYELOMA WITH A GRIM PROGNOSIS

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### Background

Immunoglobulin D (IgD) multiple myeloma (MM) is a rare isotype of MM, comprising less than 2% of all cases. It's prevalence may be underestimated because immunofixation for IgD is not routinely performed and may not be recognised on electrophoresis since the serum IgD level is extremely low. It has been considered more aggressive, often associated with advanced disease at diagnosis, and poor outcome despite autologous hematopoietic stem cell transplantation (aHSCT). However, data about IgD MM prognosis in the era of novel agents (NA) are scarce.

### Aims

Evaluate the clinical characteristics, treatment pattern, outcomes, and prognosis of IgD MM patients (pts).

### Methods

We performed a retrospective, single-centre study of IgD MM pts diagnosed between 2000 and 2022. CRAB criteria and response were evaluated by IMWG criteria. High-risk cytogenetics (HRC) was defined according mSMART v3.0 classification.

### Results

We included 25 pts, 60% male, with a median age 64 (36-83) years old (yrs): 22 (88%) pts had a IgD lambda monoclonal gammopathy (MG), 20 (80%) had a free-light chain component and 3 pts were previously diagnosed with other isotype MM (2 lambda light chain and 1 IgA lambda), latterly reviewed with the identification of IgD MG.

At diagnosis, 9 (36%) pts had renal compromise, 17 (68%) had bone disease, 7 (28%) had extramedullary disease (EMD), and 16/22 (73%) had Bence-Jones protein. The median IgD serum level was 2.4 (0.176-40) g/L.

From 11 pts that had cytogenetics by fluorescence in situ hybridization (FISH) available, 9 (82%) had HRC and 5 (46%) had del17p.

The majority of pts had advanced stage MM – 12/22 (55%) had International Staging System (ISS) III and 8/15 (53%) Revised-ISS III.

The median number of treatment lines was 2 (0-6). Eleven pts (44%) received aHSCT and 9 (36%) radiotherapy.

From 24 pts that received any therapeutics, 16 (67%) received a NA in 1st line – 8 proteasome inhibitor (PI), 3 immunomodulator (IMID) and 4 both. The overall response rate to the 1st line (R1) was 64% (n=15), with 56% (n=14) attained at least a very good partial response.

The median progression free survival (PFS) for 1st line was 15.1 months, being higher, although non-significantly in pts who received a NA (43.6 vs 10.3 months; OR 0.49; p=0.143) or aHSCT (34.5 vs 10.3 months; OR 0.11; p=0.169). From the different prognostic factors tested, only R1 was associated to a significantly increased PFS (4.7 vs 43.6 months; OR 0.50; p<0.001) (Fig. 1).

Eighteen pts progressed: 5 (28%) with EMD, 2 with plasma cell leukaemia. Thirteen pts (72%) received a 2nd line therapy, including a NA in all of them (IP in 8 pts, IMID in 4, both in 1 and anti-CD8 in 1), with PFS for 2nd line of 8.6 months.

After a median follow-up of 34.6 months, the median overall survival (OS) was 40.9 months, with only R1 line being associate with improved survival (8.3 vs 70.8 months; OR 0.21; p=0.001) (Fig. 1). The majority of pts died due to progressive disease (n=12; 70.6%) followed by infection (n=4; 23.5%).

**Conclusion**

In our cohort, the median age at diagnosis was higher (64 vs 55-59 yrs ) than other cohorts published in literature (Liu, 2022; Egan, 2022; Agbuduwe, 2022) but presented a predominance for males and lambda light chain isotype as reported. Most patients presented an advanced stage and a HRC (particularly del17p) at diagnosis. The median OS was similar to published results (38-48 months). Surprisingly, the use of NA was associated to an improved but not significantly different PFS and OS values, probably due to the small sample size, with R1 being the only significant prognostic factor for PFS and OS.