THE ARISING

OCTOBER 29, 2026 · JOHN GRIFFIN, MD

Metabolism, muscle and the next clinical test



Original conceptual illustration · Three signals, an open question

New therapies can change what seems possible, but their value depends on the details: the comparison, the outcome, the harms and the next test. This edition ranges from metabolic medicines and muscle biology to Parkinson’s research and dementia-risk coaching. Human outcomes and early laboratory findings occupy different places in the story.

Ten full written articles · Alive. Awake. Aware.

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01 / Lilly's Triple-Hormone Drug Retatrutide Beat Ozempic on Blood Sugar and Weight at Its Top Dose

An experimental drug that acts on three hormone signals produced average weight loss of 20% to 21% in a head-to-head diabetes trial. Ozempic produced 9%. The drug, retatrutide, also led to more people stopping treatment because of side effects.

According to BioPharma Dive, Eli Lilly announced the Phase 3 results on Wednesday. The trial compared retatrutide with Novo Nordisk's Ozempic over 80 weeks. The article does not say how many people took part.

On blood sugar, the 12 milligram weekly dose of retatrutide lowered the measure by an average of 2.2 percentage points. Ozempic lowered it by 1.8, and Lilly called the 12 mg result significantly better. The 9 mg dose also lowered blood sugar by 2.2 points. But Lilly described its difference from Ozempic as statistically "nominal."

The weight gap was larger. Average weight loss was 21% on the 12 mg dose and 20% on the 9 mg dose.

The tradeoff showed up in people who quit. In the trial, 3% of Ozempic recipients stopped treatment because of side effects. That compared with 5% on the 9 mg dose of retatrutide and 8% on the 12 mg dose. BioPharma Dive reports that the top dose was also linked to higher side effect rates overall. The article does not detail which side effects occurred.

For people with diabetes, the open question is whether greater benefit is worth a higher chance of stopping. These data do not answer that. Ozempic acts on one hormone pathway. Lilly's Zepbound and Mounjaro act on two. Retatrutide adds a third, called glucagon. The evidence has limits. These are company-reported results, and the article does not describe a full publication. The drug is not approved. Earlier this week the paper reported real-world data on a different drug, tirzepatide, compared with semaglutide in England. That report added observational findings on a different drug, while this one is a company-reported trial of retatrutide.

BioPharma Dive also notes that strong interest has pushed many people toward a "black market" for retatrutide. Leerink analyst David Risinger forecasts $15 billion in annual sales by 2032. That is a projection, not a finding.

Whether Lilly publishes the full data, including participant numbers and side effect details, and whether regulators approve retatrutide. Nobody should start or stop any diabetes or weight medication without talking to their own clinician.

Source: BioPharma Dive

Read the cited source: Source 1



Original issue inset. Read alongside the study design and limitations above.

Source edition: October 29, 2026 · AR-20261029-FEATURE-01 · original printed page 6

02 / Probiotic Lowered Alzheimer's Blood Marker in Six-Month Placebo- Controlled Trial

Older adults with early memory and thinking problems who took a multistrain probiotic for 24 weeks had lower blood levels of an Alzheimer's-linked protein than those who took a placebo, according to a new trial in the Journal of Alzheimer's Disease.

This is a randomized, double-blind, placebo-controlled trial, the standard design for testing whether an intervention works. Neither participants nor researchers knew who got the probiotic. The study enrolled 87 people from the Gwangju Alzheimer's Disease and Related Dementias cohort: 40 received the probiotic and 47 received placebo. All had early cognitive impairment.

The main result concerns plasma pTau181, a form of the tau protein measured in blood. Tau is a protein that builds up abnormally in Alzheimer's disease. Compared with placebo, the probiotic group showed a significant reduction in pTau181 ($p < 0.001$).

Two other blood markers, GFAP and NfL, stayed stable in the probiotic group. In the placebo group, both rose significantly over the 24 weeks ($p = 0.014$ and $p = 0.041$). The authors describe these as neuroinflammatory biomarkers.

The researchers also tested thinking and daily function. The probiotic group had improved scores on the Clinical Dementia Rating Sum of Boxes ($p = 0.010$), a clinician-rated scale. The authors say the change was driven mainly by the memory domain. The probiotic group also did better on two visuospatial tasks, Constructional Praxis ($p = 0.036$) and the Rey-Osterrieth Complex Figure copy ($p = 0.027$). These tasks involve copying drawings and shapes. Recall of those drawings was preserved in the probiotic group, while the placebo group declined significantly ($p = 0.025$).

The benefits were not broad. There were no significant between-group differences on the Mini-Mental State Examination, verbal memory or executive function scores. The authors conclude that the probiotic "selectively preserved" visuospatial cognition.

Several limits matter for anyone weighing this. The trial was small and short. It drew on one cohort. It measured blood markers, not brain scans, so it cannot show that tau tangles in the brain were reduced. The authors themselves call the findings preliminary and say further studies are needed to confirm the mechanisms. The abstract also does not say how

the many comparisons were handled statistically, and a run of modest p-values across many tests can be less reliable than a single pre-planned result.

ScienceAlert, which covered the study, reports that the product was a three-strain formulation including Bifidobacterium animalis, Limosilactobacillus fermentum and Levilactobacillus brevis. It also reports that the inflammation marker IL-1β fell more in the probiotic group. That outlet cautions that how probiotics might affect the brain through the gut is poorly understood, and that animal results do not always carry over to people. The coverage said 100 people were originally randomized, while the study abstract reports 87 randomized participants.

So is a probiotic worth considering for early memory concerns? This trial gives a reason to study the question, not an answer. It tested one specific formulation in one group, and the cognitive gains were limited to certain measures. A single small trial cannot show whether the effects last or matter in daily life.

The authors call for larger and longer trials that include tau and amyloid-beta PET brain imaging, to test how durable and clinically relevant the effects are. Whether visuospatial testing works as a meaningful endpoint is another open question. Anyone with memory concerns or considering a supplement should not start or stop anything without talking to their own clinician.

Sources: Journal of Alzheimer's disease : JAD (2026), ScienceAlert (Journal of Alzheimer's Disease)

Read the cited sources: Source 1 · Source 2



Original issue inset. Read alongside the study design and limitations above.

Source edition: October 29, 2026 · AR-20261029-FEATURE-02 · original printed page 7

03 / First Parkinson's Patient Dosed With Drug Designed to Clear Damaged Mitochondria

A drug built to help brain cells clear out their damaged power units has now been given to its first person with Parkinson's disease, but the trial is not designed to show whether it helps.

According to Longevity.Technology's report, the British company Mission Therapeutics has dosed the first patient in a Phase 1b study of MTX325. The patient was treated at the Royal Liverpool University Hospital in the UK. This article is based on that report. The company announcement and the underlying research papers were not reviewed. Here is the idea. Mitochondria are the parts of a cell that produce its energy. They wear out. Cells have a cleanup process, called mitophagy, that removes the damaged ones. Mitochondrial decline is widely studied as one of the biological changes that come with aging, and the report says Parkinson's is one of the diseases where it is suspected to play a role.

According to the report, MTX325 is a first-in-class pill that can enter the brain. It blocks USP30, an enzyme found on mitochondria. USP30 acts as a brake on mitophagy. By releasing that brake, the drug is designed to improve clearance of dysfunctional mitochondria, support cell health and reduce inflammation. The company says this could slow or stop the processes thought to drive Parkinson's progression. That is the company's claim, not a result.

The supporting evidence described so far comes from animals and early human work. Longevity.Technology says a study in Nature Communications found that deleting the gene for USP30 protected dopamine-producing neurons in a mouse model of Parkinson's. The company says MTX325 produced a similar result in the same model. In its own preclinical studies, it reports increased mitophagy and beneficial effects on alpha-synuclein, a protein that builds up in Parkinson's, and on the dopamine cells the disease targets. Mouse models do not always predict what happens in people.

In humans, the report says an earlier Phase 1a study in healthy volunteers is completed. According to the company, the drug showed high penetration into the central nervous system, and a PET scan study confirmed it reaches brain tissue. Reaching the brain is a necessary step. It does not show the drug works.

The new study, called MTX325-101, will enroll 36 people with mild to moderate idiopathic Parkinson's in the UK, Europe and Australia. Recruitment is ongoing. According to the report, its stated goal is clinical proof-of-mechanism: checking whether the drug does in

people what it does in the lab. Researchers will assess biological responses using biomarkers and imaging, alongside safety and tolerability. The report describes this as a more modest question than whether patients feel better.

That is why this trial cannot yet show benefit. A small study built to test biological activity and safety is not built to show that symptoms improve or that the disease slows. A positive result would mean the drug engages its target in people. A negative result would suggest the lab findings may not carry over. Either outcome would help guide decisions about larger trials. Mission's Chief Medical Officer, Dr Suhail Nurbhai, said the drug has the potential to move "beyond management of symptoms offered by current therapies." The report notes the company is backed by investors including Pfizer Venture Investments, Sofinnova Partners, Roche Venture Fund and SR One.

The report also frames a wider question. If helping cells clear worn-out parts benefits neurons in Parkinson's, the same logic could be tested in other age-related conditions. For now, that remains a hypothesis.

A data readout from the trial is expected in late 2027, and it will show whether MTX325 acts on its target in people with Parkinson's. Anyone with Parkinson's or concerns about it should not start or stop any treatment without talking to their own clinician.

Source: Longevity.Technology

Read the cited source: Source 1

Source edition: October 29, 2026 · AR-20261029-FEATURE-03 · original printed page 9

04 / Vessel-Function Test Before Stenting Did Not Predict Renarrowing in 91 Patients

A quick, non-invasive test of blood vessel function has been linked to heart risk, so it is fair to ask whether it can also show which stented arteries will narrow again. In a new study of 91 patients, a reading taken before the stent was placed did not independently tell much about how much the artery later narrowed.

This was a retrospective, observational study in people, published on 27 October 2026 in Frontiers in Cardiovascular Medicine. Researchers at Seoul National University Boramae Medical Center reviewed 132 patients who had the test before a stent procedure between 2009 and 2016. Of these, 91 had follow-up angiography, at a median of 9.4 months. A study like this can show links. It cannot show cause.

The test is called EndoPAT. It measures the reactive hyperemia index, or RHI, a gauge of peripheral microvascular function. According to the paper, RHI reflects nitric-oxide-dependent vessel widening and is a validated stand-in for endothelial function, the health of the vessel lining. The paper also says RHI predicts cardiovascular events.

The outcome was in-stent late lumen loss. That is how much the open channel inside the stent shrank by follow-up, measured by quantitative coronary angiography.

The link was weak. RHI showed only a borderline inverse correlation with late lumen loss ($\rho = -0.19$, $p = 0.07$). After adjusting for age, diabetes, hypertension, the number of diseased vessels and the artery's width before the procedure, the association was not significant (adjusted $\beta = -0.11$, 95% CI -0.39 to $+0.18$, $p = 0.45$). The range of plausible values runs from a small benefit to a small harm. Two further analyses, one handling missing follow-up and one handling several lesions per patient, gave similar results. No correlation survived correction for multiple testing.

One subgroup looked different. Among the 33 patients with small stents (2.75 mm or less), higher RHI went with less narrowing ($\rho = -0.375$, $p = 0.032$). In larger stents the correlation was close to zero ($\rho = -0.055$). But the statistical test for a real difference between the two groups was not significant ($p = 0.48$). The authors call this signal hypothesis-generating, meaning it is an idea to test and not a finding. This is the weakest part of any reading of the study: a small group, an exploratory split, and a result that did not hold up against chance.

The small-stent group also differed in other ways. It had more diabetes (57.6% versus 27.6%) and worse kidney function. The authors say this points to a higher-risk group, not just a size category. Inflammation did not explain the results. A blood marker of

inflammation, hs-CRP, was unrelated to both RHI and late lumen loss. The study has limits. It was retrospective, and 41 of the 132 patients had no follow-up angiography. The subgroup was small, and the procedures were done years ago.

The authors call for prospective studies that separate patients by stent size and pair RHI readings before and after the procedure.

Sources: Frontiers in Cardiovascular Medicine (2026), Frontiers in Cardiovascular Medicine

Read the cited sources: Source 1 · Source 2



Original issue inset. Read alongside the study design and limitations above.

Source edition: October 29, 2026 · AR-20261029-FEATURE-05 · original printed page 13

05 / Researchers Argue Age-Related Muscle Loss Is a Nervous System Problem Too

Drugs that build muscle have often failed to make older people move better, and a group of researchers now says the reason may be that muscle was never the whole story.

The argument comes from a review in The Lancet Healthy Longevity (2026) by Orssatto, Arnold, Ferrucci, Narici and Clark. It is a review and proposal, not a trial or an experiment. It enrolled no participants and tested no treatment. It makes a case for how sarcopenia, the age-related loss of muscle strength and function, should be understood.

According to the abstract, sarcopenia is a major driver of disability, frailty and loss of independence. Official definitions have already moved away from low muscle mass. They now centre on low muscle strength and impaired physical performance. The authors say the underlying disease model has stayed focused on muscle.

That focus, they write, has produced important advances in muscle biology. It has also guided decades of research in which drugs that increase muscle mass gave inconsistent benefits for function. Muscle mass and the intrinsic quality of muscle explain an important but incomplete share of the age-related decline in strength and mobility.

The authors point to the rest of the system. Ageing, they say, disrupts the entire motor system: the brain's movement centres, the spinal circuitry, the peripheral nerves, the junctions where nerves meet muscle, and the muscle itself. The result is reduced neural drive, coordination and force generation. In plain terms, the muscle may be present, but the signal telling it what to do is weaker.

They propose calling sarcopenia a disease of the ageing motor system. Current strength and performance criteria capture the clinical picture, they write, but there is room to improve. They want diagnosis that assesses the whole system, sorts people by mechanism, and supports therapies aimed at both nerves and muscle. Without that shift, they argue, meaningful therapeutic progress will remain challenging.

The review's lead author, Lucas Orssatto of the University of Queensland, wrote a companion piece published by Medical Xpress. It goes further than the abstract on practical detail. In it, he suggests clinicians could watch how quickly someone rises from a chair, not only whether they can. Other checks include unsteadiness during sustained effort, hand dexterity, and whether walking changes when a conversation is added. He also says sedative and anticholinergic medicines can blunt motor drive, so medication review belongs alongside strength training. The abstract itself does not cover these

points, so they should be read as the author's commentary. The same piece is frank about limits. Orssatto writes that nobody has yet shown these newer measures beat existing screening tests, on outcomes or on cost. He also notes that neuromuscular expertise is unevenly available in primary care.

Trials that measure nerve function as well as muscle, and whether international working groups revise the diagnostic criteria for sarcopenia. Readers should not start or stop any exercise, medicine or treatment without talking to their own clinician.

Sources: The lancet. Healthy longevity (2026), Medical Xpress / The Lancet Healthy Longevity

Read the cited sources: Source 1 · Source 2

FOR YOU

For readers focused on healthspan, the practical question is what to measure. Strength and walking speed remain central. Whether speed of movement, power and balance add useful information is still an open question that the authors want tested.

Original issue inset. Read alongside the study design and limitations above.

Source edition: October 29, 2026 · AR-20261029-FEATURE-06 · original printed page 15

06 / Heart Mitochondria Burn Lactate Directly as Backup Fuel, Mouse Study Finds

The heart can burn lactate, a molecule often treated as a by-product of metabolism, by taking it straight into its energy-making compartments. That is the conclusion of a new study in Nature, and it challenges a standard picture of how heart cells use fuel.

The evidence comes mostly from mice. The paper, published in Nature in 2026, also reports that the key protein is present in human heart muscle cells. Only the abstract was available to us, and it does not state how many animals were studied. This article does not report details beyond what the abstract gives.

The heart is a flexible fuel user. According to the study, it can burn several fuels, including glucose and lactate, to meet its energy needs during changes in diet, exertion and injury. The textbook view is that carbohydrate fuels converge on a molecule called pyruvate. A transporter called the mitochondrial pyruvate carrier then moves pyruvate into mitochondria, the cell's power units. The researchers found that glucose-derived carbon was still burned in mouse heart muscle even when that carrier was genetically removed. Using genetic and drug tools, they showed that a different protein, MCT1, was required for this to happen. MCT1 is traditionally found on the cell's outer membrane. The study reports it also sits in the inner membrane of mitochondria in mouse and human heart muscle cells.

Inside mitochondria, MCT1 works with an enzyme called LDHB. Together, according to the authors, they convert lactate into pyruvate and NADH, which directly feed the electron transport chain, the final stage of energy production. The authors describe this as a parallel, lactate-based route for burning carbohydrate.

The pathway appeared to matter under stress. In mice, loss of MCT1 impaired lactate burning and disrupted the heart's metabolic flexibility. It also sped the development of heart failure and raised mortality after two kinds of challenge: overactivation of the body's stress-hormone signalling, and ischemia-reperfusion injury, in which blood flow to the heart is cut off and then restored.

A commentary in Nature on the work notes that lactate is abundant in human blood and has been studied for centuries, yet how cells handle it remains debated. It says the study provides "solid support for a conclusion that defies current dogma": that in the heart,

lactate can enter mitochondria directly through a specific transporter, and that this is essential for cardiac function under stress.

For later-life heart health, the implications are not yet established. The abstract shows the pathway in mouse hearts and shows MCT1's location in human heart cells. It does not show that the pathway protects people, that it declines with age, or that it can be targeted by treatment. Any therapy based on this finding remains hypothetical.

What to watch next is whether researchers confirm this lactate route in living human hearts, and whether it changes in people with heart failure.

Sources: Nature (2026), Nature

Source edition: October 29, 2026 · AR-20261029-FEATURE-08 · original printed page 19

07 / Coaching Program Linked to Greater Weight Loss in GLP-1 Users

Weight loss on a GLP-1 drug is not only fat loss, and a new study asks whether exercise coaching can change what the body gives up. The fat and muscle figures below come from press coverage, not from the abstract we could read, and the study was run by the programme's own provider.

The work is a quasi-experimental trial, published in 2026 in the journal Diabetes, Obesity and Metabolism. A quasi-experimental design compares groups without randomly assigning people to them, so it is weaker evidence than a randomised trial. It enrolled 245 adults with obesity. All had started GLP-1 therapy for weight loss no more than eight weeks before the study began. Of these, 151 joined a 12-week virtual programme and 94 received usual care. We had access only to the study's abstract, so some details are not confirmed here.

The researchers start from a known problem. According to the paper, GLP-1 receptor agonists can produce rapid weight loss, but that loss is often accompanied by a disproportionate loss of lean mass, especially early in treatment. Lean mass includes muscle. The authors note that physical activity, particularly resistance training, is the most effective behavioural strategy for boosting fat loss while preserving lean mass.

The intervention was a virtual GLP-1 lifestyle companion programme that included personalised, strength-focused physical activity coaching. The control group received usual care. Body composition was captured with home bioelectrical impedance scales. These estimate fat and muscle by passing a weak electrical current through the body. The main outcomes were differences between the groups at 12 weeks in weight, percent body fat and percent muscle mass.

The abstract reports that participants in the programme lost an adjusted average of 6.0% of their baseline body weight, compared with 3.3% in the control group. That is a between-group difference of 2.8%. The abstract text available to us cuts off before the body fat and muscle results.

Those figures come from press coverage by Longevity.Technology, which says body fat percentage fell by 3.3% in the programme group versus 1.6% in the usual care group. It also says muscle mass percentage rose by 0.6% versus 0.2%. That is a gap of about 0.4 of a percentage point. We could not check these numbers against the abstract.

The authors conclude that personalised, virtually delivered physical activity programming "may meaningfully improve the quantity and quality of weight loss during GLP-1 therapy." The wording is cautious, and it is an association rather than proof of cause.

There are reasons for caution. According to Longevity.Technology, the work came from the programme provider Omada Health's own research initiative, so the company evaluated its own programme. The coverage also says 26% of the usual care group used another lifestyle or wellness programme during the study. Twelve weeks is short, and the coverage notes it is unclear whether the gaps persist or whether people kept any muscle they gained. Home impedance scales are convenient but are generally considered less precise than clinical imaging.

Omada's Chief Medical Officer, Dr Thomas Tsang, told Longevity.Technology: "GLP-1 care is about more than how much weight you lose. It's about the quality of the weight loss, as losing too much muscle can make it harder to keep the weight off long-term." That is the company's reading, not a finding of the study.

The longevity link is muscle. Keeping lean mass matters for physical function as people age. If many people stay on these drugs for years, how much muscle they keep may matter alongside how much weight they lose. Longer follow-up, ideally with randomised groups and more precise body composition scans, to show whether the early differences last. Anyone considering changes to GLP-1 treatment or exercise should talk to their own clinician before starting or stopping anything.

Sources: Diabetes, obesity & metabolism (2026), Longevity.Technology



Original issue inset. Read alongside the study design and limitations above.

Source edition: October 29, 2026 · AR-20261029-FEATURE-11 · original printed page 25

08 / Nurse-Led Coaching Trial Trimmed Dementia Risk Scores, but Not Cognition

A year of nurse-led coaching moved a questionnaire-based dementia risk score in a better direction for middle-aged Australians, but thinking skills, quality of life and heart risk did not differ from usual care, according to News-Medical's report of a new trial.

This article is based on that report. The paper itself, published in The Lancet Regional Health – Western Pacific, was not reviewed.

According to News-Medical, the HAPPI MIND trial assigned 31 general practices in Victoria and New South Wales, by chance, to a coaching arm or a control arm. Participants were adults aged 45 to 65 with two or more modifiable dementia risk factors and access to a smartphone or tablet. The report says 201 people were in the intervention group and 202 in the control group.

The coaching group had six nurse-led sessions: five in the first year and one at 24 months. Nurses gave personalized risk reports, set goals with participants and used motivational interviewing. Participants also used an app to track goals and read education material. Controls received a risk screening, a risk report and an educational booklet, then continued usual care.

The main measure was the ANU-ADRI, a questionnaire that estimates future dementia risk from known risk and protective factors. Lower scores mean a more favorable profile. According to News-Medical, 56% of the coaching group improved their score, versus 44% of controls. The adjusted difference between groups was 1.6 points. The report says the estimated effect was smaller after further adjustment for baseline differences.

The report is clear about what did not change. The groups did not differ significantly on cognition, quality of life, cardiovascular risk, psychosocial measures, or clinical and biomarker measures. The ANU-ADRI is an estimate built from habits and health factors. It is not a dementia diagnosis, and the coverage describes no dementia outcomes.

Some component scores moved. According to the report, protective-factor scores improved more with coaching, particularly physical activity, fish intake and body mass index status. Risk-factor scores did not differ between groups. These extra comparisons were not adjusted for multiple testing, which raises the chance that some findings are noise. Both groups improved on LDL cholesterol. Diet and medication adherence scores worsened in both groups.

Several limits apply, per the coverage. Participants and nurses knew who was coaching. Groups differed at the start: physical inactivity and uncontrolled diabetes were more common in the intervention arm, and its risk scores were numerically higher. Follow-up at 12 months was 78% for coaching and 88% for controls. Exploratory analyses hinted at larger benefits for people with low socioeconomic status and high baseline risk, but the report says these need confirmation in larger studies.

So far, the evidence suggests structured primary-care coaching can shift an estimated risk score. It does not yet show effects on memory, thinking or health measures. Follow-up is planned to 36 months, and those results will show whether the score changes lead to anything measurable. Anyone considering changes to their health habits or treatments should talk to their own clinician before starting or stopping anything.

Source: News-Medical (The Lancet Regional Health – Western Pacific)



Original issue inset. Read alongside the study design and limitations above.

Source edition: October 29, 2026 · AR-20261029-FEATURE-14 · original printed page 31

09 / Elinzanetant Halved Hot Flashes in Two-Thirds of US Trial Participants

About two in three US women who took the non-hormonal drug elinzanetant had at least half of their moderate-to-severe hot flashes disappear within three months, according to Contemporary OB/GYN's report of a new analysis. About four in ten women on placebo had the same result.

This article is based on that report. The study itself, a poster presented at The Menopause Society 2026 Annual Meeting in San Diego, was not reviewed.

Hot flashes, also called vasomotor symptoms, are common during the menopause transition. According to Contemporary OB/GYN, they can hurt quality of life. Elinzanetant blocks two brain signaling targets, the neurokinin 1 and neurokinin 3 receptors. The outlet reports it is approved in the United States for moderate-to-severe hot flashes due to menopause.

The new work pooled US data from two phase 3 trials, OASIS-1 and OASIS-2. According to the report, the analysis included 410 postmenopausal participants aged 40 to 65 who had at least 50 moderate-to-severe hot flashes per week. Half received 120 mg of elinzanetant and half received placebo for 12 weeks. After that, both groups received elinzanetant for 14 more weeks. Participants logged their hot flashes in daily diaries.

From weeks 4 to 12, 66.9% of the elinzanetant group had a reduction of at least 50% in the frequency of moderate-to-severe hot flashes, compared with 40.5% of the placebo group, according to the report. A reduction of at least 75% was seen in 46.5% versus 21.4%. A reduction of at least 90% was seen in 29.1% versus 11.6%. The placebo figure matters. Four in ten people on a dummy pill still had a 50% drop. That shows hot flash counts can fall for reasons other than the drug. The gap between the groups is the more useful comparison.

The response came early. According to the report, more than half of US participants on elinzanetant had a 50% reduction by week 4. At that point, 17.4% had a reduction of at least 90%.

At week 26, everyone had been taking elinzanetant. Contemporary OB/GYN reports that 75.2% of the original elinzanetant group and 84.1% of the placebo-to-elinzanetant group had at least a 50% reduction. For a 90% reduction, the figures were 40.4% and 39.8%. Even then, about six in ten people did not reach that level.

There are limits. According to the report, this was an exploratory, post hoc analysis, meaning it looked at a subgroup after the main trials were done. Such analyses are better for raising questions than settling them. The coverage did not report safety data for this analysis. The report says the authors found results comparable to those in the overall trial population.

Whether the full poster or a peer-reviewed paper confirms these figures, and how the drug performs over longer periods and in everyday use. Anyone considering starting or stopping a menopause treatment should talk with their own clinician first.

Source: Contemporary OB/GYN



Original issue inset. Read alongside the study design and limitations above.

Source edition: October 29, 2026 · AR-20261029-FEATURE-17 · original printed page 37

10 / New Lipid Carriers Steer mRNA Cancer Vaccines to the Spleen in Mice

Chinese chemists built 40 retinoic-acid-based lipids and found one that raised spleen expression about 15-fold over a standard spleen- targeting formula. The mouse results are promising; human data do not exist yet.

An mRNA vaccine is only as good as where it lands. A cancer vaccine needs its instructions read by immune cells, not by the liver. A new study reports a family of fat-based carriers designed to send mRNA to the spleen, where many of those immune cells live. Our research desk described a 40-member library of ionizable lipids derived from retinoic acid, a vitamin A relative. The researchers call them RAILs. The goal was to make mRNA express its payload in the spleen rather than wherever it first arrives.

The desk's framing was that total protein output, often measured in the liver, is the wrong target for a cancer vaccine. What matters is expression inside antigen-presenting cells in lymphoid tissue.

The study is real. Jiang and colleagues at the University of Science and Technology of China published it in Angewandte Chemie International Edition (2026;65(40):e3823572, PMID 42585110). PubMed lists online publication on August 12, 2026, with the September 28 issue date, so the September date our desk gave refers to the issue.

The library was described as modular, and paired lab and mouse screening picked a lead formulation, AT4-13CRA, with the highest spleen-to-liver expression ratio. It gave about 15-fold more splenic reporter expression than a single comparator, the DLin-MC3/18PA SORT formulation. The abstract we reviewed does not itemize which parts of the lipid were varied.

The mechanism was not just more uptake. The lead carrier showed less mRNA retained in lysosomes, the cell's waste-processing compartments, and weaker TNF-α/NF-κB-associated inflammatory activation. In reporter mice and an ovalbumin model, it drove expression in splenic macrophages and dendritic cells, raised antigen-specific T-cell and antibody responses, and improved protection against a melanoma (B16F10-OVA) tumor challenge.

Delivery has been the quiet bottleneck of mRNA medicine since 2020, and spleen-targeted lipid delivery is an active area of research.

If a dose can be aimed at the organ that should read it, that might eventually help cancer vaccines work better. That is our proposal, not a finding: the paper shows reduced inflammatory signalling in mice but no data on smaller doses or fewer side effects.

• This is a mouse study. Potency in animals does not predict tolerability in people. • A spleen-targeting formulation still must clear manufacturing-consistency and safety review before any trial. • The 15-fold figure is a comparison with one reference design, not with every method in use. This is the weakest point in the argument for how much better the carrier is.

• Dose-sparing and side-effect benefits are untested in this work.

• Nothing to act on yet; this is preclinical chemistry, not an available treatment.

• If you have cancer and are weighing an mRNA vaccine, discuss only trials that are actually enrolling with your oncologist.

What To Watch Next

• Whether any group advances a spleen-targeted mRNA vaccine toward a first human trial. • Independent replication of the spleen-to-liver expression ratio in another lab. As of late October 2026 we found none, and no retraction, correction or contradicting result.

• Safety data, since steering a dose to immune tissue changes the side-effect profile.

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