New drug candidate prolongs the lives of pancreatic cancer patients

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Every year, 42,000 Americans are diagnosed with pancreatic cancer. Few live very long, and less than 5% are still alive five years after diagnosis.

There's new hope, though, from the lab of Prof. Yoel Kloog, dean of Tel Aviv University's Faculty of Life Sciences. His drug compound Salirasib has shown positive results against pancreatic cancer and recently passed Phase I/II clinical trials. The drug, given in combination with gemcitabine, the standard drug used to combat pancreatic cancer, almost doubled the life expectancy of those who received it.

"In our study, the mean survival of pancreatic cancer patients was 10.8 months -- better by far than the 6.2 months with gemcitabine alone," says Prof. Kloog, who recently presented the results to a meeting of the American Society of Clinical Oncology. His basic research offers the promise of a weapon to attack a broader range of mankind's most prevalent diseases, including lung, prostate and breast cancers as well as diabetes.

Blocking the Ras protein

Salirasib works by inhibiting a protein called Ras, which is known to be abnormally activated in one-third of human cancers. In cancer of the pancreas, mutant forms of Ras are found in up to 90% of all tumors. Salirasib's basic component, FTS, works to block the formation of

cancer-promoting Ras nanoclusters, thus blocking a cascade of biochemical signals known as the "Ras signaling pathway" that allow Ras to wreak havoc on the body.

Early in the 1990s, many drug developers chased after a mechanism to inhibit Ras by targeting enzymes that modify it, but they were unsuccessful. "The major developers gave up, claiming Ras is not targetable," says Prof. Kloog, "but our concept takes a different approach. Now that we've shown it works in human subjects, I am definitely excited — no doubt about it." Prof. Kloog developed the Ras antagonist more than 15 years ago.

No toxic side effects

In the latest study, researchers tested for both toxicity and effectiveness. They gave 19 patients with advanced pancreatic cancer daily doses of salirasib along with a standard gemcitabine regimen. Salirasib was well tolerated by the patients, and they surpassed on average the number of months they would have lived on gentamiacine alone. There were no toxic side effects, such as heart or lung ailments. Tumor biopsies showed a significant reduction in Ras levels, suggesting that the drug is inhibiting the action of Ras in the tumor itself.

For this study, Salirasib was licensed by Concordia Pharmaceuticals, which collaborated with the Memorial Sloan Kettering Cancer Center, Johns Hopkins, the M.D. Anderson Cancer Center and other institutes in the United States.

If Phase II/III trials are successful, Prof. Kloog's drug will be the first successful Ras antagonist known to medical science. Salirabib could be medically available in as little as two years.

Source: Tel Aviv University (news : web)