

Bortezomib and autoimmune hemolytic anemia: a systematic review and meta-analysis

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Abstract. Conventional treatments for autoimmune hemolytic anemia (AIHA) are associated with drawbacks including high recurrence rates and limited therapeutic efficacy. As a proteasome inhibitor, bortezomib demonstrates potential value in relapsed/refractory AIHA, yet existing evidence mostly consists of small-sample case reports without quantitative integrated analyses. The results of this meta-analysis revealed that the pooled overall response rate (ORR) of bortezomib for AIHA was 81% (95%CI: 0.71–0.92), with extremely low inter-study heterogeneity ($I^2=0.0\%$, $P=0.950$). After excluding 2 conference abstracts, the pooled ORR of the remaining 4 full-text studies reached 82% (95%CI: 0.69–0.94), and leave-one-out sensitivity analysis identified no single study exerting a significant impact on the overall conclusions. Current evidence indicates that bortezomib can serve as a second-line salvage therapy for relapsed/refractory patients. However, the included studies were predominantly single-arm retrospective small-sample trials, lacking long-term safety data, failing to differentiate therapeutic effects between warm-type AIHA and cold agglutinin disease subgroups, and containing no controlled trials for direct comparisons with conventional regimens. In conclusion, bortezomib delivers stable efficacy and acceptable tolerability in relapsed/refractory AIHA. Large-sample, multicenter, prospective controlled studies are still required to clarify the optimal administration regimen, eligible patient populations and long-term safety profiles.

Keywords: Bortezomib; Autoimmune Hemolytic Anemia; Relapsed and Refractory; Systematic Review; Meta-Analysis; Salvage Therapy.

1. Introduction

Autoimmune hemolytic anemia (AIHA) is characterized by the binding of autoreactive antibodies to red blood cell (RBC) surface antigens, which drives hemolysis beyond the compensatory capacity of the bone marrow. Its core clinical features are anemia, jaundice, reticulocytosis, and a positive direct antiglobulin test (DAT) [1, 2]. The estimated annual incidence is 0.8–3.0 per 100,000 population [2]. Warm AIHA (wAIHA) accounts for roughly 67% of cases and cold agglutinin disease (CAD) for 15%–25%, while severe episodes may present as life-threatening hemolytic crisis or transfusion incompatibility [3]. As in other autoimmune disorders, loss of immune tolerance underlies AIHA: long-lived plasma cells and aberrant B cells sustain autoreactive antibody production, contributing to disease chronicity and treatment refractoriness [4].

Current management follows a tiered immunosuppressive strategy. Glucocorticoids are first-line for wAIHA, whereas rituximab forms the backbone of therapy for CAD. Refractory or relapsed cases may require splenectomy, additional immunosuppressants, or complement inhibitors [2]. Each option, however, has clear drawbacks. Long-term glucocorticoid use is complicated by infection, metabolic disturbance, and osteopenia; rituximab monotherapy achieves only modest response rates (~50%) with delayed onset; and splenectomy carries perioperative risk and is ineffective in CAD [2]. Given these limitations, attention has turned to novel regimens, including those built around proteasome inhibitors. Bortezomib-containing combinations have emerged as one such approach, yet the magnitude of their benefit in AIHA remains uncertain. The present study addresses this question through a meta-analysis of the response rates reported for bortezomib in AIHA.

Bortezomib was the first selective proteasome inhibitor to be approved and is widely used in hematological malignancies such as multiple myeloma and mantle cell lymphoma. It acts by targeting plasma cells and inducing apoptosis of aberrant lymphocytes [5]. Preclinical studies have shown that bortezomib can deplete long-lived plasma cells and reduce autoantibody production, providing a

rationale for its use as immunotargeted therapy in AIHA [6]. In recent years, several clinical studies and case reports have suggested that bortezomib, alone or combined with rituximab, is effective in relapsed/refractory wAIHA, rapidly controlling hemolysis, reducing transfusion dependence, and lowering—or in some cases eliminating—glucocorticoid requirements [5]. A scoping review of relapsed/refractory wAIHA reported an overall response rate (ORR) of 78% for bortezomib monotherapy and 64.7% when combined with rituximab, with a median time to response of approximately 21 days [7]. In a separate report, seven patients with wAIHA treated with low-dose rituximab plus bortezomib and dexamethasone (the LowR-BD regimen) achieved an ORR of 85.71% at 4 weeks with acceptable tolerability [4]. Most of this evidence, however, comes from small case series or individual reports; large, high-quality trials and pooled syntheses are lacking. The optimal dose, treatment duration, combination partners, and long-term safety of bortezomib in AIHA all remain to be defined [2].

Previous reviews have largely addressed general advances in AIHA management or newer modalities such as complement inhibitors and CAR-T cell therapy; few have focused specifically on bortezomib [2]. In particular, no quantitative synthesis has yet examined its efficacy, safety, and appropriate target population in a systematic way, which limits its translation into clinical guidance. We therefore set out to integrate the available evidence, quantify the efficacy of bortezomib in AIHA, and provide a clearer basis for individualized treatment of relapsed/refractory disease.

2. Methods

2.1. Search strategy and eligibility criteria

This study was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement (checklist provided as a supplement). We systematically searched PubMed, Embase, Web of Science, and the Cochrane Library from database inception to December 2025, with no restriction on geography or publication type. The search strategy was first developed in PubMed and then adapted for Embase and Web of Science (Science Citation Index Expanded, Social Sciences Citation Index, and Arts & Humanities Citation Index); the full strategies are provided in the Supplementary Materials. An initial scoping search was performed in September 2025 and updated in December 2025. We included peer-reviewed clinical studies—case series, observational studies, and trials—that reported the use of bortezomib, alone or in combination, for AIHA and provided response data sufficient to derive a proportion. Reviews and qualitative studies were excluded. Grey literature was not searched.

Records were imported into EndNote for deduplication and screening. Two reviewers independently screened titles and abstracts and assessed full texts against the eligibility criteria; disagreements were resolved by discussion or by a third reviewer.

Exclusion criteria were: (1) studies addressing non-autoimmune hemolytic anemias; (2) studies in which bortezomib was not administered; and (3) studies that did not report a response or remission outcome from which a response proportion could be calculated.

2.2. Data extraction

Two investigators independently extracted data using a standardized form, capturing first author, publication type, year, study population, sample size, treatment regimen, outcomes, and the number of responders. Discrepancies were resolved by a third investigator. For each study, the number of patients achieving a response was recorded together with the total number treated, allowing calculation of response proportions for pooling.

2.3. Quality assessment

Two investigators independently appraised methodological quality. Because all eligible studies were uncontrolled (single-arm) case series or observational studies, we used a tool appropriate to that design—the methodological items of the Methodological Index for Non-Randomized Studies

(MINORS)—rather than instruments developed for randomized trials or diagnostic-accuracy studies. Disagreements were resolved by discussion with a third investigator. Details are provided in the Supplementary Materials.

2.4. Statistical analysis

We performed a single-arm meta-analysis of response proportions. Because the included studies differed in design, population, and regimen, a random-effects model (DerSimonian–Laird) was used throughout. Between-study heterogeneity was assessed with the I^2 statistic and the corresponding χ^2 test; an $I^2 > 50\%$ or $P < 0.05$ was taken to indicate substantial heterogeneity. A pre-specified sensitivity analysis excluded studies published only as conference abstracts, and a leave-one-out analysis was performed by sequentially omitting each study. Publication bias was to be examined by funnel plot only if at least 10 studies were available. Meta-analysis was undertaken only when more than one study was available for a given outcome. Risk-of-bias figures were prepared in Review Manager 5.4 and all analyses were performed in Stata 17.0. Tests were two-sided, with significance set at $P < 0.05$.

3. Results

3.1. Study selection and characteristics

The initial search retrieved 259 records, of which 108 duplicates were removed. Title screening excluded a further 92 records, leaving 59 bortezomib-related articles for abstract review. Abstract screening excluded 35 records (including one with no retrievable full text), and 24 articles proceeded to full-text assessment. After full-text review, 14 were excluded. Ten articles were included in the systematic review, six of which reported sufficient data for meta-analysis (Table 1).

Table 1. Characteristics of the included studies.

Study (year)	Type	Population (n)	Regimen	Key outcome
Khandelwal P. (2014) [8]	Conference abstract	7 children, median age 9 y; refractory autoimmune cytopenias	Bortezomib 1.3 mg/m ² , 4 doses 72 h apart (IV n=6, SC n=1); single rituximab dose 375 mg/m ² in 6; plasmapheresis in all	6/7 (85%) responded; 2 AIHA patients normalized reticulocytes by day 13 and remained transfusion-independent despite persistent DAT
Ratnasingam S. (2015) [9]	Conference abstract	7, median age 53 y; all rituximab-exposed	Bortezomib 1.3 mg/m ² days 1, 4, 8, 11 q21d, reduced to weekly for repeat cycles	ORR 75% (50% durable CR, 25% PR); generally well tolerated
Ratnasingam S. (2016) [10]	Blood Adv	13 treatment episodes in 10 patients (AIHA n=8)	Bortezomib 1.3 mg/m ² IV days 1, 4, 8, 11 q21d, modified to weekly SC	ORR 77% (10/13), including 38% (5/13) CR
Rossi G. (2018) [11]	Comment	21 CAD, median age 70.4 y	Single course bortezomib 1.3 mg/m ² IV days 1, 4, 8, 11; acyclovir prophylaxis	ORR 31.6% (3 CR, 3 PR of 19 evaluable); transfusion independence in 4
Zine M. (2017) [12]	Conference abstract	4 (AIHA n=2; AIHA with red cell aplasia n=1)	Bortezomib 1.3 mg/m ² days 1, 4, 8, 11, 1–2 courses; immunosuppressants in 2	Resolution of cytopenia in 3 cases at a median of 33 days
Fadlallah J. (2019) [13]	Observational	8, median age 48.5 y; multi-refractory wAIHA	Btz 1.3 mg/m ² days 1, 4, 8, 11 q21d × 6 + weekly oral dexamethasone 20 mg LowR-BD: rituximab 100 mg day 1 + bortezomib 1.3 mg/m ² SC day 2 + dexamethasone 20 mg days 2–3	6/8 responded (3 CR, 3 PR) after a median of 2 cycles
Yao M. (2022) [14]	Medicine (Baltimore)	7 wAIHA		ORR 85.71% (CR 28.57%, PR 57.14%) after 4 cycles

Study (year)	Type	Population (n)	Regimen	Key outcome
McGlothlin J. (2023) [15]	Am J Hematol	8 (wAIHA n=6, CAD n=2)	Bortezomib ± daratumumab	ORR 88% (7/8); CR 63%, PR 25%; median response duration 24.5 months
Jain A. (2024) [16]	Indian J Hematol Blood Transfus	5 RR wAIHA	Weekly bortezomib 1.3 mg/m ² SC + dexamethasone 40 mg/week	ORR 100%; 3 achieved CR; durable transfusion-free remission

3.2. Risk of bias

Across the MINORS domains, the included studies generally reported a clearly stated aim, prospective or clearly defined data collection, and endpoints consistent with the study objective; these items were rated as adequately addressed in most studies. Two recurring weaknesses were evident. First, because every included study was uncontrolled and single-arm, the absence of a comparator group is an inherent limitation. Second, several studies did not pre-specify their outcome measures or define follow-up loss, so reporting bias cannot be excluded (Figure 1).

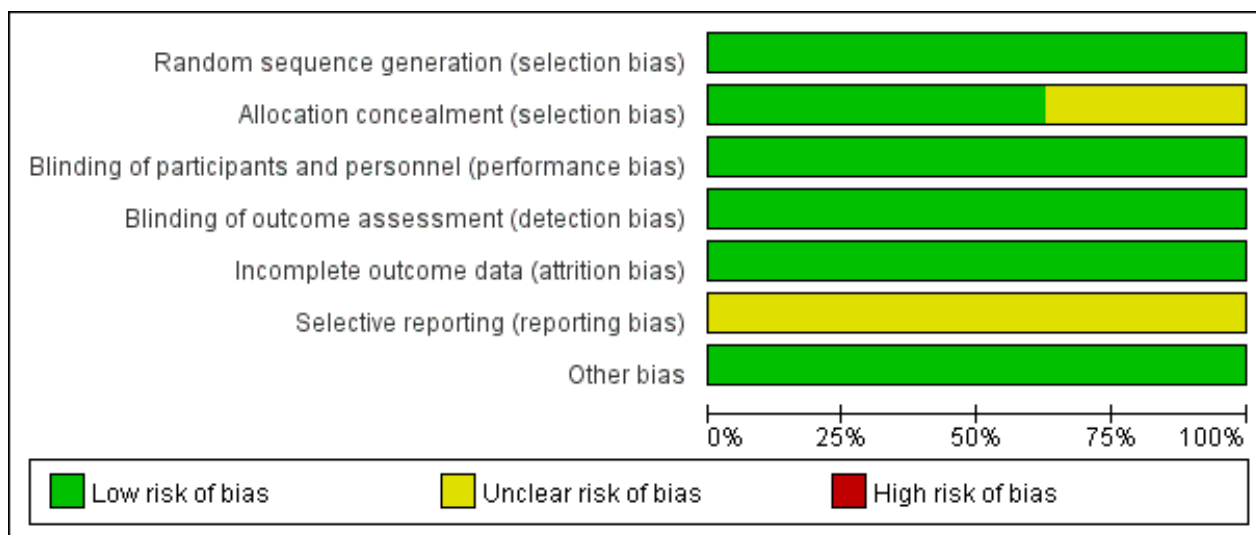
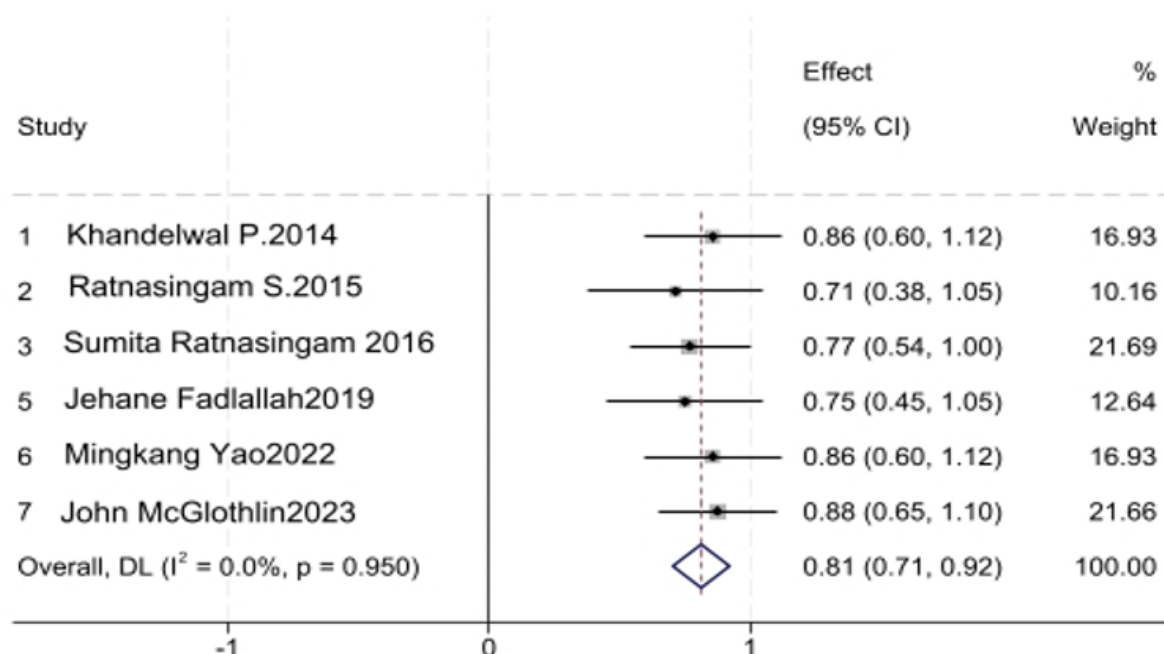


Figure 1. Methodological quality of the included studies. Risk-of-bias assessment of the 10 included single-arm studies across MINORS domains. Each item was rated as low (green), unclear (yellow), or high (red) risk. The uncontrolled study design (no comparator group) and incomplete pre-specification of outcomes were the main limitations across studies.

3.3. Meta-analysis

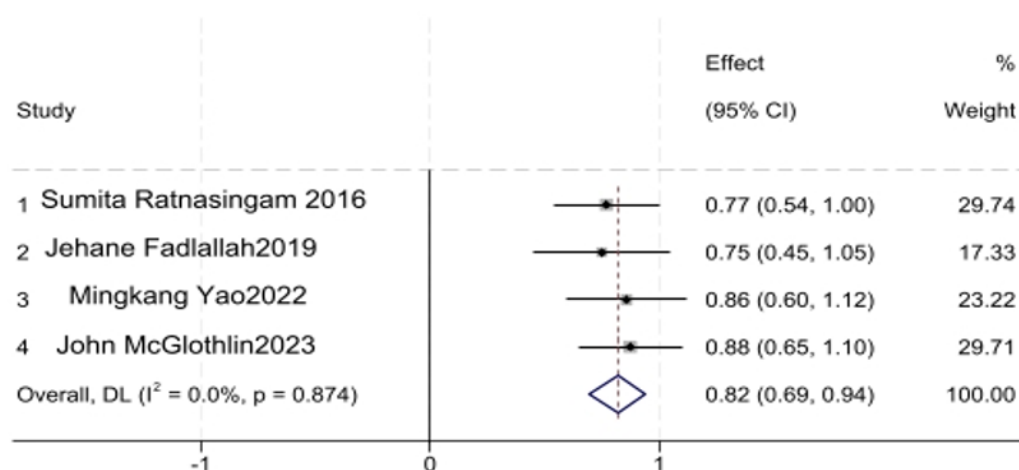
Six studies were pooled in the primary single-arm meta-analysis of bortezomib for AIHA using a random-effects model. The pooled response proportion was 0.81 (95% CI 0.71–0.92). Between-study heterogeneity was negligible ($I^2 = 0.0\%$, $P = 0.950$). Individual study estimates ranged from 0.71 to 0.88, with study weights between 10.16% and 21.69% (Figure 2).



NOTE: Weights are from random-effects model

Figure 2. Pooled response rate of bortezomib in autoimmune hemolytic anemia. Forest plot of the single-arm random-effects meta-analysis (DerSimonian–Laird) of six studies. Squares represent the response proportion of each study (size proportional to study weight), horizontal lines the 95% confidence intervals (CIs), and the diamond the pooled estimate. The pooled response proportion was 0.81 (95% CI 0.71–0.92), with no detectable heterogeneity ($I^2 = 0.0\%$, $P = 0.950$).

In the pre-specified sensitivity analysis excluding the two conference abstracts, the four remaining studies—all addressing refractory/relapsed AIHA—yielded a pooled response proportion of 0.82 (95% CI 0.69–0.94), again with no detectable heterogeneity ($I^2 = 0.0\%$, $P = 0.874$) and study weights of 17.33%–29.74%. The leave-one-out analysis, omitting each study in turn, produced essentially unchanged estimates, indicating that no single study drove the result (Figure 3).



NOTE: Weights are from random-effects model

Figure 3. Sensitivity analysis excluding conference abstracts. Forest plot of the single-arm random-effects meta-analysis (DerSimonian–Laird) restricted to the four full-text studies of refractory/relapsed autoimmune hemolytic anemia. Squares represent the response proportion of each study (size proportional to study weight), horizontal lines the 95% confidence intervals (CIs), and the open diamond the pooled estimate. The pooled response proportion was 0.82 (95% CI 0.69–0.94), with no detectable heterogeneity ($I^2 = 0.0\%$, $P = 0.874$). Weights are from the random-effects model.

Taken together, the six studies indicate a consistent response to bortezomib in AIHA. The very low heterogeneity ($I^2 = 0.0\%$, $P = 0.950$) made subgroup analysis and meta-regression unnecessary. With only six studies, a funnel plot was underpowered to assess small-study effects and is not presented; publication bias therefore cannot be formally ruled out. The pooled estimate was stable across analyses and its 95% confidence interval excluded the null, supporting a clinically meaningful effect.

4. Discussion

This systematic review and meta-analysis examined the efficacy and safety of bortezomib in AIHA. The pooled data suggest that bortezomib is effective, with a manageable safety profile, in relapsed/refractory disease. All included studies evaluated bortezomib as monotherapy or in combination. Individual response proportions ranged from 0.71 to 0.88 (study weights 10.16%–21.69%). After excluding the two conference abstracts, the pooled estimate for the remaining four studies was 0.82 (95% CI 0.69–0.94), with no detectable heterogeneity ($I^2 = 0.0\%$, $P = 0.874$) and stable results across sensitivity analyses. The included studies also showed clinical diversity in subtype and prior treatment, which we describe in Table 1. Overall, bortezomib achieved a high response rate, and reported adverse events fell within an acceptable range, supporting its use particularly in relapsed/refractory AIHA.

4.1. Bortezomib versus conventional therapy

Bortezomib compares favorably with standard options in terms of overall response, complete response, and duration of response. Glucocorticoids, the first-line treatment, achieve an ORR of 80%–90%, but only 20%–30% of patients maintain long-term remission after tapering or withdrawal, and more than 60% relapse. As monotherapy, bortezomib has been reported to achieve an ORR of 77% and a CR rate of 38%, with 66.7% of responders maintaining remission. In a prospective study from Peking Union Medical College Hospital, bortezomib combined with rituximab produced a response rate of 86.7% after initial treatment [17], with a median time to response of 15 days. The ORR at 6 months was 80.0% and the CR rate 56.7% [18], and the 24-month relapse-free survival rate reached 76.0%, compared with 20.8% historically reported for other regimens [5].

Relapse in responders is closely linked to ongoing autoantibody production. By targeting the plasma cells responsible for sustained antibody secretion, bortezomib offers a mechanistically distinct option for refractory AIHA [19]. Stratified by disease severity and refractoriness, the benefit appears greatest in patients resistant to both glucocorticoids and rituximab. Its principal mechanism is proteasome inhibition, which induces apoptosis of long-lived plasma cells and reduces autoantibody secretion [2]. In doing so, bortezomib can interrupt the pathological immune cascade and limit RBC destruction, leading to rapid improvement in hematological parameters. As clinical experience accumulates and regimens are refined, bortezomib may take on a larger role in refractory AIHA.

4.2. Combination regimens and clinical use

Bortezomib-containing combinations show efficacy broadly similar to monotherapy, though some studies report higher response rates and lower relapse rates with combination treatment. Pairing bortezomib with rituximab or glucocorticoids may enhance overall efficacy, reflecting the complementary effects of plasma cell and B cell depletion [2]. The case series included here suggest that both acute and chronic AIHA can be brought under better control after bortezomib, and that the drug can reduce reliance on high-dose glucocorticoids. Earlier work likewise indicates that effective targeted therapy can improve clinicians' ability to manage refractory disease. On this basis, bortezomib appears to be a useful salvage option for patients with severe AIHA.

That said, our findings do not support bortezomib as a routine first-line agent for uncomplicated AIHA. Despite the well-known toxicities of glucocorticoids and the limited availability and cost-effectiveness of rituximab in some settings, glucocorticoids remain the cornerstone of treatment for

newly diagnosed wAIHA [2]. Bortezomib requires parenteral administration and carries risks of peripheral neurotoxicity, infection, and gastrointestinal toxicity, all of which can affect quality of life [2]. AIHA is highly heterogeneous, with wide variation in severity and comorbidity, and without careful patient selection and risk stratification there is a real risk of overuse. The gap between trial populations and real-world patients must therefore be kept in view. Management is also multifaceted, involving close monitoring, supportive care, and prevention and treatment of complications; relying on targeted therapy alone risks underestimating this complexity. Because some patients develop life-threatening acute hemolysis requiring urgent intervention, clinicians should weigh disease severity, comorbidity, prior treatment, and patient tolerance together, and seek specialist input when needed. For now, bortezomib should not be considered a routine first-line therapy.

Although the efficacy of bortezomib in relapsed/refractory AIHA is encouraging, high-quality evidence to justify its use in unselected patients is still lacking, and the field continues to evolve. Prospective controlled trials are needed to confirm efficacy and, in particular, to identify the patients most likely to benefit, such as those with rituximab resistance [2]. At present, bortezomib is best regarded as an important second-line or salvage agent that can serve several practical roles—as salvage therapy, as a bridge to definitive treatment, or as a steroid-sparing option. Further work is needed to define optimal doses, dosing intervals, and combination partners so that safer and more effective regimens can be established [20].

4.3. Strengths of this review

To our knowledge, this is the first quantitative synthesis focused specifically on bortezomib for relapsed/refractory AIHA. Most prior reviews addressed conventional treatments or newer modalities such as complement inhibitors and CAR-T cell therapy, and evidence on bortezomib existed only as scattered small series. By pooling data across centers, the single-arm meta-analysis yielded a response proportion of 0.81 (95% CI 0.71–0.92) with very low heterogeneity ($I^2 = 0.0\%$, $P = 0.950$), providing a more reliable quantitative estimate than was previously available.

We also used several approaches to test robustness. Excluding conference abstracts left the pooled estimate essentially unchanged at 0.82 (95% CI 0.69–0.94), and the leave-one-out analysis showed no influential single study, indicating that small or non-standardized studies did not distort the conclusions. The review followed PRISMA 2020 throughout, with standardized screening and risk-of-bias assessment, and identified the main methodological weaknesses—chiefly the uncontrolled design and incomplete outcome reporting—of the available evidence.

4.4. Limitations

High-quality evidence is essential for judging how well bortezomib works in AIHA, and adequately powered, well-designed studies are needed to confirm its efficacy and safety. Most included studies, however, were retrospective, single-arm, and small, often enrolling only a few to a few dozen patients.

The proportion of refractory or rituximab-resistant cases varied widely between studies, which could destabilize the pooled estimate and inflate heterogeneity. These small sample sizes largely reflect the low incidence of severe refractory AIHA and the ethical constraints on studying it. Much of the evidence comes from single-center experience, and the non-standardized, dose-adjusted, and individualized regimens used in some reports may overestimate true treatment effects. Multicenter collaboration and shared databases would help make better use of scarce data in this rare disease, and larger, more representative cohorts are needed to define the role of bortezomib more precisely.

Long-term safety also warrants attention. Most studies report only short-term efficacy and acute toxicities such as peripheral neuropathy, gastrointestinal effects, and cytopenias, while data on delayed neuropathy, secondary malignancy, and late infection remain sparse. It is not yet clear which patients are most susceptible to severe toxicity, or how best to prevent and manage it. Compared with conventional immunosuppressants, long-term data on bortezomib in autoimmune disease are limited,

and standardized follow-up protocols—developed jointly by hematologists, pharmacologists, and clinical researchers—would help close this gap.

4.5. Future directions

This review was designed and conducted in accordance with PRISMA 2020 to evaluate the efficacy and safety of bortezomib in AIHA. The analyses point to genuine clinical potential in refractory disease and support a role for bortezomib as salvage therapy. Several caveats apply. The search was limited to major databases, so some small studies and conference proceedings may have been missed. Comparisons with alternative agents rested on indirect evidence, so confounding should be considered when interpreting the results. The included studies did not stratify outcomes by AIHA subtype (warm, cold, or mixed), and pooling across subtypes may reduce the reliability of the combined estimate. As interest in targeted therapy for AIHA grows, rigorous prospective studies will be essential to generate definitive evidence. Recently published consensus and reporting standards for autoimmune cytopenias should help harmonize study design and outcome measures, and further controlled trials are expected in the coming years.

4.6. Conclusion

In this analysis, bortezomib showed consistent efficacy in AIHA with very low between-study heterogeneity and robust results on sensitivity analysis, and it improved hemolysis control and clinical outcomes in refractory patients. These findings nonetheless require confirmation in high-quality, large-scale, multicenter prospective studies, which are also needed to resolve practical questions of dosing, treatment duration, combination regimens, and long-term safety in the standardized management of AIHA.

References

- [1] Hill, Q.A., et al., The diagnosis and management of primary autoimmune haemolytic anaemia. *Br J Haematol*, 2017. **176**(3): p. 395-411.
- [2] Chinese guideline for the diagnosis and treatment of adult autoimmune hemolytic anemia (2023)]. *Zhonghua Xue Ye Xue Za Zhi*, 2023. **44**(1): p. 12-18.
- [3] Berentsen, S. and W. Barcellini, Autoimmune Hemolytic Anemias. *N Engl J Med*, 2021. **385**(15): p. 1407-1419.
- [4] Yue, W.R., T. Wu, and X.Q. Wang, [The treatment strategies of autoimmune hemolytic anemia]. *Zhonghua Xue Ye Xue Za Zhi*, 2024. **45**(6): p. 615-620.
- [5] Lin, X., et al., Rituximab Plus Bortezomib for Relapsed and Refractory Warm Autoimmune Hemolytic Anemia: A Prospective Phase 2 Trial. *Am J Hematol*, 2025. **100**(2): p. 326-329.
- [6] Pasquale, R., et al., Bortezomib in autoimmune hemolytic anemia and beyond. *Ther Adv Hematol*, 2021. **12**: p. 20406207211046428.
- [7] Johnson, E., et al., Bortezomib for the Management of Relapsed or Refractory Warm Autoimmune Hemolytic Anemia: A Scoping Review. *Blood*, 2021. **138**.
- [8] Khandelwal, P., et al., Bortezomib Is a Successful Therapeutic Agent for Refractory Autoimmune Cytopenias in Children: A Single Center Experience. *Biology of Blood and Marrow Transplantation*, 2014. **20**(2): p. S174-S174.
- [9] Ratnasingam, S., et al., Bortezomib Yields High Response Rates in Antibody-Mediated Autoimmune Hematological Diseases Refractory to Conventional Immunosuppression. *Blood*, 2015. **126**(23).
- [10] 10. Ratnasingam, S., et al., Bortezomib-based antibody depletion for refractory autoimmune hematological diseases. *Blood Advances*, 2016. **1**(1): p. 31-35.
- [11] Rossi, G., et al., Short Course of Bortezomib in Anemic Patients with Refractory or Relapsed Cold Agglutinin Disease. a Phase II Prospective Study By the Gimema Group. *Blood*, 2017. **130**.

- [12] Zine, M., et al., BORTEZOMIB FOR STEROID-REFRACTORY RITUXIMAB AUTOIMMUNITY AFTER ALLOGENEIC HAEMATOPOIETIC STEM CELL TRANSPLANTATION. *Haematologica*, 2017. **102**: p. 858-858.
- [13] Fadlallah, J., et al., Bortezomib and dexamethasone, an original approach for treating multi-refractory warm autoimmune haemolytic anaemia. *British Journal of Haematology*, 2019. **187**(1): p. 124-128.
- [14] Yao, M.K., et al., Combination of low-dose rituximab, bortezomib and dexamethasone for the treatment of autoimmune hemolytic anemia. *Medicine*, 2022. **101**(4).
- [15] McGlothlin, J., et al., Bortezomib and daratumumab in refractory autoimmune hemolytic anemia. *American Journal of Hematology*, 2023. **98**(10): p. E263-E265.
- [16] Jain, A., et al., Efficacy and Safety of Weekly Bortezomib-dexamethasone as the Third-Line Therapy for Warm Autoimmune Hemolytic Anemia: a Case Series of 5 Patients. *Indian Journal of Hematology and Blood Transfusion*, 2025. **41**(1): p. 144-150.
- [17] Chao, S.H., et al., Efficacy and safety of rituximab in autoimmune and microangiopathic hemolytic anemia: a systematic review and meta-analysis. *Exp Hematol Oncol*, 2020. **9**: p. 6.
- [18] Reynaud, Q., et al., Efficacy and safety of rituximab in auto-immune hemolytic anemia: A meta-analysis of 21 studies. *Autoimmun Rev*, 2015. **14**(4): p. 304-13.
- [19] Barcellini, W., et al., Clinical heterogeneity and predictors of outcome in primary autoimmune hemolytic anemia: a GIMEMA study of 308 patients. *Blood*, 2014. **124**(19): p. 2930-6.
- [20] Birgens, H., et al., A phase III randomized trial comparing glucocorticoid monotherapy versus glucocorticoid and rituximab in patients with autoimmune haemolytic anaemia. *Br J Haematol*, 2013. **163**(3): p. 393-9.