Approved and Emerging Options for Oncology Treatment-Related Toxicities: A Targeted Literature Review of the Landscape and Remaining Unmet Needs

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Poster #CO30

OBJECTIVES, METHODS, AND REVIEW FRAME

Objectives

- Characterize the burden of oncology treatment-related toxicity
- Evaluate the real-world adoption and clinical outcomes associated with the use of rescue / protective agents
- Identify residual unmet needs and emerging therapeutic approaches

Methods

- Targeted PubMed review of published literature: 2010-2025
- Prioritized RCTs, RWE studies and pharmacoeconomic analyses
- Structured queries: (1) Epidemiology of treatment-related toxicities and (2) Management, utilization, and outcomes of toxicity-mitigation strategies across oncology settings.
- Agents were catalogued by intended use (Table 1)

Table 1: Therapeutic categories and intended use

Categories	Intended use	Therapeutic Agents
Acute rescue	Reverse or mitigate overdose-related or early severe toxic effects	Glucarpidase for HDMTX toxicity; uridine triacetate for 5-FU or capecitabine overdose or early onset severe toxicity
Organ-protective prophylaxis	Proactive organ protection from treatment-related toxicity	Mesna; amifostine; dexrazoxane; sodium thiosulfate; palifermin; trilaciclib
CAR-T immune countermeasures	Manage immune-mediated adverse effects after CAR-T therapy	Tocilizumab for cytokine release syndrome
Radiation protectants (in development)	Protect normal tissue from radiation injury	Superoxide dismutase mimetics; avasopasem (GC-4419)

ILLUSTRATIVE BURDEN OF TREATMENT-RELATED TOXICITY

Results

HDMTX-related kidney toxicity [1,2,3]

- **~2-15%** experience delayed elimination due to impaired kidney function following high-dose methotrexate (>500 mg/m²) infusion;
- **Grade 3-4 acute kidney injury** has been associated with serum creatinine increases and MTX levels >10 umol/L at 48 hours.
- **Nephrotoxicity** was reported in 2% of patients with osteosarcoma
- **Grade ≥3 kidney toxicity** occurred in 15% of patients with primary CNS lymphoma.

Toxicities driving prophylaxis [4-6]

Reported incidence without mesna:

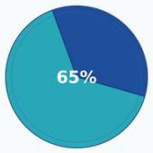
- ~20-40% ifosfamide-associated hemorrhagic cystitis
- ~20-30% cisplatin nephrotoxicity
- In the pivotal palifermin trial, 98% of patients in the PBO arm had WHO grade 3-4 oral mucositis

CAR-T immune-mediated toxicities

42.1%	56.1%	40.7%	66.6%
B-ALL CAR-T recipients receiving tocilizumab for CRS	LBCL CAR-T recipients receiving tocilizumab for CRS	Pediatric CAR-T patients requiring PICU admission	PICU patients receiving tocilizumab

CRS was the most common reason for pediatric intensive care admission.

Radiation-induced SOM in patients with head and neck cancer [7-9]



In the PBO arm of the Phase IIb trial of avasopasem manganese (GC4419) in head and neck cancer:

- **65%** of patients developed **grade 3-4 SOM**
- **30%** developed **grade 4 SOM**
- Median duration was **19 days**

Current management remains supportive and symptom-focused (basic oral care, pain control, topical agents), with no preventive therapies yet approved.

KEY TAKEAWAYS

Available rescue and protective agents provide substantial benefit, but mostly in **narrow and time-sensitive** clinical scenarios.

- Glucarpidase, uridine triacetate, dexrazoxane, sodium thiosulfate, palifermin, and tocilizumab illustrate meaningful benefit in selected populations.
- Real-world uptake varies with **toxicity recognition**, **timing requirements**, **operational logistics**, **drug access**, and **site readiness**.
- Utilization appears more consistent when rescue or prophylaxis is embedded in **protocol-based pathways** (e.g., leucovorin rescue, mesna prophylaxis, CAR-T CRS algorithms).
- Important gaps remain for common or chronic toxicities and for patient-centered outcomes linked to persistent low-grade symptoms.

Remaining unmet needs

Persistent gaps remain despite available rescue and protective options:

- **Chemotherapy-induced peripheral neuropathy**
- **Non-anthracycline cardiotoxicity**
- **Chronic immune-related adverse events**
- **Adult ototoxicity**
- **Broad chemoradiation-associated mucositis**
- **Underutilization or delayed administration of available antidotes**

Low-grade symptoms with lasting quality-of-life impact remain underrecognized.

Early recognition • Timely administration • Protocol-driven care

CLINICAL EFFECTIVENESS OF RESCUE AND PROTECTIVE AGENTS (Table 2)

Across drug classes, toxicity-mitigating agents showed the greatest benefit when paired with rapid recognition, prompt administration, or protocol-based use.

Category	Agent(s)	Selected evidence of effectiveness
Acute rescue	**Glucarpidase (Voraxaze®)**	• 97% reduction in plasma MTX levels within 15 min when given 48-60 hours after the start of HDMTX infusion [14] • Improved kidney recovery, reduced time to kidney recovery, and lower grade ≥2 neutropenia/transaminitis vs no treatment [15] • Patients were able to undergo rechallenge without requiring additional glucarpidase administration [16]
	Uridine triacetate (Vistogard®)	• Survival was 96% vs 16% in historical when uridine triacetate was given within 96 hours after fluorouracil or capecitabine overdose or early-onset severe toxicity [11,12]
Protocol-mandated Intervention following HDMTX infusion	**Leucovorin rescue**	• Early rescue, beginning 24 hours after HDMTX infusion, mitigates myelosuppression and neurotoxicity • Up to 75% may experience AEs, and fatality rates of 1-3% were reported in leukemia • PK-guided rescue reduced toxicities to 8%
Cytoprotection	**Mesna**	• Reduced hematuria (53% vs 76%) and UTI (14% vs 27%) • Was protective against hemorrhagic cystitis with high-dose cyclophosphamide
	Amifostine / dexrazoxane / sodium thiosulfate / palifermin / trilaciclib	• Reduced cisplatin nephro-, neuro-, and ototoxicity; anthracycline cardioprotection; pediatric cisplatin otoprotection when given within 6 h; reduced grade 3-4 oral mucositis in selected HSCT regimens [6] • Reduced incidence / duration of grade 4 neutropenia before chemotherapy in small cell lung cancer
Immune-mediated countermeasure	**Tocilizumab**	• Recommended for grade ≥2 cytokine release syndrome and reported to resolve symptoms in 31 of 45 patients within 14 days
Radiation protectant (investigational)	**Avasopasem manganese (GC-4419)**	• Reduced incidence (43% vs 65%), grade 4 severity (16% vs 30%) and duration (1.5 vs 19 days) of SOM during concurrent radiation and cisplatin for head and neck cancer [9-10] • Reduced cisplatin-associated renal toxicity

IMPLEMENTATION BARRIERS, UNMET NEED, AND IMPLICATIONS

Uptake barriers

- **Limited institutional awareness** and lack of recognition of toxicity
- **Operational logistics:** site readiness for protocol-driven monitoring and drug stocking and handling
- **Cost and payer access barriers:** Cost-driven dose capping may reduce drug acquisition costs, but published evidence for reduced-dose remains limited to uncontrolled case reports in time-sensitive rescue settings. [13]
- **Absence of standardized toxicity management protocols:** rapid-response agents appear less consistently adopted than protocol-embedded interventions

Remaining unmet need

- Persistent gaps remain for chemotherapy-induced peripheral neuropathy, non-anthracycline cardiotoxicity, chronic immune-related adverse events, broad chemoradiation-associated mucositis, and adult ototoxicity.
- Evidence remains limited for patient-centered outcomes and for low-grade symptoms that still impair quality of life and treatment experience.
- Higher rates of CRS and severe ICANS with some CAR-T products reinforce the need for early recognition and protocol-driven management.

Conclusions and call to action

Currently available toxicity-mitigating therapies can deliver substantial benefit in selected oncology settings, particularly when paired with early recognition, timely administration, and established care pathways. Greater recognition and documentation of toxicity burden, earlier risk stratification, standardized protocols, and access-enabling care models may help reduce avoidable morbidity and treatment disruption while supporting continued development of next-generation protective strategies.

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Abbreviations

AEs, adverse events; B-ALL, B-cell acute lymphoblastic leukemia; CAR-T, chimeric antigen receptor T-cell; CRS, cytokine release syndrome; HDMTX, high-dose methotrexate; HSCT, hematopoietic stem cell transplantation; ICANS, immune effector cell-associated neurotoxicity syndrome; LBCL, large B-cell lymphoma; MTX, methotrexate; PBO, placebo; PK, pharmacokinetic; PICU, pediatric intensive care unit; SOM, severe oral mucositis; UTI, urinary tract infection; WHO, World Health Organization

Disclosures

No financial disclosures were reported in the submitted abstract.

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Presented at the ISPOR Annual Meeting • Philadelphia, PA, USA • May 17-20, 2026

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