Serious Adverse Events in Oncology Trials: Novel Risk Assessment and Management Approaches

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ABSTRACT

Serious adverse events (SAEs) remain a critical concern in oncology clinical trials, directly impacting patient safety and the development of new therapies. With the growing use of targeted treatments and immunotherapies, treatment-related toxicities have become more complex and less predictable than with conventional chemotherapy. Traditional reactive approaches are increasingly inadequate, necessitating proactive strategies for early identification and management of SAEs. Advances in artificial intelligence (AI) and predictive analytics have enabled the early detection of adverse events and the identification of high-risk patients (6,7,20). Additionally, decentralized trials and wearable technologies now allow continuous, real-world patient monitoring (16). Despite these innovations, challenges such as data quality, algorithm transparency, and evolving regulatory frameworks limit their widespread adoption. This review synthesizes current knowledge on SAE risk factors, discusses monitoring and management strategies, and highlights emerging technologies aimed at enhancing patient safety in oncology trials.

Keywords: Serious Adverse Events, Oncology Trials, Risk Assessment, Patient Safety, Pharmacovigilance, Artificial Intelligence

INTRODUCTION

Clinical trials are essential for advancing cancer treatment but are frequently associated with a high incidence of SAEs, due to both the toxicity of therapies and the vulnerable condition of patients (1,3). Factors such as advanced age, comorbidities, prior treatments, and organ dysfunction further increase SAE risk (10). Different categories of oncology therapies present distinct toxicity profiles: Chemotherapy (e.g., cisplatin, doxorubicin) is commonly associated with bone marrow suppression and organ toxicity. Immune checkpoint inhibitors (e.g., nivolumab, pembrolizumab) can trigger immune-related adverse events affecting multiple organs (4). Targeted therapies (e.g., trastuzumab, imatinib) carry mechanism-specific risks, including cardiac or hepatic complications (12).

Standardized reporting frameworks such as the Common Terminology Criteria for Adverse Events (CTCAE) ensure consistency in grading and classifying toxicities (18). However, conventional trial designs face challenges including complex protocols, delayed recruitment, and intensive monitoring requirements (5). Emerging strategies, including AI-assisted tools and real-time patient monitoring, are being explored to improve SAE management.

Objectives

To identify key risk factors contributing to SAEs in oncology trials.

To review current monitoring and management strategies.

To explore emerging technologies for enhancing patient safety.

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MATERIALS AND METHODS

Study Design

This review follows a narrative approach, supported by a structured literature search to identify studies related to SAE risk and management in oncology trials.

Data Sources and Search Strategy

A comprehensive search was conducted in PubMed, Scopus, Web of Science, and Google Scholar for studies published between 2010 and 2026. Keywords included “oncology clinical trials,” “serious adverse events,” “SAE management,” “pharmacovigilance,” and “artificial intelligence.”

Inclusion and Exclusion Criteria

Inclusion: Peer-reviewed studies focused on oncology and reporting SAE incidence, risk factors, or management strategies.

Exclusion: Preclinical studies, non-oncology research, or articles without full text.

Study Selection

Approximately 100 studies were initially screened; after reviewing titles, abstracts, and full texts, 50 studies were included in this review.

Data Analysis

Selected studies were analyzed qualitatively and organized by patient-related, therapy-related, and study-related risk factors, as well as monitoring and management strategies.

RISK FACTORS FOR SERIOUS ADVERSE EVENTS

Patient-Related Factors

Patient characteristics strongly influence SAE risk. Older age, multiple comorbidities, and impaired organ function increase susceptibility (8). Genetic polymorphisms affecting drug metabolism also contribute to variability in toxicity (9). Patients with weakened immune systems or prior exposure to aggressive treatments are at higher risk of adverse outcomes.

Therapy-Related Factors

Chemotherapy: Predictable toxicities like myelosuppression and organ damage.

Immunotherapy: Immune-related adverse events can be unpredictable and multi-systemic (4).

Targeted therapies: Organ-specific complications may arise based on mechanism of action (12).

Additional risks: Drug interactions and dosing errors further increase SAE probability.

Study-Related Factors

Trial phase: Early-phase studies (Phase I) often involve dose escalation, increasing risk (13).

Protocol complexity: Complex or high-dose regimens heighten SAE incidence.

Multicenter variability: Differences in monitoring and reporting practices can lead to inconsistencies (14).

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MONITORING AND MANAGEMENT STRATEGIES

Risk-Based Monitoring

Risk-based approaches prioritize high-risk patients and therapies, enabling efficient allocation of monitoring resources. AI and machine learning tools are increasingly applied to detect early warning signals (6).

Early Detection

Regular laboratory evaluations, imaging studies, and patient-reported outcomes are key for timely recognition. Wearable devices allow continuous monitoring of physiological parameters, enabling rapid response to emerging toxicities (16).

Management Approaches

SAE management often involves:

Dose adjustments or temporary treatment interruptions.

Supportive care, including antiemetics, corticosteroids, or immunosuppressants (17).

Multidisciplinary intervention for rapid and effective response.

Pharmacovigilance

Mandatory reporting to regulatory authorities and ethics committees is essential. Standardized tools like CTCAE help maintain uniformity and reliability in SAE classification (18).

CHALLENGES IN SAE MANAGEMENT

Despite advances, SAE management faces several challenges:

Underreporting and delayed documentation (10).

Variability in regulatory requirements across countries (2,15).

Ethical dilemmas when balancing patient safety with trial continuation (19).

Lack of standardized reporting and monitoring practices.

SAE REPORTING TIMELINES AS PER CDSCO:

1. **Investigators: Must report all SAEs to the DCGI, sponsor, and Ethics Committee within 24 hours of occurrence.**
2. **Detailed Report:** A follow-up detailed report must be submitted by the investigator within 14 calendar days**.**
3. **Sponsors: Must analyze the SAE and submit a report to CDSCO within 14 days** of occurrence.
4. **Ethics Committees: Must review and forward SAE reports to CDSCO within 21 calendar days.**

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ROLES AND RESPONSIBILITIES:

Investigator	Sponsor	Ethics Committee (EC)
Initial SAE notification to sponsor, DCGI, and EC within 24 hours	Conduct independent SAE analysis and causality assessment	Review the SAE report and perform causality analysis
Submit complete SAE form including medical history and assessments within 14 days	Submit a full SAE report to CDSCO, EC, and investigator within 14 days	Submit opinion to CDSCO within 21 calendar days
Provide causality assessment and documentation for the event	Assess eligibility for compensation under CDSCO guidelines	Maintain documentation of the review process
Maintain SAE records and provide updates as required	Ensure payment of compensation, if applicable	Monitor investigator compliance and safety of trial participants

DISCUSSION

The occurrence of SAEs in oncology trials is influenced by patient characteristics, therapy modalities, and study design (8,9,4,12,13,14). Traditional monitoring strategies are increasingly inadequate, particularly for immunotherapies and targeted therapies, which often cause unpredictable multi-system toxicities.

Emerging technologies, including AI and predictive analytics, have shown potential in early identification of high-risk patients and preemptive intervention (6,7,20). Similarly, wearable devices and decentralized trials enable real-time, continuous monitoring, allowing rapid detection of adverse changes in patient physiology (16,17). These innovations promise not only improved patient safety but also more efficient trial conduct.

Challenges remain, particularly regarding data quality, algorithm transparency, and evolving regulatory standards (2,6,15,20). Multinational trials may face additional obstacles due to inconsistencies in reporting practices (19). Ethical considerations, especially decisions on continuing treatment in patients at high risk, remain paramount.

Integrating traditional clinical expertise with validated AI tools and digital monitoring is likely the most effective strategy for proactive, patient-centered SAE management. Future studies should focus on validating predictive models and developing standardized protocols for technology integration (7,20).

LIMITATIONS

This review has several limitations:

It is a qualitative synthesis, not a quantitative meta-analysis, limiting statistical conclusions (10).

Only English-language studies were included, potentially introducing language bias.

Variability in study design, SAE definitions, and reporting standards may affect generalizability (14,18).

Evidence on emerging technologies, while promising, is still limited, and implementation challenges remain (6,16,20).

Despite these limitations, the review provides a comprehensive overview of SAE risk factors, management strategies, and emerging tools for enhancing patient safety.

FUTURE PERSPECTIVES

Predictive Models: Improved AI-based risk prediction can identify high-risk patients and guide personalized monitoring (6,7,20).

Wearable Technologies & Decentralized Trials: Real-time monitoring allows early intervention and may reduce trial-related complications (16,17).

Personalized Medicine: Genomic and biomarker data can further tailor safety protocols (9,12).

Global Standards: Harmonization of regulatory frameworks will enhance SAE reporting consistency across trials (2,15,19).

CONCLUSION

Serious adverse events continue to challenge oncology clinical trials. Addressing this issue requires proactive, patient-centered strategies combining traditional clinical expertise with emerging technologies such as AI, predictive analytics, and wearable monitoring. Continuous improvement in predictive models, real-time monitoring, and standardized reporting protocols will be critical to enhancing patient safety and ensuring more efficient trial outcomes. Collaborative research and harmonized global standards are essential for the successful integration of these innovations into clinical practice.

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