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FDA approves Merck's Keytruda in combination with Inlyta

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Approval is based on results of KEYNOTE-426, where KEYTRUDA in combination with Axitinib reduced the risk of death by nearly half compared to Sunitinib.

Merck has announced that the U.S. Food and Drug Administration has approved KEYTRUDA, Merck's anti-PD-1 therapy, in combination with Inlyta (axitinib), a tyrosine kinase inhibitor, for the first-line treatment of patients with advanced renal cell carcinoma (RCC). The approval is based on findings from the pivotal Phase 3 KEYNOTE-426 trial, which demonstrated significant improvements in overall survival (OS), progression-free survival (PFS) and objective response rate (ORR) for KEYTRUDA in combination with axitinib (KEYTRUDA-axitinib combination) compared to sunitinib. Consistent results were observed across pre-specified subgroups, IMDC risk categories and PD-L1 tumor expression status. For the main efficacy outcome measures of OS and PFS, the KEYTRUDA-axitinib combination reduced the risk of death by 47% compared to sunitinib (HR=0.53 [95% CI, 0.38-0.74]; p<0.0001); for PFS, the KEYTRUDA-axitinib combination showed a reduction in the risk of progression of disease or death of 31% compared to sunitinib (HR=0.69 [95% CI, 0.57-0.84]; p=0.0001). The ORR, an additional efficacy outcome measure, was 59% for patients who received the KEYTRUDA-axitinib combination (95% CI, 54-64) and 36% for those who received sunitinib (95% CI, 31-40) (p<0.0001). This is the first indication for KEYTRUDA in advanced RCC, the most common type of kidney cancer, and the first anti-PD-1 therapy FDA-approved as part of a combination regimen that significantly improved OS, PFS, and ORR versus sunitinib in patients with advanced RCC.

"This represents a new treatment option for patients with advanced renal cell carcinoma, who will now have access to KEYTRUDA as part of a first-line combination regimen," said Dr. Scot Ebbinghaus, vice president, clinical research, Merck Research Laboratories. "Today's approval reflects Merck's commitment to patients with cancer and further supports the use of KEYTRUDA to help improve survival outcomes for patients with advanced renal cell carcinoma."

Immune-mediated adverse reactions, which may be severe or fatal, can occur with KEYTRUDA, including pneumonitis, colitis, hepatitis, endocrinopathies, nephritis and renal dysfunction, severe skin reactions, solid organ transplant rejection, and complications of allogeneic hematopoietic stem cell transplantation (HSCT). Based on the severity of the adverse reaction, KEYTRUDA should be withheld or discontinued and corticosteroids administered if appropriate. KEYTRUDA can also cause severe or life-threatening infusion-related reactions. Based on its mechanism of action, KEYTRUDA can cause fetal harm

when administered to a pregnant woman. For more information, see “Selected Important Safety Information” below.

“Given the aggressive nature of the disease, many patients with advanced renal cell carcinoma need additional treatment options that can help improve survival outcomes,” said Dr. Brian Rini, medical oncologist at Cleveland Clinic Cancer Center and professor of medicine at the Cleveland Clinic Lerner College of Medicine of Case Western Reserve University. “Pembrolizumab in combination with axitinib offers an important new therapeutic option for physicians to consider when approaching initial treatment for patients newly diagnosed with advanced renal cell carcinoma.” Dr. Rini reports consulting and research funding from Merck.

The approval was based on data from the pre-specified interim analysis of Phase 3 KEYNOTE-426 trial, a randomized, multi-center, open-label trial conducted in 861 patients who had not received systemic therapy for advanced RCC. Patients were enrolled regardless of PD-L1 tumor expression status. Randomization was stratified by International Metastatic RCC Database Consortium (IMDC) risk categories (favorable versus intermediate versus poor) and geographic region (North America versus Western Europe versus “Rest of the World”). Patients with an active autoimmune disease requiring systemic immunosuppression within the last two years were ineligible.