NEW THERAPIES HELPING PATIENTS WITH ADVANCED MELANOMA
Targeted therapies attack and stall growth of melanoma cells

Information presented at American Academy of Dermatology’s 70th Annual Meeting by Darrell S. Rigel, MD, FAAD, clinical professor in the department of dermatology, NYU Langone Medical Center, New York, New York.

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OVERVIEW:
While melanoma, the most serious form of skin cancer, is highly curable when it is detected and treated early, the same is not true for more advanced cases of melanoma – particularly when the disease has spread to lymph nodes or other areas of the body.

Recently, two new drugs approved by the U.S. Food and Drug Administration (FDA) – vemurafenib and ipilimumab – that target the genetic makeup of melanoma are showing promise in slowing the progression of this disease and, in some cases, extending survival in patients with advanced melanoma.

TWO NEW DRUGS INTRODUCED FOR ADVANCED MELANOMA:
Research has shown that certain melanomas have specific genetic abnormalities within the melanoma cells. With targeted therapy, the abnormal gene responsible for these melanomas is targeted in an attempt to undo the damage it is causing the cells. Dr. Rigel noted that while a number of targets have been identified, a gene known as BRAF is mutated in 40 to 80 percent of melanoma cells. This mutation causes the cells to grow uncontrollably and cancer to form.

- Vemurafenib – When a BRAF mutation is present, a pathway known as the MAP Kinase Pathway essentially gets “stuck” in the “on” position and the cells start growing very rapidly. The drug vemurafenib attacks the switch of this pathway (or blocks the “on” switch) so that the cells don’t continue to grow uncontrollably. If effective, the cancer is prevented from getting worse.
  o While not a cure for melanoma, researchers found during clinical trials that on average, patients who responded lived 6.2 months without the melanoma getting worse.
  o In some studies it was found that within six to 10 months on average, the melanoma cells develop resistance to the drug. In this case, melanoma cells either develop other Kinase proteins to sidestep the pathway, or they simply use another pathway that is not currently active. Either way, they activate to make cells continue to grow.

- Ipilimumab – This new targeted therapy blocks a specific molecule, which may allow the patient’s body to recognize, target and attack melanoma cells. Researchers now are looking at using ipilimumab in combination with vemurafenib, as they each block two different pathways – with the theory being that there is less chance for resistance to occur.
  o While not a cure for melanoma, researchers found during clinical trials that the patients who received only ipilimumab and responded to it lived about 10 months longer. For a few patients given ipilimumab, the results were dramatic – a few patients have had no signs of cancer for as long as six years.
SIDE EFFECTS CAN POSE PROBLEMS:
Dr. Rigel cautioned that patients taking vemurafenib or ipilimumab may experience troublesome side effects and should be closely monitored by their dermatologist.
- Studies have shown that significant rashes have been reported in approximately 40 percent of patients using vemurafenib.
- One-third of patients taking vemurafenib developed multiple, aggressive squamous cell carcinomas (another common type of skin cancer).

AMERICAN ACADEMY OF DERMATOLOGY (ACADEMY) EXPERT ADVICE:
“Before vemurafenib and ipilimumab were introduced, beating advanced melanoma used to be virtually hopeless and now there is at least some hope for these patients,” said Dr. Rigel.
“Targeted therapy is still in its infancy, but already it has been successful in some cases of advanced melanoma. The technique shows that it will work, and I expect we’ll see even more effective treatments in the future as we fine-tune our targeting of melanoma.”

The Academy urges everyone to examine their skin regularly. This means looking over your entire body including your back, your scalp, your palms, your soles and between your toes. If you notice a mole different from others, or which changes, itches or bleeds, even if it is smaller than 6mm, you should make an appointment to see a dermatologist.

STATISTICS:
According to the American Cancer Society’s 2012 Cancer Facts and Figures:
- 9,180 Americans are estimated to die from melanoma in 2012
- In 2012, it is estimated that the number of Americans diagnosed with melanoma will be 7 percent greater than in 2011
- While the five-year survival rate for localized melanoma is 98 percent, the survival rate of distant, or advanced stage, melanoma is 15 percent

FOR MORE INFORMATION:
To learn more about melanoma, visit the Academy’s Dermatology A to Z section at www.aad.org and SkinCancerNet at www.skincarephysicians.com.

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