Transcript Details
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Understanding the Biology to Target K-RAS Driven Tumors: Notes from a Presentation at ESMO 2021

Announcer Introduction
Welcome to *Project Oncology* on ReachMD. On this episode, sponsored by AstraZeneca and Daiichi-Sankyo, we're joined by Dr. James G. Christensen who's involved in Clinical Discovery at Mirati Theraeutics, Inc. in San Diego, California. Dr. Christensen is here to recap his presentation from the European Society of Medical Oncology 2021 Congress exploring K-RAS driven tumors. Let's hear from Dr. Christensen now.

DR. CHRISTENSEN:
The presentation at the ESMO meeting covered the activity of adagrasib in colorectal cancer patients as either a monotherapy or in combination.

So for the ESMO meeting, the key top line data was essentially illustrating the monotherapy activity of adagrasib in colorectal cancer patients harboring G12C mutations, KRAS G12C mutations. And these were essentially patients that had a median of three and a half lines of prior therapy and were heavily pretreated. This is a treatment setting where the standard of care exhibits a low response rate generally in the low single digit response rate and those patients along with a low progression-free survival and overall survival. The adagrasib monotherapy data illustrated a response rate of around 22 percent. The response rate in combination with cetuximab was an additional therapy that is designed to augment the activity of adagrasib in this patient population. The response rate was approaching 45 percent in that particular setting, with early signs of durability for those particular patients. So an opportunity to evolve the standard of care treatment for late-line colorectal cancer patients harboring KRAS G12C mutations.

So together I think a nice illustration of the opportunity to evolve targeted cancer therapies in the colorectal and pancreatic cancer space.

In this presentation, we also noted that KRAS can act as an oncogenic driver in pancreatic ductal adenocarcinoma using adagrasib data in G12C-positive patients to illustrate this point, and there are 5 out of 10 patients had illustrated or had had partial responses to therapy,in this particular population, illustrating this as a potential population for use of KRAS mutation specific inhibitors as well.

You know, of course, these are early data, and we need to continue to evaluate the drug and especially with respect to the durability of response, the progression-free survival, and ultimately the survival for these particular patients in the disease setting. We'll just say that with regard to the standard of care for patients that are heavily pretreated in colorectal cancer, that it's likely that these results represent a true treatment advance for this setting. If those results should hold up, that's an opportunity to change or evolve standard of care for patients that have no other treatment options.

And we'll just note for the pancreatic ductal adenocarcinoma patients, again, very early data, 5 out of 10 patients had exhibited a partial response to therapy. These patients that are third line or plus in pancreatic cancer, there are very few treatment options for those patients. And again, if the data should hold up, including the duration of response, andeventually theprogression-free or overall survival, again, an opportunity to continue to evaluate toshow the opportunity to evolve standard of care in these particular patients.

And finally, with regard to the discovery of the KRAS G12D inhibitorjust to note that these particular patients are about three times more prevalent than those harboring G12C mutations. And the opportunities are stronger in the setting, particularly of pancreatic ductal adenocarcinoma or colorectal cancer. And again, this is a drug discovery projects. If we can find a way to effectively move that discovery project into a development project, the data highlighted for adagrasib in G12C-positive patients, if that is able to hold true for G12D-positive patients, again, I think an opportunity to evolve the treatment paradigm for those patients.

Announcer Close

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