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A multi-targeted approach for treating pancreatic cancer

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Pancreatic cancer often presents as inoperable, locally-advanced or metastatic disease. With traditional forms of chemotherapy, long-term survival for patients with metastatic disease is less than 5%. Due to the heterogeneity within pancreatic lesions, investigators are beginning to tailor treatment regimens to the pathology and biology of individual tumors. Using a systems engineering approach, we have developed both targeted and untargeted nanoliposomal molecules as well as signaling inhibitors to combat malignant solid tumors like pancreatic cancer. Nal-IRI (liposomal irinotecan, ONIVYDE®), MM-310 (EphA2-targeted docetaxel nanoliposome), and istiratumab (a tetravalent IGF-1R and ErbB3 inhibitor) are three examples of novel therapeutic candidates designed to utilize the tumor biology and microenvironment to improve anti-tumor efficacy. Nal-IRI takes advantage of both leaky vasculature and tumor associated macrophages within the tumor environment to enhance delivery and activity of SN-38. With an EphA2-targeting arm, MM-310 is a next generation nanoliposome providing enhanced delivery of and specificity docetaxel to EphA2-positive malignancies. Lastly, istiratumab inhibits pro-survival signaling through the PI3K/AKT/mTOR pathway by blocking and subsequently stripping IGF-1R and ErbB3 from the surface of tumor cells. Nal-IRI is currently being investigated in combination with 5FU, leucovorin, and oxaliplatin in patients with newly diagnosed metastatic pancreatic cancer. Targeted ()biomarker-driven patient selection is being utilized in both the phase 1 study of MM-310 for patients with EphA2-positive cancers, and in the phase 2 study of istiratumab in combination with nab-paclitaxel and gemcitabine in newly diagnosed metastatic pancreatic cancer patients who have elevated levels of free IGF-1 in their serum.

Biography

Chrystal U Louis has obtained her MD from Tulane University School of Medicine and her MPH from Tulane University School of Public Health and Tropical Medicine. She completed her Pediatric Oncology Training from the Texas Children's Cancer and Hematology Centers and Baylor University School of Medicine. As a member of the Center for Cell and Gene Therapy, she became a successful Translational Researcher in the field of virus-specific and chimeric antigen receptor-specific cellular immunotherapy. She has joined the Discovery division of Merrimack Pharmaceuticals in 2014 and is currently the Medical Director and Project Leader of the Istiratumab (MM-141) team.

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