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Belantamab Mafodotin: Ocular Toxicity and Comparative Evaluation across Antibody–Drug Conjugates

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Abstract

Background: Multiple myeloma (MM) remains a therapeutic challenge, especially in relapsed or refractory disease. Belantamab mafodotin, a B-cell maturation antigen (BCMA)-directed antibody–drug conjugate (ADC), has demonstrated antimyeloma activity, but is associated with distinctive ocular toxicity.

Aim: This review summarizes the pharmacological and clinical characteristics of belantamab mafodotin, focusing on the manifestations, mechanisms, and management of its ocular toxicity, and compares its ocular safety profile with other ADCs.

Materials and Methods: A narrative literature review was conducted using PubMed. Clinical trials, real-world studies, systematic reviews, meta-analyses, and relevant mechanistic and ophthalmological studies published up to 2026 were considered.

Results: Belantamab mafodotin demonstrated clinically meaningful activity in relapsed or refractory MM. Ocular toxicity was mainly characterized by corneal epithelial abnormalities, particularly microcyst-like epithelial changes. Mechanistic evidence supports target-independent uptake by corneal epithelial cells and intracellular effects of the MMAF payload. Ocular findings commonly emerged during early treatment and required dosage modifications. Other ADCs showed heterogeneous ocular toxicity, ranging from corneal epithelial abnormalities to conjunctival and ocular surface involvement.

Conclusions: Belantamab mafodotin illustrates the importance of balancing the therapeutic potential of ADCs with tissue-specific toxicity. Ocular adverse events illustrate the interplay between ADC molecular properties and the biological characteristics of ocular tissues, highlighting this toxicity as a heterogeneous class effect. Continued investigation of tissue susceptibility and optimization of ADC design and treatment strategies may widen the therapeutic window.

Key words: Belantamab mafodotin; multiple myeloma; antibody–drug conjugates; ocular toxicity; corneal toxicity; keratopathy

Introduction

Continuous advances in medicine are driven by ongoing discoveries that expand our understanding of disease mechanisms and enable the development of innovative therapeutic strategies. These targeted therapies are subsequently used in the treatment of multiple myeloma (MM), which is a type of hematological malignancy defined by the proliferation of terminally differentiated plasma cells.¹ Although MM ranks only 21st in terms of incidence and 17th in terms of mortality worldwide, these rankings may underestimate its true clinical impact.² The disease represents a growing and significant public health burden, with approximately 36,000 new cases and more than 10,800 deaths projected in the United States in 2026 alone.³ Despite the introduction of proteasome inhibitors, immunomodulatory agents, and anti-CD38 monoclonal antibodies, many patients with MM eventually experience relapse or develop refractory disease. Data from a large retrospective analysis indicate that the median overall survival (OS) rate of triple-class-refractory myeloma is 9.2 months and it progressively declines with increasing resistance to therapy.⁴ The poor prognosis of this patient subgroup highlights

a substantial unmet medical need that has driven the development of Antibody-Drug Conjugates (ADCs). ADCs combine the specificity of monoclonal antibodies with the cytotoxic potency of chemotherapeutic agents, enabling selective elimination of malignant cells. This approach offers a strategy to enhance treatment efficacy while minimizing systemic toxicity.⁵ In the context of MM, B-cell maturation antigen (BCMA) has emerged as a key target for ADCs due to its positive correlation with augmented plasma cell persistence and elevated expression in relapsed or refractory disease.^{6,7} Belantamab mafodotin represents a pioneering anti-BCMA, approved for the treatment of relapsed or refractory MM. Although it has demonstrated promising antimyeloma activity in heavily pretreated patients, its clinical application is complicated by a distinctive toxicity profile.⁸ Among the adverse events associated with this agent, ocular toxicity has attracted particular attention because of its high frequency and potential impact on visual function.⁹ Belantamab mafodotin-associated keratopathy represents an important limitation requiring dedicated ophthalmic monitoring and, in some cases, treatment interruption or dose modification.¹⁰ Moreover, ocular adverse events are not exclusive to belantamab mafodotin and have been reported with other antibody–drug conjugates, raising the possibility of shared or ADC-specific mechanisms underlying these toxicities.¹¹ Characterizing the similarities and differences in ocular toxicity among ADCs may therefore provide valuable insights into its clinical significance.

1. Belantamab Mafodotin: Pharmacological and Clinical Characteristics

1.1. Molecular structure and mechanism of action

Belantamab mafodotin (belamaf; BLENREP™; previously known as GSK2857916) is a first-in-class antibody–drug conjugate (ADC) directed against B-cell maturation antigen (BCMA) and developed for the treatment of multiple myeloma (MM).¹² Structurally, belamaf consists of a humanized IgG1 monoclonal antibody directed against BCMA, which is covalently linked via a non-cleavable maleimidocaproyl (mc) linker to the cytotoxic payload monomethyl auristatin F (MMAF), a potent microtubule polymerization inhibitor.¹³ BCMA, also known as tumor necrosis factor receptor superfamily member 17 (TNFRSF17), is a transmembrane receptor predominantly expressed on mature plasma cells and malignant plasma cells, where it is involved in signaling pathways associated with plasma-cell survival.⁶ The receptor interacts with the ligands B-cell activating factor (BAFF) and a proliferation-inducing ligand (APRIL), which contribute to the regulation and maintenance of plasma-cell populations.¹⁴ The preferential expression of BCMA on malignant plasma cells has established this receptor as an attractive target for the development of targeted therapies in MM.¹² An important structural

feature of belantamab mafodotin is the afucosylation of its Fc region, which enhances interaction with FcγRIIIa expressed on immune effector cells and thereby increases Fc-mediated effector functions. These properties contribute to antibody-dependent cellular cytotoxicity (ADCC) and antibody-dependent cellular phagocytosis (ADCP), providing additional mechanisms of elimination of BCMA-expressing myeloma cells beyond the activity of the cytotoxic payload. Following binding to BCMA on the surface of malignant plasma cells, belantamab mafodotin is internalized and subsequently transported through the endocytic pathway to the lysosomal compartment. Intracellular processing of the ADC results in the formation of an active MMAF-containing catabolite, which subsequently interacts with tubulin and interferes with microtubule polymerization. Disruption of the microtubule network impairs mitotic progression and leads to G2/M cell-cycle arrest followed by activation of apoptotic pathways, including caspase-dependent apoptosis.¹⁵ The antimyeloma activity of belantamab mafodotin therefore results from complementary mechanisms involving targeted antigen recognition, intracellular delivery of a potent microtubule inhibitor, and Fc-mediated immune effector functions.¹² Importantly, the ability of belantamab mafodotin to undergo cellular uptake and deliver the MMAF payload is also relevant to its characteristic safety profile, as recent evidence suggests that the ADC can be internalized by non-BCMA-expressing cells, including human corneal epithelial cells.¹³

1.2. Clinical development and efficacy

The clinical development of belantamab mafodotin was initiated in patients with heavily pretreated relapsed or refractory multiple myeloma (RRMM), a population characterized by limited therapeutic options and poor clinical outcomes. Early evidence from the first-in-human DREAMM-1 study demonstrated that BCMA-directed ADC therapy could induce objective responses in patients with advanced disease, providing the rationale for subsequent clinical development of belantamab mafodotin. The antimyeloma activity observed in early-phase investigation was confirmed in the pivotal phase II DREAMM-2 trial, which enrolled patients with RRMM who had received at least three prior lines of therapy and were refractory to an immunomodulatory agent and a proteasome inhibitor, as well as refractory or intolerant to an anti-CD38 monoclonal antibody. At the recommended dose of 2.5 mg/kg administered every three weeks, belantamab mafodotin achieved an overall response rate (ORR) of 31%, demonstrating clinically meaningful antimyeloma activity in this heavily pretreated population.¹⁶ The therapeutic effect was not limited to short-term tumor reduction, as longer follow-up of the 2.5 mg/kg cohort demonstrated a median duration of response (DoR) of 11.0 months, while median progression-free survival (PFS) and overall survival (OS) were 2.8 and 13.7 months.¹⁷

The final analysis of DREAMM-2, including 223 treated patients, further confirmed the durability of clinical activity, with ORRs of 32% and 35% in the 2.5 and 3.4 mg/kg cohorts, while median DoR reached 12.5 months in the 2.5 mg/kg group.¹⁸ The efficacy of belantamab mafodotin was generally maintained across several patient subgroups, although less favorable outcomes were observed in patients with extramedullary disease.¹⁷ Despite encouraging results in heavily pretreated patients, belantamab mafodotin monotherapy failed to demonstrate a statistically significant progression-free survival benefit over pomalidomide + low-dose dexamethasone in the phase III DREAMM-3 trial.¹⁹ These findings shifted subsequent development toward combination regimens, as demonstrated by the phase III DREAMM-7 trial, in which belantamab mafodotin combined with bortezomib and dexamethasone significantly prolonged progression-free survival compared with daratumumab, bortezomib, and dexamethasone in patients with RRMM who had received at least one prior line of therapy.²⁰ The phase III DREAMM-8 trial further supported the efficacy of combination therapy, demonstrating significantly prolonged PFS with belantamab mafodotin plus pomalidomide and dexamethasone (BPd) compared with bortezomib, pomalidomide, and dexamethasone (PVd) in patients with RRMM previously exposed to lenalidomide. After a median follow-up of 21.8 months, the estimated 12-month PFS was 71% with BPd compared with 51% with PVd, corresponding to a hazard ratio for disease progression or death of 0.52. The BPd regimen also resulted in deeper responses, with complete response or better achieved in 40% of patients compared with 16% receiving PVd, despite similar overall response rates between the two groups (77% vs 72%).²¹ Overall, clinical data demonstrate substantial antimyeloma activity of belantamab mafodotin, with its therapeutic role evolving from salvage monotherapy toward combination-based treatment strategies that provide deeper and more durable disease control.

18,20,21

1.3. Safety profile

The safety profile of belantamab mafodotin has been characterized across clinical trials involving both heavily pretreated patients receiving monotherapy and patients treated with belamaf-containing combination regimens. In the final analysis of DREAMM-2, the most frequently reported grade 3–4 adverse events included keratopathy, thrombocytopenia, and anemia.¹⁸ Hematologic toxicities, particularly thrombocytopenia and anemia, were among the most commonly observed non-ocular adverse events and were generally manageable with appropriate clinical intervention.¹⁸ The safety profile remained broadly consistent when belantamab mafodotin was evaluated in combination regimens. In DREAMM-7, grade 3 or higher adverse events occurred in 95% of patients receiving belantamab mafodotin plus

bortezomib and dexamethasone, compared with 78% of those receiving daratumumab, bortezomib, and dexamethasone, with thrombocytopenia being the most frequent grade 3 or higher adverse event.²⁰ Similarly, in DREAMM-8, grade 3 or higher adverse events occurred in 94% of patients treated with belantamab mafodotin, pomalidomide, and dexamethasone, compared with 76% receiving pomalidomide and dexamethasone with bortezomib.²¹ Among these adverse events, ocular toxicity represents the most distinctive safety concern associated with belantamab mafodotin and is discussed in detail in the following section.

2. Ocular Toxicity Associated with Belantamab Mafodotin

2.1. Clinical characteristics and incidence

Belantamab mafodotin-associated ocular toxicity is one of the most characteristic adverse events observed during treatment and predominantly affects the corneal epithelium. In the pivotal DREAMM-2 trial, keratopathy was reported in approximately 70% of patients receiving belantamab mafodotin, making it the most frequently observed treatment-related adverse event.¹⁶ The hallmark of belantamab mafodotin-associated keratopathy is the development of microcyst-like epithelial changes (MECs), which can be detected by slit-lamp examination. In DREAMM-2, MECs were identified in 72% of patients receiving the recommended dose of 2.5 mg/kg, with the median time to onset of the first corneal finding being 37 days.²² Most patients who developed keratopathy experienced their first corneal finding within the first four treatment cycles, indicating that ocular toxicity commonly emerges relatively early during therapy.²² These epithelial changes may initially appear in the peripheral cornea and subsequently progress toward the central cornea, potentially involving the visual axis.²³ Corneal changes may be accompanied by reduced visual acuity, blurred vision, dry-eye symptoms, photophobia, and ocular discomfort, although the severity of symptoms does not necessarily correspond to the extent of corneal findings.⁹ Although ocular findings may remain asymptomatic or cause only mild visual disturbances in some patients, more severe keratopathy can result in clinically meaningful reductions in visual acuity and affect daily functioning. In the final analysis of DREAMM-2, grade 3 keratopathy occurred in 29% of patients receiving belantamab mafodotin at 2.5 mg/kg, demonstrating that ocular toxicity may reach clinically significant severity despite being generally manageable.¹⁸

2.2. Pathophysiology

The pathophysiology of belantamab mafodotin-associated ocular toxicity has not been fully elucidated, but current evidence indicates that the cytotoxic MMAF payload plays a central role in the development of corneal epithelial damage. Importantly, corneal epithelial cells do not

express BCMA at levels sufficient to account for conventional antigen-dependent ADC uptake, suggesting that the ocular toxicity is predominantly mediated through a target-independent mechanism.^{9,13} Belantamab mafodotin may reach the cornea through the tear film and, potentially, via the limbal vasculature, where it can be internalized by corneal epithelial cells independently of BCMA expression. Earlier studies proposed nonspecific cellular uptake, including macropinocytosis, as a potential mechanism underlying this process.^{8,9} More recent experimental data provide direct support for this hypothesis, demonstrating concentration- and time-dependent uptake of belantamab mafodotin by primary human corneal epithelial cells despite the absence of BCMA expression.¹³ Following cellular internalization, belantamab mafodotin is trafficked through the endocytic pathway and undergoes intracellular processing, resulting in the release of a cytotoxic MMAF-containing catabolite. MMAF can subsequently disrupt tubulin polymerization and the integrity of the microtubule network, impairing essential cellular processes and ultimately inducing apoptosis of corneal epithelial cells.^{13,24} This mechanism is consistent with the characteristic microcyst-like epithelial changes observed clinically and may explain the progressive accumulation and subsequent shedding of damaged epithelial cells from the corneal surface.²⁴ The distribution of these changes may also reflect the biology of the corneal epithelium. Damage to basal and limbal epithelial cells can interfere with cell migration, differentiation, and replacement of the superficial epithelium, allowing affected cells to migrate toward the central cornea before undergoing apoptosis and desquamation.²⁴ In addition to epithelial injury, corneal confocal microscopy studies have suggested that belantamab mafodotin may exert neurotoxic effects, with marked alterations and loss of subbasal corneal nerve fibers observed during treatment.²⁵ The emerging evidence therefore supports a multifactorial model in which BCMA-independent uptake of belantamab mafodotin, intracellular release of MMAF, disruption of microtubule function, and subsequent epithelial apoptosis collectively contribute to the development of corneal toxicity. However, the precise mechanisms governing ADC uptake and the variability in individual susceptibility remain incompletely understood.^{13,24}

2.3. Dose modifications based on ocular findings

Management of belantamab mafodotin-associated ocular toxicity relies on regular ophthalmic monitoring and treatment modification according to the severity of corneal findings and changes in visual acuity. Importantly, treatment decisions are guided primarily by objective ophthalmic assessment, as corneal abnormalities may develop without corresponding ocular symptoms.²⁶ The Keratopathy and Visual Acuity (KVA) scale was introduced to provide a standardized approach to grading corneal findings and changes in best-corrected visual acuity

and to facilitate treatment decisions. Based on the severity of ocular findings, management may range from continuation of therapy with close monitoring to temporary treatment interruption, dose reduction, or extension of the dosing interval.²⁶ The importance of dose modification was already demonstrated in DREAMM-2. Among patients receiving belantamab mafodotin at 2.5 mg/kg who developed microcyst-like epithelial changes, 47% experienced at least one dose delay and 25% required a dose reduction. Despite the high frequency of these interventions, permanent treatment discontinuation due to corneal events remained relatively uncommon.²² Subsequent studies have supported the feasibility of maintaining treatment with modified dosing schedules. In DREAMM-7 and DREAMM-8, ocular adverse events were predominantly managed through dose delays and reductions rather than permanent discontinuation, allowing patients to remain on belantamab mafodotin-containing regimens while ocular findings were monitored for recovery. Importantly, treatment modifications were incorporated into the overall management strategy while maintaining the clinical benefit observed with the combination regimens.²⁷ More recent evidence has also highlighted the potential role of extending the dosing interval as an alternative to repeated dose interruptions or permanent treatment discontinuation. This approach is based on the relatively slow recovery of the corneal epithelium and aims to provide sufficient time for resolution of ocular findings while maintaining exposure to belantamab mafodotin.²⁸ Overall, dose modification has become an integral component of belantamab mafodotin therapy, allowing ocular toxicity to be managed while preserving the possibility of continued antimyeloma treatment.

2.4. Clinical trial versus real-world evidence

The high incidence of ocular toxicity observed in clinical trials has been broadly confirmed in real-world practice, although reported rates vary between patient cohorts. In a multicenter real-world study of 106 patients with RRMM, keratopathy occurred in 68.4% of patients, with grade ≥ 3 events reported in 40.5%. Despite the frequency of ocular events, permanent treatment discontinuation because of ocular toxicity was uncommon, supporting the feasibility of managing keratopathy through treatment modifications.⁴ More recent real-world data have similarly demonstrated a high incidence of corneal toxicity, while also highlighting differences in its reported severity. In a single-center cohort of 30 patients, keratopathy of any grade occurred in 93% of patients, whereas only 2% of keratopathy events were grade ≥ 3 . Dose reductions and treatment delays were frequently required, but treatment could generally be continued despite these modifications.²⁹ A large US real-world observational study further confirmed that ocular adverse events were common during belantamab mafodotin treatment, with keratopathy reported in 41.3% of patients and discontinuation specifically attributed to

keratopathy occurring in 4.3% of patients.³⁰ Differences in the reported incidence and severity of ocular events between clinical trials and real-world cohorts may reflect variations in patient characteristics, ophthalmic monitoring, diagnostic criteria, and treatment management. Overall, real-world evidence supports the clinical trial findings that ocular toxicity is a frequent complication of belantamab mafodotin, but that it can often be managed with treatment modifications without permanent treatment discontinuation.⁴

3. Ocular Toxicity across Antibody-Drug Conjugates (ADCs)

3.1. Clinical characteristics and incidence

Ocular adverse events are increasingly recognized as a clinically relevant toxicity associated with several antibody–drug conjugates (ADCs), although their incidence and clinical presentation vary substantially between individual agents. Reported manifestations include dry eye, blurred vision, conjunctivitis, keratitis, and corneal epithelial abnormalities, with the cornea and conjunctiva representing the most frequently affected ocular structures. A 2025 systematic review and meta-analysis of 31 randomized clinical trials involving 18,490 patients estimated the pooled incidence of all-grade ocular adverse events associated with ADC therapy at 10.45%, although substantial heterogeneity was observed across individual ADCs. The analysis also indicated a higher risk of ophthalmotoxicity with ADCs carrying monomethyl auristatin E (MMAE) or monomethyl auristatin F (MMAF) payloads, suggesting that the cytotoxic component may contribute to the development of ocular toxicity.³¹ Among ADCs with a well-characterized ocular safety profile, mirvetuximab soravtansine is associated predominantly with corneal events and blurred vision. In an integrated analysis of 682 patients, blurred vision occurred in 43% of patients, while grade ≥ 3 keratopathy occurred in 5%; most ocular events were low grade and reversible.³² Tisotumab vedotin demonstrates a different clinical pattern, with ocular toxicity occurring predominantly at the conjunctival and ocular surface level. In the pivotal phase II study, ocular treatment-related adverse events occurred in 53% of patients, most commonly conjunctivitis, dry eye, and keratitis, and were predominantly grade 1–2.³³ Corneal epithelial changes have also been described with other ADCs, including trastuzumab emtansine, where characteristic corneal epithelial lesions may occur despite being clinically asymptomatic in many patients.³⁴ Overall, ADC-associated ocular toxicity encompasses a heterogeneous spectrum ranging from mild and reversible ocular surface symptoms to clinically significant corneal disease. The marked differences in incidence and phenotype between ADCs provide a basis for evaluating how individual ADC components and mechanisms contribute to ocular toxicity, which is discussed in the following section.

3.2. Mechanisms of ADC-associated ocular toxicity

The mechanisms underlying ADC-associated ocular toxicity are not fully understood and appear to involve both target-dependent and target-independent processes. Unlike the intended uptake of ADCs by antigen-expressing tumor cells, ocular toxicity may result from direct binding to antigens expressed on ocular tissues or from nonspecific internalization of the intact ADC by cells lacking the target antigen.³⁵ Target-dependent toxicity has been proposed for ADCs whose target antigens are expressed on ocular surface tissues. Tisotumab vedotin, for example, targets tissue factor, which is expressed in the conjunctiva, and its uptake by conjunctival cells may result in intracellular delivery of the cytotoxic payload and subsequent cellular injury.³⁶ Conversely, target-independent toxicity may occur through nonspecific endocytosis or pinocytosis, including macropinocytosis, allowing ADCs to enter ocular cells despite limited or absent target-antigen expression.³⁷ The cytotoxic payload represents an additional determinant of ocular toxicity. Auristatin-based payloads, particularly MMAE and MMAF, have been associated with a higher risk of ophthalmotoxicity, consistent with their potent inhibition of microtubule function.³¹ The intracellular retention and physicochemical properties of the released payload may further influence the extent and distribution of tissue injury.³⁵ Linker characteristics may also affect ocular safety by determining the stability of the ADC in circulation and the conditions under which the payload is released. Premature linker cleavage can increase systemic exposure to the free cytotoxic drug and potentially enhance off-target toxicity, whereas more stable linkers may reduce nonspecific payload release.³⁷ In addition, the physicochemical properties of the complete ADC, including molecular structure and interactions with cellular uptake pathways, may influence its distribution to ocular tissues and subsequent intracellular processing.³⁵ Taken together, ADC-associated ocular toxicity is likely determined by the interaction of several factors rather than by a single mechanism. The antibody target, uptake pathway, linker stability, payload characteristics, and susceptibility of individual ocular tissues may collectively determine the specific pattern and severity of ocular injury observed with each ADC.³⁵

3.3. Comparative profile of ocular toxicity

Although ocular toxicity is a recognized adverse effect of several ADCs, its frequency, anatomical distribution, and clinical severity differ considerably between individual agents. Belantamab mafodotin is distinguished by the high frequency of corneal epithelial toxicity, with microcyst-like epithelial changes representing its characteristic ocular manifestation. In contrast, other ADCs demonstrate different patterns of ocular involvement, reflecting differences in their molecular structure and pharmacological properties. Mirvetuximab

soravtansine, which also contains a tubulin-targeting payload, is associated predominantly with corneal epithelial changes, blurred vision, and dry eye. However, compared with belantamab mafodotin, its ocular toxicity has generally been reported as lower grade and reversible, with grade ≥ 3 keratopathy reported in approximately 5% of patients in an integrated analysis of 682 participants.³² Tisotumab vedotin exhibits a distinct ocular phenotype, with toxicity primarily involving the conjunctiva and ocular surface. In the pivotal phase II trial, ocular treatment-related adverse events occurred in 53% of patients, most commonly conjunctivitis, dry eye, and keratitis, and were predominantly grade 1–2.³³ Corneal epithelial abnormalities have also been described with trastuzumab emtansine (T-DM1). Prospective ophthalmic evaluation demonstrated characteristic, predominantly asymptomatic epithelial lesions, which were generally reversible and did not require discontinuation of systemic therapy.³⁴ More recent evidence has further demonstrated ocular surface and corneal changes associated with HER2-targeted ADCs, supporting the relevance of both target biology and ADC-specific properties in determining the ocular phenotype.³⁸ Overall, belantamab mafodotin appears to have a particularly prominent corneal toxicity profile, whereas other ADCs may produce predominantly conjunctival, ocular surface, or less clinically significant corneal abnormalities. Direct comparison of incidence rates should nevertheless be interpreted cautiously because clinical trials differ in patient populations, ophthalmic surveillance, definitions of ocular events, and grading systems.

Table 1. Comparative profile of ocular toxicity^{22,32–34,39}

ADC	Target	Payload	Predominant ocular toxicity	Reported incidence/severity	Characteristic features
Belantamab mafodotin	BCMA	MMAF	Keratopathy/MECs	~70% keratopathy; grade ≥ 3 events common	Microcyst-like epithelial changes; blurred vision
Mirvetuximab soravtansine	FR α	DM4	Keratopathy, blurred vision, dry eye	~50% ocular AEs; grade ≥ 3 ocular AEs ~5%	Predominantly corneal; generally reversible
Tisotumab vedotin	Tissue factor	MMAE	Conjunctivitis, dry eye, keratitis	53% ocular TRAEs; predominantly grade 1–2	Predominantly conjunctival/ocular surface
Trastuzumab emtansine (T-DM1)	HER2	DM1	Corneal epithelial changes	Mainly low-grade/asymptomatic in ophthalmic studies	Characteristic epithelial lesions; often reversible

Abbreviations: ADC, antibody–drug conjugate; AE, adverse event; BCMA, B-cell maturation antigen; DM1, maytansine derivative 1; DM4, maytansine derivative 4; FR α , folate receptor alpha; HER2, human epidermal growth factor receptor 2; MECs, microcyst-like epithelial changes; MMAE, monomethyl auristatin E; MMAF, monomethyl auristatin F; TRAE, treatment-related adverse event.

4. Conclusions and Future Perspectives

Belantamab mafodotin represents an important advance in the development of targeted therapies for relapsed or refractory multiple myeloma, demonstrating meaningful antimyeloma activity in patients with limited therapeutic options. Its clinical use, however, is associated with a distinctive pattern of ocular toxicity, predominantly affecting the corneal epithelium and representing one of the main challenges associated with treatment. The analysis presented in this review demonstrates that ocular toxicity is not uniform across antibody–drug conjugates. Differences in clinical presentation, affected ocular structures, and severity reflect the complex interplay between the molecular characteristics of individual ADCs and the biological properties of ocular tissues. Belantamab mafodotin is particularly characterized by a high frequency of corneal epithelial changes, whereas other ADCs may predominantly affect the conjunctiva, ocular surface, or produce less clinically significant corneal abnormalities. Despite its high incidence, belantamab mafodotin-associated ocular toxicity can generally be managed through systematic ophthalmic monitoring and appropriate treatment modification. Dose interruptions, reductions, and adjustment of dosing intervals provide an opportunity to control ocular adverse events while maintaining antimyeloma treatment. This highlights the importance of integrating ophthalmic assessment into the overall therapeutic strategy rather than considering ocular toxicity solely as a reason for treatment discontinuation. Overall, the experience with belantamab mafodotin emphasizes that the clinical value of ADCs depends not only on their antitumor efficacy but also on their tolerability and the possibility of effectively managing treatment-related toxicities. Further development of ADCs should aim to improve the therapeutic window through optimization of their molecular structure and more individualized approaches to toxicity monitoring and management. A better understanding of the mechanisms underlying ocular injury may ultimately contribute to the development of ADCs that retain potent antitumor activity while minimizing their impact on visual function and quality of life.

Disclosure

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Declaration of the Use of Generative AI and AI-assisted technologies in the Writing Process

During the preparation of this work, the authors used Google Gemini and ChatGPT for the purpose of language improvement, readability enhancement, and text formatting. After using this tool/service, the authors reviewed and edited the content as needed and take full responsibility for the substantive content of the publication.

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