International Journal of Clinical and Translational Medicine
https://www.sciltp.com/journals/ijctm

Mini-Review

Monoclonal Gammopathy of Undetermined Significance: A Perspective from Laboratorians

Ishwarlal Jialal [1,*] and Perumal Thiagarajan [2]

[1] School of Medicine, University of California, Davis, 2616 Hepworth Drive, Davis, CA 95618, USA
[2] Center for Translational Research on Inflammatory Diseases (CTRID), Michael E. DeBakey Veterans Affairs Medical Center & Department of Pathology and Medicine, Baylor College of Medicine, Houston, TX 77030, USA
* Correspondence: kjialal@gmail.com; Tel.: +1-530-902-0125

How To Cite: Jialal, I.; Thiagarajan, P. Monoclonal Gammopathy of Undetermined Significance: A Perspective from Laboratorians. *International Journal of Clinical and Translational Medicine* **2025**, *1*(4), 3. https://doi.org/10.53941/ijctm.2025.1000024

Received: 2 July 2025
Accepted: 11 July 2025
Published: 9 October 2025

Abstract: Monoclonal Gammopathy of Undetermined Significance (MGUS) is defined as the presence of a monoclonal protein (M-protein) detected by electrophoresis in serum or urine or an abnormal free light chain ratio (FLCR). The concentration of M protein is <3.0 g/dl, with <10 percent plasma cells on bone marrow biopsy (if performed). Moreover, patients lack CRAB-related clinical features such as hyperCalcemia, Renal dysfunction, Anemia and lytic Bone lesions. MGUS is present in over 3% of persons > 50 years of age. Most MGUS are of the IgG subtype. For non-IgM –MGUS (IgG, IgA, IgD, IgE), the risk of progression to multiple myeloma, amyloidosis or a related disorder is 1.0 percent per year. For IgM-MGUS the risk of progression to Waldenstrom's macroglobulinemia or IgM myeloma is 1.5 percent per year. For light chain MGUS the risk of progression to light chain myeloma or amyloidosis is 0.3% per year. The Mayo Clinic criteria for greatest progression over 20 years include a M-protein level ≥ 1.5 g/dl, non-IgG M-protein and an increase in the FLCR. In any patient with an M protein and unexplained end organ dysfunction, it is imperative to rule out Monoclonal Gammopathy of Clinical Significance manifesting as renal disease, neuropathy etc. since potential treatments could be offered. Most importantly, studies have suggested that MGUS screening should be actively discouraged. Finally, much further research is needed to identify biomarkers that will more accurately predict progression to malignancies in patients with MGUS.

Keywords: monoclonal protein; myeloma; free light chains; protein electrophoresis

1. Introduction and Diagnosis

This mini review was based on a PubMed search from January 2000–June 2025 focusing on MGUS as the key term.

Monoclonal Gammopathy of Undetermined Significance (MGUS) is defined by the International Myeloma Working Group (IMWG) as the presence of a monoclonal protein (M-protein) detected by electrophoresis in serum or urine (SPE, UPE, respectively) or an abnormal free light chain ratio (FLC) [1–3]. The M protein is <3.0 g/dl with <10 percent plasma cells on bone marrow biopsy. Also the patients should have no CRAB-related clinical features such as hyperCalcemia, Renal dysfunction, Anemia and lytic Bone lesions. Table 1 summarizes the different subtypes of MGUS. The majority of MGUS is of the IgG subtype, accounting for at least 59% of MGUS [4]. For non-IgM–MGUS (IgG, IgA, IgD, IgE), the risk of progression to MM, amyloidosis or a related disorder is 1.0 percent per year. For IgM-MGUS the risk of progression to Waldenstrom's macroglobulinemia (WM), IgM myeloma is 1.5 percent per year. For light chain MGUS the risk of progression to light chain myeloma or amyloidosis is 0.3% per year [1].

Table 1. International Myeloma Working Group Diagnostic Criteria for Classification of the Subtypes of MGUS.

Disorder	Disease Definition/Criteria *
IgM MGUS	Serum IgM monoclonal protein level < 3 g/dL Bone marrow lymphoplasmacytic infiltration < 10% No evidence of anemia, constitutional symptoms, hyperviscosity, lymphadenopathy, or hepatosplenomegaly that can be attributed to the underlying lymphoproliferative disorder
Non-IgM MGUS	Serum monoclonal protein level (non-IgM type) < 3 g/dL Clonal bone marrow plasma cells < 10% Absence of end-organ damage, such as hyperCalcemia, Renal insufficiency, Anemia, and Bone lesions (CRAB), that can be attributed to the plasma cell proliferative disorder
Light-Chain MGUS	Abnormal FLC ratio (<0.26 or >1.65)–higher in renal disease Increased level of the appropriate involved light chain (increased kappa FLC in patients with ratio > 1.65 and increased lambda FLC in patients with ratio < 0.26) No immunoglobulin heavy-chain expression on immunofixation Absence of end-organ damage that can be attributed to the plasma cell proliferative disorder Clonal bone marrow plasma cells < 10% Urinary monoclonal protein level < 500 mg/24 h

AL = light-chain; FLC = free light-chain; MGUS = monoclonal gammopathy of undetermined significance. * All criteria must be met. Adapted from Rajkumar et al. [1].

MGUS is largely an incidental laboratory finding that is present in over 3% of patients >50 years old and is asymptomatic [1–3]. It is more prevalent in males than females. In addition to age, obesity is a risk factor [2,3]. Studies have shown that it is frequent in African Americans and those with a family history of plasma cell dyscrasias such as multiple myeloma [5,6]. Other risk factors include chronic immunosuppression and history of auto-immune diseases [2,3,7,8]. Furthermore, exposure to pesticides and to Agent Orange among veterans are recognized as risk factors [7,8].

Screening for MGUS should be actively discouraged given its low risk of progression to serious disorders and MGUS, per se, does not qualify for treatment [2]. Also, it is not certain that early diagnosis improves survival. In addition, it exacts a major psychological toll (anxiety, depression etc.) on patients knowing they harbor a pre-cancerous disorder and might be at risk for a malignancy. A large prospective study (n = 75,422) conducted in the Icelandic population with age over 40 years old, Iceland Screens, Treats or Prevents of Multiple Myeloma (iStopMM) will help define the validity if any of screening strategies for MGUS [9].

Smoldering Multiple Myeloma (SMM) appears to be transition stage from MGUS to multiple myeloma and other serious disorders. It is defined by M-protein (≥ 3.0 g/dl) and presence of plasma cells or lymphoplasmacytic cells in the bone marrow which are ≥10% with no end organ damage i.e., CRAB manifestations [2,3]. The risk of progression to myeloma and other related disorders from SMM is much higher at 10 percent per year for the first 5 years.

2. Progression of MGUS

Since the majority of patients with MGUS do not progress to myeloma, WM and amyloidosis it is crucial to identify factors that predict progression.

A commonly accepted risk stratification model derives from the Mayo Clinic experience [3,10]. This model uses the M-protein concentration, subtype of M-protein and FLC ratio to define low risk, intermediate risk and high risk. The 3 factors include a M-protein < 1.5 g/dl, Ig-G subtype and normal FLC ratio to define low risk of progression (5%) over 20 years. If only one factor is abnormal it connotes an intermediate risk of 21% at 20 years and if any 2 risk factors are abnormal it denotes a 37% risk of progression over 20 years. High risk is present when all 3 factors are abnormal and the 20 year risk of progression is 58%. Since a bone marrow biopsy and imaging were not reported it is possible that these risks for progression was contaminated by SMM patients and thus an over estimate. Also a decrease in normal gamma globulins, hypogammaglobinemia or immune-paresis confers an increased risk of progression [11]. Another risk stratification model, the PANGEA model includes hemoglobin trajectory, FLC ratio, M spike concentration, age, and creatinine concentration (without bone marrow) as risk progression predictors [12].

The general consensus is that in low risk patients with MGUS, one could defer on bone marrow biopsy and skeletal imaging. Though all myelomas are preceded by MGUS, karyotyping and gene-expression studies in purified plasma cells from bone marrow have shown similar finding in MGUS and MM [13]. In smoldering myeloma, del(17p), t(4;14), 1q gain and hyperdiploidy are associated with progression to overt myeloma. No differences in gene expression were observed between WM and IgM MGUS patients [14]. Similarly, flow

cytometric also show similar immunophenotypic expression between clonal B-cells of IgM MGUS, Waldenstrom's macroglobulinemia [15].

All patients should be monitored within 6 months of diagnosis and low risk patients at yearly intervals or longer thereafter if stable. In high-risk patients, after the 6 month visit, monitoring every 6 to 12 months to determine disease progression is prudent.

3. Laboratory Testing

Tests used to diagnose MGUS include SPE/UPE, Immunofixation electrophoresis (IFE) and the serum free light chain (FLC) assay [1]. Testing for monitoring MGUS should include SPE, UPE, FLC assay, serum calcium, creatinine and complete blood count [2,3]. Since MGUS is largely a laboratory-based diagnosis, it is important to comment on the recommended tests.

High resolution serum protein electrophoresis (SPEP) and urine protein electrophoresis (UPEP), traditionally performed using agarose gel, are often the initial tests for identifying monoclonal proteins. SPEP will also detect hypogammaglobinemia and hypoalbuminemia which can be used to correct serum calcium. The presence of monoclonal proteins are confirmed and isotyping with immunofixation electrophoresis (IFE) for both the heavy and light chain e.g., IgA -kappa. SPEP can also be used to quantify the M-spike for disease staging and monitoring. If the M-protein is in the beta or alpha-2 area it is prudent to also assay immunoglobulin levels by nephelometry since normal migrating proteins in these areas can interfere with accurate quantification of M-protein. The limit of detection for M-proteins by SPEP is affected by the background of polyclonal immunoglobulins, and it is approximately 0.1 g/dl [16].

Capillary zone electrophoresis (CZE), has some advantages over agarose electrophoresis, such as faster throughput and automation [17]. The proteins are quantified by an ultraviolet absorbance detector without any staining, which improves the reproducibility. The immune subtraction with capillary zone electrophoresis is performed after adding specific antibodies to the serum, and the immune complexes that form migrate to the albumin region, allowing precise detection of the M-component. Occasionally, CZE may fail to detect an M-protein due to its precipitation in the CZE buffer. Iodinated contrast agents, certain medications such as 5-fluorocytosine and hydroxycobalamin can cause abnormal peaks due to their capacity to absorb at a wavelength in the UV spectrum [18]. These interferences can be resolved in subsequent immune-subtraction electrophoresis.

Thus, both SPE and CZE are comparable and acceptable first-line tests depending on work load and technical expertise available at the respective institutions globally [19].

Serum FLC levels are measured by nephelometry and expressed as a kappa/lambda ratio. The importance of FLC measurement was recently highlighted by the introduction of a new definition of MM disease by the International Myeloma Working Group (IMWG) [20]. The reported reference range is 0.26–1.65, with the upper limit increasing with chronic kidney disease and chronic inflammation (polyclonal gammopathy on SPE). Long et al. reported reference ranges for severity of CKD; 0.46–2.62, 0.48–3.38 and 0.54–3.3 for eGFR of 45–59, 30–44 and <30 mL/min, respectively [21]. These results are solely based on a single assay method (Freelite assay). Also the FLC assay is subject to the prozone phenomena due to excess antigen and can display lot-to-lot variation. If the prozone phenomenon is suspected, the assay should be repeated with sample dilution. Additional assays, N Latex FLC and ELISA-based Sebia FLC, are now available and the ratio showed significant discrepancies among these assays [22]. Most of the data used by the guideline committees is based on the Freelite assay which is well validated.

Recently, mass spectrometric methods are more sensitive and specific in detecting M-proteins but are not widely available [23–25]. However, their value in the workup of MGUS is unclear since high risk is defined as a value >1.5 g/dl which is easily quantified by SPE or CZE. Its main value appears to be in differentiating M proteins from monoclonal antibodies in patients being treated with these antibodies, and in detecting minimal residual disease in patients with myeloma on treatment and possibly in primary amyloidosis [23]. In this regard, we have previously shown that therapeutic monoclonal antibodies like, daratumumab, do not interfere with the FLC assay [26].

Serum creatinine and estimated glomerular filtration rate (eGFR) should be reported and serum calcium corrected if there is hypoalbuminemia as determined by the formula: Corrected Serum calcium = Measured total calcium + 0.8(4.0 - serum albumin in g/dl). The serum anion gap may be decreased due to the unmeasured contribution of cations by the M-protein [27].

The complete blood count is normal in MGUS and useful in assessing progression to overt myeloma e.g., detection of anemia. Sometimes the M-spikes in MGUS may cause prolongation of PTT due to lupus anticoagulant effect [28] or an acquired von Willebrand disease [29].

4. MGUS of Clinical Significance

The term monoclonal gammopathies of clinical significance (MGCS) defines a heterogeneous group of disorders in which the monoclonal protein is implicated in unexplained end-organ dysfunction in the absence of diagnostic criteria for plasma cell neoplasm [30–33]. MGCS should be suspected in all patients with an M-protein and unexplained end-organ damage. In monoclonal Gammopathy of Renal Significance (MGRS) renal damage is caused by the deposition of monoclonal proteins [33]. Several renal pathologies have been described, including cryoglobulinemic nephropathy, monoclonal immunoglobulin deposition disease, glomerulonephritis and renal Fanconi syndrome. Unlike MGUS, MGRS requires treatment to prevent further deterioration renal function. In addition to renal damage, monoclonal proteins can cause pathologies in other organs without fulfilling the criteria for plasma cell malignancy. These disorders include neuropathy syndromes, POEMS syndrome (Polyneuropathy, Organomegaly, Endocrinopathy, Monoclonal spike and Sclerotic bone lesions), recurrent urticaria (Schnitzler syndrome), TEMPI syndrome, (Telangiectasias, Erythrocytosis due to elevated erythropoietin, Monoclonal gammopathy, Perinephric fluid collections and Intrapulmonary shunt), thrombosis and cold haemagglutinin disease, ocular disease (keratopathy), angioneurotic edema due to due to acquired C1 inhibitor deficiency and acquired von Willebrand disease among other rare disorders. This is a fast-evolving area and is beyond the purview of this mini-review, which focused on classical MGUS and thus MGCS is briefly mentioned.

5. Conclusions

MGUS is a common precancerous disorder of persons >50 years of age in which a minority of patients progress to a malignancy. Better risk stratification for progression of MGUS to myeloma, WM, amyloidosis will be clinically useful and most welcome. Currently available models are useful only in a minority of patients. Further in-depth analysis of genomics and epigenetics, microRNAs, and tumor microenvironment are recommended to provide more meaningful and relevant markers of disease progression.

Author Contributions

Both I.J. and P.T. generated the idea for this publication. Both generated the original version following a PubMed search and edited multiple iterations. All authors have read and agreed to the published version of the manuscript.

Funding

There was no funding for this present report.

Institutional Review Board Statement

Not applicable for review article

Informed Consent Statement

Not applicable for review article

Data Availability Statement

The data is available from the senior author for review on reasonable request.

Conflicts of Interest

The authors declare no conflict of interest. Given their editorial roles, Ishwarlal Jialal (Editor-in-Chief) and Perumal Thiagarajan (Editorial Board Member) had no involvement in the peer review of this paper and had no access to information regarding its peer-review process. Full responsibility for the editorial process of this paper was delegated to another editor of the journal.

Use of AI and AI-Assisted Technologies

No AI tools were utilized for this paper.

References

1. Rajkumar, S.V.; Dimopoulos, M.A.; Palumbo, A.; et al. International Myeloma Working Group updated criteria for the diagnosis of multiple myeloma. *Lancet Oncol.* **2014**, *15*, e538–e548. https://doi.org/10.1016/S1470-2045(14)70442-5.

2. Liu, Y.; Parks, A.L. Diagnosis and Management of Monoclonal Gammopathy of Undetermined Significance: A Review. *JAMA Intern. Med.* **2025**, *185*, 450–456. https://doi.org/10.1001/jamainternmed.2024.8124.
3. Gonsalves, W.I.; Rajkumar, S.V. Monoclonal Gammopathy of Undetermined Significance. *Ann. Intern. Med.* **2022**, *175*, ITC177–ITC192. https://doi.org/10.7326/AITC202212200; Erratum in *Ann. Intern. Med.* **2023**, *176*, 288. https://doi.org/10.7326/L22-0509.
4. Willrich, M.A.; Katzmann, J.A. Laboratory testing requirements for diagnosis and follow-up of multiple myeloma and related plasma cell dyscrasias. *Clin. Chem. Lab. Med.* **2016**, *54*, 907–919. https://doi.org/10.1515/cclm-2015-0580.
5. Landgren, O.; Graubard, B.I.; Katzmann, J.A.; et al. Racial disparities in the prevalence of monoclonal gammopathies: A population-based study of 12,482 persons from the National Health and Nutritional Examination Survey. *Leukemia* **2014**, *28*, 1537–1542. https://doi.org/10.1038/leu.2014.34.
6. Landgren, O.; Kristinsson, S.Y.; Goldin, L.R.; et al. Risk of plasma cell and lymphoproliferative disorders among 14621 first-degree relatives of 4458 patients with monoclonal gammopathy of undetermined significance in Sweden. *Blood* **2009**, *114*, 791–795. https://doi.org/10.1182/blood-2008-12-191676.
7. Hofmann, J.N.; Beane Freeman, L.E.; Murata, K.; et al. Lifetime Pesticide Use and Monoclonal Gammopathy of Undetermined Significance in a Prospective Cohort of Male Farmers. *Environ. Health Perspect.* **2021**, *129*, 17003. https://doi.org/10.1289/EHP6960.
8. Liu, L.W.; Wang, M.; Grandhi, N.; et al. The Association of Agent Orange Exposure with the progression of monoclonal gammopathy of undetermined significance to multiple myeloma: A population-based study of Vietnam War Era Veterans. *J. Hematol. Oncol.* **2024**, *17*, 3. https://doi.org/10.1186/s13045-023-01521-6.
9. Rögnvaldsson, S.; Thorsteinsdóttir, S.; Kristinsson, S.Y. Screening in Multiple Myeloma and Its Precursors: Are We There Yet? *Clin. Chem.* **2024**, *70*, 128–139. https://doi.org/10.1093/clinchem/hvad148.
10. Kyle, R.A.; Larson, D.R.; Therneau, T.M.; et al. Long-Term Follow-up of Monoclonal Gammopathy of Undetermined Significance. *N. Engl. J. Med.* **2018**, *378*, 241–249. https://doi.org/10.1056/NEJMoa1709974.
11. Landgren, O.; Hofmann, J.N.; McShane, C.M.; et al. Association of Immune Marker Changes with Progression of Monoclonal Gammopathy of Undetermined Significance to Multiple Myeloma. *JAMA Oncol.* **2019**, *5*, 1293–1301. https://doi.org/10.1001/jamaoncol.2019.1568.
12. Cowan, A.; Ferrari, F.; Freeman, S.S.; et al. Personalised progression prediction in patients with monoclonal gammopathy of undetermined significance or smouldering multiple myeloma (PANGEA): A retrospective, multicohort study. *Lancet Haematol.* **2023**, *10*, e203–e212. https://doi.org/10.1016/S2352-3026(22)00386-6; Erratum in *Lancet Haematol.* **2024**, *11*, e181. https://doi.org/10.1016/S2352-3026(24)00040-1.
13. Dhodapkar, M.V. MGUS to myeloma: A mysterious gammopathy of underexplored significance. *Blood* **2016**, *128*, 2599–2606. https://doi.org/10.1182/blood-2016-09-692954.
14. Trojani, A.; Di Camillo, B.; Bossi, L.E.; et al. Identification of a Candidate Gene Set Signature for the Risk of Progression in IgM MGUS to Smoldering/Symptomatic Waldenström Macroglobulinemia (WM) by a Comparative Transcriptome Analysis of B Cells and Plasma Cells. *Cancers* **2021**, *13*, 1837. https://doi.org/10.3390/cancers13081837.
15. García-Sanz, R.; Jiménez, C.; Puig, N.; et al. Origin of Waldenstrom's macroglobulinaemia. *Best Pract. Res. Clin. Haematol.* **2016**, *29*, 136–147. https://doi.org/10.1016/j.beha.2016.08.024.
16. Jacobs, J.F.M.; Turner, K.A.; Graziani, M.S.; et al. An international multi-center serum protein electrophoresis accuracy and M-protein isotyping study. Part II: Limit of detection and follow-up of patients with small M-proteins. *Clin. Chem. Lab. Med.* **2020**, *58*, 547–559. https://doi.org/10.1515/cclm-2019-1105.
17. Cho, H.; Jung, J.; Chae, H.; et al. Assessment of M-protein quantification using capillary electrophoresis and immunosubtraction-based integration in clinical samples with low M-protein concentrations. *Clin. Biochem.* **2022**, *107*, 7–12. https://doi.org/10.1016/j.clinbiochem.2022.05.011.
18. Booth, R.A.; McCudden, C.R.; Balion, C.M.; et al. Candidate recommendations for protein electrophoresis reporting from the Canadian Society of Clinical Chemists Monoclonal Gammopathy Working Group. *Clin. Biochem.* **2018**, *51*, 10–20. https://doi.org/10.1016/j.clinbiochem.2017.10.013.
19. Keren, D.F.; Bocsi, G.; Billman, B.L.; et al. Laboratory Detection and Initial Diagnosis of Monoclonal Gammopathies. *Arch. Pathol. Lab. Med.* **2022**, *146*, 575–590. https://doi.org/10.5858/arpa.2020-0794-CP.
20. Dispenzieri, A.; Kyle, R.; Merlini, G.; et al. International Myeloma Working Group guidelines for serum-free light chain analysis in multiple myeloma and related disorders. *Leukemia* **2009**, *23*, 215–224. https://doi.org/10.1038/leu.2008.307.
21. Long, T.E.; Indridason, O.S.; Palsson, R.; et al. Defining new reference intervals for serum free light chains in individuals with chronic kidney disease: Results of the iStopMM study. *Blood Cancer J.* **2022**, *12*, 133. https://doi.org/10.1038/s41408-022-00732-3.
22. Schieferdecker, A.; Hörber, S.; Ums, M.; et al. Comparison of three different serum-free light-chain assays-implications on diagnostic and therapeutic monitoring of multiple myeloma. *Blood Cancer J.* **2020**, *10*, 2. https://doi.org/10.1038/s41408-019-0267-8.

23. Willrich, M.A.V.; Murray, D.L.; Kyle, R.A. Laboratory testing for monoclonal gammopathies: Focus on monoclonal gammopathy of undetermined significance and smoldering multiple myeloma. *Clin. Biochem.* **2018**, *51*, 38–47. https://doi.org/10.1016/j.clinbiochem.2017.05.001.
24. Moore, L.M.; Cho, S.; Thoren, K.L. MALDI-TOF mass spectrometry distinguishes daratumumab from M-proteins. *Clin. Chim. Acta* **2019**, *492*, 91–94. https://doi.org/10.1016/j.cca.2019.02.017.
25. Tzasta, A.; Wijnands, C.; Baalman, K.; et al. Advances in multiple myeloma blood-based monitoring and its clinical applications. *Crit. Rev. Clin. Lab Sci.* **2025**, 1–19. https://doi.org/10.1080/10408363.2025.2512466.
26. Rosenberg, A.S.; Bainbridge, S.; Pahwa, R.; et al. Investigation into the interference of the monoclonal antibody daratumumab on the free light chain assay. *Clin. Biochem.* **2016**, *49*, 1202–1204. https://doi.org/10.1016/j.clinbiochem.2016.07.016.
27. Keshgegian, A.A. Anion gap and immunoglobulin concentration. *Am. J. Clin. Pathol.* **1980**, *74*, 282–284. https://doi.org/10.1093/ajcp/74.3.282.
28. Yasin, Z.; Quick, D.; Thiagarajan, P.; et al. Light-chain paraproteins with lupus anticoagulant activity. *Am. J. Hematol.* **1999**, *62*, 99–102. https://doi.org/10.1002/(sici)1096-8652(199910)62:2<99::aid-ajh6>3.0.co;2-n.
29. Abou-Ismail, M.Y.; Rodgers, G.M.; Bray, P.F.; et al. Acquired von Willebrand syndrome in monoclonal gammopathy—A scoping review on hemostatic management. *Res. Pract. Thromb. Haemost.* **2021**, *5*, 356–365. https://doi.org/10.1002/rth2.12481.
30. Iberri, D.; Liedtke, M. MGCS: Where do we stand today? *Hematol. Am. Soc. Hematol. Educ. Program* **2024**, *2024*, 482–488. https://doi.org/10.1182/hematology.2024000572.
31. Cho, H. Diagnosis and management of monoclonal gammopathy of clinical significance. *Blood Res.* **2022**, *57*, 20–26. https://doi.org/10.5045/br.2022.2022035.
32. Oganesyan, A.; Gregory, A.; Malard, F.; et al. Monoclonal gammopathies of clinical significance (MGCS): In pursuit of optimal treatment. *Front. Immunol.* **2022**, *13*, 1045002. https://doi.org/10.3389/fimmu.2022.1045002.
33. Leung, N.; Bridoux, F.; Nasr, S.H. Monoclonal Gammopathy of Renal Significance. *N. Engl. J. Med.* **2021**, *384*, 1931–1941. https://doi.org/10.1056/NEJMra1810907.