Combination therapy shows potent tumor growth inhibition in preclinical studies

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Combining the investigational agents REGN910 and aflibercept yielded statistically significant improvements in antitumor effects in animal models compared with either agent alone, according to results presented at the AACR-NCI-EORTC International Conference: Molecular Targets and Cancer Therapeutics, held Nov. 12-16, 2011.

"These preclinical findings suggest that combining REGN910 (SAR307746) and aflibercept in the clinic could be an attractive approach for future clinical research," said Alshad S. Lalani, Ph.D., director of strategic oncology development at Regeneron Pharmaceuticals Inc. in Tarrytown, N.Y. "The rationale is that inhibition of tumor angiogenesis by combining antiangiogenesis treatments could translate into more potent and durable antitumor responses than those observed with single-agent therapy."

In this preclinical mouse study, researchers from Regeneron and BC Cancer Agency in Vancouver, British Columbia, Canada, monitored how REGN910 and aflibercept blocked vascular endothelial growth factor (VEGF) and angiopoietin-2 (Ang2), which are critical growth factors for tumor angiogenesis, or blood vessel formation.

REGN910 is a fully human monoclonal antibody discovered using Regeneron VelocImmune antibody technology that binds and inhibits Ang2. Aflibercept is a fully human fusion protein that binds all forms of VEGF-A, as well as VEGF-B and placental growth factor. REGN910 and aflibercept are being developed by Regeneron and Sanofi.

In addition, researchers performed tissue analyses to monitor the number of tumor blood vessels, tumor hypoxia (oxygen deprivation), tumor cell death and tumor perfusion.

"When used alone in animal studies, both REGN910 and aflibercept blocked tumor angiogenesis and growth; however, the combination of the two led to increased tumor hypoxia and consequently to the death of a large percentage of the tumor cells," Lalani said. "Consistent with its ability to promote rapid and widespread tumor cell death in histology, the combination treatment inhibited tumor growth to a significantly greater extent than the single agents in multiple tumor models - colorectal, mammary and prostate. In particular, it caused dramatic tumor regression in the colorectal tumor models. Importantly, no visible evidence of toxicities or enhanced body weight loss was observed following the combination treatment."

In ongoing animal studies, Lalani and colleagues are studying the reasons behind the results with the combined therapy. They are also investigating biomarkers that will allow them to monitor the combination therapy treatment effect and/or to identify which tumors are most likely to respond to treatment.

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