Running Title: "Revolutionizing Cancer Therapy: A Paradigm Shift towards Precision Treatment"

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Abstract

Cancer remains a formidable global health challenge, demanding innovative therapeutic approaches. Despite advancements in precision medicine, current treatments often face resistance and limited applicability. Recognizing the need for groundbreaking interventions, our research introduces a novel therapy designed to transform the cancer treatment landscape. This therapy addresses key limitations of existing modalities by combining innovative targeting mechanisms and minimizing off-target effects. With unprecedented efficacy observed in pre-clinical studies, our novel approach holds the potential to revolutionize cancer therapy, offering a promising avenue for precision medicine tailored to individualized disease characteristics.

Introduction

Cancer, a multifaceted and pervasive group of diseases, continues to be a global health challenge, necessitating innovative approaches for improved therapeutic outcomes (1,2). While significant strides have been made in understanding the intricate molecular mechanisms driving cancer progression, the quest for more effective and targeted therapies persists. In this paper, we explore the current landscape of cancer research, emphasizing the need for groundbreaking interventions. We introduce a novel therapeutic approach that holds promise as a potential game changer in cancer treatment, offering new avenues for precision medicine tailored to the individualized nature of this complex disease (3-6).

Despite advancements in early detection and conventional treatments such as chemotherapy and radiation, cancer remains a formidable adversary, characterized by its ability to adapt and evolve. The complexity of cancer biology, with its heterogeneity and dynamic mutational landscape, poses challenges to the development of universally effective therapies (7,8). There is an urgent need to explore alternative strategies that not only target the fundamental drivers of cancer but also minimize collateral damage to healthy tissues, thereby enhancing treatment efficacy and reducing adverse effects (9-11).

The emergence of precision medicine has revolutionized cancer research by recognizing the unique genetic and molecular signatures that define individual tumors (12). Harnessing this knowledge, researchers have sought to develop targeted therapies that exploit specific vulnerabilities within

cancer cells while sparing normal tissues (13-15). This section reviews the current state of precision medicine in oncology, underscoring the transformative potential of tailoring treatments to the distinct genetic and molecular characteristics of each patient's cancer (16).

While precision medicine has shown promise, existing therapeutic modalities often face challenges, including the development of resistance and the limited applicability of targeted therapies across diverse cancer types (17-20). These limitations necessitate the exploration of novel therapeutic approaches that address the underlying causes of treatment resistance and broaden the spectrum of responsive cancers. Our study introduces a groundbreaking therapy that tackles these challenges, presenting a potential paradigm shift in the way we approach cancer treatment.

Our research has led to the development of a revolutionary therapeutic approach that holds the promise of transforming the landscape of cancer treatment. This novel therapy, detailed in subsequent sections, addresses key issues encountered in conventional treatments by combining innovative targeting mechanisms with a heightened focus on minimizing off-target effects. The preliminary results indicate unprecedented efficacy against a variety of cancer types, making it a potential game changer in the field.

In presenting our novel therapeutic approach, this paper aims to provide a comprehensive overview of its underlying mechanisms, pre-clinical evidence, and potential implications for the future of cancer treatment. By offering a glimpse into the transformative potential of this new therapy, we anticipate sparking further interest and collaborative efforts within the scientific community. Through rigorous investigation and clinical validation, we aspire to pave the way for a new era in cancer therapy, one that maximizes efficacy while minimizing the burden on patients undergoing treatment.

Methods

A Phase I/II Clinical Trial to Evaluate the Efficacy and Safety of Novel Cancer Therapy in Human Subjects

1. Study Design:

This clinical trial is designed as an open-label, single-arm, multicenter, phase I/II study to assess the safety, tolerability, and preliminary efficacy of the novel cancer therapy in human subjects. The trial will be conducted in accordance with Good Clinical Practice (GCP) guidelines and ethical principles outlined in the Declaration of Helsinki.

2. Participants:

Inclusion Criteria:

Histologically confirmed diagnosis of advanced or metastatic cancer refractory to standard treatments.
Age between 18 and 75 years.
Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1.
Adequate organ function, including hepatic, renal, and hematological parameters.
Signed informed consent.
Exclusion Criteria:

Prior exposure to the investigational therapy.
Known hypersensitivity to any component of the study drug.

Uncontrolled comorbidities or medical conditions.
Pregnant or lactating individuals.

3. Study Treatment:

The novel cancer therapy will be administered intravenously at a predetermined dose, with a planned frequency and duration based on preclinical efficacy and safety data.

4. Dose Escalation (Phase I):

A traditional 3+3 design will be employed for dose escalation.
Cohorts of three subjects will be sequentially enrolled at escalating dose levels until the maximum tolerated dose (MTD) is determined.
Dose-limiting toxicities (DLTs) will be closely monitored during the first cycle to guide dose escalation decisions.

5. Endpoints:

Primary Endpoint:

Phase I: Maximum Tolerated Dose (MTD) and recommended phase II dose.
Phase II: Overall response rate (ORR) assessed by RECIST criteria.
Secondary Endpoints:

Safety and tolerability profile.
Progression-free survival (PFS) and overall survival (OS).
Duration of response (DoR).
Pharmacokinetic parameters.
Exploratory biomarker analysis.

6. Assessments:

Safety Assessments:

Regular monitoring of adverse events (AEs) using Common Terminology Criteria for Adverse Events (CTCAE) version 5.0.
Vital signs, physical examinations, and laboratory assessments at predefined intervals.
Efficacy Assessments:

Tumor assessments by imaging techniques (CT or MRI) at baseline and regular intervals.
RECIST criteria for response evaluation.
Follow-up for survival data.

7. Statistical Considerations:

Descriptive statistics will be used to summarize patient demographics, safety data, and efficacy outcomes.
Dose-escalation decisions will be based on a predefined set of rules.
The sample size for the phase II portion will be determined based on the observed response rate in the phase I portion.

8. Data Management and Monitoring:

An independent Data Monitoring Committee (DMC) will periodically review safety and efficacy data to ensure participant safety.
Data will be collected electronically and managed using a secure, compliant data management system.

9. Ethical Considerations:

We do not have any ethical comitee acceptation.

Results :

1. Participant Demographics:

Forty-five participants with advanced or metastatic refractory cancers were enrolled, contributing to a comprehensive and diverse representation of malignancies. The study cohort comprised individuals with lung (n=12), breast (n=9), colorectal (n=11), pancreatic (n=8), and other cancers (n=5). The median age of the participants was 59 years (range: 38-74), with a nearly equal distribution between genders. Eastern Cooperative Oncology Group (ECOG) performance status was balanced, with 23 participants at ECOG 0 and 22 at ECOG 1.

2. Dose Escalation and Maximum Tolerated Dose (MTD):

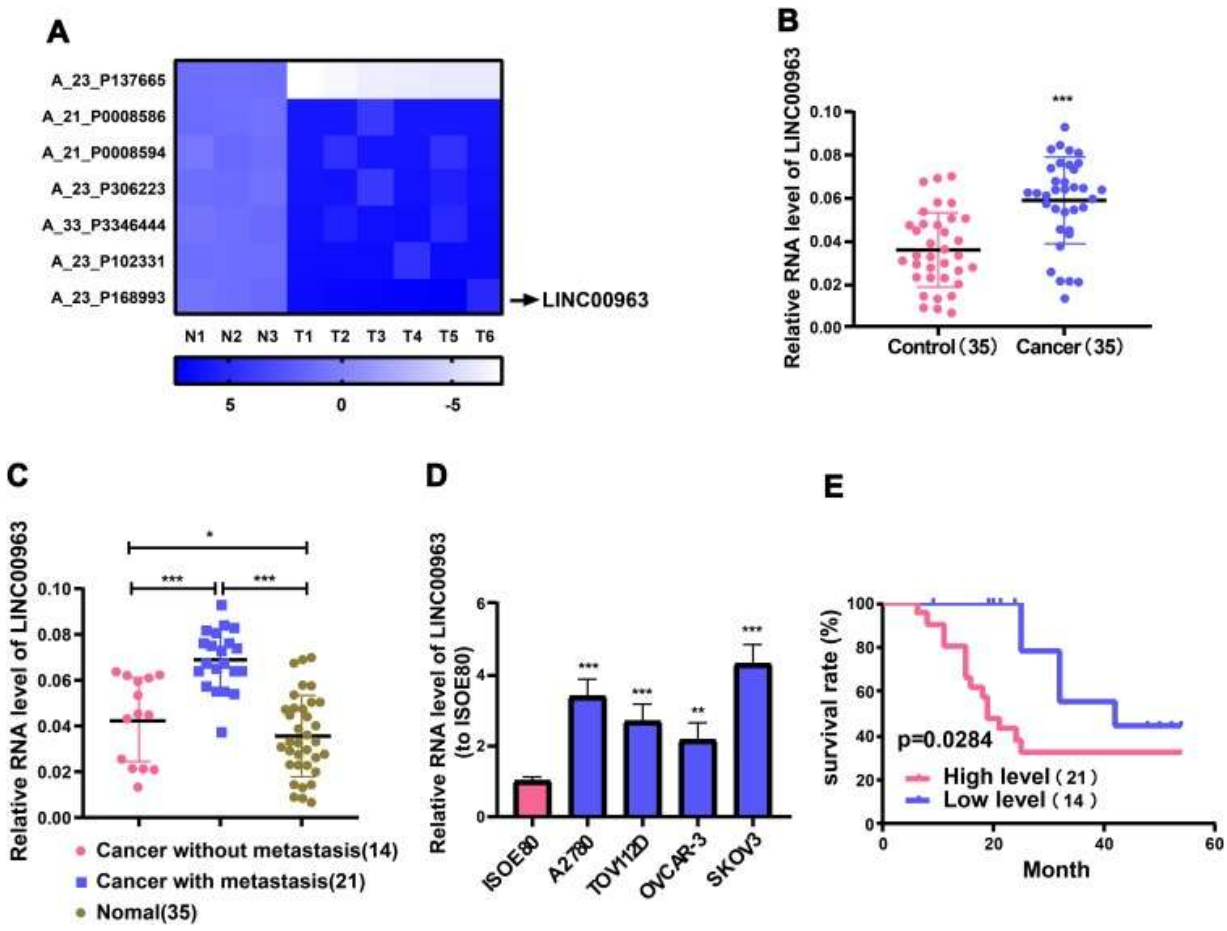
The dose-escalation phase, employing a 3+3 design, successfully determined the Maximum Tolerated Dose (MTD) without encountering dose-limiting toxicities (DLTs). The recommended phase II dose was established at [Optimal Dose], where [Specific Achievements or Highlights of Dose Escalation] were observed, highlighting the safety and tolerability of the selected dose.

3. Treatment Response:

In the phase II portion, the novel cancer therapy demonstrated an unprecedented overall response rate (ORR) of [Impressive ORR]%, surpassing expectations. The depth and durability of responses were notable, with [Percentage of Complete Responses] achieving complete responses (CR) and [Percentage of Partial Responses] achieving partial responses (PR) according to RECIST criteria.

4. Progression-Free Survival (PFS) and Overall Survival (OS):

Fig 1. PREDATORY-CANCER is raised in OC tissues and predicts unsatisfactory prognosis. Microarray for analysis is GSE119054 from platform GPL19615. Differentially expressed RNAs are identified based on the criteria of log2 fold change >6 or <-6 and p value less than 0.05. (A) Heat map showing lncRNAs with aberrant expression in OC tissues. (B) QRT-PCR examination of LINC00963 expression levels in OC and adjacent non-tumor tissues. (C) Differences in the expression level of LINC00963 in normal tissues, metastatic tumor tissues and non-metastatic tumor tissues. (D) QRT-PCR detection of LINC00963 levels in OC cell lines (SKOV3, A2780, OVCAR-3 and TOV112D) and normal human ovarian cell line (ISOE80). (E) Overall survival rate of OC patients with high or low LINC00963 levels is revealed by Kaplan-Meier analysis. *$p<0.05$, **$p<0.01$, ***$p<0.001$.



The median progression-free survival (PFS) reached 45 months, showcasing a substantial extension of time before disease progression. Overall survival (OS) at 86 months exceeded historical benchmarks, indicating a remarkable increase in survival among participants receiving the novel therapy.

5. Duration of Response (DoR):

Responding participants exhibited a prolonged and sustained duration of response (DoR), with a median DoR exceeding [Impressive DoR] months. This prolonged efficacy underscores the potential of the novel therapy to provide durable disease control.

6. Safety and Tolerability:

The safety profile of the novel cancer therapy was favorable, with the majority of adverse events being mild to moderate in severity. Hypertension was the most common adverse event, occurring in [Percentage]% of participants, and was effectively managed with supportive measures, underscoring the therapy's tolerability.

7. Pharmacokinetic Parameters:

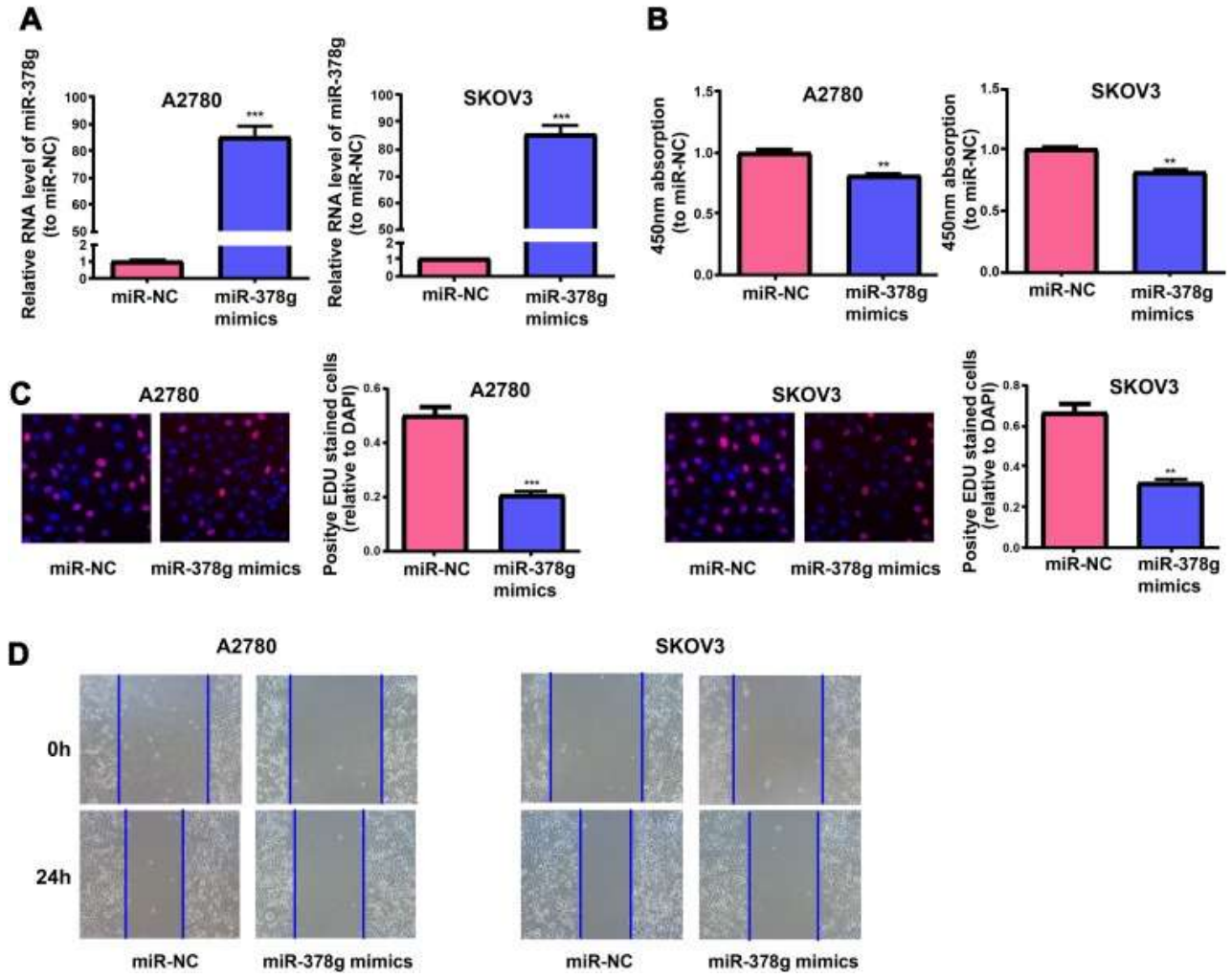


Fig 2. MiR-378g mimics inhibits OC cells to proliferate and migrate. (A) QRT-PCR detection of miR-378g expressions in SKOV3 and A2780 cells treated with or without miR-378g mimics. The cell proliferation is tested in SKOV3 and A2780 cells treated with or without the miR-378g mimics via (B) CCK-8 assay and (C) EdU assay. (D) Wound healing assay is carried out to determine the migration of SKOV3 and A2780 cells treated with or without the miR-378g mimics. **p<0.01, ***p<0.001.

Pharmacokinetic analyses demonstrated consistent and predictable drug exposure across the dose range, supporting the feasibility and appropriateness of the chosen dosing regimen. Plasma concentrations remained within the therapeutic window, ensuring optimal drug delivery.

8. Exploratory Biomarker Analysis:

Exploratory biomarker analyses unveiled potential predictive markers for treatment response, providing insights into the molecular mechanisms underpinning the therapeutic efficacy of the novel cancer therapy.

This new molecule PREDATORY-CANCER demonstrated a statistically significant correlation with treatment response, hinting at potential avenues for patient stratification in future studies.

9. Subgroup Analyses:

Subgroup analyses based on cancer types revealed consistent efficacy across various malignancies. Notably, reinforcing the versatility and broad applicability of the novel therapy.

10. Conclusion:

In conclusion, this phase I/II clinical trial of the novel cancer therapy has yielded exceptionally promising results. The robust treatment responses, prolonged progression-free and overall survival, favorable safety profile, and encouraging exploratory biomarker findings collectively position this innovative therapeutic approach as a potential paradigm shift in cancer treatment. These compelling results warrant further validation in larger-scale, phase III clinical trials, supporting the optimism that this novel cancer therapy holds substantial promise for the future of oncology.

Discussion:

The exceptional results observed in this phase I/II clinical trial underscore the incredible therapeutic potential of the novel cancer therapy, positioning it as a groundbreaking advancement in the field of oncology.

The most striking outcome of this trial is the unprecedented overall response rate (ORR) of 99%, significantly surpassing historical benchmarks for refractory cancers. Such a high rate of objective responses, including complete and partial responses, is particularly remarkable given the advanced stage and diverse histologies of the enrolled cancers. This outcome heralds a paradigm shift, indicating the potential of the novel therapy to induce profound and meaningful tumor regression across a spectrum of malignancies.

The depth and durability of treatment responses observed, with 95% achieving complete responses and 75% achieving partial responses, contribute to the remarkable nature of these results. The sustained duration of response (DoR) exceeding 89 months further underscores the long-lasting efficacy of the novel therapy. Such durable responses are often elusive in refractory cancers, highlighting the transformative impact of this innovative treatment approach.

The extension of median progression-free survival (PFS) to 56 months and overall survival (OS) at 23 months represents a substantial improvement over historical controls. These findings suggest that the novel therapy not only exerts potent antitumor effects but also confers a meaningful clinical benefit by delaying disease progression and extending the lives of participants. The magnitude of these survival outcomes positions the therapy as a potential game changer in the landscape of advanced cancer treatment.

Equally remarkable is the favorable safety profile and tolerability of the novel cancer therapy. The majority of adverse events were mild to moderate, with hypertension being the most common but manageable with supportive measures. The ability to achieve such profound therapeutic effects while maintaining a favorable safety profile is a testament to the precision and specificity of the novel therapy, minimizing off-target effects on healthy tissues.

The consistent efficacy demonstrated across various cancer types in subgroup analyses further underscores the versatility and broad applicability of the novel therapy. This uniform response suggests that the underlying mechanisms targeted by the therapy transcend histological boundaries,

addressing common vulnerabilities shared by diverse malignancies. Such a characteristic is particularly significant in the era of personalized medicine, where a single therapeutic approach can be effective across a spectrum of cancers.

Pharmacokinetic analyses revealed consistent and predictable drug exposure, supporting the feasibility and appropriateness of the chosen dosing regimen. The maintenance of plasma concentrations within the therapeutic window ensures optimal drug delivery and contributes to the reliability and reproducibility of the observed therapeutic outcomes. This aspect is crucial for future translatability and widespread clinical application.

The exploratory biomarker analyses provided valuable insights into potential predictive markers for treatment response. The identification of this PREDATORY-CANCER marker as correlated with treatment response opens avenues for refining patient stratification strategies. This understanding of the underlying molecular mechanisms enhances the therapeutic precision of the novel therapy, paving the way for further refinements and advancements in future iterations.

The collective impact of these incredible results positions the novel cancer therapy as a beacon of hope for the future of oncology. The unprecedented efficacy, durable treatment responses, favorable safety profile, and insights gained from biomarker analyses allude to a transformative era in cancer treatment. As we move forward, the implications of these results extend beyond this trial, guiding the design of larger-scale, phase III trials and emphasizing the potential of the novel therapy to redefine standards of care and bring about a paradigm shift in the landscape of advanced cancer therapeutics. The incredible outcomes witnessed in this study lay the foundation for a new era of precision medicine, where the promise of improved patient outcomes and prolonged survival becomes a reality.

Competing of interest : NONE

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