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Outpatient CAR-T therapy in adult hematologic malignancies: Systematic review of feasibility, toxicity, hospitalization, and resource use

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ABSTRACT

Background: Outpatient and ambulatory models of chimeric antigen receptor T-cell (CAR-T) therapy have been developed to reduce inpatient bed use and improve patient-centered delivery. However, safety and feasibility are difficult to interpret because published evidence differs by CAR-T product, costimulatory domain, disease context, monitoring pathway, and definition of outpatient care.

Objective: To synthesize evidence on feasibility, toxicity, hospitalization burden, intensive care use, healthcare resource utilization, and cost-related outcomes associated with outpatient CAR-T therapy in adults with hematologic malignancies.

Methods: A PRISMA-structured systematic review was conducted using PubMed/MEDLINE, Web of Science core collection, Scopus, and Cochrane CENTRAL for studies published from 1 January 2017 to 1 January 2026. Eligible studies included adults receiving CAR-T therapy in outpatient infusion, ambulatory monitoring, early-discharge, telemedicine-supported, remote-monitoring, or community-site pathways and reported extractable clinical or resource-use outcomes. Meta-analysis was not performed because of heterogeneity; synthesis followed SWiM principles.

Results: Twelve original studies published from 2022 to 2025 were included. Selected 4-1BB-based pathways showed the clearest signal for admission avoidance: in one tisa-cel cohort, 68 of 72 patients were managed outpatient and 36.1% were admitted within 30 days; in the multicenter tisa-cel cohort, 45% of outpatient recipients required unplanned admission. OUTREACH showed feasible community-site liso-cel monitoring, with 70% monitored outpatient and 25% of outpatient-monitored patients never hospitalized. CD28-based outpatient axi-cel/brexu-cel pathways were feasible but often still led to admission: in a prospective outpatient axi-cel trial, 19 of 20 patients were admitted within four weeks, and in ZUMA-24, 93% were hospitalized after outpatient axi-cel. Claims analyses suggested lower index or 30-day costs for outpatient site of care, but they lacked toxicity grading and detailed pathway information.

Conclusions: Outpatient CAR-T therapy is feasible for carefully selected adults, but outpatient initiation should not be equated with hospital-free treatment. Current evidence supports structured, product- and risk-adapted outpatient programs rather than unselected ambulatory administration.

Keywords: CAR-T therapy, outpatient care, ambulatory monitoring, cytokine release syndrome, ICANS, hospitalization, healthcare resource utilization, lymphoma, multiple myeloma

INTRODUCTION

Hematologic malignancies represent a substantial global disease burden, accounting for 6.6% of all cancer cases and 7.2% of cancer-related deaths worldwide in 2022 [1]. Patients with hematologic malignancies may develop serious and potentially life-threatening complications related to the disease or its treatment, including sepsis, acute respiratory failure, tumor lysis syndrome, thrombocytopenia, and venous thromboembolism, highlighting the need for timely and multidisciplinary management [2]. Treatment is tailored to the disease subtype, stage, prior therapy, and patient characteristics and may include chemotherapy, targeted agents, monoclonal antibodies, hematopoietic stem-cell transplantation, and cellular immunotherapies [3]. Among these approaches, chimeric antigen receptor T-cell (CAR-T) therapy has transformed the treatment landscape for selected

patients with relapsed or refractory hematologic malignancies, particularly aggressive B-cell lymphomas and other CD19-positive non-Hodgkin lymphoma subtypes [4, 5].

Commercial CD19-directed products, including tisagenlecleucel, axicabtagene ciloleucel, lisocabtagene maraleucel, and brexucabtagene autoleucel, have shown clinically meaningful activity in heavily pretreated populations and are now integrated into routine cellular-therapy practice [4-7]. However, these benefits are accompanied by substantial healthcare resource use, largely related to early monitoring and management of cytokine release syndrome, immune effector cell-associated neurotoxicity syndrome, infections, cytopenias, and other post-infusion complications [8, 9].

Historically, CAR-T infusion and early monitoring were performed in inpatient settings because toxicities can evolve rapidly and require immediate access to specialized interventions. With increasing institutional experience, standardized toxicity-management algorithms, and improved supportive-care pathways, outpatient and hybrid CAR-T models have emerged. These include outpatient infusion with daily clinic assessment, ambulatory post-infusion monitoring, telemedicine-supported follow-up, remote patient monitoring, early-discharge pathways, and community-site models with predefined escalation procedures [10-17].

The rationale for outpatient CAR-T delivery is clinically and operationally compelling: it may reduce inpatient bed use, shorten hospital length of stay, lower index resource utilization, and improve convenience for patients and caregivers [18, 19]. Beyond resource use, reducing inpatient exposure may also be relevant to patient well-being, as hospitalized patients with leukemia, including older adults, may have substantial physical and psychological supportive-care needs [20]. Nevertheless, outpatient CAR-T introduces distinct safety and logistical requirements, including careful patient selection, reliable caregiver support, proximity to the treating center or temporary lodging, patient and caregiver education, rapid admission capacity, and institutional readiness to manage CRS and ICANS without delay [19]. Therefore, outpatient initiation should not be assumed to mean hospital-free treatment.

Differences between outpatient models may partly reflect CAR-T product biology. Products with 4-1BB costimulation, such as tisagenlecleucel and lisocabtagene maraleucel, are often associated with later and more gradual toxicity kinetics, whereas CD28-based constructs, including axicabtagene ciloleucel and brexucabtagene autoleucel, may produce earlier CRS and more intensive toxicity patterns [21]. However, product biology alone does not explain outpatient feasibility; tumor burden, comorbidity, lymphodepletion, prophylactic corticosteroid use, monitoring intensity, caregiver support, proximity to the treatment center, and institutional admission thresholds are also important [19].

Published evidence remains fragmented because studies differ in CAR-T product, disease context, patient selection, definition of outpatient care, monitoring strategy, admission thresholds, and outcome assessment windows.

Therefore, the aim of this systematic review was to synthesize the available evidence on the feasibility and safety of outpatient CAR-T therapy in adults with hematologic malignancies, with particular emphasis on toxicity, hospitalization burden, intensive care use, healthcare resource utilization, and cost-related outcomes.

MATERIALS AND METHODS

Study Design and Reporting Framework

This study was conducted in line with PRISMA 2020, with search reporting aligned to PRISMA-S and narrative synthesis structured according to SWiM guidance [22-24]. The protocol was predefined before review initiation with respect to eligibility criteria, information sources, search concepts, extraction domains, and synthesis framework. The protocol was not registered in PROSPERO or OSF. This is explicitly acknowledged as a reporting limitation rather than left implicit.

Scope of the Review

The review focused on adult outpatient CAR-T delivery in hematologic malignancies. Most included evidence related to CD19-directed CAR-T therapy in B-cell lymphomas. Mixed-product cohorts were retained when they reported outpatient outcomes for commercial CD19-directed and/or BCMA-directed products, because they directly inform outpatient infrastructure and hospitalization burden. These mixed cohorts were interpreted separately and were not used to generalize lymphoma-specific findings to multiple myeloma or acute lymphoblastic leukemia.

This scope resolves a key ambiguity in earlier drafts: the review is not limited strictly to B-cell lymphoma, but product-specific conclusions are stratified. Statements about tisa-cel, liso-cel, axi-cel, and brexu-cel are confined to the disease contexts studied in the cited reports.

Information Sources and Search Strategy

A systematic search was conducted in PubMed/MEDLINE, Web of Science core collection, Scopus, and the Cochrane CENTRAL. The final search update covered 1 January 2017 to 1 January 2026, corresponding to the era of clinical implementation of commercial CAR-T therapy. No formal language restriction was applied; however, only studies with extractable English-language data were ultimately included.

Search strategies combined controlled vocabulary and free-text terms for CAR-T therapy, commercial CAR-T products, outpatient or ambulatory delivery, and outcomes related to feasibility, toxicity, hospitalization, ICU use, resource utilization, and cost. In the final manuscript version, the search concepts were explicitly broadened to include BCMA/myeloma terms because one included mixed-product outpatient cohort reported both CD19- and BCMA-directed commercial CAR-T therapy. The core PubMed/MEDLINE strategy is provided in **Appendix A**. Equivalent concepts were adapted for Web of Science topic fields, Scopus TITLE-ABS-KEY fields, and Cochrane CENTRAL.

Reference lists of relevant articles and key reviews were screened manually. Clinical trial registries were checked when appropriate, but only studies with available published results were included.

Eligibility Criteria

Studies were eligible if they met all of the following criteria: original research; adult patients with hematologic malignancies receiving CAR-T therapy; outpatient infusion, outpatient monitoring, ambulatory management, early-discharge, telemedicine-supported, remote-monitoring, or community-site pathway; and extractable data on at least one

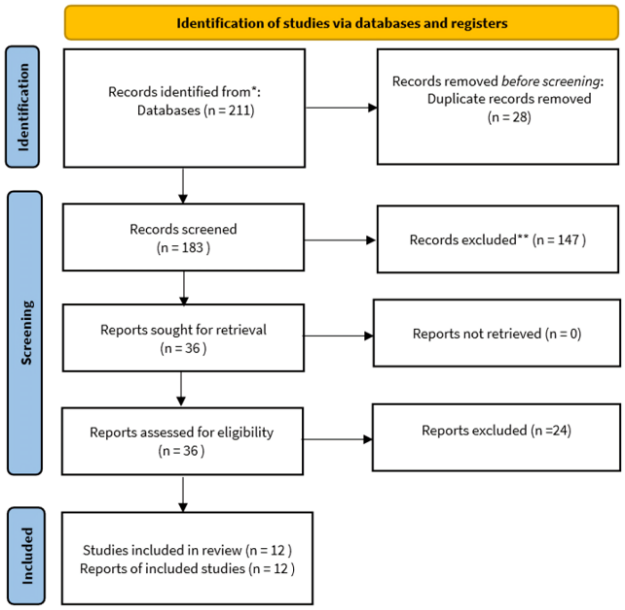

Figure 1. PRISMA flow diagram of study selection (adapted from the PRISMA 2020 flow diagram template [22])

relevant outcome, including feasibility, CRS, ICANS, hospitalization, length of stay, ICU use, healthcare resource utilization, or cost. Both comparative and non-comparative designs were eligible.

Studies were excluded if they were inpatient-only without separable outpatient data, preclinical or animal studies, pediatric-only studies, reviews without original clinical data, expert opinion papers, implementation papers without patient-level outcomes, or duplicate/overlapping reports of the same cohort. When overlapping datasets were suspected, the most complete and most recent report with extractable outpatient-relevant outcomes was retained (**Appendix B**).

Outcomes

The primary outcomes were feasibility of outpatient initiation or monitoring and hospitalization burden after outpatient CAR-T infusion or monitoring. Secondary outcomes were CRS and ICANS, grade ≥ 3 CRS/ICANS when reported, ICU utilization, length of stay, healthcare resource utilization, and cost-related outcomes. The terms outpatient, ambulatory, community-site, early-discharge, telemedicine-supported, and remote monitoring were treated as related but not interchangeable models.

Study Selection and Data Extraction

A total of 211 records were identified through database searching and supplementary manual screening. After removal of 28 duplicate records, 183 records underwent title and abstract screening. One hundred forty-seven records were excluded at this stage. Thirty-six reports were assessed in full text or detailed eligibility review; 24 were excluded for reasons including lack of outpatient-specific outcomes, inpatient-only design, absence of original clinical data, duplicate or overlapping cohorts, ineligible population, or publication outside the predefined search period. Twelve original studies were included in the final qualitative synthesis (**Figure 1**).

Search outputs were exported and de-duplicated in a single screening library. Database-specific pre-deduplication yields were not available in the source extraction file; therefore the PRISMA diagram reports verified aggregate counts rather than unsupported database-level numbers. This avoids the earlier error of leaving blank database fields or inserting non-verifiable counts.

Data were extracted independently by two reviewers using a standardized form. Extracted items included author, year, design, setting, population, malignancy type, CAR-T product, outpatient model, sample size, comparator group where available, feasibility outcomes, CRS and ICANS outcomes, hospitalization rate, length of stay, ICU utilization, healthcare resource utilization, cost-related outcomes, and key limitations. Discrepancies were resolved by discussion; a third reviewer was available if consensus could not be achieved.

Risk of Bias and Evidence Limitations

Risk of bias was assessed using a domain-based approach informed by the Newcastle-Ottawa Scale for observational cohort evidence and the Joanna Briggs Institute framework for case-series and non-comparative evidence. Domains included selection bias, comparability and confounding, outcome completeness, and adequacy of follow-up. Each study was classified as low concern, some concerns, or high concern. Risk-of-bias assessment was performed independently by two reviewers, with disagreements resolved by consensus. Overall evidence limitations were evaluated narratively, considering risk of bias, inconsistency, indirectness, imprecision, and reporting limitations. Formal GRADE ratings were not assigned because of heterogeneous designs, non-randomized comparisons, variable outpatient definitions, and lack of common effect measures.

Data Synthesis

A meta-analysis was not performed because included studies differed substantially in CAR-T product, costimulatory domain, disease context, patient selection, monitoring pathway, comparator structure, outcome definition, and follow-up window. Studies were grouped by product/pathway type: predominantly ambulatory 4-1BB products, community-site liso-cel pathway, CD28-based outpatient initiation, coordinated outpatient care without intensive remote monitoring, and administrative claims-based outpatient site-of-care analyses. Outcomes were interpreted hierarchically, prioritizing feasibility, severe CRS/ICANS, hospitalization avoidance, length of stay, ICU use, and cost/resource-use measures.

RESULTS

Study Selection and General Characteristics

Twelve original studies published from 2022 to 2025 were included. The evidence base consisted of early single-center cohorts, multicenter retrospective cohorts, prospective outpatient studies, phase II studies, and administrative claims analyses. Most studies evaluated adults with relapsed or refractory B-cell non-Hodgkin lymphoma, diffuse large B-cell lymphoma, or related large B-cell lymphoma subtypes. One cohort included a mixed outpatient population with CD19- and BCMA-directed products.

CAR-T products included 4-1BB-based constructs, mainly tisagenlecleucel and lisocabtagene maraleucel [25-27], and CD28-based constructs, mainly axicabtagene ciloleucel and brexucabtagene autoleucel [10-12].

Table 1. Characteristics of original studies included in the qualitative synthesis

Study	Design/setting	Population	Product	Outpatient model	Sample/comparator	Main contribution
[10]	Single-center cohort	LBCL / MCL	Axi-cel, brexu-cel	Telemedicine-supported outpatient pathway	13/no formal comparator	Early CD28 outpatient experience; hospital-free recovery uncommon
[11]	Prospective trial	R/R DLBCL	Axicabtagene ciloleucel	Protocolized outpatient axi-cel with RPM/telemedicine	20 treated	Prospective axi-cel feasibility; most patients hospitalized after outpatient start
[12]	Phase II open-label multicenter study	R/R LBCL	Axicabtagene ciloleucel	Outpatient axi-cel with prophylactic corticosteroids	30 treated	Prospective multicenter axi-cel outpatient evidence
[13]	Single-center cohort	Adults with hematologic malignancies	Mixed commercial CAR-T	Outpatient infusion and monitoring	Approximately two dozen/no formal comparator	Early tertiary-center feasibility evidence; most patients still required admission
[14]	Real-world cohort	Adults receiving commercial CAR-T	Mixed commercial CAR-T	Outpatient optimization pathway	32 outpatient of 40 total	Operational feasibility in routine practice
[15]	Prospective cohort	R/R NHL	Anti-CD19 CAR-T	Ambulatory pathway with preemptive tocilizumab	48 / no comparator	Shows proactive CRS management may support ambulatory care
[16]	Single-center cohort	33 myeloma, 24 lymphoma, 1 ALL	CD19 and BCMA commercial products	Coordinated outpatient care without intensive home monitoring	58 outpatient/no formal comparator	Mixed-product model using daily clinic follow-up and early CRS intervention
[25]	Retrospective cohort	NHL	Tisagenlecleucel	Predominantly ambulatory management	68 outpatient/4 inpatient starters	Strong tisa-cel outpatient signal with admission avoidance in most patients
[26]	Multicenter retrospective cohort	B-cell NHL	Tisagenlecleucel	Outpatient vs.inpatient treatment	93 outpatient/64 inpatient	Multicenter tisa-cel comparison; demonstrates selection bias
[27]	Phase II multicenter community-site study	R/R LBCL	Lisocabtagene maraleucel	Community-site outpatient or inpatient monitoring	82 treated; 70% outpatient monitored	Prospective liso-cel evidence at community sites with structured procedures
[28]	Medicare claims analysis	DLBCL	CAR-T across settings	Outpatient vs.inpatient site of care	391 Medicare claims	Index cost and utilization comparison; weak toxicity granularity
[29]	Commercial claims analysis	DLBCL	CAR-T across settings	Outpatient vs.inpatient site of care	Commercial claims cohort	Real-world HCRU/cost analysis; limited clinical detail

Claims-based studies compared site of care but lacked detailed information on monitoring intensity, toxicity grade, tumor burden, caregiver status, and institutional escalation criteria (**Table 1**).

Feasibility, Safety, and Hospitalization Outcomes

Across included studies, outpatient CAR-T was feasible only when embedded in a structured monitoring and escalation system (**Table 2**). Common operational elements were patient selection, caregiver availability, proximity or lodging near the center, frequent clinical assessment, clear fever/neurologic symptom pathways, tocilizumab and corticosteroid access, and direct admission capacity.

The most consistent signal for admission avoidance was seen in selected 4-1BB-based cohorts. It was identified 72 patients with relapsed or refractory NHL treated with commercial tisagenlecleucel; 68 (94.4%) received outpatient tisa-cel [25]. Twenty-six patients (36.1%) were admitted within 30 days and 14 (19.4%) within 72 hours, with median length of stay of 5 days among admitted patients; no grade 3-4 CRS occurred and two patients had grade 3-4 neurotoxicity [25]. It provided multicenter confirmation but also showed selection bias: outpatient tisa-cel recipients had lower comorbidity and disease burden; CRS was 29% versus 56%, ICANS 10% versus 16%, unplanned admission 45%, and ICU transfer 5% versus 8% for outpatient versus inpatient cohorts [26].

OUTREACH extended evidence to liso-cel at community sites. Eighty-two patients received liso-cel; 70% were monitored outpatient and 30% inpatient. Grade ≥ 3 CRS occurred in 0% of both groups; grade ≥ 3 neurologic events occurred in 12% of outpatient-monitored and 4% of inpatient-monitored patients. Among outpatients, 25% were never hospitalized after infusion, 32% were hospitalized within 72 hours, and median initial hospitalization duration was 6.0 days for outpatients versus 15.0 days for inpatients [27].

For CD28-based products, outpatient initiation was feasible but was less often equivalent to hospital-free care. It was shown feasibility of outpatient axi-cel/brexu-cel using telemedicine tools, but any-grade CRS and neurologic toxicity were frequent and hospital-free recovery was uncommon [10]. In the later prospective outpatient axi-cel trial, 20 patients were treated, 19 were admitted within four weeks, median hospitalization was 5.5 days, no grade ≥ 3 CRS occurred, grade 3 ICANS occurred in 20%, and two ICU admissions occurred in patients with pre-existing conditions exacerbated during CRS [11]. ZUMA-24 similarly showed outpatient axi-cel feasibility

Table 2. Key feasibility, toxicity, hospitalization, and resource-use outcomes

Study	Feasibility/pathway outcome	CRS and ICANS signal	Hospitalization/LOS	ICU/HCRU/cost interpretation
[10]	Outpatient axi-cel/brexu-cel initiation feasible using telemedicine tools.	Any-grade CRS and neurologic toxicity frequent in CD28 pathway.	Hospital-free recovery is uncommon; median inpatient stay about 7 days.	Supports CD28 outpatient initiation as admission-minimization, not admission avoidance.
[11]	20 treated with outpatient axi-cel; 90% received prophylactic steroids.	Grade 2 CRS 40%; no grade ≥ 3 CRS; grade 3 ICANS 20%; no grade ≥ 4 ICANS.	19/20 admitted within 4 weeks; median LOS 5.5 days; 1 remained outpatient to day 30.	2 ICU admissions linked to pre-existing condition exacerbation during CRS.
[12]	30 treated with outpatient axi-cel and prophylactic steroids.	Grade 1-2 CRS 90%; no grade ≥ 3 CRS; neurologic events any grade 80%, grade ≥ 3 23%.	93% hospitalized; median time to first hospitalization 4 days; median stay 8 days.	ICU 4/30 (13%); supports feasibility but not hospital-free axi-cel.
[13]	Outpatient CAR-T program feasible in a tertiary center.	Toxicities manageable with rapid admission capacity.	Most patients required admission; median LOS reported around 8 days.	No formal cost analysis; key message is feasibility with mature infrastructure.
[14]	32 of 40 patients infused outpatient in optimized program.	Safety acceptable in experienced center.	Hospitalization after outpatient start remained common.	Operational feasibility report; not definitive for comparative cost reduction.
[15]	Ambulatory anti-CD19 pathway with preemptive tocilizumab feasible.	ICANS 10/48; grade 3/4 ICANS in 5; no toxicity-related deaths.	Hospitalization is influenced by proactive CRS management.	ICU admission 19%; mainly ICANS management; no ICU admission for CRS.
[16]	58 outpatient infusions; no intensive remote home monitoring.	Early outpatient tocilizumab was used for grade ≥ 1 CRS.	Admissions: 17 days 0-3, 16 days 4-7, 9 days 8-30.	Tocilizumab prevented hospitalization in 15/35 CRS cases; still high admission burden.
[25]	68/72 received outpatient tisa-cel.	Any CRS 40.3%; no grade 3-4 CRS; 2 grade 3-4 neurotoxicity.	26/72 (36.1%) admitted by 30 days; 14/72 (19.4%) by 72 h; median LOS 5 days.	Strongest tisa-cel admission-avoidance signal; no CAR-T toxicity death.
[26]	93 outpatient vs.64 inpatient tisa-cel recipients across 9 centers.	CRS 29% vs. 56%; ICANS 10% vs.16% (outpatient vs.inpatient).	42/93 (45%) unplanned admission; LOS 5 vs.13 days.	ICU transfer 5% vs.8%; outpatient group had lower comorbidity/disease burden.
[27]	82 treated; 70% outpatient monitored at community sites.	Grade ≥ 3 CRS 0% in both groups; grade ≥ 3 neurologic events 12% outpatient vs.4% inpatient.	25% of outpatients are never hospitalized; 32% hospitalized ≤ 72 h; LOS 6 vs.15 days.	Strong prospective community-site liso-cel evidence but requires SOPs and escalation.
[28]	Medicare claims; outpatient use minority (21%) vs.inpatient (79%).	Toxicity grade unavailable in claims.	30-day post-period inpatient admission higher after outpatient index CAR-T (59% vs.21%).	Average index Medicare cost lower outpatient ($414,393) vs.inpatient ($498,723).
[29]	Commercial claims; DLBCL CAR-T across settings.	Toxicity grade unavailable in claims.	Inpatient service utilization lower in outpatient group in claims analysis.	30-day post-index costs lower outpatient vs.inpatient overall and for axi-cel; clinical selection not visible.

with prophylactic corticosteroids, but 93% of patients were hospitalized after infusion, median time to first hospitalization was 4 days, median stay was 8 days, and ICU admission occurred in 13% [12].

The coordinated outpatient cohort in [16] is important because it included both CD19- and BCMA-directed products and did not rely on intensive at-home remote monitoring. Fifty-eight patients received outpatient CAR-T; 17 were admitted on days 0-3, 16 on days 4-7, and 9 on days 8-30. The most common reason for admission was CAR-T-related toxicity. Outpatient tocilizumab for CRS prevented hospitalization in 15 of 35 CRS cases, suggesting that early CRS intervention can reduce some admissions but does not eliminate the need for robust escalation capacity [16].

Claims-based studies should be interpreted separately from clinical cohorts. It was evaluated medicare fee-for-service claims and found that outpatient index claims were less costly on average than inpatient claims, but outpatient site of care did not necessarily reduce subsequent hospital use; 30-day post-period inpatient admission was higher after outpatient index CAR-T in that analysis [28]. It used commercial claims and reported lower 30-day post-index costs for outpatient administration compared with inpatient administration, but claims data cannot capture CRS/ICANS grades, tumor burden, caregiver reliability, or local monitoring protocols [29].

Outpatient Pathway Characteristics

Outpatient CAR-T was not a uniform intervention. The included studies described at least five clinically distinct models: predominantly ambulatory 4-1BB pathways; community-site liso-cel monitoring; telemedicine-supported CD28 outpatient initiation; coordinated outpatient care without intensive remote home monitoring; and administrative site-of-care classification in claims databases. Predominantly ambulatory 4-1BB pathways relied on frequent clinic-based assessment, caregiver support, proximity to the treating center, rapid admission access, and tocilizumab availability [25, 26]. The OUTREACH study is important because it tested liso-cel monitoring at community sites, but it does not support unstructured decentralization. Rather, it shows that outpatient monitoring may be feasible outside traditional academic inpatient models only when standard procedures, trained staff, and escalation criteria are in place [27]. CD28-based outpatient care was more intensive. Telemedicine-supported axi-cel/brexu-cel and protocolized outpatient axi-cel pathways required close monitoring, prophylactic or early corticosteroid strategies in some studies, rapid admission thresholds, and readiness for ICU-level events [10]. These pathways are best interpreted as models to reduce inpatient days or shift initial monitoring location, not as models that reliably avoid hospitalization [11, 12] (**Table 3**).

Table 3. Comparative structure of outpatient CAR-T pathways

Pathway type	Representative studies	Monitoring model	Key safety infrastructure	Interpretation
Telemedicine-supported CD28 pathway	[10]	Telemedicine plus symptom escalation	Strict caregiver and rescue-admission pathway	Feasible, but hospital-free recovery uncommon
Protocolized outpatient axi-cel	[11, 12]	Daily visits, RPM/telemedicine where used, toxicity prevention	Prophylactic corticosteroids, early intervention, rapid admission	Mostly inpatient-days minimization rather than admission avoidance
Coordinated outpatient care without intensive home monitoring	[16]	Clinic-centric follow-up; daily early visits	Early CRS recognition, outpatient tocilizumab, direct admission	Feasible mixed-product model, but admission burden remains high
Predominantly ambulatory 4-1BB pathway	[25, 26]	Daily or frequent clinic-based assessment	Caregiver, proximity/lodging, rapid admission, tocilizumab access	Best signal for true admission avoidance in selected patients
Community-site liso-cel pathway	[27]	Structured community-site monitoring	Multidisciplinary SOPs, trained site teams, predefined escalation	Strongest prospective community-site evidence; not ordinary decentralization
Administrative outpatient site-of-care	[28, 29]	Not clinically granular	Not visible in claims data	Useful for cost/HCRU; weak for safety/pathway inference

Table 4. Risk of bias and methodological appraisal of included original studies

Study	Selection bias	Comparability/ confounding	Outcome completeness	Overall concern	Main limitation
[10]	High	High	Moderate	High concern	Small CD28 cohort; selected patients; no comparator
[11]	Moderate	Moderate	Moderate	Some concerns	Small prospective single-center trial
[12]	Moderate	Moderate	Moderate-to-good	Some concerns	Single-arm phase II design; sponsor trial context
[13]	High	High	Moderate	High concern	Small early cohort; no formal comparator
[14]	High	High	Low-to-moderate	High concern	Operational report; limited comparative inference
[15]	Moderate	Moderate	Moderate	Some concerns	No control group; intervention/pathway confounding
[16]	Moderate	Moderate	Moderate	Some concerns	Mixed diseases/products; no comparator
[25]	Moderate	Moderate	Moderate	Some concerns	Single-center retrospective design
[26]	Moderate	Moderate-to-high	Moderate	Some concerns	Outpatient patients had lower disease burden and comorbidity
[27]	Low-to-moderate	Moderate	Good	Some concerns	Non-random outpatient vs. inpatient monitoring
[28]	Moderate	High	Good for claims outcomes	Some concerns	No CRS/ICANS grade or pathway detail
[29]	Moderate	High	Good for claims outcomes	Some concerns	Commercial claims; unmeasured clinical selection

Methodological Appraisal

The included evidence was limited mainly by non-randomized design, small cohorts, heterogeneity of outpatient definitions, and strong confounding by patient selection. Early single-center feasibility studies were useful operationally but had high risk of selection bias and limited comparability [10, 13, 14]. Later multicenter and prospective studies improved outcome completeness but still lacked randomized allocation to outpatient versus inpatient care.

Claims-based analyses had a different limitation profile. They were stronger for measuring reimbursed costs and service utilization but weak for toxicity grading, disease burden, patient eligibility, caregiver status, and monitoring-pathway detail. Their findings should therefore inform payer and resource-use hypotheses rather than clinical safety conclusions (**Table 4**).

DISCUSSION

This review supports a cautious but clinically useful conclusion: outpatient CAR-T therapy is feasible in selected adults. Although outpatient initiation reduced initial inpatient exposure in selected cohorts, subsequent hospitalization remained common, particularly with CD28-based products. Some 4-1BB-based pathways appear capable of avoiding hospitalization in a meaningful proportion of patients, whereas CD28-based outpatient pathways often still require admission soon after infusion and mainly reduce initial inpatient exposure or total hospital days.

The strongest part of the evidence is operational consistency. Across studies, safe outpatient delivery depended on the same core elements: careful selection, patient and caregiver education, frequent clinical assessment, local lodging or proximity, immediate access to tocilizumab and corticosteroids, and a direct admission pathway. These requirements align with ASTCT expert opinion that outpatient CAR-T is a program-level intervention, not simply a change in infusion location [19].

The weaker part is comparative inference. Most studies were observational and small. Outpatient recipients were often clinically more stable, had lower tumor burden, fewer comorbidities, stronger caregiver support, or better proximity to treatment centers. The authors in [26] clearly illustrate this issue: outpatient tisa-cel recipients had lower comorbidity and disease burden, which likely contributed to lower observed toxicity and resource use. Claims-based analyses cannot resolve this bias because key clinical variables are absent.

The product-specific pattern is biologically plausible but not proven by randomized comparisons. Tisa-cel and liso-cel are 4-1BB-based products and have generally been more favorable for outpatient monitoring in selected cohorts. Axi-cel and brexu-cel are CD28-based products and outpatient administration appears feasible, but the high admission

frequency in the study in [11] and ZUMA-24 [12] shows that feasibility should be interpreted as safe structured initiation with rapid escalation, not as reliable admission avoidance.

Economic interpretation requires particular care. Outpatient site of care may reduce index reimbursement or 30-day costs, as suggested in [28, 29]. However, lower index cost does not automatically mean lower total clinical burden. In [28], outpatient index claims were less costly, but subsequent 30-day inpatient admission was higher after outpatient index CAR-T. Cost analyses therefore need standardized episode windows, payer perspective, subsequent admissions, ICU care, outpatient visits, caregiver burden, and indirect patient costs.

For clinical practice, the evidence supports a tiered approach. Selected patients receiving 4-1BB-based products may be candidates for outpatient infusion or monitoring when center infrastructure is mature. CD28-based outpatient delivery should be considered an intensified hybrid pathway requiring early admission thresholds and high vigilance for neurotoxicity. Mixed CD19/BCMA outpatient pathways are promising but should not be generalized across malignancies without product- and disease-specific reporting.

Study Strengths and Limitations

A key strength of this review is its focus on whether outpatient CAR-T therapy leads to meaningful hospitalization avoidance rather than merely demonstrating the feasibility of outpatient infusion. By comparing different CAR-T products and care pathways, the review provides a clinically relevant interpretation of safety, hospitalization, and resource-use outcomes.

This review has several limitations. The available evidence was heterogeneous and predominantly non-randomized, with variable definitions of outpatient care and several small, single-center studies; therefore, meta-analysis was not considered appropriate. Claims-based studies also lacked detailed clinical information, including CRS and ICANS severity, tumor burden, caregiver availability, and monitoring pathways. In addition, the review protocol was not prospectively registered, and publication bias could not be formally assessed.

Future studies should use standardized definitions of outpatient CAR-T therapy, distinguish outpatient infusion from outpatient monitoring, and report product-specific outcomes using consistent hospitalization windows. Comparative and economic studies should also account for patient selection, treatment characteristics, center experience, subsequent admissions, intensive care use, and patient and caregiver burden.

CONCLUSIONS

Outpatient CAR-T therapy is feasible for selected adult patients with hematologic malignancies when delivered through structured programs with rapid toxicity recognition and direct inpatient escalation. The evidence is strongest for selected 4-1BB-based pathways, especially tisa-cel and liso-cel, where meaningful admission avoidance has been observed. For CD28-based products such as axi-cel and brexu-cel, outpatient initiation is feasible but often requires subsequent hospitalization.

In practice, outpatient CAR-T should be viewed as a structured strategy for selective reduction of inpatient resource use rather than a universal replacement for hospitalization, and it requires mature infrastructure, trained teams, caregiver support, proximity, and rapid access to CRS/ICANS treatment

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APPENDIX A

Table A1. Search concepts used for the final manuscript version

Database	Search concept/query
PubMed/MEDLINE	("Chimeric Antigen Receptor T-Cell Therapy" [Mesh] OR CAR-T [tiab] OR "CAR T" [tiab] OR "chimeric antigen receptor T-cell" [tiab] OR tisagenlecleucel [tiab] OR axicabtagene [tiab] OR lisocabtagene [tiab] OR brexucabtagene [tiab] OR idecabtagene [tiab] OR ciltacabtagene [tiab] OR BCMA [tiab] OR "B-cell maturation antigen" [tiab]) AND (outpatient [tiab] OR ambulatory [tiab] OR "outpatient setting" [tiab] OR "same-day discharge" [tiab] OR "early discharge" [tiab] OR telemedicine [tiab] OR "remote patient monitoring" [tiab]) AND (feasibility [tiab] OR safety [tiab] OR toxicity [tiab] OR CRS [tiab] OR ICANS [tiab] OR hospitalization [tiab] OR "length of stay" [tiab] OR ICU [tiab] OR cost [tiab] OR "healthcare resource utilization" [tiab]) AND Humans [Mesh].
Web of Science core collection	TS = (CAR-T OR "chimeric antigen receptor T cell" OR tisagenlecleucel OR axicabtagene OR lisocabtagene OR brexucabtagene OR idecabtagene OR ciltacabtagene OR BCMA OR "B-cell maturation antigen") AND TS = (outpatient OR ambulatory OR "early discharge" OR "same day discharge" OR telemedicine OR "remote monitoring") AND TS = (feasibility OR safety OR toxicity OR CRS OR ICANS OR hospitalization OR "length of stay" OR ICU OR cost OR "resource utilization").
Scopus	TITLE-ABS-KEY (CAR-T OR "chimeric antigen receptor T-cell" OR tisagenlecleucel OR axicabtagene OR lisocabtagene OR brexucabtagene OR idecabtagene OR ciltacabtagene OR BCMA OR "B-cell maturation antigen") AND TITLE-ABS-KEY (outpatient OR ambulatory OR "early discharge" OR "same-day discharge" OR telemedicine OR "remote patient monitoring") AND TITLE-ABS-KEY (feasibility OR safety OR toxicity OR CRS OR ICANS OR hospitalization OR "length of stay" OR ICU OR cost OR "healthcare utilization").
Cochrane CENTRAL	(CAR-T OR "chimeric antigen receptor T-cell" OR BCMA) AND (outpatient OR ambulatory OR "early discharge") AND (safety OR toxicity OR hospitalization OR cost).

APPENDIX B

Table B1. Grouped full-text exclusion reasons

Exclusion category	Comment
Not outpatient CAR-T or no outpatient-specific outcomes	Records described CAR-T therapy but did not report separable outpatient, ambulatory, early-discharge, or remote-monitoring outcomes.
Inpatient-only pathway	Reports evaluated inpatient infusion/monitoring only or did not allow separation of inpatient and outpatient outcomes.
Not original clinical research	Reviews, expert opinions, guidelines, commentaries, operational descriptions, or implementation papers without original patient-level outcomes.
Duplicate or overlapping cohort	More complete or more recent cohort retained.
Ineligible population or timing	Pediatric-only, preclinical/animal, outside predefined search period, or no published results.