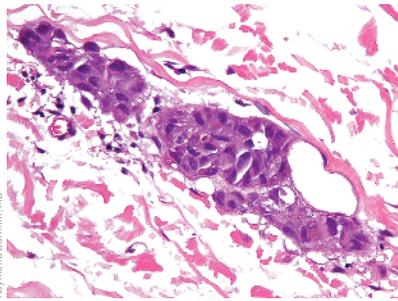


## NEWS IN BRIEF



An angiotropic microscopic satellite is developing away from the primary melanoma. Melanoma cells (dark purple) are wrapping around the abluminal surface of a microvascular channel (at right).

from metastatic disease. “We need more research teams working on this new field of angiotropism and EVMM,” Lugassy says. “There’s still a lot of work left to find the right target to hopefully control melanoma metastasis.” ■

## FGFR Inhibitor Works in Multiple Cancers

A pan-FGFR inhibitor yielded positive safety and efficacy results in multiple cancers, particularly invasive bladder cancer. Investigators reported findings from the phase I trial on April 8 at the American Association for Cancer Research Annual Meeting 2014 in San Diego, CA.

FGFRs are a family of receptor tyrosine kinases involved in cell proliferation and survival. Mutations, amplifications, and translocations in these receptors have been implicated in the development of numerous cancers, including urothelial bladder cancer, squamous non-small cell lung cancer (NSCLC), and breast cancer.

The pan-FGFR inhibitor BGJ398 (Novartis Oncology) selectively blocks FGFR signaling. Various doses—ranging from 5 mg to 150 mg—given once or twice a day were tested in 43 patients with advanced solid tumors showing any FGFR genetic alteration. The maximum tolerated dose of BGJ398 was identified as 125 mg a day.

In the expansion phase of the study, 64 patients with cancers harboring FGFR genetic alterations were separated into three groups that all received 125 mg daily. The first group included 18 patients with *FGFR1*-amplified

squamous NSCLC. The second group included 21 patients with other types of cancer harboring FGFR genetic alterations. The third group also included patients with various FGFR-altered cancer types, but the 25 patients in this group were treated on a 3-weeks-on, 1-week-off schedule rather than taking the drug continuously.

Six patients achieved a partial response: two with *FGFR3*-mutated bladder cancer—one of whom saw her tumor shrink by 45% and has remained on treatment more than 8 months—and four with *FGFR1*-amplified squamous NSCLC. Two other bladder cancer patients experienced tumor shrinkage of greater than 25%. One patient with cholangiocarcinoma with an *FGFR2* gene fusion and four patients with *FGFR1*-amplified breast cancer also experienced some tumor shrinkage.

“These findings suggest that certain types of cancer, specifically bladder cancers and squamous lung cancers that are dependent on FGFR for survival, can be treated with FGFR blockers,” said principal investigator Lecia V. Sequist, MD, an associate professor of medicine at Harvard Medical School and Massachusetts General Hospital in Boston.

The most common drug-related adverse event was an abnormally high serum phosphate level, a side effect that can be managed through diet, phosphate-lowering therapy, or drug interruptions, Sequist said. Other adverse events were generally mild and included stomatitis, hair loss, decreased appetite, and fatigue.

No targeted drugs are currently approved to treat bladder cancer or squamous NSCLC. “This agent could open up a new treatment realm for a significant subset of these populations,” Sequist said. Indeed, *FGFR3* is mutated in 15% of invasive bladder cancers, and *FGFR1* is amplified in about 20% of squamous NSCLC.

Researchers chose the 3-weeks-on, 1-week-off treatment schedule based on its better safety profile. Researchers are planning phase II trials of BGJ398 in cholangiocarcinoma and bladder, lung, and endometrial cancers. A phase II trial in glioblastoma is already under way. ■

## NOTED

- As part of its implementation of the 2009 Family Smoking Prevention and Tobacco Control Act, **the FDA issued a proposed rule (available at [www.federalregister.gov](http://www.federalregister.gov)) that would extend its authority to regulate additional tobacco products** including electronic cigarettes, cigars, pipe tobacco, nicotine gels, water-pipe (or hookah) tobacco, and dissolvables. The FDA currently regulates cigarettes, cigarette tobacco, roll-your-own tobacco, and smokeless tobacco.
- **Novartis announced that it will acquire GlaxoSmithKline’s (GSK) oncology products for as much as \$16.1 billion** and send its vaccines business (excluding flu vaccines) to GSK for \$7.1 billion plus royalties. GSK oncology drugs include the BRAF inhibitor Tafenlar (dabrafenib) and the MEK inhibitor Mekinist (trametinib), both for metastatic melanoma, and the VEGFR inhibitor Votrient (pazopanib) for renal cell carcinoma. The two companies also agreed to combine their consumer divisions to create a world-leading consumer healthcare business.
- **Indianapolis, IN-based Eli Lilly received FDA approval to market Cyramza (ramucirumab) as a single-agent treatment for patients with advanced or metastatic gastric cancer or gastroesophageal junction adenocarcinoma** with disease progression. Approval was based on results of the REGARD trial, which showed significant improvements in median overall and progression-free survival.
- **The agent IMCgp100, a new type of immunotherapy, was well tolerated and showed efficacy in some patients with advanced melanoma in a phase I clinical trial**, according to data reported on April 8 at the American Association for Cancer Research (AACR) Annual Meeting in San Diego, CA. IMCgp100 attaches to cancer cells, activates any adjacent T cells to kill the cancer cells, and recruits other immune cells to help clear the disease.
- **“Overweight and obesity are contributing just about as many excess cancers now in the United States as is current smoking,” commented Walter Willett, MD, MPH, DrPH, of the Harvard School of Public Health in Boston, MA, during a plenary presentation at the AACR meeting on April 6.**

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# CANCER DISCOVERY

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