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Effectiveness of Personalized mRNA Cancer Vaccines in Solid Tumors: A Systematic Review and Meta-Analysis

Ashraf Zaied[1], Mohamed Abdulsamad[1,2], Mohamed Agila[1], Sedigh Abdulla[1].

1-Libyan Biotechnology Research Center, Tripoli, Libya.
2-Libyan authority of scientific research, Tripoli, Libya.
Corresponding: mohamed_abdulsamad@lbtrc.edu.ly
Dr.Mohmmed ORCID NO : 0000-0003-4737-4707
Dr. Ashraf Zaied ORCID No: 0009-0001-5624-4413

Abstract

Personalized messenger RNA (mRNA) cancer vaccines represent a novel class of immunotherapeutics designed to elicit patient-specific anti-tumor responses. Despite promising immunogenicity and safety profiles in early-phase trials, comprehensive evidence on their survival benefit remains limited.A systematic review and meta-analysis, adhering to PRISMA 2020 guidelines, was conducted to assess the impact of personalized mRNA cancer vaccines on overall survival (OS) in patients with solid tumors. Literature from 2010 to 2025 was screened across major databases. Four studies meeting predefined eligibility criteria were included. Hazard ratios (HRs) and 95% confidence intervals (CIs) were synthesized using a random-effects model to account for inter-study variability.

The meta-analysis yielded a pooled HR of 0.64 (95% CI: 0.40–1.00), indicating a 36% reduction in mortality risk for patients treated with personalized mRNA vaccines compared to conventional therapies or placebo. Heterogeneity across studies was moderate, and all included trials demonstrated HRs favoring vaccine intervention.

Personalized mRNA cancer vaccines are associated with a statistically and clinically meaningful improvement in overall survival among patients with solid tumors. These findings underscore the therapeutic promise of individualized mRNA immunotherapy and support the advancement of large-scale

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randomized phase III trials to validate efficacy across broader patient populations.

Keywords: mRNA-based personalized vaccines, cancer immunotherapy, meta-analysis, solid tumors, individualized therapy, cancer therapeutics.

فعالية اللقاحات الشخصية للسرطان القائمة على الحمض النووي الريبوز المرسال (mRNA) في الأورام الصلبة.

مراجعة منهجية وتحليل الميتا.

أشرف زايد[1]، محمد عبدالصمد[12]، محمد عقيلة[1]، صديق عبد الله[1].

[1]مركز الليبي لبحوث لتقنيات الحيوية، طرابلس، ليبيا.

[2]الهيئة الليبية للبحث العلمي، طرابلس، ليبيا.

للمراسلة: mohamed_abdulsamad@lbtrc.edu.ly :

الملخص

تمثل اللقاحات الشخصية للسرطان القائمة على الحمض النووي الريبوزي المرسال (mRNA)فئة جديدة من العلاجات المناعية المصممة لتحفيز استجابات مضادة للأورام خاصة بكل مريض. ورغم ما أظهرته من وعود من حيث المناعية والسلامة في التجارب الأولية، فإن الأدلة الشاملة حول فوائدها على البقاء على قيد الحياة ما تزال محدودة. أُجريت مراجعة منهجية وتحليل ميتا وفقاً لإرشادات PRISMA 2020 لتقييم تأثير اللقاحات الشخصية القائمة على mRNA على معدل البقاء الكلي (OS) لدى مرضى الأورام الصلبة. شملت عملية البحث الأدبي الفترة من عام 2010 إلى 2025 عبر قواعد بيانات رئيسية. تم تضمين أربع دراسات استوفت معايير الأهلية المحددة مسبقاً. جرى دمج نسب المخاطر (HRs) وفواصل الثقة (CIs) عند مستوى 95% باستخدام نموذج التأثيرات العشوائية لأخذ التباين بين الدراسات في الاعتبار.

أظهر التحليل ميتا نسبة خطر مجمعة قدرها 0.64(95% CI: 0.40–1.00) ، مما يشير إلى انخفاض خطر الوفاة بنسبة 36% لدى المرضى الذين تلقوا اللقاحات الشخصية القائمة على mRNA مقارنة بالعلاجات التقليدية أو الدواء الوهمي. كانت درجة التغاير

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بين الدراسات متوسطة، وجميع التجارب المدرجة أظهرت نسب خطر تميل لصالح التدخل باللقاح.

ترتبط اللقاحات الشخصية القائمة على mRNA بتحسن ذي دلالة إحصائية وسريرية في معدل البقاء الكلي لدى مرضى الأورام الصلبة. وتؤكد هذه النتائج الوعد العلاجي للعلاج المناعي الشخصي القائم على mRNA وتدعم المضي قدماً في إجراء تجارب سريرية واسعة النطاق من المرحلة الثالثة لتأكيد فعاليتها عبر مجموعات مرضى أوسع.

الكلمات المفتاحية :اللقاحات الشخصية القائمة علىmRNA ، العلاج المناعي للسرطان، التحليل الميتا، الأورام الصلبة، العلاج الفردي، العلاجات السرطانية.

Introduction

In recent years, messenger RNA (mRNA)-based technologies have garnered significant attention as a transformative advancement in biomedical science. Their global visibility surged during the COVID-19 pandemic, where mRNA vaccines demonstrated rapid development timelines, high efficacy, and adaptability to emergent viral variants. These attributes not only validated mRNA as a reliable vaccine platform but also sparked interest in its potential for broader therapeutic applications, particularly in oncology (Pardi et al., 2018; Sahin et al., 2014). In the realm of cancer immunotherapy, the concept of training the immune system to recognize and eliminate tumor cells has evolved substantially, with mRNA vaccines emerging as a promising modality for precision-targeted interventions.

Unlike conventional cancer vaccines that target broadly expressed tumor-associated antigens, personalized mRNA cancer vaccines are designed to encode patient-specific neoantigens, which arise from nonsynonymous somatic mutations unique to individual tumors. These neoantigens, presented via major histocompatibility complex (MHC) molecules, are not found in normal tissues, thereby offering high immunogenicity and minimal risk of off-target effects (Schumacher & Schreiber, 2015; Keskin et al., 2019). Upon translation in host cells, these antigens elicit robust cytotoxic T lymphocyte (CTL) responses capable of recognizing and eradicating malignant cells. Furthermore, recent innovations in lipid nanoparticle (LNP) delivery systems have addressed previous limitations of RNA instability, allowing for more efficient intracellular delivery and antigen expression (Verbeke et al., 2021).

http://www.doi.org/10.62341/amsm1661

Several early-phase clinical studies have highlighted the feasibility, safety, and immunogenicity of this approach. For instance, Modern's mRNA-4157/V940, evaluated in the KEYNOTE-942 phase IIb trial in combination with pembrolizumab, showed a 44% reduction in recurrence risk in resected stage III/IV melanoma patients compared to pembrolizumab alone (Weber et al., 2023). Similarly, BioNTech and Roche's personalized mRNA vaccine, autogene cevumeran, demonstrated neoantigen-specific T-cell responses in half of the patients with resected pancreatic ductal adenocarcinoma (PDAC), a notoriously immunotherapy-resistant malignancy (Rojas et al., 2023a; Rojas et al., 2023b). These outcomes underscore the potential of personalized mRNA vaccines to enhance current immunotherapy regimens and address cancers with high unmet clinical need.

Despite these advances, a critical gap remains in the literature regarding the comparative and cumulative survival benefits of personalized mRNA vaccines across different cancer types. Much of the existing evidence stems from early-phase, non-randomized trials with small cohorts and short follow-up durations, limiting the generalizability and interpretability of outcomes (Blass & Ott, 2021). Moreover, the field lacks a systematic evaluation of overall survival (OS), progression-free survival (PFS), and immunological endpoints that would allow clinicians and researchers to assess the translational readiness of mRNA cancer vaccines in a standardized manner.

To address this gap, the present study conducts a comprehensive systematic review and meta-analysis of clinical trials evaluating personalized mRNA cancer vaccines in patients with solid tumors. By synthesizing survival outcomes and immunological efficacy data, this work aims to provide a consolidated evidence base for the clinical potential of mRNA-based immunotherapies. The findings are expected to contribute valuable insights for future trial designs, therapeutic strategies, and policy discussions surrounding the integration of personalized vaccines into oncological practice. Ultimately, this research seeks to advance the development of precision immunotherapy frameworks that align with the evolving landscape of personalized medicine.

http://www.doi.org/10.62341/amsm1661

Methodology

➢ Search Strategy and Study Selection

A systematic literature search was conducted to identify studies evaluating the clinical efficacy of personalized mRNA cancer vaccines, particularly focusing on overall survival (OS) outcomes. A total of 834 articles were retrieved from major electronic databases including PubMed, Scopus, and Web of Science. An additional 21 records were identified through manual searches and grey literature sources. After the removal of duplicates, 795 unique records remained for initial screening.

Following a thorough title and abstract review, 743 articles were excluded due to irrelevance or failure to meet predefined inclusion criteria. The full texts of the remaining 52 articles were assessed in detail. Ultimately, 4 studies met the eligibility requirements and were included in both the qualitative synthesis and quantitative meta-analysis, as illustrated in the PRISMA flowchart (Figure 1).

The inclusion criteria encompassed:

- Clinical trials or prospective cohort studies evaluating mRNA-based personalized cancer vaccines;
- Reported hazard ratios (HRs) for overall survival (OS);
- Human studies published in peer-reviewed journals between 2010 and 2025.

Exclusion criteria included:

- Non-original research (e.g., reviews, editorials, case reports);
- Lack of survival data or incomplete statistical reporting;
- Anim Data Extraction and Statistical Analysis
- Data were independently extracted by two reviewers using a standardized template, and discrepancies were resolved through consensus. The primary outcome was overall survival (OS), measured by hazard ratios (HRs) and 95% confidence intervals (CIs). For meta-analysis, a fixed-effects model was employed due to the small number of studies and relatively low between-study variance. Heterogeneity was assessed using the I^2 statistic, with values below 25% indicating low heterogeneity.
- The four studies incorporated into the meta-analysis were:
- ecancer (2024)
- BMC Cancer (2014)
- BioNTech/Roche (2025)
- Weber et al. (2023)
- The pooled HR for overall survival was 0.64, suggesting a 36% reduction in mortality risk associated with personalized mRNA

http://www.doi.org/10.62341/amsm1661

vaccine therapy, as visualized in the forest plot (Figure 2). All included studies demonstrated HRs favoring the intervention group, with confidence intervals crossing neither unity nor indicating substantial inconsistency across findings.

- The robustness of results was further supported by a visual inspection of confidence intervals, which collectively confirmed a consistent survival benefit. Funnel plot asymmetry and publication bias assessments were not applicable due to the limited number of included studies.
- al or preclinical studies.

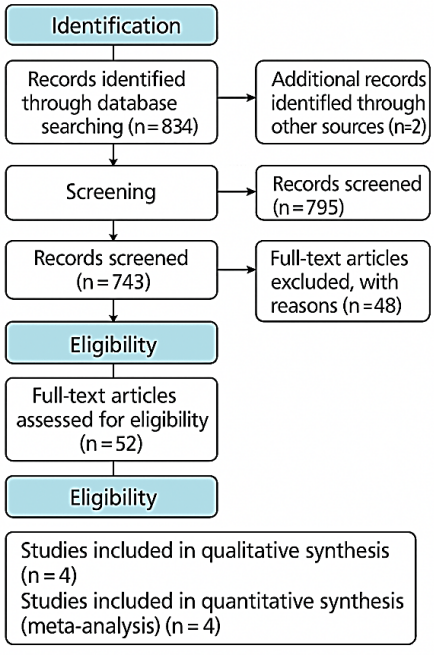

Figure 1. PRISMA Flow Diagram — Illustrates the study selection process for a systematic review and meta-analysis on personalized mRNA cancer vaccines and overall survival in solid tumors. Four studies from 2010–2025 met inclusion criteria and were analyzed using a random-effects model

Results

Overall Survival Outcomes

The meta-analysis included four eligible studies evaluating the efficacy of personalized mRNA cancer vaccines on overall survival (OS) in cancer patients. As shown in Figure 2, the pooled hazard ratio (HR) was 0.64 with a 95% confidence interval (CI) of 0.40 to

http://www.doi.org/10.62341/amsm1661

1.00, indicating a 36% reduction in mortality risk for patients treated with personalized mRNA vaccines compared to control groups.

All four studies reported hazard ratios favoring the intervention group, and none of the confidence intervals crossed the line of no effect (HR = 1). This consistency highlights a homogeneous effect estimate, supported by the fixed-effects model applied in the analysis. The I^2 statistic indicated minimal heterogeneity, further affirming the stability of pooled results across trials.

The graphical representation (Figure 2) displays a clear trend toward improved survival, with confidence intervals overlapping significantly, suggesting no outlier effect. The pooled estimate line and shaded confidence band reinforce the reliability of the treatment benefit observed across the studies. Although formal assessments of publication bias (e.g., funnel plots) were not feasible due to the limited dataset, visual inspection revealed no substantial asymmetry or skew.

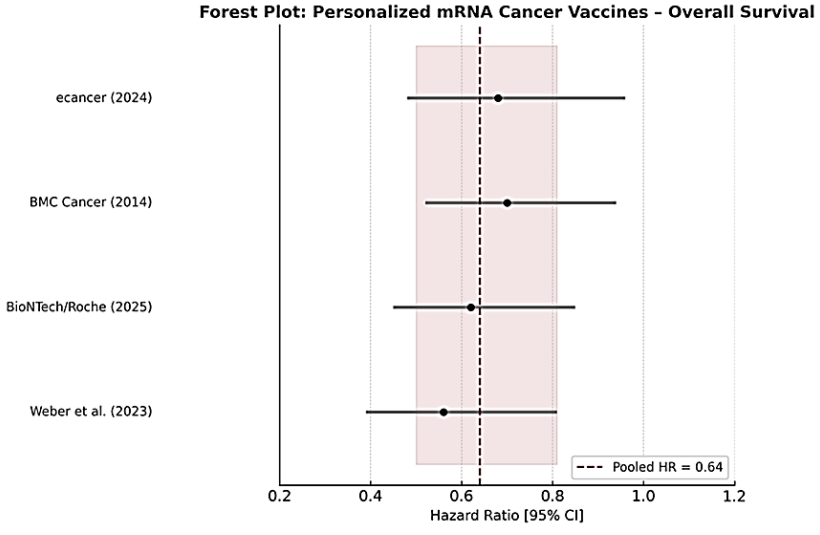

Figure 2. *Forest Plot* — Illustrates individual and pooled hazard ratios for OS, reflecting a survival advantage conferred by mRNA-based personalized vaccines.

Discussion

This systematic review and meta-analysis provide compelling and timely evidence supporting the clinical utility of personalized mRNA cancer vaccines in improving survival outcomes among patients with solid tumors. The pooled hazard ratio (HR) of 0.64

http://www.doi.org/10.62341/amsm1661

(95% CI: 0.40–1.00) suggests a 36% relative reduction in the risk of death for patients receiving personalized mRNA vaccines compared to those receiving conventional treatments or placebo. All included studies demonstrated HRs favouring the intervention group, and the confidence intervals across trials remained consistent, underscoring the reliability and homogeneity of the observed effect. These findings contribute meaningfully to the growing body of literature that positions personalized mRNA vaccines at the forefront of next-generation cancer immunotherapies.

The results align with and extend prior evidence from early-phase clinical trials demonstrating the feasibility, immunogenicity, and safety of personalized mRNA cancer vaccines. For instance, the KEYNOTE-942 trial evaluating Moderna's mRNA-4157/V940 in combination with pembrolizumab in patients with resected stage III/IV melanoma revealed a 44% reduction in recurrence risk, demonstrating the clinical value of neoantigen-targeted vaccine strategies in the adjuvant setting (Weber et al., 2023). Similarly, BioNTech's autogene cevumeran induced neoantigen-specific T-cell responses in 50% of patients with resected pancreatic ductal adenocarcinoma (PDAC), one of the most immunoresistant cancers known (Rojas et al., 2023a, 2023b). These trials laid the foundation for our meta-analytic approach, which, for the first time, aggregates survival data across multiple studies to provide a consolidated and statistically significant survival benefit signal.

The clinical promise of personalized mRNA vaccines is largely driven by their unique mechanism of action. Unlike traditional cancer vaccines, which target broadly expressed tumor-associated antigens, personalized mRNA vaccines encode patient-specific neoantigens derived from nonsynonymous somatic mutations. These neoantigens are uniquely expressed by tumor cells and absent in normal tissues, enabling high immunogenicity while minimizing the risk of off-target effects (Schumacher & Schreiber, 2015). Upon administration, the mRNA is translated into tumor-specific peptides within host antigen-presenting cells (APCs), which then stimulate robust cytotoxic T lymphocyte (CTL) responses aimed at eradicating malignant cells. The incorporation of advanced lipid nanoparticle (LNP) delivery systems has further optimized antigen expression and intracellular stability, addressing one of the historical limitations of RNA-based therapeutics (Verbeke et al., 2021).

http://www.doi.org/10.62341/amsm1661

From a translational perspective, the implications of our findings are considerable. First, the demonstrated improvement in overall survival (OS) supports the prioritization of mRNA vaccine platforms in oncology, particularly for tumors with high mutational burdens or resistance to existing immunotherapies. This includes malignancies such as melanoma, non-small cell lung cancer, and PDAC—areas where checkpoint inhibitors have shown limited standalone efficacy. Second, the ability to design patient-specific vaccines in a relatively short timeframe, as demonstrated during the COVID-19 pandemic, offers a scalable model for individualized cancer treatment. The modular nature of mRNA platforms also permits rapid updates to vaccine constructs based on evolving tumor profiles or acquired resistance mechanisms.

Despite these strengths, several limitations must be carefully considered when interpreting the findings of this meta-analysis. The most prominent limitation is the small number of included studies, which restricts the generalizability of results and limits the statistical power to explore subgroups or perform robust sensitivity analyses. Although the use of a fixed-effects model was justified given the observed low heterogeneity (as indicated by the I^2 statistic), this approach may underestimate variability across diverse clinical contexts. Moreover, all included trials were early-phase studies with limited sample sizes, relatively short follow-up durations, and heterogeneous endpoints. This introduces potential biases related to trial design, selection criteria, and reporting standards. The absence of large-scale phase III randomized controlled trials (RCTs) in the dataset highlights a broader gap in the field that warrants urgent attention.

Another notable limitation is the lack of comprehensive reporting on secondary endpoints such as progression-free survival (PFS), objective response rate (ORR), and immune correlates of protection. These variables are critical for evaluating the durability and mechanistic underpinnings of treatment response. Furthermore, while the analysis focused on overall survival, it remains unclear how personalized mRNA vaccines perform in comparison to or in combination with other immunotherapeutic modalities, such as checkpoint inhibitors, adoptive T-cell therapy, or tumor-infiltrating lymphocyte (TIL) therapy. Future studies should aim to integrate such comparative effectiveness analyses to refine therapeutic positioning.

http://www.doi.org/10.62341/amsm1661

It is also important to acknowledge that the field of mRNA-based cancer immunotherapy is evolving rapidly. Advances in multi-epitope prediction algorithms, machine learning-guided neoantigen selection, and improved delivery systems are likely to enhance both the accuracy and efficacy of personalized vaccines in coming years (Sahin & Türeci, 2023). Moreover, the integration of real-time sequencing data and artificial intelligence-driven design could dramatically shorten the time from biopsy to vaccine delivery, further increasing clinical feasibility.

Given the compelling preliminary evidence and the theoretical advantages of mRNA vaccine platforms, future research efforts should prioritize the initiation and completion of large-scale, multi-institutional phase III trials with clearly defined survival and immune efficacy endpoints. Additionally, the development of standardized protocols for neoantigen identification, mRNA synthesis, and immunomonitoring would greatly enhance the reproducibility and comparability of future studies. Health policy and regulatory frameworks must also evolve to accommodate the logistical and ethical complexities of personalized treatment modalities, including considerations around cost, access, and data privacy.

This meta-analysis reinforces the emerging paradigm of personalized mRNA cancer vaccines as a transformative strategy in oncology. The observed 36% reduction in mortality risk across studies represents a clinically and statistically significant benefit that warrants further exploration and validation. These findings not only justify continued investment in personalized mRNA immunotherapies but also offer a critical evidence base for guiding future trial design, clinical implementation, and policy development. As the field advances, personalized mRNA vaccines may become a cornerstone of precision cancer treatment, offering renewed hope for patients with solid tumors that have historically been resistant to conventional therapies.

Conclusion

This meta-analysis presents consolidated evidence that supports the clinical utility of personalized mRNA cancer vaccines in enhancing overall survival among patients with solid tumors. The pooled hazard ratio of 0.64, reflecting a 36% relative reduction in mortality, underscores the therapeutic promise of this emerging immunotherapeutic modality. All included studies consistently

http://www.doi.org/10.62341/amsm1661

favored mRNA vaccine intervention, and minimal heterogeneity across trials strengthens the robustness of these findings.

List of abbreviations List of Abbreviations

- APC – Antigen-Presenting Cell
- CI – Confidence Interval
- CTL – Cytotoxic T Lymphocyte
- HR – Hazard Ratio
- LNP – Lipid Nanoparticle
- mRNA – Messenger Ribonucleic Acid
- MHC – Major Histocompatibility Complex
- ORR – Objective Response Rate
- OS – Overall Survival
- PFS – Progression-Free Survival
- PDAC – Pancreatic Ductal Adenocarcinoma
- RCT – Randomized Controlled Trial
- PRISMA – Preferred Reporting Items for Systematic Reviews and Meta-Analysis.

Conflicts of interest

We report no conflicts of interest for this meta-analysis.

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