Efficacy and Safety of BCMA-Targeted CAR-T Cell Therapy in Chinese Patients with Relapsed/Refractory Multiple Myeloma: A Meta-Analysis (Postprint)

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Abstract

Background Chimeric antigen receptor (CAR) T cells targeting B-cell maturation antigen (BCMA) have demonstrated favorable clinical efficacy in clinical studies for relapsed/refractory multiple myeloma (RRMM), but currently there is limited evidence regarding their efficacy and safety in Chinese RRMM patients. Objective To investigate the safety and efficacy of anti-BCMA CAR-T cell therapy in Chinese patients with RRMM. Methods A computerized search was conducted of PubMed, Web of Science, Embase, CNKI, Wanfang Data Knowledge Service Platform, and VIP databases. Studies published from database inception to May 2024 on anti-BCMA CAR-T cell therapy for Chinese RRMM patients were screened, with two researchers independently screening literature, extracting data, and evaluating the risk of bias in included studies. Meta-analysis was performed using Stata 16.0 software, with efficacy indicators, safety indicators, and prognostic indicators as the primary outcome measures. Results A total of 18 studies involving 684 patients were included. Meta-analysis results showed: the overall response rate to anti-BCMA CAR-T cell therapy in RRMM patients was 86% (95%CI=76%~94%), the stringent complete response rate was 67% (95%CI=58%~75%), the complete response rate was 54% (95%CI=44%~65%), the very good partial response rate was 16% (95%CI=8%~24%), and the partial response rate was 17% (95%CI=13%~22%). The incidence of cytokine release syndrome (CRS) was 76% (95%CI=56%~92%), and grade 3 or higher CRS was 16% (95%CI=8%~26%). The incidence of leukopenia was 91% (95%CI=74%~100%), and grade 3 or higher leukopenia was 70% (95%CI=47%~90%). The incidence of neutropenia was 82% (95%CI=54%~99%), and grade 3 or higher neutropenia was 74% (95%CI=52%~92%). The incidence of thrombocytopenia was

81% (95%CI=64%~95%), and grade 3 or higher thrombocytopenia was 54% (95%CI=37%~70%). The incidence of anemia was 78% (95%CI=44%~99%), and grade 3 or higher anemia was 55% (95%CI=38%~70%). The incidence of immune effector cell-associated neurotoxicity syndrome (ICANS) was 13% (95%CI=4%~24%), and grade 3 or higher ICANS was 0 (95%CI=0~2%). The 1-year mortality rate was 3% (95%CI=1%~7%), and the 2-year or longer mortality rate was 35% (95%CI=10%~66%). The 1-year relapse or progression rate was 35% (95%CI=19%~52%), and the 2-year or longer relapse or progression rate was 35% (95%CI=18%~54%). The 1-year disease stability rate was 60% (95%CI=34%~83%). The 1-year progression-free survival rate was 52% (95%CI=44%~60%). The 6-month overall survival rate was 90% (95%CI=76%~99%), and the 1-year or longer overall survival rate was 74% (95%CI=66%~80%). Conclusion Anti-BCMA CAR-T therapy is effective and safe for Chinese RRMM patients; however, there are issues such as small sample sizes and varying quality among the included studies, necessitating larger-scale studies and higher-quality randomized controlled trials for further validation.

Full Text

Efficacy and Safety of BCMA-Targeted Chimeric Antigen Receptor T-Cell Therapy for Chinese Patients with Relapsed/Refractory Multiple Myeloma: A Meta-Analysis

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Abstract

Background: Chimeric antigen receptor (CAR) T-cell therapy targeting B-cell maturation antigen (BCMA) has demonstrated promising clinical efficacy in relapsed/refractory multiple myeloma (RRMM). However, evidence regarding its effectiveness and safety specifically in Chinese RRMM patients remains limited.

Objective: To evaluate the safety and efficacy of anti-BCMA CAR-T cell therapy in Chinese patients with RRMM.

Methods: We systematically searched PubMed, Web of Science, Embase, CNKI, Wanfang Data, and VIP databases for studies on anti-BCMA CAR-T cell therapy in Chinese RRMM patients published from inception to May 2024. Two investigators independently screened literature, extracted data, and assessed risk of bias. Primary outcomes included efficacy indicators, safety indicators, and prognostic indicators. Meta-analysis was performed using Stata 16.0 software.

Results: Eighteen studies involving 684 patients were included. The pooled objective response rate (ORR) was 86% (95%CI=76%-94%), stringent complete response (sCR) rate was 67% (95%CI=58%-75%), complete response (CR) rate was 54% (95%CI=44%-65%), very good partial response (VGPR) rate was 16% (95%CI=8%-24%), and partial response (PR) rate was 17% (95%CI=13%-22%). Cytokine release syndrome (CRS) occurred in 76% of patients (95%CI=56%-92%), with grade $ $3 CRS reported in 16% (95%CI=8%-26%). Leukopenia was observed in 91% (95%CI=74%-100%), with grade $ $3 leukopenia in 70% (95%CI=47%-90%). Neutropenia occurred in 82% (95%CI=54%-99%), with grade $ $3 neutropenia in 74% (95%CI=52%-92%). Thrombocytopenia was reported in 81% (95%CI=64%-95%), with grade $ $3 thrombocytopenia in 54% (95%CI=37%-70%). Anemia occurred in 78% (95%CI=44%-99%), with grade $ $3 anemia in 55% (95%CI=38%-70%). Immune effector cell-associated neurotoxicity syndrome (ICANS) was observed in 13% (95%CI=4%-24%), with no grade $ $3 ICANS cases (95%CI=0-2%). The 1-year mortality rate was 3% (95%CI=1%-7%), while the $ $2-year mortality rate was 35% (95%CI=10%-66%). The 1-year recurrence/progression rate was 35% (95%CI=19%-52%), and the $ $2-year rate was 35% (95%CI=18%-54%). The 1-year stable disease rate was 60% (95%CI=34%-83%). The 1-year progression-free survival (PFS) rate was 52% (95%CI=44%-60%). The 6-month overall survival (OS) rate was 90% (95%CI=76%-99%), and the $ $1-year OS rate was 74% (95%CI=66%-80%).

Conclusion: Anti-BCMA CAR-T therapy demonstrates efficacy and acceptable safety for Chinese RRMM patients. However, limitations include small sample sizes and variable study quality. Larger-scale, high-quality randomized controlled trials are needed for further validation.

Keywords: Relapsed/refractory multiple myeloma; B-cell maturation antigen; Chimeric antigen receptor T-cell therapy; Meta-analysis

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Multiple myeloma (MM) is a B-cell malignancy characterized by clonal plasma cell proliferation, presenting clinically with hypercalcemia, anemia, and bone lesions. It accounts for approximately 10% of hematological malignancies in China, ranking second in incidence among hematological cancers [1]. The treatment of relapsed/refractory multiple myeloma (RRMM) has long challenged hematologists. Despite rapid development of various therapeutic agents over recent decades—including immunomodulatory drugs, proteasome inhibitors, and monoclonal antibodies—nearly all patients eventually relapse, necessitating

novel therapeutic approaches [2-5]. CAR-T cell therapy combines specific tumor antigen recognition with potent T-cell antitumor activity, demonstrating remarkable efficacy in malignant tumors, particularly hematological malignancies [6]. B-cell maturation antigen (BCMA) is essential for plasma cell survival and is typically highly expressed in malignant myeloma cells [7-8], making it a promising therapeutic target for RRMM patients. Numerous clinical trials have reported excellent efficacy and safety of anti-BCMA CAR-T therapy, with responses observed even in patients who have undergone multiple relapses or developed drug resistance after various treatments (proteasome inhibitors, immunomodulatory agents) [9]. However, clinical studies have reported high incidence rates of adverse events during CAR-T treatment, such as cytokine release syndrome (CRS) and cytopenias [10]. Therefore, additional clinical data are needed to further confirm the efficacy and safety of anti-BCMA CAR-T therapy. Moreover, no meta-analysis has systematically evaluated the evidence for its safety and efficacy in Chinese RRMM patients. To address this gap, we conducted this meta-analysis to better assess the effectiveness and safety of anti-BCMA CAR-T therapy for Chinese RRMM patients.

Methods

Study Design: Single-arm studies.

Participants: Chinese patients meeting the International Myeloma Working Group (IMWG) diagnostic criteria for RRMM. All patients had BCMA expression in RRMM cells at enrollment and were observed for over 12 months post anti-BCMA CAR-T cell therapy unless death occurred due to RRMM.

Exclusion Criteria: (1) Duplicate publications; (2) Studies with unavailable or insufficient data; (3) Non-Chinese or non-English literature; (4) Reviews, case reports, editorials, animal studies, or cell studies.

Search Strategy: We searched Web of Science, PubMed, Embase, VIP, Wanfang Data, and CNKI databases for studies on anti-BCMA CAR-T cell therapy in Chinese RRMM patients. Searches combined subject terms and free-text terms, adjusted according to database characteristics. Search terms included: refractory/relapsed multiple myeloma, multiple myeloma, BCMA chimeric antigen receptor T-cell, B-Cell Maturation Antigen, Receptors, Chimeric Antigen, Multiple Myeloma, etc.

Study Selection: Two investigators independently screened titles and abstracts, reviewed full texts of potentially relevant articles, extracted data, and cross-checked results. Disagreements were resolved by a third reviewer. Extracted data included basic study information, baseline participant characteristics, key elements for bias risk assessment, and outcome indicators.

Risk of Bias Assessment: Two investigators independently evaluated the risk of bias using the MINORS (Methodological Index for Non-Randomized Studies) scale, which contains 12 items scored 0-2 points each (0=not mentioned,

1=mentioned but incomplete, 2=adequately reported). Since all studies lacked control groups, only 8 applicable items were used, with a maximum score of 16 points per study. Publication bias was assessed using funnel plots and Egger' s test [11].

Statistical Analysis: Meta-analysis of single-arm studies was performed using Stata 16.0 software. Heterogeneity was assessed using the I^2 statistic. A fixed-effects model was used when no or low heterogeneity was detected ($P>0.1$ and $I^2<50\%$). For substantial heterogeneity ($P<0.1$ or $I^2>50\%$), we investigated potential causes and used a random-effects model after excluding studies causing significant clinical heterogeneity. The significance level was set at $\alpha=0.05$. For obvious clinical heterogeneity, sensitivity analysis was performed by sequentially removing individual studies, or descriptive analysis was conducted [12].

Results

The database search yielded 3,356 relevant articles: PubMed (n=462), Embase (n=1,495), Web of Science (n=1,108), CNKI (n=56), Wanfang (n=207), and VIP (n=28). After removing duplicates (n=1,794) and screening titles/abstracts (n=1,926), 48 articles underwent full-text review. Thirty articles were excluded: 17 non-single-arm studies, 6 registered trials without results, 4 lacking outcome indicators, and 3 duplicate publications. Ultimately, 18 studies [9,13-29] involving 684 patients were included in the qualitative and quantitative synthesis. The literature screening flowchart is shown in Figure 1 [Figure 1: see original paper].

The 18 studies included 684 RRMM patients with a median age of 56 years. All were single-arm studies without control groups, with sample sizes ranging from 4 to 105 patients. Basic characteristics of included studies are presented in Table 1 .

Efficacy Outcomes Objective Response Rate (ORR): Eleven studies [9,15-16,18-21,23,25,27-28] reported ORR. High heterogeneity was observed ($I^2=82.68\%$, $P<0.01$), so a random-effects model was used. The pooled ORR was 86% (95%CI=76%-94%), as shown in Figure 2 [Figure 2: see original paper].

Stringent Complete Response (sCR) Rate: Seven studies [9,16,18-19,21-22,26] reported sCR. Low heterogeneity was found ($I^2=40.24\%$, $P=0.12$), so a fixed-effects model was used. The pooled sCR rate was 67% (95%CI=58%-75%).

Complete Response (CR) Rate: Thirteen studies [13,16-18,20-28] reported CR. High heterogeneity was observed ($I^2=78.82\%$, $P<0.01$), requiring a random-effects model. The pooled CR rate was 54% (95%CI=44%-65%), as shown in Figure 3 [Figure 3: see original paper].

Very Good Partial Response (VGPR) Rate: Eight studies [13,16,19,21-22,24,26-27] reported VGPR. High heterogeneity was present ($I^2=61.40\%$,

P<0.01), and the random-effects model yielded a pooled VGPR rate of 16% (95%CI=8%-24%).

Partial Response (PR) Rate: Eight studies [9,13,17,21-22,24,26-27] reported PR. Low heterogeneity was found (I^2=35.86%, P=0.14), and the fixed-effects model showed a pooled PR rate of 17% (95%CI=13%-22%), as shown in Figure 4 [Figure 4: see original paper].

Sensitivity Analysis: For outcomes with I^2>50%, we performed sensitivity analysis by sequentially removing individual studies. Excluding the study by Liu et al. [27] substantially changed ORR and VGPR results. ORR heterogeneity decreased (I^2=49.19%, P=0.04) with a pooled ORR of 92% (95%CI=88%-95%), as shown in Figure 5 [Figure 5: see original paper]. VGPR heterogeneity also decreased (I^2=29.23%, P=0.21) with a pooled VGPR rate of 17% (95%CI=12%-22%), as shown in Figure 6 [Figure 6: see original paper]. After excluding studies by Liu et al. [27], Zhang et al. [28], and Wang et al. [26], CR heterogeneity decreased (I^2=51.47%, P=0.03) with a pooled CR rate of 46% (95%CI=38%-55%), as shown in Figure 7 [Figure 7: see original paper]. These findings suggest that efficacy results should be interpreted cautiously.

Safety Outcomes Cytokine Release Syndrome (CRS): Seventeen studies [9,13-28] reported CRS. High heterogeneity was observed (I^2=96.04%, P<0.01), and the random-effects model showed a pooled CRS rate of 76% (95%CI=56%-92%), as shown in Figure 8 [Figure 8: see original paper]. Eighteen studies [9,13-29] reported grade $ 3$CRSwithhighheterogeneity(I^{2}$=88.62%, P<0.01), yielding a pooled rate of 16% (95%CI=8%-26%).

Leukopenia: Eight studies [9,14-18,20,25] reported leukopenia. High heterogeneity was present (I^2=83.90%, P<0.01), and the random-effects model showed a pooled leukopenia rate of 91% (95%CI=74%-100%). Nine studies [9,14-18,20-21,25] reported grade $ 3$leukopeniawithhighheterogeneity(I^{2}$=88.16%, P<0.01), yielding a pooled rate of 70% (95%CI=47%-90%).

Neutropenia: Seven studies [9,15-16,18,20,23,25] reported neutropenia. High heterogeneity was observed (I^2=94.90%, P<0.01), and the random-effects model showed a pooled neutropenia rate of 82% (95%CI=54%-99%). Seven studies [9,15-16,18,20,23,25] reported grade $ 3$neutropeniawithhighheterogeneity(I^{2}$=91.63%, P<0.01), yielding a pooled rate of 74% (95%CI=52%-92%).

Thrombocytopenia: Nine studies [9,14-15,17-18,20,23-25] reported thrombocytopenia. High heterogeneity was present (I^2=89.37%, P<0.01), and the random-effects model showed a pooled thrombocytopenia rate of 81% (95%CI=64%-95%), as shown in Figure 9 [Figure 9: see original paper]. Nine studies [9,14-15,17-18,20,23-25] reported grade $ 3$thrombocytopeniawithhighheterogeneity(I^{2}$=82.68%, P<0.01), yielding a pooled rate of 54% (95%CI=37%-70%).

Anemia: Nine studies [9,14-18,20,23,25] reported anemia. High heterogeneity was observed (I^2=96.00%, P<0.01), and the random-effects model showed

a pooled anemia rate of 78% (95%CI=44%-99%), as shown in Figure 10 [Figure 10: see original paper]. Ten studies [9,14-18,20-21,23,25] reported grade $ 3*anemiawithhighheterogeneity*(I^{2}=82.07%, P<0.01), yielding a pooled rate of 55% (95%CI=38%-70%).

Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS): Seven studies [16,19,20-21,24,26,28] reported ICANS. High heterogeneity was present (I^2=71.38%, P<0.01), and the random-effects model showed a pooled ICANS rate of 13% (95%CI=4%-24%). Six studies [14,16,20-21,24,26] reported grade $ 3*ICANSwithlowheterogeneity*(I^{2}=0, P=0.92), and the fixed-effects model showed no grade $ $3 ICANS cases (95%CI=0-2%). Sensitivity analysis of safety indicators showed that no individual study significantly affected the meta-analysis results, indicating relatively stable findings.

Prognostic Outcomes **Mortality:** Six studies [9,14,17,23,24,28] reported 1-year mortality with low heterogeneity (I^2=0, P=0.60). The fixed-effects model showed a pooled 1-year mortality rate of 3% (95%CI=1%-7%), as shown in Figure 11 [Figure 11: see original paper]. Six studies [14,17-18,20,22,29] reported $ 2 − *yearmortalitywithhighheterogeneity*(I^{2}=91.03%, P<0.01), and the random-effects model showed a pooled rate of 35% (95%CI=10%-66%).

Recurrence or Progression: Four studies [9,16-17,19] reported 1-year recurrence/progression rate with low heterogeneity (I^2=38.92%, P=0.18). The fixed-effects model showed a pooled rate of 35% (95%CI=19%-52%). Seven studies [18,20,22-23,25,28-29] reported $ 2−*yearrecurrence/progressionratewithhighheterogeneity*(I^{2}=91.71%, P<0.01), and the random-effects model showed a pooled rate of 35% (95%CI=18%-54%).

Stable Disease: Two studies [9,21] reported 1-year stable disease rate with low heterogeneity (I^2=0). The fixed-effects model showed a pooled rate of 60% (95%CI=34%-83%).

Progression-Free Survival (PFS): Five studies [14,19,21,25,28] reported 1-year PFS rate with low heterogeneity (I^2=36.08%, P=0.18). The random-effects model showed a pooled 1-year PFS rate of 52% (95%CI=44%-60%).

Overall Survival (OS): Two studies [14,21] reported 6-month OS rate with low heterogeneity (I^2=0, P>0.05). The fixed-effects model showed a pooled 6-month OS rate of 90% (95%CI=76%-99%). Six studies [14-15,19,21,25,27] reported $ 1 − *yearOSratewithlowheterogeneity*(I^{2}=0, P=0.51). The fixed-effects model showed a pooled $ $1-year OS rate of 74% (95%CI=66%-80%), as shown in Figure 12 [Figure 12: see original paper].

Publication Bias Funnel plots for ORR, CR, and CRS were constructed. The CRS funnel plot was essentially symmetrical, showing no significant publication bias. Egger' s test for ORR and CR yielded P-values of 0.178 and 0.409, respectively, indicating no obvious publication bias, as shown in Figures 13-15

[Figure 13: see original paper][Figure 14: see original paper][Figure 15: see original paper].

Discussion

Cancer treatment has evolved from traditional chemotherapy to specific immune-based therapeutic strategies. Despite the emergence of novel agents such as immunomodulatory drugs, proteasome inhibitors, and monoclonal antibodies that have substantially improved multiple myeloma outcomes [30], relapse and refractory disease remain problematic, with nearly all patients eventually relapsing and those with high-risk cytogenetic features or treatment-refractory disease experiencing poor survival outcomes [31-34]. A study by Kumar et al. [35] showed that 6-year OS rates improved from 31% in 2001-2005 to 56% in 2006-2010. However, due to factors such as antigen escape, poor CAR-T cell persistence, complex tumor microenvironment, defective DNA repair mechanisms, and altered or mutated drug target expression [36], many patients still respond poorly to novel agents or develop resistance, ultimately experiencing disease progression and relapse. Thus, developing new treatments for RRMM is urgently needed.

Previous studies have demonstrated that CAR-T therapy can improve life expectancy in RRMM patients. In a study of 16 RRMM patients receiving anti-BCMA CAR-T cell therapy, the median event-free survival was 7.1 months [37]. However, research on anti-BCMA CAR-T cell therapy for Chinese RRMM patients remains exploratory, with varying methodologies and sample sizes across studies, necessitating systematic analysis. Therefore, this meta-analysis was conducted to systematically evaluate the efficacy and safety of anti-BCMA CAR-T cell therapy for Chinese RRMM patients.

Our results demonstrate that anti-BCMA CAR-T cell therapy shows favorable outcomes and tolerable toxicity in RRMM patients. BCMA-targeted CAR-T and BCMA-containing regimens contribute to improved efficacy and demonstrate excellent response quality. The National Cancer Institute' s Brudno et al. [37] reported the first-in-human study of anti-BCMA CAR-T therapy for RRMM, showing an ORR of 81.3% in the high-dose cohort. Another meta-analysis reported an ORR of 82% for anti-BCMA CAR-T therapy in RRMM, consistent with our findings. Notably, CAR-T therapy demonstrates superior response rates compared to some other regimens: bortezomib/dexamethasone (ORR 82.9%) [38], ixazomib/lenalidomide/dexamethasone (ORR 78%) [39], and carfilzomib/dexamethasone (ORR 77%) [40]. Conventional treatments rarely achieve CR, with even autologous transplantation yielding only 40% CR [41], highlighting the remarkable efficacy of anti-BCMA CAR-T therapy for RRMM.

BCMA, also known as CD269 and TNF receptor superfamily 17 (TNFRSF17), is selectively expressed in multiple myeloma cell lines and plays an important role in malignant B-lymphocyte proliferation and differentiation, making it an ideal antigenic target [42]. Studies show BCMA expression is limited to mature B-lymphoid compartments, making it a promising target for RRMM patients

[43]. To generate CAR-T cells that specifically recognize tumor surface antigens, T cells from patients or healthy donors are genetically modified with a specific tumor-targeting receptor called CAR. The CAR structure contains a single-chain variable fragment (scFv) that enables specific recognition of tumor surface antigens without MHC-restricted antigen presentation. Similar to effector T cells, CAR-T cells mediate tumor killing through multiple mechanisms, including secretion of cytotoxic granules containing perforin and granzyme, production of pro-inflammatory cytokines such as interferon (IFN)-γ and tumor necrosis factor (TNF)-α, and activation of the Fas/Fas ligand (Fas/FasL) pathway. Numerous BCMA-targeted CAR-T products have been applied in active clinical trials, with many RRMM patients achieving objective responses after anti-BCMA CAR-T cell infusion, suggesting imminent clinical application.

Nevertheless, CAR-T cell therapy application may be limited by adverse reactions. CRS is the most common CAR-T-related toxicity, representing a systemic inflammatory reaction caused by immune activation associated with CAR-T cell proliferation. It releases massive amounts of cytokines, particularly interleukin (IL)-6, IL-10, and IFN-γ, overwhelming self-regulatory homeostatic control mechanisms [46]. Clinical manifestations range from mild symptoms such as muscle and joint pain, rash, headache, fever, and fatigue to severe conditions including shock, coagulation problems, fluid leakage, and organ failure. In rare cases, clinical and laboratory findings may resemble macrophage activation syndrome (MAS) [46-47]. Our analysis found CRS occurred in 76% of patients, highlighting the importance of CRS monitoring and management.

ICANS represents a neuropsychiatric condition associated with immune cell activity, appearing as a consequential complication after CAR-T cell infusion. ICANS exhibits variable clinical presentations, initially manifesting as toxic encephalopathy, dysphagia, and impaired motor function. In some cases, additional symptoms such as weakness, cerebral edema, and seizures may occur [48]. Our study found fewer patients experienced any-grade ICANS (13%) after treatment, demonstrating relative safety. Notably, a large proportion of ICANS patients had previously experienced and recovered from CRS, which may serve as an early indicator of ICANS. The primary goal of ICANS management is to alleviate inflammatory responses; one approach involves administering IL-6 antagonists. Siltuximab, an IL-6 antagonist, can prevent IL-6 from crossing the blood-brain barrier [49].

Our study showed rates of neutropenia, leukopenia, thrombocytopenia, and anemia of 82% (95%CI=54%-99%), 91% (95%CI=74%-100%), 81% (95%CI=64%-95%), and 78% (95%CI=44%-99%), respectively. In a study by Yu et al. [44], hematologic toxicities included neutropenia (75%), anemia (70%), and thrombocytopenia (65%), with febrile neutropenia in 20%. Our results are consistent with these findings. Except for delayed reactions occurring around 4 weeks post CAR-T infusion in a minority of patients, most cytopenias recover within 1 month. The vast majority of patients recover through appropriate interventions such as cytokine support (e.g., G-CSF for neutropenia, TPO for thrombocy-

topenia) [45].

Our results demonstrate that anti-BCMA CAR-T cell therapy shows favorable prognostic outcomes in RRMM patients, with low mortality rates and other prognostic indicators revealing high-quality prognosis and long-term efficacy and safety.

This study has several limitations. First, heterogeneity existed among studies. Although sensitivity analysis reduced heterogeneity for ORR, VGPR, and CR, most sensitivity analyses showed relatively robust results while significant heterogeneity remained. Heterogeneity may stem from multiple factors, including disease characteristics and patient attributes. For instance, patients in this meta-analysis spanned a wide age range and included patients with highly variable disease characteristics (e.g., cytogenetics). Additionally, studies employed different designs/methodologies and follow-up durations. Differences in baseline characteristics, performance status, disease status, and median prior treatment lines among study participants may also contribute. Nevertheless, sensitivity analyses indicated robustness of meta-analysis results. Second, included studies had high risk of bias and small sample sizes, comprising single-arm clinical trials that may be subject to selection and performance bias due to lack of randomization. Third, response duration was not analyzed due to variable follow-up durations. Fourth, quantitative analysis could not be performed for factors such as disease type, stage, and tumor burden due to the small number of articles and heterogeneity across studies. Additionally, confounding bias may exist due to differences in baseline characteristics, performance status, or disease status after different prior treatment lines.

This study provides insights into the efficacy and safety of anti-BCMA CAR-T cell therapy for Chinese RRMM patients. We believe that with further research, the efficacy of anti-BCMA CAR-T therapy in Chinese RRMM patients will become more reliable, and adverse reactions will be better prevented and controlled.

Author Contributions: Zhan Li and Xing Jinshan conceived and designed the study and analyzed feasibility. Zhan Li, Heng Zhaoyang, and He Liangyu collected data. He Liangyu, Zhao Jie, and Chen Jie organized data. Zhan Li and Heng Zhaoyang analyzed and interpreted results. Zhan Li drafted the manuscript. Zhan Li and He Liangyu revised the manuscript. Xing Jinshan provided overall responsibility and supervision.

Conflict of Interest: The authors declare no conflicts of interest.

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