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ORIGINAL ARTICLE

From toxicity assessment to adaptive safety care: implementing comprehensive fast-track safety evaluation for anticancer drug development

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Background: The conventional drug development pathway in oncology, spanning 10-15 years, has long been slow, costly, and complex, often marked by late-stage failures due to efficacy or safety concerns.

Materials and methods: We aimed to develop this position paper, based on a literature review and by sharing experience, skills, and works of the different co-authors, in order to propose a new approach to the clinical trials' process.

Results: In the past decade, the field has undergone major transformation. Innovative trial designs and fast-track regulatory pathways, such as priority review, breakthrough designation, accelerated approval, and fast-track processes, have significantly shortened timelines from phase I to market approval. While these approaches have enabled quicker access to promising therapies, they have also exposed gaps in postmarketing safety and highlighted the need for tailored adverse event management strategies. These emerging safety challenges call for multidisciplinary evaluation and the integration of advanced monitoring technologies.

Conclusions: This manuscript introduces a comprehensive, adaptive fast-track safety evaluation framework designed to support oncology drug development. It aims to enhance patient safety while preserving the benefits of accelerated regulatory pathways.

Key words: drug development, drug safety, adverse event, clinical trials, fast-track safety evaluation

INTRODUCTION

Current anticancer drug development typically follows a sequence: discovery, dose-limiting toxicity (DLT) identification, then safety and efficacy evaluation. Although early trials define toxicities, strategies for prediction and management often emerge late, during advanced phases or after approval. Multidisciplinary networks and predictive models are available, but there is an urgent need for a tailored, structured approach earlier in the process. To ensure timely market access, oncology drugs should be supported by integrated safety and efficacy data, along with clear guidelines for toxicity management.

RECENT EVOLUTION OF THE DRUG DEVELOPMENT PROCESS IN ONCOLOGY

The historic drug development process (Figure 1), from drug discovery, preclinical work, through phase I/II/III trials, to submission for review by the relevant health authority, has always been a complex and costly journey for drug development companies, typically taking 10-15 years to complete.[1] A review from 2013 to 2015 revealed that failures in phase II and III trials were primarily due to lack of efficacy (52%) or safety concerns (24%), with toxicity-related issues more frequent in phase II (25%) than in phase III (14%).[2] Over the past decade, a notable shift has occurred: the focus is now on shortening the time between

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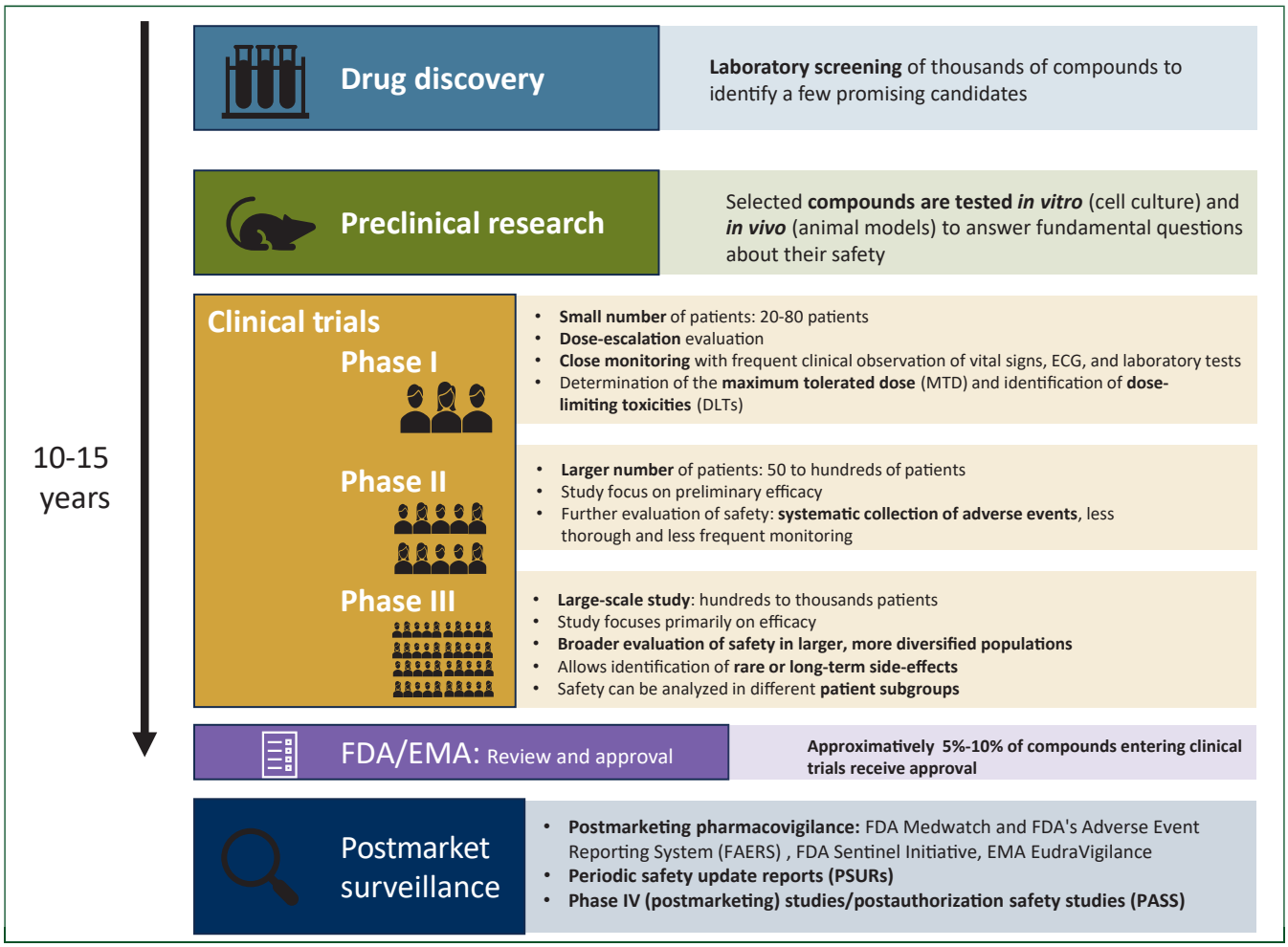

Figure 1. Drug development process in oncology.
ECG, electrocardiogram; EMA, European Medicines Agency; FDA, Food and Drug Administration.

phase I initiation and regulatory approval. Innovative phase I/II trial designs,[3] alongside fast-track programs led by health authorities, have helped speed up the development of treatments for serious conditions with unmet needs.[4] Both the Food and Drug Administration (FDA)[5] and the European Medicines Agency (EMA)[6] now offer multiple pathways for accelerated approval (Table 1), significantly reducing preapproval timelines and increasing the rate of new oncology drug authorizations.[7,8]

Overall, regulatory frameworks developed by the EMA and FDA play a vital role in expediting access to promising oncology therapies, while upholding high safety and efficacy standards. However, accelerated approval pathways often limit the time and patient data available to fully assess a drug's safety profile. To address this, regulators have strengthened postapproval monitoring requirements, ensuring continued evaluation of real-world safety outcomes[9,10]:

- **Pharmacovigilance:** The FDA and EMA collect voluntary reports from health care professionals and consumers (via the MedWatch program for the FDA, EudraVigilance for the EMA) and mandatory reports from drug manufacturers. All these safety data are accessible to the general public via the FDA's Adverse Event Reporting System (FAERS) or the EMA's EudraVigilance online tool.
- **Risk evaluation and mitigation strategies/risk management plan:** These are required by the FDA/EMA to describe specific strategies for identifying, characterizing, preventing, or minimizing risks associated with a drug.
- **Periodic safety update reports:** These are regular reports produced by manufacturers and required by the FDA/EMA to summarize all known adverse events (AEs), safety data, and an assessment of the risk—benefit balance.
- **Phase IV (postmarketing) studies/postauthorization safety studies:** These may be requested by the FDA/EMA after a drug's approval to gather additional information on a drug's safety, to better understand a drug's real world.
- **Sentinel Initiative:** This is an active surveillance system that the FDA uses to monitor the safety of drugs and other medical products by analyzing data from multiple sources including electronic medical records or insurance claims.

Table 1. FDA and EMA approaches to grant accelerated approval

FDA approaches	
Fast track	A process designed to facilitate the development and expedite the review of drugs to treat serious conditions and fill an unmet medical need.
Breakthrough therapy	A process designed to expedite the development and review of drugs that are intended to treat a serious condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over available therapy on a clinically significant endpoint(s).
Accelerated approval	These regulations allowed drugs for serious conditions that filled an unmet medical need to be approved based on a surrogate endpoint.
Priority review	A Priority Review designation means FDA's goal is to take action on an application within 6 months (compared with 10 months under standard review).
EMA approaches	
Conditional marketing authorization (CMA)	CMA allows the approval of a medicine on the basis of less complete clinical data than normally required, provided that the benefits of immediate availability outweigh the risks of less comprehensive data.
Accelerated assessment	This process reduces the time frame for the Committee for Medicinal Products for Human Use (CHMP) to review a marketing authorization application from 210 days to 150 days.
Rolling review	This is a tool used during public health emergencies to review data as they become available from ongoing studies. It accelerates the review process by allowing the EMA to start evaluating data before the full application is submitted.

EMA, European Medicines Agency; FDA, Food and Drug Administration.

Overall, this integrated approach ensures that any emerging safety concerns are promptly identified and addressed, safeguarding patient health in the oncology field.

LIMITATIONS OF THE CURRENT SAFETY ASSESSMENT PROCESS DURING DRUG DEVELOPMENT

Safety evaluation across drug development phases faces persistent challenges (Figure 2). During drug discovery, target selection is often guided by anticipated therapeutic activity rather than potential toxicity, leading to unforeseen safety issues later in development. In the preclinical phase, animal models lack predictive accuracy for human toxicity.[11] Early clinical trials typically detect only high-frequency toxicities, while delayed or rare events are underreported. The use of maximum tolerated dose (MTD) is increasingly questioned, as lower doses may offer efficacy with reduced toxicity.[12] It is in this context that initiatives such as the OPTIMUS project are developed.[13] An analysis of 85 match trials ranging from phase I to phase II/III by the FDA from 1990 to 2012 showed that the dose from the later trials was within 20% of the recommended phase II dose and only 70% of toxicity observed in later trials was seen previously in phase I.[14] The concept of DLT is also reductive, focusing only on severe toxicities in the first treatment cycle, while many dose-reducing toxicities emerge later.[3,15-17] Although drug-related mortality in early trials declined in the early 2000s,[18] attributing causality for serious AEs (SAEs), especially in combination therapies, remains complex and often relies solely on investigator judgment.[19,20] Overall, there is a serious underreporting of AEs, either in phase I[21] or in later phases,[22-28] with low-grade toxicities frequently overlooked despite their impact on quality of life and treatment adherence.[29]

Physician-reported AEs often differ from patient-reported[30] or nurse-reported AEs,[31] highlighting the need for patient-reported outcomes (PROs) like the Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE).[32] The evolving CTCAE grading system has added complexity, with inconsistent definitions and grading misuse.[33,34] CTCAE criteria also tend to underestimate the accumulation and persistence of low-grade AEs. AE evaluation is often led by oncologists, though organ-specific specialists may offer more nuanced insights and improve toxicity management. Lastly, clinical trial populations typically exclude patients with comorbidities or poor performance status, limiting generalizability, even though these patients may face higher toxicity risks.[35,36]

As clinical trials move from phase I to phase III, the increase in the number of participants necessarily leads to a reduction in safety monitoring, affecting the quality of AE recording and qualification. Key safety features such as impact on quality of life, treatment adherence, or mid—long-term safety issues are rarely monitored.[37-39] Post-marketing safety surveillance is even more limited, with reduced sensitivity for AE detection and difficulty in linking events to the drug. Finally, phase IV studies, which could validate mitigation strategies, are seldom conducted.[40]

In recent years, multiple safety concerns have emerged following the approval of oncology drugs. Immune checkpoint inhibitors (ICIs), for instance, have prompted the development of multidisciplinary strategies to manage acute, delayed, and long-term immune toxicities. These efforts have led to the publication of guidelines aimed at improving long-term safety monitoring and management.[41]

Bruton tyrosine kinase inhibitors such as ibrutinib, approved in 2013 for B-cell malignancies, were later linked to cardiac toxicities, most notably atrial fibrillation, affecting up to 38% of patients.[42] This prompted a reassessment of its pharmacologic profile and the creation of management protocols.[43] Enfortumab vedotin, an antibody—drug conjugate targeting nectin-4, received accelerated FDA approval in 2019 for metastatic urothelial carcinoma.[44] By 2022, serious dermatologic AEs such as Stevens—Johnson syndrome and toxic epidermal necrolysis were reported, leading to FDA warnings and restricted access in some countries.[45] Chimeric antigen receptor (CAR)-T-cell therapies targeting B-cell maturation antigen (BCMA) have also raised safety concerns. In 2024, the FDA issued a boxed warning for the risk of secondary T-cell malignancies, applicable to all approved BCMA- and CD19-directed CAR-T products.[46] Similarly, phosphoinositide 3-

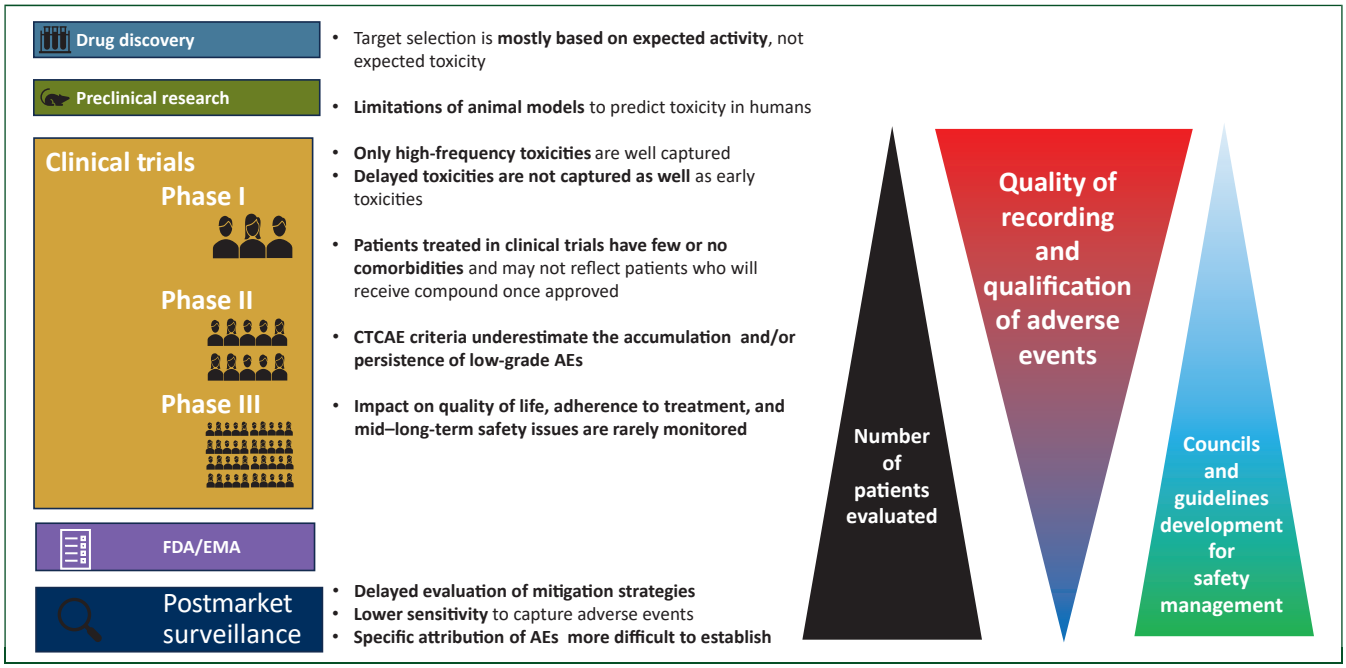

Figure 2. Safety evaluation and limitations during the drug development process.
AE, adverse event; EMA, European Medicines Agency; FDA, Food and Drug Administration.

kinase inhibitors such as duvelisib, approved in 2018 for lymphoma, were withdrawn in 2022 after data from the DUO trial revealed increased mortality due to infections compared with standard care.[47] ICIs, approved since the early 2010s, continue to reveal a wide spectrum of post-marketing toxicities. Myocarditis,[48,49] sometimes overlapping with myositis or myasthenia gravis, has emerged as a particularly lethal complication, underscoring the importance of early diagnosis.[50,51] The broad spectrum of toxicities that can be associated with ICIs[52,53] has led to the formation of organ-specific specialist teams to better understand and manage such AEs.[41] These examples highlight the inherent risks of accelerated drug approvals, where safety issues may only surface after marketing.[54] Delays in developing management guidelines can hinder treatment access, compromise patient quality of life, and result in irreversible harm.

'MANAGEABLE SAFETY PROFILE': CURRENT BIASES IN THE REPORTING OF SAFETY DATA IN CONGRESSES, PEER-REVIEWED LITERATURE, AND DRUG LABELING

The term 'manageable safety profile' is commonly used in congress presentations and peer-reviewed publications, often without regard to the true frequency or severity of side-effects. AEs may be selectively reported and grouped as 'events of interest', filtered by frequency thresholds, or combined with non-treatment-related AEs, obscuring the full safety picture. For example, several limitations in the reporting and analysis of immunotherapy trials have been highlighted,[55] such as incomplete reporting of AEs, discrepancies in the collection, coding, and reporting of AEs, and extreme variations in follow-up and/or duration of exposure and concurrent risk with death.

A more transparent approach is needed. All treatment-related AEs, including low-grade ones, should be reported with onset, duration, and impact on treatment exposure. Persistent, mild AEs can lead to discontinuations and are often under-recognized without PROs, which are still too rarely included. SAEs or fatal AEs occurring during therapy, even if not deemed related, must be disclosed, as they are frequently underestimated by investigators.[56]

Effective safety management requires personalized, real-time supportive care alongside cancer therapies under development. This ensures the approach considers individual tolerance, comorbidities, and lived experience, blending the precision of targeted therapies with the responsiveness of patient-centered medicine.

Even after approval, drug labeling often omits critical safety data: rates of dose reductions, interruptions, or discontinuations due to AEs. Such omissions make it harder for clinicians to manage risks and slow down the learning curve in everyday practice.

Partial or filtered safety data weaken clinical decision making and undermine the optimal integration of new therapies into routine care. Addressing these reporting biases is essential for improving patient outcomes and building trust in cancer drug development.

NEW TOOLS FOR THE ASSESSMENT OF ADVERSE EVENTS

Traditional AE reporting methods often fall short in capturing patient-specific risks and long-term effects. To close these gaps, new tools have emerged that shift the focus toward personalized and data-driven safety evaluation.

Contemporary phase I designs now seek an optimal dose that balances efficacy and toxicity, moving beyond the sole

focus on MTD. Contemporary and adaptive dose-finding designs now strive to determine an optimized dose by thoughtfully balancing efficacy and toxicity. Model-assisted designs such as modified toxicity probability interval (mTPI),[57] mTPI-2, keyboard, and toxicity and efficacy probability interval (TEPI)[58,59] use predefined probability intervals and decision rules to guide dose escalation. These approaches emphasize selecting a dose that carefully weighs therapeutic benefit against patient safety. Model-based approaches, including efficacy—toxicity trade-off (EffTox),[60] time-to-event continual reassessment method (TITE-CRM),[61] data augmentation CRM (DA-CRM), and time-to-event Bayesian optimal interval (TITE-BOIN),[62] apply Bayesian statistical models to continuously estimate toxicity and efficacy. Many of these methods accommodate delayed outcomes; for instance, TITE-CRM integrates partial follow-up data to address late-onset toxicities, while DA-CRM leverages Bayesian data augmentation to handle missing toxicity information. Furthermore, utility-based designs such as those featured in TEPI and EffTox aim to identify doses that maximize clinical value, combining efficacy and safety into a single composite score. These designs are particularly compelling when both endpoints are crucial and when trial teams wish to embed their preferences directly into decision-making algorithms.

The multisystem toxicity profile of immune agents has prompted the formation of multidisciplinary committees bringing together oncologists, organ specialists, radiologists, and pharmacists. These collaborative networks, centered around individual patients, enhance the characterization of AEs and improve AE attribution. Specific management of AEs is improved through collaborative case reviews and shared clinical experience. Leveraging their biological and clinical expertise accelerates the overall learning curve, fostering a deeper understanding of toxicity mechanisms and more effective, individualized interventions.[63,64]

Innovative technologies can now be incorporated into phase I trials to identify safety biomarkers and improve patient monitoring for side-effects. Technologies such as cell-free DNA (cfDNA) methylome profiling enable the detection of organ-specific damage signals by tracing the tissue of origin of cfDNA fragments in plasma.[65] In immunotherapy, tools like cytokine profiling,[66] antibody signatures,[67] T-cell receptor sequencing,[68] or genetic predisposition assessments[56] can uncover susceptibility to drug-related toxicities. These approaches hold promise for identifying early, noninvasive markers of toxicity during initial drug exposure.

Integration of PROs into clinical trials provides a more continuous and patient-centered view of treatment impact. These measures often identify AEs missed by clinical metrics and enable earlier intervention.[69,70] PROs can better capture patients' perspectives on their health, treatment, and quality of life during and after cancer therapy. These measures often identify AEs missed by clinical metrics and enable earlier intervention. Unlike clinical measures, PROs can assess multiple dimensions of patients' health depending on selected questionnaires. For example, health-related quality of life questionnaires (such as the 36 item short form health survey questionnaire and EuroQol - 5 dimension) assess overall health and quality of life across various domains such as physical functioning, emotional well-being, and social roles.[71] Some questionnaires can be more specific to cancer patients, such as the European Organisation for Research and Treatment of Cancer (EORTC) QLQ-C30,[72] and/or focus on symptoms or side-effects experienced by cancer patients, such as the Functional Assessment of Cancer Therapy (FACT) questionnaire.[73]

Table 2. Key advantages from artificial intelligence that can significantly improve the capture and management of patient adverse events during drug development

Enhanced data mining and signal detection	Analysis of large volumes of clinical data from various sources (electronic health records, patient-reported outcomes, etc.) to identify and categorize adverse events more effectively and detect unexpected safety signals, earlier in the drug development process.
Natural language processing	Extraction of relevant information from unstructured data sources (clinical notes, patient narratives, etc.) to identify potential adverse events that might be missed by traditional reporting systems.
Predictive analytics	Machine learning models can help to predict the risk of adverse events based on patient characteristics or treatment regimen.
Real-time monitoring and automated reporting	Continuous monitoring of datasets or wearable sensors to provide real-time alerts for potential adverse events and automatically generate adverse events reports to regulatory agencies.

With rising public adoption, wearable devices are becoming powerful tools in clinical research. Smartwatches, patches, and connected wearables can track multiple physiological parameters such as heart rate, blood pressure, electrocardiography, temperature, respiratory rate, oxygen saturation, weight, electroencephalography, or glucose[74] level. By analyzing changes in skin conductance or sweat composition, some patch sensors can even detect variation in biological markers.[75,76] Their portability and continuous feedback enhance AE tracking inside and outside clinical settings.

Innovative imaging techniques or analysis, such as immuno-positron emission tomography (immunoPET) or radiomics, are currently being developed to better assess drug activity and identify predictive biomarkers of response.[77-79] ImmunoPET uses radiolabeled antibodies targeting markers such as programmed death-ligand 1 or CD8 to produce high-resolution images of immune cell distribution. Radiomics applies advanced algorithms to extract features (such as texture, shape, or intensity) from scans, offering deeper insights into tumor biology and response likelihood. These technologies go beyond efficacy: imaging healthy tissue can help detect off-target effects and early signs of toxicity before they become clinically apparent. As interest from regulators and clinicians grows, successful integration will hinge on standardization, interoperability, and smooth incorporation into workflows.

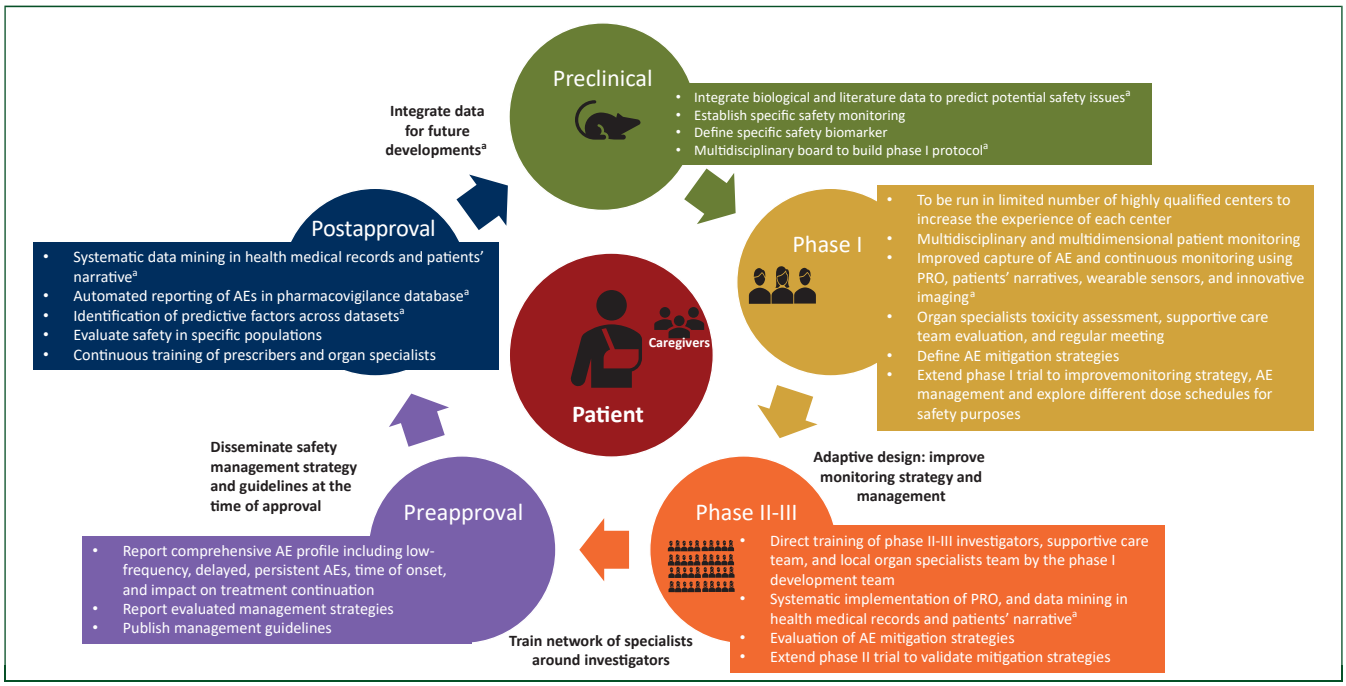

Figure 3. Implementing an innovative, comprehensive, and adaptive fast-track safety evaluation for drug development in oncology.
AE, adverse event; AI, artificial intelligence; PRO, patient-reported outcome.
[a]AI empowered.

Real-world data (RWD) play an increasingly vital role in oncology by capturing diverse populations and care settings. Initiatives like the European Union's DARWIN network and the FDA's Sentinel Initiative demonstrate how clinical records, registries, and reimbursement data can generate real-world evidence to assess drug effectiveness and safety more broadly. At the same time, the integration of artificial intelligence (AI) into these RWD streams is transforming safety assessments. By leveraging its ability to analyze vast amounts of data and identify patterns that might be missed by traditional methods, AI has the potential to considerably enhance drug safety assessments in oncology[80] (Table 2). AI-driven predictive models can streamline compounds' selection and the design of safety studies, or help to optimize dosing and mitigation strategies. Machine learning models can process clinical trial data, electronic health records, or patient narratives to identify potential AEs that might be missed by traditional reporting systems. Furthermore, by using its power for deep data mining and automated reporting, AI can uncover correlations that might not be apparent through conventional analysis and facilitate the reporting process by automatically generating and submitting AE reports. Overall, incorporating AI capacities into safety monitoring can achieve more accurate, timely, and comprehensive capture of AEs.

IMPLEMENTING AN INNOVATIVE, COMPREHENSIVE, AND ADAPTIVE FAST-TRACK SAFETY EVALUATION FOR DRUG DEVELOPMENT IN ONCOLOGY

The drug development process has been significantly transformed and accelerated in recent years thanks to the emergence of highly innovative compounds, improved study designs, and a more favorable framework from health authorities. Yet safety evaluation has not evolved at the same pace.

Based on our experience in drug development and AE assessment and management, we believe that safety evaluation in oncology should also shift to an innovative fast-track model by implementing an early, multidisciplinary, and multidimensional approach supported by new technologies.

To address this need, we have developed a comprehensive and adaptive fast-track safety evaluation plan, applied throughout all phases of development (Figure 3).

Safety prediction should begin early during the preclinical phase by integrating biological knowledge and literature to identify risks and define specific monitoring strategies, including safety biomarkers. We propose forming a multidisciplinary committee, including safety officers, biologists, pharmacists, and specialized researchers, but also drug development experienced oncologists, organ specialists, and supportive care experts, to design a robust safety plan for the phase I protocol.

Phase I trials should be conducted at select, highly qualified centers to ensure consistent treatment volumes and cumulative expertise. These centers should operate with established networks of organ and supportive care specialists experienced in early drug development. While phase Ib expansion cohorts focus primarily on early efficacy signals within a given tumor indication, they should also deepen safety insights. When deployed across diverse tumor types, they can be used to reveal transtumoral safety data, such as organ-specific toxicities and tolerability

differences. Tailored 'safety expansion cohorts' may be added to address drug interactions or population-specific risks, allowing for adaptive protocols.

Phase I-II safety strategies must extend beyond high-grade acute toxicities to include underreported, persistent low-grade AEs. Trials should incorporate multidimensional monitoring using PROs, wearable sensors, and innovative imaging to capture a more complete AE profile. Regular review by multidisciplinary teams, including sponsors, preclinical experts, investigators, and organ/symptom specialists, can refine mitigation strategies, considering pharmacokinetic and pharmacodynamic data.

Beyond guidance on informed consent and procedural acceptability, the active inclusion of patients, caregivers, and patient advocates throughout the drug development process is essential. Their participation can enrich safety assessments by ensuring meaningful representation of clinical endpoints and lived experiences. From the earliest phases, patient advocates can contribute to the development of relevant PROs and co-develop symptom monitoring tools that reflect real-world concerns. During clinical trials, their participation in safety monitoring discussions, particularly within data monitoring committees, can provide valuable context for interpreting AE profiles, especially for persistent low-grade toxicities. Their insights can also guide the design of personalized supportive care strategies tailored to real-time symptom management and patient needs. Including patient voices in monitoring committees ensures that real-world concerns inform safety decisions, boosting trial participant retention and relevance of the data collected.

As the drug progresses to phase II and III, we emphasize direct training of the phase II-III investigators and local organ specialists' team by the phase I development team.

Trials should continue to use PROs and integrate advanced data mining of medical records and patient narratives. Phase II should also offer an opportunity to evaluate previously defined AE mitigation strategies. Finally, phase II-III trials should be the opportunity to train the health care network around the investigators' teams.

Preapproval efforts should focus on presenting the safety profile at academic congresses or peer-reviewed publications. Data should cover full AE scope, including delayed, persistent, and low-frequency events, with evaluations of management approaches to inform future clinical practice and regulatory review. Sponsors must be ready to release safety guidance alongside drug launch.

Throughout the multiphase process of drug development, including postmarketing surveillance, extensive safety data are collected from increasingly diverse patient populations. Thus, the integration of prospectively collected RWD using master observational protocols[81] could significantly improve safety assessment strategies, both across multiple clinical trials and from sources outside traditional trials. By connecting diverse data streams, these frameworks facilitate and enrich safety assessments with insights from everyday treatment contexts. Thanks to the support of AI technologies, we think that the postapproval strategies will be profoundly transformed by the systematic data mining of health medical records and patients' narratives, and also the automated reporting of AEs in the pharmacovigilance database, which should facilitate identification of predictive factors across datasets. Therefore, these next-generation AI-empowered phase IV studies will become the cornerstone for evaluating any new safety signals, new management strategies, and the safety profile in specific populations.

Despite their promise, we acknowledge that novel tools face cost and feasibility barriers. RWD platforms continue to face barriers related to cost, data quality, and scalability, particularly due to the expense of data acquisition, integration, and management across fragmented health care systems. Wearable devices remain constrained by limitations in sensor accuracy, battery life, user adherence, affordability, and workflow integration. Innovative imaging technologies demand significant infrastructure and investment, and their routine clinical use hinges on continued efforts in standardization, interoperability, and seamless integration. Finally, AI-based approaches hold promise for scalable solutions, yet rely heavily on diverse, high-quality datasets and smooth clinical system integration, both of which require substantial financial and technical resources. Overcoming these barriers demands coordinated, cross-sector collaboration, multistakeholder engagement, and alignment with evolving regulatory frameworks, with careful consideration of cost-effectiveness and sustainability at every step.

Conclusion

The evolution of the drug development process in oncology has been marked by significant advancements aimed at accelerating the time from initial trials to drug approval. This shift has been facilitated by innovative trial designs and regulatory frameworks that streamline the approval process for drugs addressing serious conditions with unmet needs. Despite these advancements, challenges remain, particularly in ensuring comprehensive safety assessments throughout the drug development lifecycle.

We believe that the early generation and integration of multidisciplinary and multidimensional safety data is an iterative process that will inform, accelerate, and improve future oncology drug development.

This strategy is especially critical for first-in-human compounds, given their unknown pharmacological risks. While second-generation and me-too drugs often benefit from pre-existing safety data, they may still require tailored safety assessments when applied to new populations, indications, or dosing regimens. A risk-adapted approach allows for selective implementation of these tools where they add value, ensuring a rigorous and resource-efficient assessment.

This approach should optimize patient outcomes by improving early and late toxicity management and reducing emergency visits and hospitalizations. Long term, this could ease health care costs and improve survivorship. With this

proactive strategy, we aim to improve both the immediate and future health of cancer patients while delivering broader economic and societal benefits.

By embedding such innovative, comprehensive, and adaptive safety assessment in oncology drug development, we support faster learning, earlier mitigation of AEs, and safer transitions from trials to real-world care.

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