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Mechanism and Clinical Role and Application of DNA
Methyltransferase Inhibitors Combination Therapy for the Treatment
of Solid Tumor

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#### Abstrac

According to the results of a global phase 2 clinical trial, the new drug sotorasib reduces tumor size and promises to improve and increase survival in patients with lung tumors caused by specific DNA mutations. It is designed to counteract the effects of mutations that are seen in about 13% of patients with non-small cell lung adenocarcinoma (a common type of lung cancer). The Food and Drug Administration (FDA) on May 28 approved the drug as a targeted treatment for patients with small cell lung cancer whose tumors express a specific mutation called G12C in the KRAS gene. Small cell lung cancer accounts for more than 80% of lung cancers. More than 200,000 new cases of non-small cell lung cancer are diagnosed in the United States each year.

**Keywords**: Cancer; Cells; Tissues, Tumors; Prevention, Prognosis; Diagnosis; Imaging; Screening; Treatment; Management

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#### Introduction

Also known as the Lumakras brand, it was manufactured by Amgen and paid for by testing. "The new drug addresses the unmet needs of these patients and targets the most common mutation." To improve or not. This drug is for those patients whose tumors are difficult to treat and for whom we have not provided targeted therapies. The study included 126 patients with non-small cell lung cancer who had specific mutations in the KRAS gene. A DNA error inhibits an important protein

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structure and puts cysteine where glycine should be. Mutated tumors produce a copy of the KRAS protein that is almost continuously active and promotes tumor growth. Sotorasib, taken orally daily, inhibits tumor growth by inactively trapping KRAS protein. Most patients in this trial have already received standard chemotherapy with an immunotherapy drug that targets a protein called PD-1. To evaluate this new treatment, all patients enrolled in this study were treated with sotorasib. Phase 2 trials evaluating safety and efficacy often do not include the placebo group. It inhibited tumor spread in 102 of 126 patients (82%). About 37% of patients' tumors shrink by at least 30% in size. In contrast, the response rate to standard treatment in these patients is from 6% to 20%. Forty-two patients (34%) showed a relative response to treatment, meaning that the tumor was significantly smaller and its growth was controlled for some time, and four patients (3%) showed a complete response, leaving no evidence of disease. For tumors that have shrunk, on average, about 60% of the tumor shrinks. The effects of sotorasib lasted an average of 11 months, the drug showed no progression survival, patients with this type of lung cancer receiving standard treatment have an average progression of two to four months without progression. The mean overall survival of patients in this experiment was 12 months [1-510].

#### **Results and Discussion**

We hope this is a new option for patients with lung cancer who are driven by this particular type of KRAS gene mutation. KRAS gene modification has long been unacceptable for targeted therapies. A number of combination diets are being tested here at the Cytman Cancer Center and other leading cancer centers around the world. These are highlights of what the University of Washington has done in the past to study the genomic variations of tumors to identify therapeutic targets; this preliminary

research on the cancer genome is now in full swing to help our patients.

"The excitement of this test result is that sotorasib is currently the first targeted treatment for patients with lung cancer," said Welchti, another specialist in the field. KRAS-targeted treatments are needed for these patients with limited immediate treatment options.

About 7% of patients discontinued sotorasib treatment due to severe side effects, but no life-threatening side effects and no disease died as a result of treatment. This drug caused severe side effects that required a reduction in the dose of the drug in about 22% of patients. Approximately 70% of patients experienced some drug-related side effects. The most common of these were diarrhea, fatigue, nausea, and elevated liver enzyme levels, which are indicators of liver damage.

#### **Conclusions**

Clinically demonstrated KRAS mutant lung cancer in patients with this particular type without any new safety concerns. Moving forward, the team is working to learn about the development of combination therapies with sotorasib and other emerging drugs, and to determine which direction is best for each patient's cancer cells. Researchers are currently conducting a phase 3 clinical trial to compare the effectiveness of sotorasib with a chemotherapy drug called docetaxel in 345 patients with non-small cell lung cancer and this KRA mutation.

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