SERUM FREE LIGHT CHAINS MEASUREMENT FOR AL AMYLOIDOSIS DETECTION IN PATIENTS WITH SUSPECTED AMYLOID CARDIOMYOPATHY

S Soledad [a], AM Adela [a], MM Agustina [a], B Gisela [a], C Delfina [a], C Malena [b], V Mariana [a], C Marcelina [a], V Eugenia [a], D Santiago [a], PA Diego [a], S Patricia [b], NE Mercedes [a], PM Lourdes [a], DF M [c], SE M [c]

[a] *Hospital Italiano de Buenos Aires (HIBA), Ciudad Autónoma de Buenos Aires, Argentina*
[b] *Instituto Universitario del Hospital Italiano de Buenos Aires (IUHIBA), Ciudad Autónoma de Buenos Aires, Argentina*
[c] *Binding Site, empresa do Grupo Thermo Fisher*

Aim: To assess serum free light chains (SFLCs) behavior in heart failure patients with preserved systolic function and ventricular wall thickness suggestive of cardiac amyloidosis (CA) and their performance as an initial test for detecting light chain (AL) amyloidosis. **Methodology:** Ambispective, observational study in a high complexity hospital in Buenos Aires from March 2020 to October 2022. Inclusion criteria were hospitalization in Cardiologic ICU due to heart failure and echocardiographic evidence of left-ventricular ejection fraction >55% and ventricular wall thickness ≥1,2 mm in any segment. Inclusion was prospective for 6 months and retrospective for 2 years. Heart failure cases due to any other cardiovascular affections were excluded. The minimum follow up was 3 months. Sampling was consecutive. SFLCs values and the kappa/lambda ratio were registered (normal range was assumed between 0,26 and 1,65). Requests of urine and serum immunofixation and other complementary studies were registered as well as their results. Diagnosis based on medical criteria served as the reference standard for AL and transthyretin amyloidosis (ATTR) diagnosis. For the evaluation of diagnostic performance, sensitivity, specificity, likelihood ratios and predictive values and their respective confidence intervals were calculated with software Stata13. **Results:** 29 patients were included, with a median age of 81 years old (IQI 75-85). Amyloidosis was diagnosed in 12 patients (41%, IC95 24-61%), from which 7 (58%) were ATTR and 5 (42%) AL. Eighty-six percent (n = 6) of the patients with ATTR diagnosis and 100% of those with AL amyloidosis presented alterations of at least one free light chain value (lambda or kappa). Kappa/lambda ratio was altered in 100% patients with AL amyloidosis and in 43% of ATTR patients. Sensitivity of kappa/lambda ratio for the diagnosis of AL amyloidosis was 100% (IC95 48%-100%) and specificity was 58% (37-78%). Positive likelihood ratio (PLR) was 2.4 (1,49-3,85) and negative predictive value was 100% (76%-100%). **Discussion:** Altered kappa/lambda ratio for diagnosis of AL cardiac amyloidosis showed high sensitivity but a PLR of 2.4 and low specificity, suggesting its convenience as a screening method for AL amyloidosis. Subsequent immunofixation studies would be required for diagnostic confirmation. Negative predictive value of 100% suggests it might be a reliable method to rule out AL amyloidosis. The main limitations of the research are the small number of patients involved, its ambispective character, the fact that a unique range of the kappa/lambda ratio was used disregarding renal function, and the possible distortion of kappa/lambda ratio in clinical situations associated with polyclonal hypergammaglobulinemia. Also, the definition of a suspected case of CA does not cover all possible suspicion scenarios and is based on operator-dependent findings. **Conclusions:** Currently, diagnostic methods allow early diagnosis of CA. Differentiating between its two main etiologies, ATTR and AL, is a key point. SFLCs dosing turned out to be highly sensitive for diagnosis of AL amyloidosis, though not very specific. Considering it is a simple and rapid method, it could be useful for the initial evaluation of CA, as it allows to increase the grade of suspicion of AL, an entity with earlier mortality that requires prompt therapeutic action.

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IGA MULTIPLE MYELOMA ASSESMENT WITH HEVYLITE ASSAY

G Virginia [a], C Silvina [a], F Delgado [b], EM Soares [b]

[a] *1MANLAB, Diagnóstico Bioquímico y Genómico, Área de Proteínas, Buenos Aires, Argentina*
[b] *Binding Site, empresa do Grupo Thermo Fisher*

Introduction: A key element on Multiple Myeloma (MM) evaluation is the quantification of monoclonal proteins. Current techniques include Serum Protein Electrophoresis (SPE), Immunofixation (IFE) and Free Light Chain Assay (FLC, Freelite). All assays are clinically relevant but have some limitations. Especially for IgA MM patients, SPE could be inaccurate, insensitive due to comigration, lack of sensitivity below 10 g/L and has subjective interpretation, among other limitations. IFE have greater sensitivity but is only qualitative. Hevylite, an immunoassay based on polyclonal antibodies that measure IgA-κ and IgA-λ independently, quantifies these proteins while identifying clonality through its ratio (IgA-κ/IgA-λ, HLCr) and gives additional clinical information, especially for difficult IgA MM patients serum samples. **Aim:** To test Hevylite assay and to evaluate its lab and clinically relevance for IgA MM patients. **Material and methods:** 44 IgA MM patients were evaluated in this study. All were received at protein lab for MM query between Feb-May 2023. Patients were selected according to: CZE: Monoclonal component or distortion of alfa-2 or beta fraction. IFE: Monoclonal component IgA-Kappa or IgA-Lambda isotype. Measurement of IgA-κ and IgA-λ were performed using Hevylite™assay (The Binding Site) according to manufacture recommendations in a turbidimetry (Optilite, The Binding Site). CZE with Capillarys 3 (Sebia) and IFE with Hydrasys 2 (Sebia). Patients were classified: IgA-κ MM, IgA-λ MM and non-MM. Patient's evaluation was performed following IMWG recommendations. **Results:** Serum level of monoclonal protein and discrimination between monoclonal and polyclonal components are crucial in the follow up of MM patients. All IgA MM patients in the study showed an abnormal HLCr IgAκ/IgAλ indicating clonality. IgAκ or IgAλ levels were abnormally high when the isotype was monoclonal. HLCr allowed a better discrimination between groups and an accurate identification of myeloma patients at diagnosis.

Concordance grade (0,927) between HLCr and IFE qualitative results were analyzed with Cohen k coefficient. Hevylite allowed accurate identification and quantification of M protein in 10 IgA MM patients that couldn't be resolved by CZE. Case#1. IgAκ: 3,849 g/L, IgAλ: 0,032 g/L. HLCr: 120,28. CZE β1-2 fraction alteration without signs of monoclonal component. Hevylite solved this patient's evaluation. **Conclusions:** The performance of Hevylite assay as a biomarker in IgA monoclonal gammopathies allow us: To use a full automated lab assay, easy to run in daily routine. To better discriminate monoclonal components that co-migrates in CZE, especially IgA monoclonal proteins. To increase the sensitivity to detect monoclonal protein compared to CZE, given a quantitative and reproducible results of both monoclonal isotype (involved) and non-monoclonal isotype (uninvolved) in the patient serum sample. To use as a clinical tool to overcome traditional methods'limitations on monoclonal gammopathies detections and follow up. Overall, our results showed that Hevylite could be a useful clinical tool, with increased sensitivity compared with electrophoretic methods and that can provide additional clinical information overcoming electrophoresis limitations and allowing more MM serum samples to be accurate evaluated and, and the end, to better manage IgA MM patients.

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ELRANATAMAB, A B-CELL MATURATION ANTIGEN-CD3 BISPECIFIC ANTIBODY, FOR PATIENTS WITH RELAPSED/REFRACTORY MULTIPLE MYELOMA: EXTENDED FOLLOW UP AND BIWEEKLY ADMINISTRATION FROM THE MAGNETISMM-3 STUDY

M Mohty [a], M Tomasson [b], B Arnulf [c], N Bahlis [d], M Prince [e], R Niesvizky [f], P Rodrgue-Otero [g], J Martine-Lopez [h], G Koehne [i], Y Jethava [j], A Gabayan [k], D Stevens [l], A Nooka [m], N Raje [n], S Iida [o], E Leip [p], U Conte [q], A Czibere [q], A Viqueira [r], V Blunk [s], A Lesokhin [t]

[a] *Sorbonne University, Hôpital Saint-Antoine, and INSERM UMRs938, Paris, France*
[b] *Holden Comprehensive Cancer Center, University of Iowa, Iowa City, United States*
[c] *Hôpital Saint-Louis, Paris, France*
[d] *Arnie Charbonneau Cancer Institute, University of Calgary, Calgary, Canada*
[e] *Epworth Healthcare, Melbourne, Australia*
[f] *Weill Cornell Medical College – New York Presbyterian Hospital, New York, United States*
[g] *Clinica Universidad de Navarra, Madrid, Spain*
[h] *Hospital Universitario 12 DE OCTUBRE, Madrid, Spain*
[i] *Miami Cancer Institute, Miami, United States*
[j] *Indiana Blood & Marrow Transplant, Indianapolis, United States*
[k] *Beverly Hills Cancer Center, Beverly Hills, United States*
[l] *Norton Cancer Center, Louisville, United States*
[m] *Winship Cancer Institute, Atlanta, United States*
[n] *Massachusetts General Hospital Cancer Center, Harvard Medical School, Boston, United States*
[o] *Department of Hematology & Oncology, Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan*
[p] *Pfizer Inc, Cambridge, United States*
[q] *Pfizer Inc, New York, United States*
[r] *Pfizer SLU, Madrid, Spain*
[s] *Pfizer, São Paulo, Brazil*
[t] *Division of Hematology and Oncology, Memorial Sloan Kettering Cancer Center/Weill Cornell Medical College, New York, United States*

Introduction/Objectives: To report the findings of extended follow-up and biweekly administration of elranatamab monotherapy in patients (pts) with relapsed/refractory multiple myeloma (RRMM) naïve to BCMA-directed therapies enrolled in Cohort A of MagnetisMM-3. **Materials and methods:** MagnetisMM-3 (NCT04649359) is an open-label, multicenter, registration phase 2 study evaluating the efficacy and safety of elranatamab monotherapy in pts with RRMM. Eligible pts were refractory to at least 1 proteasome inhibitor, 1 immunomodulatory drug, and 1 anti-CD38 antibody. Pts received subcutaneous elranatamab in 28-d cycles with step-up doses of 12 mg on cycle 1 day 1 (C1D1) and 32 mg on C1D4 followed by 76 mg once-weekly beginning C1D8. Pts treated for 6 cycles and achieving partial response (PR) or better, lasting ≥2 mo, were switched to 76 mg once every two weeks (Q2W). **Results:** Overall, 123 pts received elranatamab. Median pt age was 68.0 y (range, 36-89); 63.4% of pts had an ECOG PS ≥1. The median number of prior lines of therapy was 5.0 (2-22), with 96.7% and 42.3% of pts having triple-class- and penta-drug refractory disease, respectively. At data cutoff (≈12 mo after last pt initial dose), the median follow up was 12.8 mo (0.2-22.7); 34.1% of pts remained on treatment. The most common reasons for treatment discontinuation were progressive disease (39.0%) and adverse events (AE; 13.8%). Objective response rate per blinded independent central review (BICR) was 61% (95% CI 51.8-69.6), with 39 (31.7%) pts with complete response (CR) or stringent CR (sCR); very good partial response (VGPR) and PR were achieved in 29 (23.6%) and 7 (5.7%) pts, respectively. MRD-negativity (threshold 10−−5) was achieved by 92.0% (n = 23/25) of evaluable pts. Median duration of response (mDOR) has not been reached (95% CI 12.9-NE), and DOR at 12 mo was 74.1% (95% CI 60.5-83.6). In pts with CR/sCR or VGPR, mDOR was not reached by 12 mo; in pts with PR, mDOR was 5.2 mo (95% CI 1.6-NE). There were 46 responders by BICR who switched to Q2W dosing ≥24 wk prior to the data cutoff; among these pts, 80.4% maintained/improved their response ≥24 wk after the switch. Median progression-free and overall survival have not been reached by 12 mo, and the respective rates (95% CI) at 12 mo were 57.1% (47.2-65.9) and 62.0% (52.8-70.0). Most common grade 3/4 treatment emergent AEs were hematologic; grade 3/4 nonhematologic events reported in ≥5% of pts were COVID-pneumonia (10.6%), hypokalemia (9.8%), pneumonia (7.3%), sepsis (6.5%), hypertension (6.5%), ALT increased (5.7 %), and SARS-COV-2 test positive (5.7%). Among pts who switched to Q2W dosing (n = 58), the incidence of grade 3/4 AEs decreased