Safety and Activity of the First-in-Class Sym004 Anti-EGFR Antibody Mixture in Patients with Refractory Colorectal Cancer


Précis: Sym004, a mixture of two EGFR-targeting monoclonal antibodies, induces sustained EGFR downregulation and shows antitumor activity in patients with metastatic anti-EGFR antibody-resistant colorectal cancer.

See commentary, p. 578

Next-Generation Sequencing of Stage IV Squamous Cell Lung Cancers Reveals an Association of PI3K Aberrations and Evidence of Clonal Heterogeneity in Patients with Brain Metastases


Précis: PI3K pathway aberrations in squamous cell lung cancer are associated with increased incidence of brain metastases, which are clonally divergent from their matched primary tumors.

The p53 Target Gene SIVA Enables Non–Small Cell Lung Cancer Development

J.L. Van Nostrand, A. Brisac, S.S. Mello, S.B.R. Jacobs, R. Luong, and L.D. Attardi

Précis: SIVA promotes NSCLC cell proliferation and tumorigenesis independent of p53 via activation of mTOR and stimulation of mitochondrial metabolic function.

See commentary, p. 581
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ON THE COVER

Dienstmann and colleagues found that Sym004, a mixture of two recombinant monoclonal antibodies targeting nonoverlapping EGFR epitopes, induced significant EGFR degradation and growth inhibition in a panel of colorectal cancer cell lines in the presence of EGFR ligands. In a first-in-human phase I trial, Sym004 treatment resulted in sustained EGFR downregulation in tumor samples and was associated with grade 3 skin toxicities and hypomagnesemia that were consistent with known adverse events of anti-EGFR drugs and manageable with dose reductions and supportive care. Furthermore, Sym004 induced tumor shrinkage in 17 (44%) patients with metastatic colorectal cancer and acquired resistance to anti-EGFR therapy, including 5 (13%) patients who achieved a partial response. These findings demonstrate that Sym004 has clinically relevant antitumor activity and may overcome cetuximab or panitumumab resistance in patients with metastatic colorectal cancer. For details, please see the article by Dienstmann and colleagues on page 598.
## CANCER DISCOVERY

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