

Re: Synta says drug (in combination with chemos) delays worsening of melanoma

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*Source:* <http://sci.tech-archive.net/Archive/sci.med.diseases.cancer/2007-09/msg00055.html>

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- *From:* J <[nswex@nald;anon](mailto:nswex@nald;anon)>
  - *Date:* Wed, 26 Sep 2007 15:34:16 -0400
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J wrote:

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<http://uk.reuters.com/article/governmentFilingsNews/idUKL2690074520070926>

Synta says drug delays worsening of skin cancer  
Wed Sep 26, 2007 3:43pm BST

By Michael Kahn

BARCELONA, Sept 26 (Reuters) – An experimental drug that spurs cancer cells to commit suicide helped melanoma patients live longer and delayed worsening of their disease, the drug's maker said on Wednesday.

Patients with skin cancer that had spread to other parts of the body lived four months longer when using the drug — called STA-4783 — in combination with the standard chemotherapy treatment paclitaxel, said Anthony Williams, vice president of clinical research at Synta Pharmaceuticals (SNTA.O: Quote, Profile, Research).

And the cocktail more than doubled how long patients survived without their cancer getting worse, he told the European Cancer Conference.

Alexander Eggermont, incoming president of the European Cancer Organisation and who was not involved in the study, said the way the trial was done and the results merit further research.

"It is a novel mechanism," he said. "If you have these results, you have a green light to do a Phase III trial." Phase III is the final stage of human testing before a drug can win licensing approval.

Melanoma is an aggressive, difficult to treat cancer with an average survival rate of about six months for people with advanced the stages of the disease. Current therapies have only a limited impact or are highly toxic.

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The new treatment centres on unstable charged molecules called free radicals that can damage the body and which people often try to get rid of by consuming food or drink rich in anti-oxidants such as vitamin E.

But Synta found that increasing the level of free radicals in melanoma patients using the drug caused the tumour cells to kill themselves without impacting normal cells,

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[http://www.boston.com/news/globe/health\\_science/articles/2007/07/16/from\\_industry\\_castoff\\_to\\_potential\\_medicine/](http://www.boston.com/news/globe/health_science/articles/2007/07/16/from_industry_castoff_to_potential_medicine/)

From industry castoff to potential medicine

Scientists turn to old chemicals for cure for melanoma, other cancers

By Robert Cooke, Globe Correspondent | July 16, 2007

By poking through thousands of industrial chemicals, scientists report that they have found a new drug that, for the first time, improves the grim outlook for patients with the most dangerous form of skin cancer.

Although the research and clinical trials are still in early stages, preliminary data suggest that the new drug, called STA-4783, doubles patients' survival time to 12 months, with very few side effects, said Safi Bahcall, president and chief executive of Synta Pharmaceuticals, a small biotechnology firm in Lexington that developed the drug. His company recently announced the results at the annual meeting of the American Society for Clinical Oncology in Chicago.

"It's the first time anyone has seen a drug that extends the survival time of people with metastatic melanoma," Bahcall said. "Normally, half of the people who come in with malignant melanoma are dead in six months."

"The key thing will be to validate these early, significant results," said Dr. John Kirkwood, a leading melanoma specialist at the University of Pittsburgh Cancer Institute.

"We are encouraged with the pilot results with this new agent," he said, adding that further testing, on a larger scale, is required.

STA-4783's anticancer properties were uncovered by a drug-screening program in which Synta scientists are carefully testing chemicals one by one to assess their medical potential.

The company has several other drug candidates derived from industrial chemicals in the research pipeline, including a possible drug for arthritis, a newer oral version of STA-4783, a second oral drug for cancer, an antipsoriasis skin drug, and an inhibitor of autoimmune diseases.

All these came from Synta's focus on small-molecule compounds that exhibit unexpected

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and unexplored medical properties. Hundreds of thousands of such chemicals exist, originally made for industrial purposes, but they are rarely studied for medical potential.

In the past, of course, some industrial chemicals were discovered, often by accident, to have medical uses.

Mustard gas, for example, which is notorious as a frightful chemical warfare agent during World War I, opened the door to modern chemotherapy for childhood leukemia. Bayer AG in Germany became a major pharmaceutical supplier after discovering medical uses for its industrial chemicals.

Lan Bo Chen, an emeritus professor of pathology at the Dana–Farber Cancer Institute in Boston, came up with the idea in 1979 of searching through industrial chemicals, particularly photographic dyes, for cancer treatments.

One early dye, rhodamine 123, for instance, was found to selectively seek out and damage the energy factories within cancerous cells, killing them while leaving healthy cells untouched. (It was later abandoned because it wasn't potent enough.)

STA–4783 appears to work in much the same way, causing cancer cells to self–destruct, while leaving normal ones unscathed.

The new research findings come from a Phase II clinical trial of 81 patients at 21 medical centers, who were given STA–4783 along with a version of the standard cancer drug, Taxol. The encouraging results prompted the US Food and Drug Administration to grant STA–4783 fast–track status last November to speed up the review process.

A far larger trial, enrolling 600 patients at 150 hospitals in 15 countries, is now getting under way, Bahcall said, and results are expected in late 2008.

Synta found STA–4783 from among a stockpile of chemicals from Russia, bought with money donated by junk–bond guru Michael Milken, a cancer survivor who is supporting two drug development programs involving Synta with a gift of \$10 million.

If the drug is proven safe and effective, it would offer the first real hope for advanced melanoma patients, whose tumors are now considered essentially unstoppable.

Most of the 60,000 new melanoma cases seen annually in the United States are treated successfully with surgery, but about 8,200 patients per year don't spot the disease early enough, and only 16 percent of them are expected to survive at least five years.

Chen believes there are many more drugs waiting to be discovered in chemical stockpiles.

"The chemical libraries are gold mines, but they're all sitting in warehouses at the moment," said Chen, because winning permission to test them "is virtually impossible right now."

Companies are leery of participating in drug development research because it is very expensive, time–consuming, highly uncertain, and fraught with legal hazards.

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Kodak, for instance, made its chemicals available to Chen in earlier days, but not anymore.

"Kodak exited the pharmaceuticals business in 1994 and subsequently has not pursued further follow-up on this earlier work," said company spokesman Christopher K. Veronda.

"Since a representative sample of the chemical library was already screened, it's unlikely there are undiscovered compounds that may have therapeutic value."

But Chen disagrees.

"I think these companies should have a sense of social responsibility and allow scientists to study their precious compounds," he added. "They were synthesized over many decades by gifted chemists, at the expense of hundreds of millions of dollars, yet we let it sit in the warehouse."

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