Nanoparticles in Cancer Treatment

I have been asked by multiple patients recently about nanoparticles for use in the treatment of cancer. Nanoparticle research has generated considerable coverage in the lay press over the past year and a half, including a CBS 60 Minutes episode titled “The Kanzius Machine: A Cancer Cure?".

The term “nanoparticles” refers to very tiny particles, much smaller than cancer cells or even standard chemotherapy drugs. A nanoparticle ranges between 1 and 100 nanometers (a metric unit of length equal to one billionth of a meter) in diameter. Nanoparticles have industrial uses in creating surface coatings for scratch-resistant glass, skid-resistant roads, in strengthening metals, and in the development of more efficient solar panels. This post will concentrate on the applications related to cancer therapy.

There are basically two main areas in which nanoparticles are being explored in relation to cancer: molecular imaging and therapy. In molecular imaging, nanoparticles are injected into the body and taken up by cancer cells, with the uptake causing the cancer cells to show up differently than normal surrounding cells (from Google images).

Molecular imaging might allow more detailed evaluations of tumors to assess which cancer cells may be surviving and which may be dying. On a full-body scale, the imaging may be used to stage cancer by detecting tumor metastases, or to measure response to therapy (similar to PET scans). A cartoon animation of nanoparticles used to highlight a cancer cell is available on www.cancer.gov.

The use of nanoparticles in molecular imaging is still investigational, with most studies having been conducted thus far in cellular and animal models. The primary imaging method studied so far is the coupling of iron nanoparticles with MRI (the magnet of which detects the metal). It is hoped that this type of imaging may detect smaller deposits of cancer than PET scans may detect. MD Anderson Cancer Center conducted a small study evaluating this method (lymphotrophic nanoparticle-enhanced MRI) to look for lymph node metastases in patients with high-risk prostate cancer. The authors concluded that more patients and longer follow up were needed to assess the potential utility of this technique.

In the realm of active therapy, nanoparticles are being evaluated in coupling with standard chemotherapy agents (paclitaxel, cisplatin, etc), with targeted therapy agents (Map-kinase targets), with gene therapy (Rexin-G), and with a novel technique coupling nanoparticles with radiowaves (the Kanzius machine). The investigation of all techniques is still extremely early, and most studies currently involve either cellular models (looking at the effects on cancer cells growing in a petri dish) or in mice.

There are currently two main agents with nanoparticles that are being evaluated in human trials. Rexin-G is a nanoparticle designed to deliver a fatal gene directly into tumor cells. It was recently granted fast-track approval status by the FDA for research in pancreatic cancer based on the outcomes of a phase I/II trial presented this year at the ASCO GI Cancer symposium. In
this trial, designed to test the safety of the drug primarily, the agent was well-tolerated, without treatment-related side effects. There were only 9 patients enrolled in this study, but what the authors found interesting was that all 9 patients had either stable disease or partial response (more responses with the higher dose tested) of their tumors. Rexin-G is now being evaluated in larger phase II studies in pancreatic, colorectal, breast cancers, and sarcomas.

The “Trojan Horse” therapy uses a “mini-cell” to deliver a package of RNA into cancer cells. In this case the RNA signal is called a “silencing RNA”, or siRNA. This siRNA signals a cancer cell to stop production of proteins that cause chemotherapy resistance. A second mini-cell is then injected which delivers chemotherapy drugs into the cancer cells. So far, this Trojan Horse approach (called EDV technology, for EnGeneIC Delivery Vehicle) has been tested in cellular and mouse models. The first human trial has just begun in Australia.

The Kanzui's Machine is a new treatment approach that is in early-stage development and testing. Given that this technique was highlighted in a 60 minutes special, though (generating many questions from patients), I thought it would warrant a comment. John Kanzui was a radio technician who developed lymphoma. In thinking about and going through his own chemotherapy, he developed a concept of using radiowaves to heat up and selectively “cook” cancer cells. This is basically a technique similar to radiofrequency ablation, or RFA. With RFA, a probe is inserted into a tumor and radio waves are generated which heat up the area and cook the cancer. RFA treatment is limited to a tumor in a specific, reachable area of the body, carries risks of bleeding, infection, or perforation of vital organs, and does not address systemic disease (any tumor cells not located in that immediate vicinity being treated).

Mr. Kanzui, however, was interested in coupling his radio wave machine with nanoparticles, using the theory that if cancer cells throughout the body were to take up nanoparticles that then heated up when a radio wave passed through the body, it might have the potential to “cook” the cancer cells selectively in many locations at the same time, thus treating systemic disease. Unfortunately, Mr. Kanzui passed away earlier this year, but his foundation is continuing to develop and research his theory and machine. It has not yet reached the point of human trials, and will have several hurdles yet to pass before being able to do so.

So where does this leave us? Nanoparticle technology is very interesting, and carries the potential of reducing toxicity to the patient while improving the efficacy of therapy. However, all research is still relatively early. There is no approach with nanoparticles that would be indicated as standard of care, or outside of a clinical trial setting. Many prior treatments, too many to count really, have shown similar promise in early studies but have not panned out in humans the way we would like. Unfortunately, we cure far more mice with cancer than we do humans, and mouse studies do not mean that a treatment will be effective in humans.

Also unknown thus far are the potential risks. Although in 9 patients Rexin-G was well-tolerated, more patient safety data needs to be collected on all treatment approaches with nanotechnology. In the world of industrial nanoparticles, concerns are being raised over the potential health risks with inhalation of these tiny particles during the manufacturing process or elsewhere. This raises the memory of asbestos: once thought to be one of the most important advances in safety, it is now recognized to have deadly consequences years after exposure.
The media searches avidly for an exciting headline, one that promises that in cancer treatment, problems will be fixed and a cure for all cancer would be just around the corner. In reality, treatment is not that simple. We all maintain hope and all continue to work toward a better future in cancer diagnosis and therapy. It will still take time.

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