REVIEW ARTICLE

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The role of anakinra in the treatment of CAR-T-induced cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS) – a narrative review

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Abstract

Introduction and Objective. Chimeric antigen receptor T-cell (CAR-T) therapy is a transformative immunotherapy that has achieved promising clinical efficacy in the treatment of haematologic malignancies. However, its modality is frequently complicated by cytokine release syndrome (CRS), and immune effector cell-associated neurotoxicity syndrome (ICANS). Anakinra is an immunosuppressant and antagonist of human interleukin-1 receptors, widely used to treat these syndromes. The aim of the study is to evaluate the efficacy and safety of anakinra and compare dosing regimens in patients with CRS and ICANS caused by CAR-T administration.

Review Methods. A narrative review of the literature was conducted using the PubMed/MEDLINE and Google Scholar databases, covering the period from 2020 – May 2026. English-language systematic reviews, randomized trials, retrospective studies, and case reports on anakinra usage in CRS and ICANS were included.

Brief description of the state of knowledge. Anakinra provides an effective targeted strategy for managing ICANS that mitigates neuroinflammation without the broad immunosuppression associated with corticosteroids. However, increasing the dosage of corticosteroids remains the cornerstone of treating refractory ICANS. A prophylactic anakinra strategy has been demonstrated to have limited efficacy against high-grade neurotoxicity and an increased probability for severe infections.

Summary. Anakinra has been proven most effective as a strategic second-line intervention for steroid-refractory ICANS cases. More studies are needed to determine the optimal prevention strategy for CRS and ICANS in patients receiving CAR-T therapy, as well as the optimal integration of anakinra into these protocols.

Key words

CAR-T, anakinra, Interleukin-1 receptor antagonist, cytokine release syndrome (CRS), immune effector cell-associated neurotoxicity syndrome (ICANS)

INTRODUCTION

Chimeric antigen receptor T-cell (CAR-T) therapy is a transformative immunotherapy that involves genetically reprogramming a patient's autologous T-cells to express synthetic receptors. This enables them to identify and eliminate malignant cells by targeting specific surface antigens without depending on major histocompatibility complex restriction. This precision-targeted approach has achieved promising clinical efficacy in the treatment of various relapsed or refractory haematologic malignancies [1]. However, this modality is frequently complicated by specific adverse events, including cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS), which manifest as a spectrum of neurological deficits ranging from expressive aphasia to life-threatening cerebral oedema [2].

Cytokine release syndrome (CRS) is a frequent systemic inflammatory reaction triggered by the overactivation of CAR T-cells, which induces a systemic inflammatory cascade critically mediated by elevated levels of interleukin-6. Standard clinical management focuses on mitigating this systemic inflammation with corticosteroids and the interleukin-6 receptor antagonist tocilizumab [2].

Immune effector cell-associated neurotoxicity syndrome (ICANS) occurs comparatively frequently, manifesting as a range of neurological disorders, from mild encephalopathy, such as confusion, dysgraphia, or expressive aphasia, to severe, life-threatening focal deficits, seizures, and cerebral oedema [1, 3]. The pathophysiology of ICANS is primarily

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driven by vascular endothelial activation, which promotes disruption of the blood-brain barrier, allowing systemic cytokines and immune cells to migrate into the central nervous system [4]. Severity is assessed using the American Society of Transplantation and Cellular Therapy consensus grading system, which provides standardized criteria for clinical decision-making [5]. ICANS affects 27–65% of patients who are treated with CAR T-cell therapy [6]. Treatment depends on the severity and usually involves corticosteroids, tocilizumab, anakinra, and other immunosuppressants [7].

Anakinra is an immunosuppressant and antagonist of human interleukin-1 receptors (r-metHuIL-1ra obtained through DNA recombination in an E. coli gene expression. Anakinra neutralizes the biological activity of interleukin-1α (IL-1α) and interleukin-1β (IL-1β) by competitively restraining binding with type I interleukin receptors (IL-1RI). *In vitro* anakinra inhibits consecutive steps of IL-1 response, including the production induction of NO, PGE2, and collagenase in synovial membrane cells, fibroblasts, and cartilage corposcule. Anakinra is approved for the treatment of refractory rheumatoid arthritis in adults, and both neonatal-onset multisystem inflammatory disease and deficiency of the IL-1 receptor antagonist in children. Routine off-label use of anakinra in numerous adult and paediatric autoinflammatory disorders, e.g. Catastrophic Antiphospholipid Syndrome (CAPS), Familial Mediterranean Fever, and Still's Disease, provides additional experience with safety and efficacy in toxicities resembling CRS and ICANS. Clinical trials of anakinra for refractory Kawasaki disease, haemophagocytic lymphohistiocytosis (HLH), macrophage activation syndrome (MAS), sepsis with MAS, and severe acute respiratory syndrome coronavirus 2–associated cytokine storm, have also shown benefit [8].

OBJECTIVE

The aim of the study is to evaluate the efficacy and safety of anakinra (interleukin-1 receptor antagonist) and compare dosing regimens in patients with cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS) caused by CAR-T administration.

MATERIALS AND METHOD

A narrative review of the literature was conducted using the PubMed/MEDLINE and Google Scholar databases. The search strategy was designed to identify publications evaluating the efficacy, safety, and dosing regimens of anakinra in CAR-T therapy-associated CRS and ICANS. The following combinations of key words were used: 'anakinra AND CAR-T', 'anakinra AND ICANS', 'anakinra AND immune effector cell-associated neurotoxicity syndrome'. Articles published between June 2018 – May 2026 and one from 2008 were considered, with emphasis on papers published after 2022. Peer-reviewed original research articles, review papers and conference abstracts published in English were included. Studies conducted in human populations were prioritized, including randomized controlled trials, observational studies, and systematic reviews. Due to the limited availability of large-scale studies, case reports and case series were also included. After screening and eligibility assessment, a total of 30 sources met the inclusion criteria and were included in the final qualitative synthesis.

DESCRIPTION OF THE STATE OF KNOWLEDGE

Mechanism of action of Anakinra and central nervous system penetration. The development of immune effector cell-associated neurotoxicity syndrome is driven by a complex cytokine storm, where interleukin-1 has emerged as the central mediator [3, 9]. Specifically, IL-1 serves as a proximal driver of ICANS pathophysiology, being produced upstream of the IL-6 cascade to initiate inflammatory signalling within the central nervous system [10, 11]. Unlike interleukin-6, which is primarily associated with systemic cytokine release syndrome, IL-1 is believed to play a more critical role in the early stages of neuroinflammation by contributing to blood-brain barrier disruption [4, 12]. Animal models have demonstrated that IL-1 inhibition can alleviate ICANS symptoms and reduce meningeal inflammation, a benefit not observed with IL-6 blockade via tocilizumab [13]. By blocking this primary mediator, anakinra disrupts the inflammatory feedback loops that impair blood-brain barrier permeability [14]. Moreover, anakinra can cross the blood-brain barrier when given intravenously, although its large molecular size allows only 4% penetration into cerebrospinal fluid with standard dosing regimens [15]. Preclinical models indicate that inhibiting the IL-1 pathway can mitigate ICANS without compromising the essential anti-tumour activity of CAR T-cells [6, 16]. Taking all the above into consideration, anakinra could be much more effective if prescribed earlier in the clinical scenario to reduce endothelial disruption and limit progression to established ICANS. Earlier administration could shorten the total duration of encephalopathy and delirium, thereby reducing the risks of prolonged intensive care and secondary patient distress [17].

Anakinra efficacy in the treatment of CAR-T-associated CRS and ICANS. Early clinical studies have demonstrated the feasibility of subcutaneous anakinra administration for grade 2 cytokine release syndrome and immune effector cell-associated neurotoxicity syndrome [18]. This intervention is frequently employed as an adjunct alongside high-dose corticosteroids, especially when standard-of-care treatments become insufficient [19]. Wang et al. found that implementing an early-intervention toxicity management protocol, while incorporating IL-1 blockade with anakinra, significantly improved toxicity outcomes in patients. The modified strategy led to faster resolution of CRS and ICANS events and meaningfully shorter durations of CRS and ICANS (~1.0 and 2.5 days shorter, respectively) without compromising overall response rates, survival outcomes, or health care utilization. Furthermore, the protocol resulted in lower rates of infection within one year of treatment (54% vs 77%) and directionally lower rates of severe infection (26% vs 39%). Notably, no differences in toxicity rate/severity, overall/progression-free survival, cumulative steroid dose, or health care utilization were detected [17]. Despite its role as a key adjunct, anakinra typically yields no immediate neurological recovery, serving instead to shorten the overall duration of toxicities through the normalization of systemic and laboratory inflammatory indices [7]. Furthermore, unlike tocilizumab, which has been associated with paradoxical exacerbations of neurotoxicity

by potentially increasing CNS-resident IL-6 concentrations, anakinra avoids these secondary inflammatory cascades [20, 21]. Given that high-dose corticosteroid exposure is associated with an increased risk of secondary infections and treatment failure in 16–27% of patients, anakinra has emerged as a vital therapeutic candidate for cases refractory to standard corticosteroids [3, 9]. In a study of 14 patients treated with anakinra for steroid-refractory ICANS, researchers observed significant and rapid reductions in inflammatory cytokines and fever [3]. Moreover, small case series have reported symptomatic improvement in about two-thirds of severe, refractory ICANS cases [13]. Moreover, recent data identify severe 'variant' forms of ICANS, such as those presenting with myelitis, which may remain refractory to multi-modal therapy, including anakinra. Hence, anakinra is not a universal salvage therapy for all ICANS presentations, particularly for these novel variants [22].

Despite those limits, anakinra remains appealing as clinicians try to reduce prolonged steroid exposure, partly due to concern about negative effects on T-cell expansion and long-term remission [21]. Future clinical integration must focus on identifying specific biomarkers that correlate with anakinra responsiveness to optimize patient selection and therapeutic timing.

Dosing strategies and clinical variability of Anakinra. One of the major barriers to consistent medical practice is the lack of a standardized dosing protocol for anakinra in the context of ICANS. Institutional strategies remain notably inconsistent, often falling into standard or aggressive regimens. Surveys of European centres reveal that approximately 62% of institutions utilize a standard dose of 100–200 mg/day, mirroring the established protocol for rheumatoid arthritis [23]. Conversely, 38% of centres employ more intensive regimens ranging from 300 mg – 1,000 mg daily, a strategy typically reserved for severe autoinflammatory conditions like Cryopyrin-associated periodic syndrome [23]. Furthermore, some clinical practice guidelines have suggested weight-based dosing. A starting dose of 2 mg/kg s.c./i.v. every 6 hours was generally used for CAR T-cell toxicities, with escalation based on tolerability and response. In a single-centre experience with CD22 CAR T cells and Haemophagocytic Lymphohistiocytosis-like toxicity, a high dose of anakinra (8–10 mg/kg per day IV/SC) was the typical starting dose in patients more severely impacted, with the aim of tapering down the dose to 5–7 mg/kg/day [24]. In highly refractory cases, some centres have reported using 100 mg administered every 6 hours (max 400 mg/day) to maintain constant suppression of the IL-1 pathway [7]. However, the clinical utility of anakinra remains nuanced, as administration routes, specifically the choice between subcutaneous delivery and intravenous infusions, continue to be debated for patients with poor perfusion or rapid onset of severe neurotoxicity [7]. Furthermore, the lack of standardized prospective trials emphasizes the necessity of establishing clear clinical guidelines to reduce inter-centre differences in treatment timing and dosage [5].

Preemptive and prophylactic approaches of anakinra administration. Recent clinical strategies have increasingly focused on the preemptive use of anakinra to inhibit the IL-1 receptor pathway before the onset of symptomatic neurotoxicity, effectively reducing ICANS incidence without compromising the anti-tumour efficacy of CAR-T cell therapy [6, 16]. Furthermore, clinical reports indicate that the application of prophylactic anakinra in high-risk populations, such as those receiving anti-BCMA CAR-T therapies, has correlated with a notable decrease in the severity of grade 2 adverse events, and a diminished requirement for subsequent corticosteroid intervention [25]. Nath et al. evaluated the utility of prophylactic anakinra, demonstrating a significant reduction in the incidence of severe ICANS to 9.7% in high-risk cohorts [26]. Liang et al. observed lower CRS rates and faster resolution of CRS in comparison to a real-world cohort of patients receiving CAR-T without prophylactic anakinra [27]. Moreover, emerging clinical data indicate that this intervention correlates with a decreased reliance on corticosteroids, which are known to potentially undermine the long-term antileukemic efficacy of chimeric antigen receptor T-cell therapy [21]. Emerging retrospective analyses further indicate that early anakinra initiation correlates with improved clinical and laboratory indices of inflammation, which may contribute to a reduced duration of neurotoxic events [3, 17]. Importantly, a recent multicentre retrospective study by Liang et al. evaluated 101 patients who received anakinra primarily as second-line treatment for corticosteroid-refractory or severe ICANS. The 28-day cumulative incidence of ICANS resolution was 86%, the median time to resolution after anakinra initiation was 8 days, treatment failure occurred in 28% of patients, and treatment-related mortality reached 13%, indicating that outcomes remain suboptimal [20]. Notably, only 43% of patients achieved significant neurologic improvement within 72 hours. Patients who achieved this early response experienced faster ICANS resolution, earlier hospital discharge, lower corticosteroid exposure, and lower treatment-related mortality than non-responders. These findings suggest that a 72-hour neurologic assessment may serve as a clinically useful decision point for identifying patients who are likely to benefit from continued anakinra and those who may require alternative therapies. However, because the study lacked a corticosteroid-only cohort, the independent efficacy of anakinra remains uncertain [20]. While early IL-1 blockade is a promising strategy, it does not consistently prevent neurotoxic development, with recent single-cell RNA-seq analyses demonstrating that breakthrough ICANS is driven by IFN-γ and CXCL10 pathways that are not effectively modulated by IL-1 inhibition [14]. Additionally, these findings must be balanced against recent data that challenge this optimistic perspective. A 2025 Blood report found no significant reduction in grade ≥3 ICANS with anakinra prophylaxis (13.0% vs 9.8%) and reported higher odds of any-grade ICANS (39.6% vs. 23.4%) [28]. Furthermore, Easwar et al. demonstrated that prophylactic anakinra was associated with significantly higher rates of grade ≥3 ICANS, grade ≥3 CRS, and severe infections, reinforcing caution regarding the routine adoption of this preemptive strategy in high-risk CAR T-cell therapy populations [28]. Moreover, Easton et al. reported significantly higher rates of grade ≥3 infections in patients receiving anakinra prophylaxis compared to historical controls (20.8% vs 7.8%) [29].

Recent audit findings highlight a critical safety concern regarding prophylactic anakinra that warrants careful consideration, especially as the literature also presents contradictory evidence. For instance, Kwan et al. reported that prophylactic anakinra enhances patient safety by

Table 1. Summary of anakinra administration recommendations by clinical scenarios

Clinical Phase	Scenario	Recommended Anakinra Strategy	Strength of Recommendation	Key Supporting Evidence
Pre-infusion	Pre-infusion, high-risk patient (age ≥65, CD28-CAR, high LDH)	No routine prophylaxis; individualized decision weighing infection risk	Moderate quality	No reduction in grade ≥3 ICANS (13.0% vs 9.8%); ↑ any-grade ICANS (aOR 3.05); ↑ grade ≥3 infections (HR 10.17), no response/survival benefit (ORR 87% vs 93%) [28]; A a separate cohort confirmed ↑ grade ≥3 infections (20.8% vs 7.8%) [29]
Pre-infusion	Biomarker-stratified high risk (high m-EASIX/EASIX-F, rising IL-6)	Use predictive scores to select candidates for preemptive IL-1 blockade	Low quality	m-EASIX predicts severe CRS/ICANS (AUC 80.4% at lymphodepletion; 73% for severe ICANS at day +3)[33]; EASIX+ferritin/CRP stratify CRS/ICANS risk (74% vs 23–29% across groups) [32]; IL-6 log-slope predicts CRS (AUC 0.88) [35]
Pre-ICANS escalation	Grade ≥2 CRS *or* grade 1 ICANS	Early-intervention protocol: adjunctive anakinra and early steroids at first CRS/ICANS escalation	Low quality	ICANS ↓ 2.49 d; CRS ↓ 0.93 d; 1-y infections 54% vs 77% [17]
Established ICANS	Grade ≥2 ICANS	Corticosteroids first-line; add anakinra only if steroid-refractory	Moderate quality	Corticosteroids are the cornerstone of ICANS management; tocilizumab may exacerbate ICANS via elevated CSF IL-6, so corticosteroids alone are preferred in grade 1 CRS with higher-grade ICANS [16]; The efficacy of Anakinra in combination with corticosteroids over corticosteroids alone remains undetermined [20]
Refractory ICANS	Steroid-refractory, persistent grade ≥2 ICANS	High-dose IV Anakinra (>200 mg/day) preferred over SC 100–200 mg/day	Low quality	High-dose: 0% vs 47% treatment-related mortality, median 7-day resolution vs not reached (low-dose) [40]
Refractory ICANS	Response monitoring after initiation (72-h reassessment)	Reassess at 72 h; escalate if no significant neurologic improvement	Moderate quality	72-h SNI achieved in 43% and predicted faster resolution (3 vs 9 days, p<0.001) and lower TRM (0% vs 21%) [20]; benchmarks: 86% resolution by day 28, median 8 days, TRM 13% [20]; responders had lower baseline CRP, ferritin, LDH [35]
Anakinra failure	Breakthrough ICANS despite prophylaxis	Escalate beyond IL-1 blockade: IFN-γ/GM-CSF/JAK-STAT targeting (itacitinib, lenzilumab, emapalumab)	Low quality	Breakthrough toxicity driven by IFN-γ/CXCL10 in CD14+ monocytes – not inhibited by Anakinra [14]; IFNγ/MIP-1β persist despite IL-6 blockade, supporting GM-CSF/IFN-γ targeting [25]

reducing severe ICANS and treatment-related toxicities, while improving healthcare efficiency through fewer ICU admissions and decreased reliance on high-cost therapies such as tocilizumab [30]. Such inconsistent outcomes may result from heterogeneity in patient populations, institutional risk stratification protocols, or differences in concurrent therapies and dosing regimens. Rather than treating the data as a reason to abandon preemptive use entirely, these findings support a transition toward a more nuanced, tailored approach to anakinra administration that carefully balances potential neuroprotective benefits against individual vulnerability to secondary infections. Moreover, balancing these neurotoxic mitigation benefits against the clinical vulnerability is especially relevant in patients with concurrent cytopenias, including Immune Effector Cell-Associated Haematotoxicity (ICAHT) [31]. Researchers are increasingly focused on identifying predictive biomarkers that might distinguish patients who will derive actual benefit from IL-1 blockade from those who are susceptible to secondary infectious complications. Lactate dehydrogenase, platelet count, C-reactive protein, ferritin, and EASIX-based scores could be used to identify patients at heightened risk for severe CRS or ICANS before clinical deterioration occurs [32,33]. Serial assessment may further improve risk prediction, as early increases in IL-6 have been associated with subsequent CRS and ICANS, while dynamic measurements could help distinguish patients who require intensified monitoring or preemptive intervention [34].

In patients who develop breakthrough toxicity despite IL-1 blockade, assessment of IFN-γ-related signatures and CXCL10 may indicate activation of inflammatory pathways not adequately controlled by anakinra and thereby support escalation toward complementary therapies [14]. Conversely, elevated baseline CRP, ferritin, and LDH have been associated with poorer responses to anakinra in retrospective analyses, suggesting that these markers could eventually help determine whether IL-1 blockade is likely to be beneficial or whether an alternative mechanism-based strategy should be prioritized [35].

Alternatives for anakinra and next steps in a refractory disease. It is crucial to address the clinical challenge of managing patients who remain refractory to anakinra, with recent literature suggesting the investigation of alternative agents such as ruxolitinib or emapalumab [36]. The clinical paradigm is shifting away from universal anakinra application toward a more tailored approach that carefully weighs potential neuroprotective benefits against the increased vulnerability to serious secondary infections [28, 31]. While anakinra remains a primary focus for IL-1-directed prophylaxis, alternative strategies are emerging to enhance neuroprotection; specifically, GM-CSF inhibition (e.g., via lenzilumab) is being investigated as an adjunctive or alternative approach to mitigate inflammatory cascades, offering a more comprehensive landscape of preemptive management [5]. Beyond clinical uncertainty regarding the optimal timing for escalation to alternative agents like lenzilumab, ruxolitinib, or itacitinib, recent practice suggests these should be viewed not just as rescue options, but as potential first-line or primary alternatives in select contexts. Lenzilumab has been highlighted for its potential superiority in specific ICANS models. Oluwole et al. found that the addition of Lenzilumab to the axi-cel regimen appeared to dose-dependently suppress the GM-CSF axis and reduce

markers of systemic inflammation [37]. Given these shifting perspectives and the inconsistent outcomes associated with IL-1 inhibition, strategies targeting complementary inflammatory pathways, such as GM-CSF blockade or JAK-STAT inhibition, are under rigorous investigation [6]. Furthermore, while tocilizumab is standard for CRS, its inability to effectively penetrate the blood-brain barrier or reduce elevated levels of IFNγ and MIP-1β necessitates these alternative approaches to prevent or ameliorate neurotoxicity [25]. It is important to include findings on itacitinib, which has emerged as a compelling prophylactic alternative; notably, a recent randomized controlled trial demonstrated a significant reduction in grade ≥2 CRS and a numerical reduction in ICANS, offering a potential strategy for mitigating treatment-related toxicities [38]. In addition, ongoing clinical trials are evaluating how these strategies integrate with novel engineered cell features, such as suicide switches or inhibitory domains, to provide safer therapeutic profiles without impeding effector function. Emerging data from recent retrospective analyses continue to highlight the heterogeneity of current treatment strategies, noting that sequences of IL-1 receptor antagonists are frequently adjusted based on the specific CAR T-cell product and the patient's baseline inflammatory profile [36]. Stratified management supported by real-time inflammatory monitoring is increasingly presented as a practical route to reduce outcome variability driven by the heterogeneity of ICANS.

DISCUSSION

Corticosteroids remain first-line therapy for ICANS, but questions remain regarding potential impairment of CAR T-cell persistence and overall efficacy, with research highlighting the need for further prospective evaluation to clarify the clinical significance of these concerns [7]. In contrast, anakinra functions as an IL-1 receptor antagonist with a distinct pharmacological profile; it crosses the blood-brain barrier and mitigates neurotoxicity in preclinical models without compromising the anti-tumour activity of engineered T-cells [7, 12]. Early reports suggested that prophylactic administration could significantly reduce the incidence of ICANS following CD19-targeted therapies, presenting a viable strategy to preserve the expansion of the therapeutic product [16]. However, this clinical optimism has been challenged by recent high-impact investigations. Specifically, Easwar et al. demonstrated that prophylactic anakinra failed to reduce the incidence of grade ≥3 ICANS and was paradoxically associated with increased odds of any-grade ICANS and severe infections [28]. Reconciling these findings with contrasting reports, such as those by Kwan et al., provides a more balanced view of the current clinical evidence and strengthens the argument for a stratified approach [30]. Furthermore, research by Frigault et al. identified that 'breakthrough' ICANS and CRS occurring despite prophylaxis are frequently driven by interferon-gamma pathways, suggesting a mechanistic ceiling for anakinra's efficacy within the broader context of cytokine-mediated toxicity [14]. Additionally, emerging evidence that CAR T cells may directly target CD19 on brain pericytes, contributing to blood-brain barrier disruption independently of systemic cytokines, offers one explanation for IL-1 blockade alone being insufficient in some clinical situations [39].

Collectively, these findings emphasize that prophylactic anakinra is not a universal solution. While recent high-impact investigations have tempered earlier clinical enthusiasm, the strategy remains pursued in many centres as a practical approach to facilitate outpatient CAR T-cell administration [14]. Furthermore, clinicians continue to promote its potential as a steroid-sparing agent to mitigate severe adverse events.

CONCLUSIONS

Anakinra provides a targeted strategy for managing immune effector cell-associated neurotoxicity syndrome that mitigates neuroinflammation, without the broad immunosuppression associated with steroids. However, it is important to note that increasing the dosage of corticosteroids remains the cornerstone of treating refractory ICANS. Although early clinical data suggested broad utility, particularly as a prophylactic strategy to facilitate outpatient administration, subsequent real-world analyses have raised concern, demonstrating limited efficacy against high-grade neurotoxicity and an increased probability for severe infections. Current evidence positions anakinra most effectively as a strategic second-line intervention for steroid-refractory cases, where its distinct pharmacological profile addresses the cytokine feedback loops that often persist despite standard management.

Looking ahead, optimizing outcomes requires a shift from universal prophylaxis to a stratified management strategy. By utilizing real-time inflammatory profiling and predictive biomarkers, clinicians can better match mechanism-based therapies, such as IL-1 blockade, to specific patient profiles, thereby maximizing toxicity mitigation while preserving CAR T-cell efficacy. In conclusion, further research is essential to determine the optimal prevention strategy for CRS and ICANS in patients receiving CAR-T therapy, as well as the optimal integration of anakinra into these protocols.

Supplementary materials

No supplementary materials are available.

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