Condensed version and key points from the study:

Hydrogen gas activates coenzyme Q10 to restore exhausted CD8+ T cells, especially PD-1+Tim3+terminal CD8+ T cells, leading to better nivolumab outcomes in patients with lung cancer

Study Overview

- A prospective cohort study published in Oncology Letters (November 2020) investigating whether hydrogen gas enhances the clinical outcomes of nivolumab (an immunotherapy checkpoint inhibitor) in patients with stage IV lung cancer, and exploring the role of coenzyme Q10 (CoQ10) as a marker of mitochondrial function. 56 patients were enrolled at Tamana Regional Health Medical Center, Japan between July 2016 and July 2018.

Quick Background — Key Terms Explained

- Nivolumab is an immunotherapy drug (anti-PD-1 antibody) that blocks cancer cells from suppressing the immune system. However, nivolumab has a low cure rate of only 20–30%, and many researchers have been searching for biomarkers to distinguish responders from non-responders.
- PDT+ cells (PD-1+Tim-3+ terminal CD8+ T cells) are the most severely exhausted immune cells — burned-out fighters that can no longer attack cancer effectively.
- CoQ10 (coenzyme Q10) is a key enzyme in the mitochondrial energy chain, measurable in blood, used here as a proxy for mitochondrial health.

Participants & Treatment

- Of 56 patients with stage IV lung cancer, 42 were treated with hydrogen gas combined with nivolumab (HGN), while 14 received nivolumab only. Patients inhaled hydrogen gas for 3 hours daily at home via cannula or mask. No patients reported any complaints regarding the daily hydrogen inhalation, and no adverse events were observed in up to 60 months of use.

Key Survival Results

- Patients treated with hydrogen gas and nivolumab had a significantly longer overall survival than those treated with nivolumab only. Median survival time for the combined group was 28 months — approximately three times longer than the nivolumab-only group at 9 months.
- Patients with low PDT+ had a median overall survival of 60 months, compared to only 11 months in those with high PDT+.

The Role of CoQ10 — A New Finding

- Patients with high CoQ10 levels had a median overall survival of 25 months, compared to 8 months in those with low CoQ10 — described as the first report of an association between CoQ10 and cancer prognosis.
- PDT+ showed a significant inverse correlation with CoQ10 — meaning patients with higher CoQ10 had fewer exhausted immune cells. When CoQ10 increased after hydrogen treatment, PDT+ significantly decreased.
- Hydrogen gas treatment increased CoQ10 concentration in 19 (46%) of 41 patients.

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The Proposed Mechanism — How Hydrogen Helps

- Hydrogen gas is suggested to activate CoQ10 (mitochondria), thereby enhancing the outcomes of nivolumab via reducing exhausted CD8+ T cells, especially PDT+. PDT+ and CoQ10 are proposed as reliable negative and positive biomarkers of nivolumab, respectively.
- In plain terms: hydrogen recharges the energy supply of exhausted immune cells by boosting mitochondrial function, making them capable of fighting cancer again — and making nivolumab far more effective.
- Direct mitochondrial activators synergize with PD-1 blockade therapy; however, none of the mitochondrial activation chemicals alone exert any effects on tumour growth — meaning nivolumab is also required. The better outcomes observed are not attributable to hydrogen gas alone.

Why Hydrogen Doesn't Work for Everyone

- Hydrogen gas could not restore PDT+ in 21 of 41 patients (51%), and in 22 out of 41 patients (54%) it could not increase CoQ10 concentration. This may be due to the existence of senescent (permanently aged/dysfunctional) CD8+ T cells with irreversible mitochondrial dysfunction.
- Encouragingly, the longer patients inhaled hydrogen gas, the better their prognosis, suggesting longer inhalation may cause further recovery of PDT+ even in cases of senescent CD8+ T cells.

Conclusions

- Hydrogen gas activates CoQ10 (mitochondria), thereby enhancing the outcomes of nivolumab via reducing exhausted CD8+ T cells, especially PDT+. It is assumed that nivolumab is not effective for patients with predominant exhausted CD8+ T cells in peripheral blood, which can be overcome by hydrogen gas.

Limitations to Keep in Mind

- The groups were unequal in size (42 vs. 14), partly because researchers began preferring the combined treatment once interim results looked promising — which introduces selection bias.
- The study was conducted at a single centre by the same research team as the earlier colorectal cancer hydrogen study.
- Other mitochondrial markers (NAD+, ATP, etc.) were not measured, so CoQ10's suitability as the best mitochondrial marker remains unconfirmed.
- Pulmonary function tests before and after hydrogen treatment were not performed, an acknowledged limitation.
- Larger independent multi-centre trials are needed to validate these findings.

To Read The Full Study Please CLICK HERE