VERVE *Holistic Health*

ELEVATE YOUR VITALITY

AN EDUCATIONAL GUIDE

# CAR-NK *Exosome* Therapy

*Targeted, cell-free immune signaling — the next frontier in adjunctive cancer support.*

INTEGRATIVE ONCOLOGY SUPPORT AT VERVE

VERVE HOLISTIC HEALTH · TUSTIN, CALIFORNIA

*Elevate Your Vitality*

OVERVIEW

# What are CAR-NK exosomes?

*A new class of nanoscale immune messengers — engineered to carry the targeting precision of CAR therapy and the natural cancer-fighting cargo of NK cells, without infusing live cells.*

**Natural killer (NK) cells** are a frontline component of the body's innate immune system. Their primary role is to detect and eliminate cells the body has flagged as abnormal — including stressed, infected, and cancerous cells.[8] They do this through a "triple-killing" mechanism: releasing perforin and granzyme B to induce apoptosis, engaging death receptors via FasL and TRAIL, and recruiting other immune cells through cytokine signaling.[1,2]

**Chimeric antigen receptors (CARs)** are engineered surface proteins that give an immune cell a precise, programmable target — most often a tumor-associated antigen. Adding a CAR to an NK cell creates a *CAR-NK cell*: an immune cell with the natural killing repertoire of an NK cell *plus* the targeting specificity of a designed antibody.[1,7]

**CAR-NK exosomes** are nanoscale extracellular vesicles (30–150 nm) secreted by these engineered cells. They inherit much of the parent cell's functional cargo — including the CAR, perforin, granzyme B, miRNAs, and signaling proteins — while being small enough to penetrate tissues that intact cells often cannot reach, and free of the cellular risks (cytokine release syndrome, persistence concerns) associated with live CAR-cell infusions.[2,3,5]

**30–150**
Nanometers — exosome size, small enough to traverse biological barriers including the BBB.[2]

**3 *pathways***
Perforin/granzyme · death-receptor · ADCC — the cytotoxic mechanisms inherited from parent cells.[1,2]

**Cell-*free***
No live cells, no genetic material transferred — a fundamentally different safety profile from CAR-cell therapy.

### *An important note up front*

CAR-NK exosome therapy is an *emerging*, *investigational* approach. The most rigorous evidence today comes from preclinical studies and early-phase research; it is not an FDA-approved cancer treatment and is not a replacement for conventional oncology care. At Verve, it is offered exclusively as an *adjunctive* therapy, alongside — never instead of — appropriate medical oncology management. Please see the dedicated disclosures section on page 6.

HOW THEY WORK

# The *biology* of targeted exosome therapy.

*Four mechanistic features distinguish CAR-NK exosomes from conventional exosome products and from live CAR-cell therapies.*

### *Inherited cytotoxic cargo* — *i.*

CAR-NK exosomes carry perforin, granzyme B, FasL, and TRAIL — the same cytotoxic molecules NK cells use to induce apoptosis in target cells. Studies confirm these molecules retain their function when delivered via exosomes.[1,2]

### *CAR-directed targeting* — *ii.*

Because the CAR is anchored in the exosome's lipid bilayer, the vesicle preferentially binds cells expressing its target antigen — for example, Her2-positive cells in studied platforms — concentrating delivery where it's intended.[1,4]

### *Tissue penetration* — *iii.*

At nanoscale, exosomes can reach micro-environments that intact CAR cells often cannot — including dense solid tumor tissue and, in research models, regions across the blood-brain barrier.[2,5]

### *Reduced systemic risk* — *iv.*

Because exosomes are non-replicating, non-cellular vesicles, they do not expand in the body. Preclinical work suggests this gives them a lower toxicity profile than live CAR-cell therapy, particularly regarding cytokine release syndrome.[1,2]

## *How CAR-NK exosomes engage tumor cells — a simplified mechanism*

*Step 01*
**Circulation** →
Exosomes are introduced and distribute through the bloodstream and lymphatics.

*Step 02*
**Recognition** →
CARs on the exosome surface bind tumor-associated antigens on target cells.

*Step 03*
**Cargo release** →
Bound exosomes deliver perforin, granzyme B, and other cytotoxic cargo to the target.

*Step 04*
**Apoptosis**
The target cell is signaled to undergo programmed cell death.

### *Why NK-derived rather than T-derived?*

CAR-T cell therapies have transformed care for several blood cancers, but they carry meaningful risks — most notably cytokine release syndrome and graft-versus-host concerns. NK cells natively avoid these risks, and CAR-NK platforms have shown a markedly lower rate of severe CRS in clinical research. Exosomes derived from CAR-NK cells inherit those favorable safety characteristics.[1]

CURRENT EVIDENCE

# Where the *science* stands today.

*An honest summary of what the peer-reviewed literature does — and does not yet — establish about CAR-NK exosomes.*

The scientific groundwork for CAR-NK exosome therapy spans roughly fifteen years and has accelerated significantly since 2020. Foundational research established that NK-derived exosomes carry functional cytotoxic cargo and exert measurable antitumor activity in laboratory models.[2,8] More recent work has demonstrated that exosomes from CAR-engineered NK cells inherit the parent cells' targeting specificity — for example, anti-Her2 CAR-NK92 exosomes showing selective cytotoxicity against Her2-positive tumor cell lines.[4]

Comprehensive 2024–2025 reviews now position CAR-immune-cell exosomes as one of the most active translational research areas in cancer immunotherapy.[1,3,7] Researchers cite their potential advantages over live cell therapies — better tissue penetration into solid tumors, improved safety profile, manufacturing scalability — while explicitly cataloging the open questions that remain before broad clinical use.

| | *CAR-T cells* | *CAR-NK cells* | *CAR-NK exosomes* |
|---|---|---|---|
| *Approval status* | FDA-approved for select hematologic cancers | In clinical trials (109+ studies as of 2025) | **Investigational — preclinical & early research** |
| *Cytokine release risk* | Significant (boxed warning) | Markedly lower | **Minimal (no live cells)** |
| *Solid tumor penetration* | Limited | Limited | **Promising (nanoscale)** |
| *Engraftment / persistence* | Long-lived | Shorter-lived | **Non-replicating** |
| *Manufacturing complexity* | Patient-specific, complex | Allogeneic-capable | **Scalable in principle** |

### *What is not yet established*

Translation from preclinical evidence to confirmed clinical efficacy in humans is still in progress. Open questions include large-scale manufacturing standardization, optimal dosing, biodistribution and clearance, and head-to-head comparison with live CAR-cell therapies.[3] No CAR-NK exosome product is currently FDA-approved for the treatment of any cancer.

OUR APPROACH

# Adjunctive, integrative, *physician-led.*

*At Verve, CAR-NK exosome therapy is offered as part of a coordinated integrative oncology support plan — alongside, never replacing, conventional cancer care.*

IV
INFUSION

METHOD I · SYSTEMIC DELIVERY

## *Intravenous exosome infusion*

Exosomes are delivered intravenously in a comfortable in-clinic setting under physician supervision. Systemic administration allows distribution throughout the bloodstream and lymphatic system, with closely monitored infusion protocols and a structured observation period after each session.

Adj.
ADJUNCTIVE

METHOD II · COORDINATED CARE

## *Integrative oncology support*

Therapy is coordinated with the patient's existing oncology team and complementary modalities — IV nutrient therapy, peptide protocols, lifestyle and metabolic optimization. Verve does not substitute for or interfere with chemotherapy, radiation, surgery, or immunotherapy directed by a treating oncologist.

### *Patients we may consider*

- Adults seeking adjunctive immune-system support
- Survivorship phase — interest in immune-system support post-treatment
- Patients with stable performance status and no acute decompensation
- Those whose treating oncologist is informed and supportive of integrative care
- Patients fully informed of the investigational nature of this therapy

### *Not appropriate candidates*

- Active acute medical instability or hospitalization
- Pregnancy or breastfeeding
- Active uncontrolled infection
- Documented contraindication identified during medical review

### *The structure of a course*

Therapy is structured as a course rather than a single session, with specific cadence determined by your physician based on your goals, current treatment, and response over time. Every patient begins with a comprehensive intake — including review of prior records and coordination with your treating oncology team — before any therapy is administered.

PLEASE READ CAREFULLY

# What you need to *know*.

*Transparency is foundational to integrative oncology care. This page summarizes what CAR-NK exosome therapy is — and is not — at Verve.*

### *This is not an FDA-approved cancer treatment.*

CAR-NK exosome therapy is an emerging area of biomedical research. As of the date this booklet was prepared, no CAR-NK exosome product has received FDA approval for the treatment, prevention, or cure of any cancer or other disease. The therapy offered at Verve is administered under physician supervision and is offered for adjunctive, supportive purposes — not as a curative cancer treatment, not as a replacement for chemotherapy, radiation, surgery, or any other therapy your oncologist has recommended.

### *The evidence base is largely preclinical.*

The scientific support for CAR-NK exosome therapy comes primarily from laboratory experiments, animal studies, and a small number of early-phase clinical investigations. Translation of these findings to confirmed clinical benefit in humans is ongoing and incomplete. Verve cites peer-reviewed sources to describe the science accurately; we do not present preclinical evidence as proof of clinical efficacy in the patients we treat.

### *Outcomes vary, and cannot be guaranteed.*

No reputable medical professional can guarantee a specific clinical outcome from any cancer therapy — conventional or integrative. Individual response depends on cancer type and stage, prior and concurrent treatments, performance status, and many other factors. Verve does not make claims of cure, remission, or specific survival benefit from CAR-NK exosome therapy.

### *Coordination with your oncologist is required.*

We require that patients pursuing this therapy have an active treating oncologist (or treating physician for those in survivorship) and we strongly encourage open communication between Verve and that team. We will not knowingly provide therapy that interferes with, substitutes for, or undermines a recommended conventional treatment plan.

FREQUENTLY ASKED

# Common *questions.*

*Honest answers to the questions patients and families most often ask before considering CAR-NK exosome therapy.*

### Q. *Is this a cancer cure or treatment?*

**A.** No. CAR-NK exosome therapy is offered at Verve as an adjunctive, supportive therapy — not as a treatment, cure, or replacement for conventional cancer care. We do not make claims of curing cancer, achieving remission, or extending survival. The therapy is intended to support patients alongside the oncology care directed by their treating team.

### Q. *How is this different from CAR-T or live CAR-NK therapy?*

**A.** CAR-T and CAR-NK therapies infuse engineered *live cells* into a patient — these are powerful approved or trial-stage treatments delivered in oncology settings. CAR-NK *exosomes* are nanoscale vesicles secreted by those engineered cells: cell-free, non-replicating, and currently investigational. Importantly, exosome therapy is not a substitute for clinically indicated CAR-cell therapy if your oncologist has recommended it.[1,3]

### Q. *Will it interfere with my chemotherapy or other treatments?*

**A.** Coordination with your treating oncology team is required before therapy begins. Our physicians review your current treatment plan, recent labs and imaging, and any pending procedures before scheduling. Where there is any question of interaction or interference, conventional oncology care takes precedence and we will defer or decline to administer.

### Q. *What are the known risks and side effects?*

**A.** Reported effects from exosome IV therapy in clinical settings are typically mild — transient fatigue, low-grade fever, headache, or infusion-site reaction. Because CAR-NK exosomes are an emerging therapy, the long-term safety profile in humans is not yet fully characterized. All known risks and uncertainties are reviewed during informed-consent discussions before treatment.

### Q. *How is the product sourced and prepared?*

**A.** We work only with qualified laboratories that operate under documented quality and chain-of-custody standards. Materials are characterized, screened, and handled according to applicable regulations. Your physician can review specific sourcing and quality documentation with you during consultation.

### Q. *What does a course look like?*

**A.** Therapy is structured as a course of infusions over time, with cadence determined by your physician based on your specific situation. Every course begins with a comprehensive intake and informed-consent discussion. Follow-up reviews are scheduled to assess tolerability, coordinate with your oncology team, and adjust the plan as needed.

### Q. *What if my oncologist disagrees with this approach?*

**A.** We take that seriously. Our preference is to communicate directly with your oncologist; if they have specific concerns, we want to understand them. In some cases concerns can be addressed through coordination; in others, the appropriate path is to defer integrative therapy until conventional treatment is complete or stabilized. We will not proceed against the explicit advice of a treating oncologist on a clinical-safety basis.

SCIENTIFIC REFERENCES

# The *evidence* behind this booklet.

*Selected peer-reviewed publications underpinning the science described in this guide, presented in reverse chronological order.*


1. **Brnić D, Tomić S, Brnić D, et al.** *CAR cell-derived exosomes in cancer therapy: biogenesis, engineering strategies, and antitumor mechanisms.* International Journal of Molecular Sciences. 2025;26(15):7890.

2. **Liu S, Tang H, Liu Y, et al.** *CAR-exosomes derived from immune cells: an emerging nanoscale vanguard in overcoming tumor immunotherapy hurdles.* Frontiers in Immunology. 2025;16:1655095.

3. **Mititelu R, Țuțuianu R, Stanca L, et al.** *From CAR-T cells to exosome-based immunotherapy: exploring the frontiers of cell-free targeted cancer therapeutics.* Cancers. 2025;17(13):2156.

4. **Shoae-Hassani A, Hamidieh AA, Behfar M, et al.** *Anti-Her2 CAR-NK92 cells and their exosomes: generation, characterization, and selective cytotoxicity against Her2-positive tumor cells.* Cells. 2025;14(15):1167.

5. **Khazaeli Najafabadi M, Mirzaeian E, Memar Montazerin S, et al.** *Exploring the potential of the convergence between extracellular vesicles and CAR technology as a novel immunotherapy approach.* Journal of Extracellular Biology. 2024;3(8):e159.

6. **Pace L, Marletta D, Pasquale R, et al.** *Antitumor immunity: role of NK cells and extracellular vesicles in cancer immunotherapy.* Current Issues in Molecular Biology. 2024;46(1):11.

7. **Zhang Y, Liu Q, Zhang X, et al.** *Emerging strategies to overcome current CAR-T therapy dilemmas — exosomes derived from CAR-T cells.* International Journal of Nanomedicine. 2024;19:2773–2791.

8. **Choi JW, Lim S, Kang JH, et al.** *Proteome analysis of human natural killer cell derived extracellular vesicles for identification of anticancer effectors.* Molecules. 2020;25(21):5216.


YOUR NEXT STEP

## *Begin with a consultation.*

Every CAR-NK exosome protocol at Verve begins with a thorough intake, informed-consent discussion, and coordination with your treating oncology team. We're here to answer your questions honestly.


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