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Reflexion, Merck team up on collaboration for biology-guided radiotherapy and Keytruda

By Liz Hollis

Hayward, Calif.-based Reflexion Medical Inc. reported a clinical collaboration with Merck & Co. Inc., of Kenilworth, N.J., to evaluate the safety and efficacy of Keytruda (pembrolizumab) in combination with biology-guided radiotherapy (BgRT) in multiple late-stage cancers.

The goal is to establish whether treating multiple tumors with BgRT, a novel external beam radiotherapy treatment (EBRT) modality in development, is safe and amplifies Keytruda's therapeutic effect. Keytruda is a humanized monoclonal antibody that blocks the interaction between PD-1 and its ligands, PD-L1 and PD-L2. One planned target for the collaboration is non-small-cell lung cancer.

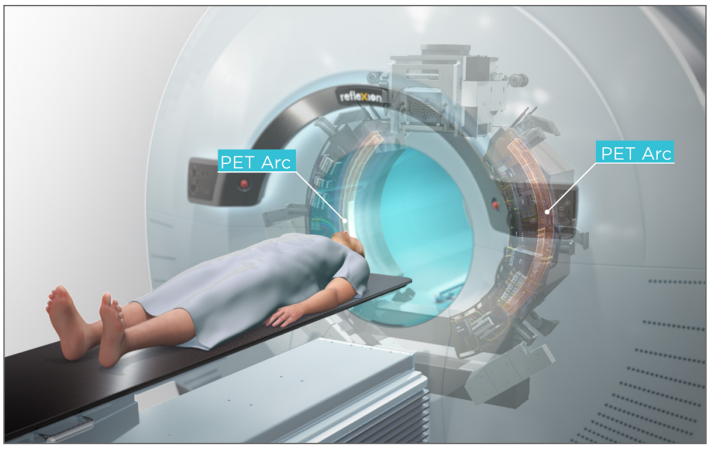
This is big news for Reflexion, which has developed the Reflexion X1 machine with BgRT. That capability, which is not available for sale, is designed to overcome the technical limitations that restrict radiotherapy delivery to one or two sites of disease. It instead allows such therapy to reach multiple areas during the same treatment session – even those sites that move due to breathing or digestion.

Earlier this year, the company revealed that it had received the green light from the U.S. FDA to market its Reflexion X1 system for standard radiation therapy treatments. Specifically, the agency cleared the system for stereotactic body radiotherapy, stereotactic radiosurgery and intensity modulated radiotherapy.

Differentiation

"BgRT ... is a novel advancement of ... EBRT technologies," Thorsten Melcher, chief business officer of Reflexion, told *BioWorld* when asked about what differentiates BgRT from other therapies. "Over the last decades, EBRT has become a very efficacious and cost-effective cancer treatment with a well-understood safety profile."

He went on to note that EBRT with curative intent serves as the standard-of-care in more than 50% of all solid tumor patients. It is a commonly used cancer therapeutic; however, its clinical applications remain limited to patients with stage I, II or III disease due to technical reasons.



Reflexion X1 machine with BgRT. Credit: Reflexion Medical Inc.

The company is hoping to make EBRT accessible for all stages of cancer, to include stage IV or metastatic disease in which patient treatment options are limited. To that end, Reflexion is developing BgRT that combines the functionality of PET/computed tomography with a linear accelerator to direct radiotherapy delivery directly to tumors with sub-second latency.

"BgRT relies on the emissions generated by an injected radiotracer to enable tumors to continuously signal their location and guide the radiotherapy beam during each fraction," Melcher noted. "As a result, BgRT has the potential to allow for real-time, tracked dose delivery to tumors, even in those subject to motion, in a highly parallel fashion that will one day enable treatment of many target lesions in the same session, while also sparing healthy tissue."

This differs from current EBRT technology, which uses anatomic imaging, fiducials, markers and gating to localize the tumor and guide radiotherapy delivery. "Because these methods are not as exact as using the biology of the tumor itself, ... they add a margin of healthy tissue around the tumor to ensure adequate radiation reaches it."

BgRT, meanwhile, has the potential to neutralize mechanisms

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that allow cancer to escape immunotherapy. "BgRT may reduce tumor bulk, tumor heterogeneity, tumor pace and potentially inflame the tumor microenvironment," he explained.

Indeed, early clinical studies combining EBRT with immunotherapy in metastatic cancers revealed a favorable safety profile and increased efficacy as measured by progression-free survival or overall survival. "Potentially, increased efficacy may come without significant added toxicity, as BgRT's toxicity profile is largely non-overlapping with the toxicity profile of systemic therapies."

When asked how long the Merck collaboration was expected to last, he noted that many factors are in play, including possible modifications of the clinical protocols. With that said, more such collaborations could come in order to make cancer a manageable, chronic disease. "The pharmaceutical industry has been very productive in creating novel immunotherapies and drugs that target certain vulnerabilities of cancer cells, and we expect several collaborative opportunities in the future," said Melcher.

FDA, other markets

When asked about going to the FDA for its BgRT capability, he noted that his company is actively engaged with the agency. "We will begin a clinical study at Stanford Cancer Institute, our first commercial site, later this year to collect clinical data in support of that application."

He also explained that the company is laser focused on the U.S. and will control its initial product rollout. "As we gain more experience with our installation and clinician training processes, we will commercialize outside of the U.S. We are currently in the planning phase for these activities," he noted.

The company recently reported the close of a $100 million equity financing round, as well as the sale of the first commercial system of the X1 machine for conventional radiotherapy applications. The equity financing was led by Public Sector Pension Investment Board. Existing investors, TPG's The Rise Fund, KCK Group, Sofinnova Partners, Venrock, T. Rowe Price, as well as Pfizer Ventures and Johnson & Johnson Innovation, JJDC Inc., all participated in the round.