



## The 65th ASH Annual Meeting Abstracts

## POSTER ABSTRACTS

## 653.Multiple Myeloma: Prospective Therapeutic Trials

**Renal Sub-Study (GEM-KyCyDex): Cystatin C Improves the Proficiency of Creatinine Alone in the Detection and Management of Myeloma-Related Renal Impairment**

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**Introduction:**

Renal impairment is an important adverse prognostic factor in patients with multiple myeloma (MM), which limits the use of certain drugs that require dose adjustment. Renal function is measured by the glomerular filtration rate (GFR) which is estimated with equations such as MDRD or CKD-EPI. In clinical practice, serum creatinine (Crea) is the main parameter used in these calculations, however, the recent IMWG recommendations suggest including other parameters such as Cystatin C (CC) to improve the management of kidney disease in patients with MM.

**AIM:**

To assess the prevalence of renal impairment in patients with multiple myeloma at relapse (MMRR), comparing the GFR (CKD-EPI), using Crea alone or including also CC in the equation and to study the potential association with the prognosis.

**Material and methods:**

Within the phase II GEM-KyCyDex clinical trial, which compared carfilzomib and dexamethasone in combination with cyclophosphamide (KcD) versus carfilzomib and dexamethasone (Kd) in MMRR, a substudy was conducted to analyze in detail the basal renal function and its potential modification during 12 months of follow-up, using CC and Crea to estimate GFR

**Results:**

87 patients were included in the renal substudy (45KcD/42Kd) with a median age of 70 years (40-89 range) and 45% were women. The mean Crea level was 1.06 mg/dL ( $\pm$  0.36) (normal range 0.7-1.4 mg/dL in men and 0.6-1.2 mg/dL in women). and the mean CC was 1.43 mg/L ( $\pm$  0.46) (normal range 0.62-1.11 mg/L).

Progressive elevations of CC were present as ISS stages increase and according to the elevations of beta2microglobulin, and patients with ISS-1 stage had lower CC levels than patients with ISS-3 stage (1.13 vs 1.63 mg/L.  $p=0.001$ ), while Crea levels did not show significant differences ( $p=0.62$ ).

According to method for estimating GFR that includes the CC and Crea parameters (CKD-EPI Crea-CC), the prevalence of patients at baseline with GFR < 60 mL/min, adjusting for body surface area, was 45% versus 24% detected by the CKD-EPI that only includes creatinine.

Interestingly, slight reductions in both CC and Crea levels were observed throughout treatment, from baseline to the end of cycle 12 (median of 1.42 mg/L vs 1.07 for CC and 1.23 mg/dL vs 0.7 for crea), although differences were not statistically significant.

When studying the association with response, those patients who maintained an abnormal kappa/lambda free light chain ratio, had higher CC levels (1.51 mg/L) compared to patients who presented a normal ratio (1.33 mg/L). However, in the case of Crea, the values remain within the normal range (1.11 mg/dL)

The equation that presented the greatest diagnostic capacity (according to ROC curves) in terms of detecting patients who dropped off the study due to toxicity or progression, was the CKD-EPI CC formula with baseline values lower than 54 mL/min (AUC 0.59 (0.44-0.72, 95% CI), with a sensitivity/specificity of 68/71% respectively. In these same patients, the CKD-EPI equation did not identify renal impairment, since values higher than 62 mL/min (AUC 0.51 (0.37-0.66, 95% CI)) presented the worst prognosis.

#### Conclusions:

In the patients included in the renal substudy of the phase II GEM-KyCyDex clinical trial, we observed a prevalence of chronic kidney disease with the CKD-EPI CC-crea equation of 45%, being 21% of them hidden (not detected by creatinine alone). Patients with elevated CC were found mainly in the stage with the worst prognosis ISS-3, they showed a more altered kappa/lambda ratio and a worse prognosis in terms of showing greater toxicity or abandonment of the study due to disease progression, situations not detected with elevations of crea. CC can improve monitoring of patients with MM, to early detect renal impairment and patients with the worst prognosis who will require close monitoring

**Disclosures Rosiñol:** Sanofi: Other: Honoraria for lectures; Takeda: Other: Honoraria for lectures; GlaxoSmithKline: Other: Honoraria for lectures; Amgen: Other: Honoraria for lectures; Bristol Myers Squibb/Celgene: Other: Honoraria for lectures; Janssen: Other: Honoraria for lectures. **Oriol:** Amgen: Consultancy, Other: Consulting fees; BMS/Celgene: Consultancy, Honoraria, Speakers Bureau; GSK: Consultancy, Honoraria, Speakers Bureau. **Gonzalez:** SOBI, Roche: Honoraria; Takeda: Honoraria, Speakers Bureau; BMS/Celgene: Honoraria; Janssen: Consultancy, Honoraria; Alexion: Consultancy, Honoraria, Speakers Bureau; Astra Zeneca: Consultancy, Speakers Bureau; Jazz Pharma: Consultancy. **Gonzalez-Calle:** Janssen: Consultancy, Honoraria, Research Funding; Prothena: Consultancy; BMS: Honoraria. **Ocio:** Oncopeptides: Consultancy, Honoraria, Research Funding; Pfizer: Consultancy, Honoraria; Regeneron: Honoraria; BMS: Consultancy, Honoraria; Takeda: Consultancy, Honoraria; Sanofi: Consultancy, Honoraria; Menarini: Consultancy; Karyopharm: Consultancy; Janssen: Consultancy, Honoraria, Speakers Bureau; GSK: Consultancy, Honoraria, Research Funding; Amgen: Consultancy, Honoraria; Abbvie: Consultancy. **Mateos:** Regeneron: Honoraria; Janssen: Honoraria, Membership on an entity's Board of Directors or advisory committees; BMS-Celgene: Honoraria, Membership on an entity's Board of Directors or advisory committees; Stemline: Honoraria, Membership on an entity's Board of Directors or advisory committees; Oncopeptides: Honoraria, Membership on an entity's Board of Directors or advisory committees; Sanofi: Honoraria, Membership on an entity's Board of Directors or advisory committees; Takeda: Honoraria; Amgen: Honoraria; GSK: Honoraria, Membership on an entity's Board of Directors or advisory committees; Abbvie: Honoraria, Membership on an entity's Board of Directors or advisory committees; Pfizer: Honoraria, Membership on an entity's Board of Directors or advisory committees; University of Salamanca/Gerencia Regional de Salud de Castilla y León: Current Employment.

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