Annals of Case Reports
Kühne FW, et al. Ann Case Rep: 10: 102493
www.doi.org/10.29011/2574-7754.102493
www.gavinpublishers.com

OPEN ACCESS

GAVIN PUBLISHERS

Case Report

Resolution of Chemotherapy-Induced Lymphopenia in Waldenström's Macroglobulinemia Following Compassionate Use of WF10

Friedrich-Wilhelm Kühne[1], Ulrike Jentzsch-Kühne[2], Jörg Flemmig[1*]

[1]OXO Translational Science GmbH, Wanzleben-Börde, Germany

[2]Praxis Jentsch-Kühne / Rosenstein, Kiel, Germany

***Corresponding Author:** Jörg Flemmig, OXO Translational Science GmbH, Vor dem Schlosstor 9, 39164 Wanzleben-Börde, Germany

Citation: Kühne FW, Jentzsch-Kühne U, Flemmig J. (2025). Resolution of Chemotherapy-Induced Lymphopenia in Waldenström's Macroglobulinemia Following Compassionate Use of WF10. Ann Case Report. 10: 2493. DOI:10.29011/2574-7754.102493

Received: 17 December 2025; **Accepted**: 22 December 2025; **Published**: 24 December 2025

Abstract

Bendamustin-Rituximab (BR) chemotherapy controls clonal B-cell expansion in Waldenström's macroglobulinemia (WM) but may aggravate anemia and induce persistent lymphopenia. In the presented patient, the drug WF10 restored immune balance, reduced inflammation, and resolved anemia without interfering with chemotherapy (CT) effects on the tumor clone. No dedicated drug exists to counteract CT-induced lymphopenia in WM, despite its link to infections and secondary malignancies.

This case highlights Immunokine as a post-CT option for resolving persistent lymphopenia, abating systemic inflammation, and restoring immune balance in WM patients. Tangible benefits included resolution of infection susceptibility, improved energy, and abatement of anemia translating into better quality of life and resilience under CT. In the presented case, persistence of grade 1 lymphopenia suggests further WF10 treatment cycles may achieve full immune reconstitution.

In summary, WF10 (Immunokine) therapy successfully counteracted chemotherapy-induced lymphopenia in a Waldenström's macroglobulinemia (WM) patient without compromising tumor control. It restored immune balance, reduced systemic inflammation, and resolved anemia, resulting in improved energy, reduced infection susceptibility, and better quality of life. These findings indicate that WF10 may serve as a post-chemotherapy immune-restorative option for managing persistent lymphopenia and inflammation in WM.

Keywords: Waldenström's Macroglobulinemia; Lymphopenia, Anemia; Myeloid-Lymphoid Dysbalance; WF10; Immunokine; TCDO.

Case Presentation

We describe a case of a male patient aged 81 with Waldenström's Macroglobulinemia (WM) treated under compassionate use with WF10 (Immunokine). The patient presented with persistent lymphopenia (ICD-10: D72.810) and recurrent infections after chemotherapy (CT) – consistent with the clinical picture of Myeloid-Lymphoid Dysbalance (MLD). This form of immune dysfunction is common after CT and represents a diagnostic and therapeutic challenge with no effective standard treatment options currently available. The treating physician identified this condition, characterized by frequent infections, as a key rationale for initiating WF10 therapy.

The patient received one CT-cycle in 01-06/2024, consisting of six infusions with Bendamustin/Rituximab (BR therapy) every four weeks. Rational for CT induction was development of anemia in Q3/2024 as well as neuropathy and poor general condition. While the first two infusions were poorly tolerated with high fever, shivers and further irritations, later cycles were tolerated better and CT improved general condition. However, CT induced a persistent immune weakness, which led to initiation of WF10

therapy. The drug was administered as five weekly infusions in 03-04/2025. Treatment started on 10th Mar 2025 (baseline, BL) with a dosage of 0.25 mL WF10 solution per kg body weight (BW). The subsequent four infusions were escalated to 0.4-0.5 mL/kg BW. The indicated amount of WF10 was thereby always diluted in physiological saline directly before usage. Patient was followed up till 16 weeks post-treatment.

Results and Discussion

MLD reduction and inflammation resolution

Before treatment, absolute lymphocyte counts were stable and in the lower physiological range. CT led to quick onset of grade 2-3 lymphopenia and increasing in Neutrophil-to-Lymphocyte Ratio (NLR) values. At BL before WF10 therapy, lymphocytes were 0.49 G/L, corresponding to grade 3 lymphopenia, with NLR of 9.3, indicating severe MLD. Under WF10, absolute lymphocytes quickly increased to 0.80 G/L and stabilized at 0.85-0.86 G/L five weeks post treatment, which corresponds to grade 1 lymphopenia. NLR stabilized at 4.9-5.1, reflecting substantial MLD reduction.

Constantly elevated C-reactive protein (CRP) levels before CT (mean: 27.5 mg/L), decreased to 1-3 mg/L post CT, but rose again on BL (24.0 mg/L). WF10 consistently reduced CRP to physiological values during follow up. Normalization of hepatic parameters, including alkaline phosphatase (ALP) reduction from 147 U/L at BL to 127 U/L 12 weeks after treatment, shows resolution of hepatic stress by WF10 therapy.

Thus, CT-derived severe lymphopenia was resolved by WF10, evidenced by NLR normalization. At WM and further B-cell malignancies, elevated NLR values (≥ 5.0) are indicative for immune imbalance (MLD) and prognostic for adverse outcomes [1,2]. Normalization of CRP and ALP further illustrates drug-mediated reduction of chronic inflammation. Reduction of MLD and systemic inflammation are predictive for better both CT response and prognosis at WM [2]. The patient experienced no further infections during at/after WF10 therapy, which also indicates drug- mediated restoration of healthy immune competence.

Effect on IgM and κLC/λLC

IgM and κLC/λLC values were highly elevated before CT (09/2020-01/2024, means: 15.26 g/L, 43.67) but efficiently and consistently reduced under CT. Starting from BL values of 4.30 g/L and 17.08, WF10 treatment had no significant effect and values of 4.50 g/L and 19.40 were obtained at the end of follow-up. Thus, adjunct application of the WF10 does not interfere with CT-mediated inhibition of lymphoplasmacytic B lymphocyte extension. While IgM plasma levels were always below estimated threshold for clinical relevance (30 g/L [3-5]), the patients reported neuropathic symptoms as part of the rationale for CT initiation.

Effect on anemia and RBC homeostasis

Main reason for CT initiation was the development of mild anemia in 06/2023-01/2024, with low absolute Red Blood Cell (aRBC) counts, hemoglobin (Hgb) and hematocrit (Hct). Anemia persisted during/post CT with mean values of 3.78 T/L, 12.5 g/dL and 0.36 L/L observed in 01/2024-03/2025. WF10 therapy led to anemia abatement with values of 4.14 T/L, 13.6 g/dL and 0.39 L/L observed at the end of follow-up. Drug-induced erythropoiesis, evidenced by elevated reticulocytes in 06-07/2025 and increasing MCV values, is likely responsible for the observed resolution of anemia and restoration of RBC homeostasis [6].

Development of anemia and resulting clinical symptoms are common at WM [3,4] and Hb values < 10 g/dL are indicative for CT initiation [7,8]. Low Hb values are also part of the International Scoring System for Waldenström's Macroalbuminuria (ISSWM) and predict poor prognosis at WM [9]. Still, while in the reported case CT did not resolve but perpetuate anemia, WF10- derived induction of erythropoiesis led to anemia resolution and sustainable restoration of RBC homeostasis.

Conclusion

Clinical symptoms at WM emerge from bone marrow infiltration of the lymphoplasmacytic B cells [3,4]. While IgM hypersecretion leads to hyperviskosity syndrome and kryoglobinemia, suppression of normal hematopoiesis lead to clinical symptoms emerging from anemia and leukopenia [9,8]. In the presented case, especially anemia-derived fatigue as well as occurrence of frequent infections were indicative for CT induction [7]. The applied CT solidified anemia and led to prompt and sustained onset of severe lymphopenia, reflecting MLD and immune exhaustion. BR therapy is well known to impair healthy B-, T- and NK-cell production, causing long-lasting lymphopenia and frequent infections in the patients at/after CT [10-12].

However, subsequent application of WF10 led to quick abatement of lymphopenia and resolution of anemia. The drug is well known for both its immune-rebalancing [13,14] and RBC homeostasis-restoring [6] properties. The drug thereby did not interfere with the CT-derived push back of the clonal expansion of lymphoplasmacytic B cells and thus represents an ideal post-CT treatment option for WM patients. To date, no drug specifically counteracts CT-induced lymphopenia, despite the known higher risk for infections and development of secondary malignancies in WM patients [3,4]. Nevertheless, while WF10 therapy significantly reduced MLD, the persistence of grade 1 lymphopenia may be indicative for applying a second treatment cycle to further improve immune balance and immune competence.

In conclusion, in patients presenting with severe MLD, persistent lymphopenia, and recurrent infections, WF10 may provide a

rational and effective immunologic reset as this drug compensates for the detrimental effects of CT on healthy lymphocyte production. The presented case supports further evaluation and prioritization of the immune-balance and immune- competence restoring drug [13,15,16] in post-chemotherapy or immune-exhausted WM settings.

Chlorine–oxygen compounds are generally considered too reactive for therapeutic use. TCDO, the active pharmaceutical ingredient in WF10, represents a rare example of molecular engineering in which intrinsically reactive chlorite–oxygen species were transformed into a stable, non-radical, pharmacologically safe oxygen carrier.

Data availability: The data supporting the findings of this case report are available from the corresponding author upon reasonable request. All data will be provided in anonymized form to protect patient privacy.

Authors' contribution: FWK conceived the idea for the report, wrote the first draft, contributed to clinical interpretation, and coordinated manuscript preparation. UJK treated the patient with WF10 (Immunokine), provided clinical data and follow-up information, and contributed to clinical interpretation. JF contributed to data interpretation, provided biochemical expertise, revised the manuscript, and finalized the text. AI assistance (ChatGPT, OpenAI) supported with language editing and structural drafting under the supervision of the authors.

All authors reviewed the final version of the manuscript, approved its submission, and agree to be accountable for the accuracy and integrity of the work.

Competing interest and funding: FWK and JF are affiliated with OXO Translational Science GmbH (OTS), an independent research entity. Their research is self-funded through personal savings and earnings. The authors declare no commercial or financial interest in Immunokine (WF10) or related products. UJ is an independent clinician in private practice and has no financial relationships to disclose.

Compliance with ethical standards

The patient, whose case is described in this report, provided written consent to this publication. The authors thank the patient for his trust and cooperation, Stefan Brunn for kindly providing pretreatment data (declining co-authorship citing insufficient contribution). The study was conducted in accordance with the Declaration of Helsinki.

References

1. Wang Z, Bao Y, Xu Z, Sun Y, Yan X, et al. (2024). A novel inflammatory-nutritional prognostic scoring system for patients with diffuse large B cell lymphoma. Journal of Inflammation Research. 17: 1-13.
2. Kaldas D, Thapa S, Modukuri S, Blue B, Alsina M, et al. (2025). The prognostic role of neutrophil-to-lymphocyte ratio (NLR) in Waldenström macroglobulinemia: An independent prognostic marker. European Hematology Association Congress Proceedings. 2025: MW011.
3. Bibas M, Sarosiek S, Castillo JJ. (2024). Waldenström macroglobulinemia – A state-of-the-art review: Part 1 epidemiology, pathogenesis, clinicopathologic characteristics, differential diagnosis, risk stratification, and clinical problems. Mediterranean Journal of Hematology and Infectious Diseases. 16: e2024061.
4. Bibas M, Sarosiek S, Castillo JJ. (2025). Waldenström macroglobulinemia – A state-of-the-art review: Part 2 focus on therapy. Mediterranean Journal of Hematology and Infectious Diseases. 17: e2025015.
5. Grunenberg A, Buske C. (2016). New developments in Waldenström's macroglobulinemia. Deutsche Medizinische Wochenschrift. 141: 170-172.
6. Yingsakmongkol N, Tanunyutthawongse C, Flemmig J, Kuehne FW. (2021). Effect of the chlorite-based drug WF10 on hemoglobin A1c and hematological biomarkers in uncontrolled diabetic patients with foot ulcer. Journal of Diabetes Treatment. 6: 1-12.
7. Hensel M. (2024). Morbus Waldenström. DLD – Deutsche Leukämie- & Lymphomhilfe e.V.
8. Buske C. (2022). Morbus Waldenström. Deutsche Leukämie- & Lymphom-Hilfe.
9. Buske C, Pott C, Hoster E, Heim D, Staber PB, et al. (2024). Morbus Waldenström (lymphoplasmacytic lymphoma). Fachgesellschaft zur Diagnostik und Therapie hämatologischer und onkologischer Erkrankungen. Retrieved from online.
10. Martínez-Calle N, Hartley S, Ahearne M, Kasenda B, Beech A, et al. (2019). Kinetics of T-cell subset reconstitution following treatment with bendamustine and rituximab for low-grade lymphoproliferative disease: A population-based analysis. British Journal of Haematology. 184: 957-968.
11. Shotton R, Broadbent R, Alchawaf A, Mohamed MB, Gibb A, et al. (2024). Safety of bendamustine for the treatment of indolent non-Hodgkin lymphoma: A UK real-world experience. Blood Advances. 8: 878-888.
12. Cona A, Tesoro D, Chiamenti M, Merlini E, Ferrari D, et al. (2019). Disseminated cytomegalovirus disease after bendamustine: A case report and analysis of circulating B- and T-cell subsets. BMC Infectious Diseases. 19: 881.
13. Giese T, McGrath MS, Stumm S, Schempp H, Elstner E, et al. (2004). Differential effects on innate versus adaptive immune responses by WF10. Cellular Immunology. 229: 149-158.
14. McGrath MS, Kodelja V. (1999). Balanced macrophage activation hypothesis: A biological model for development of drugs targeted at macrophage functional states. Pathobiology. 67: 277-281.
15. Schempp H, Reim M, Dornisch K, Elstner EF. (2001). Chlorite-hemoprotein interaction as key role for the pharmacological activity of the chlorite-based drug WF10. Arzneimittelforschung. 51: 554-562.
16. Bauerdick A, Exner T, Habicht J, Konstandin MH, Grieshaber-Bouyer R, et al. (2025) MorphoMapping reveals a RedOX-induced transition in primed neutrophils from NETosis to apoptosis. Journal of Immunology.