

# Investigational AKT inhibitor AZD5363 is active against multiple tumor types with AKT1 E17K mutations

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Treatment with the investigational pan-AKT inhibitor AZD5363 led to tumor regression in patients with a variety of types of solid tumors positive for the AKT1 E17K genetic mutation, according to data from a phase I clinical trial expressly designed to recruit patients with these types of tumors. The data were presented at the AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics, held Nov. 5–9.

"The AKT1 E17K genetic mutation was detected in a range of tumor types almost 10 years ago," said David M. Hyman, MD, acting director of developmental therapeutics at Memorial Sloan Kettering Cancer Center in New York. "Because the mutation is found in only a small fraction of cases of each tumor type and clinical trials have traditionally enrolled [patients](#) with only one type of [cancer](#), it was not possible to determine whether the mutation fuels the growth of these tumors and is a viable therapeutic target until the recent advent of basket trials, whereby patients with a range of types of tumor all harboring a defined mutation are enrolled in a single clinical trial.

"The most up-to-date results show that among the 41 patients with AKT1 E17K mutation–positive tumors for which there are data available, 33 had tumor shrinkage after receiving AZD5363," continued Hyman. "To have seen an array of tumor types respond to single-agent AZD5363 is extremely encouraging, although we need further studies to confirm the clinical benefit, and supports the utility of the basket trial design."

To date, 45 patients with tumors positive for the AKT1 E17K mutation have received AZD5363 through the phase I clinical trial. Twenty-one patients had estrogen receptor–positive breast cancer, four had triple-negative breast cancer, 14

had a gynecological cancer, and eight had another cancer type.

Among the 33 patients who had [tumor shrinkage](#), 12 had partial responses, as assessed by RECIST 1.1 criteria, including six patients with estrogen receptor–positive breast cancer.

The researchers were able to analyze circulating tumor DNA in serial blood samples from 15 patients. Persistent declines in levels of the AKT1 E17K mutation in circulating tumor DNA were associated with durable [tumor regression](#) and increasing levels preceded clinically or radiologically defined disease progression in seven of seven patients.

"Our circulating [tumor](#) DNA data highlight the potential of liquid biopsies as a useful tool to help monitor treatment responses to targeted therapeutics," said Hyman.

The adverse events were consistent with a previous report, with the most common being diarrhea, rash, and elevated blood glucose levels.

According to Hyman, the major limitations of the current study are that it involves only small numbers of patients and it is ongoing, which means that the response rates may change over time.

Provided by American Association for Cancer Research

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