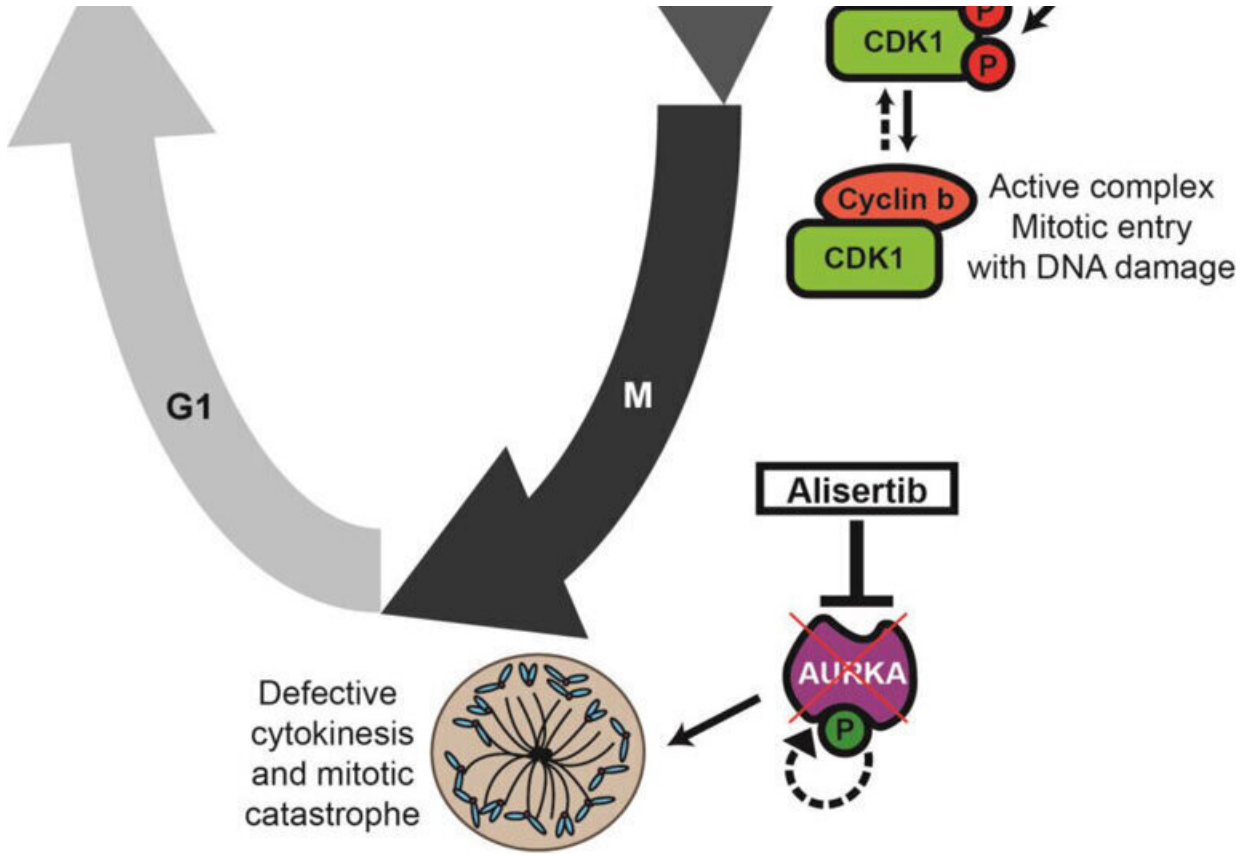
Medical Xpress

New findings support novel combination treatment for head and neck cancers

April 5 2023



Schematic model of the effect by the combined inhibition of AURKA and WEE1 in this study. The addition of the WEE1 inhibitor adavosertib would prevent the checkpoint kinase WEE1 with dephosphorylating CDK1 therefore leading to mitotic entry in the presence of DNA damage. When the AURKA inhibitor alisertib is concomitantly added, a failure in cytokinesis including spindle formation and centrosome maturation would in turn lead to mitotic catastrophe and cell death. Credit: *Clinical Cancer Research* (2019). DOI:

10.1158/1078-0432.CCR-18-0440

Human papillomavirus (HPV)-negative head and neck squamous cell carcinoma (HNSCC) and lung cancer can have disruptive mutations in TP53 and/or CDKN2A tumor suppressor genes, which are associated with poor patient survival.

Division Chief of Head and Neck Cancers/Sarcoma at Yale Cancer Center and Smilow Cancer Hospital, Barbara Burtness, MD, will join fellow researchers to share new findings, building on a 2019 study published in Clinical Cancer Research at the April American Association for Cancer Research (AACR) annual meeting in Orlando, FL. Dr. Burtness is co-author of the study, which suggested a combination treatment with adavosertib and alisertib led to antitumor effects.

"Head and neck cancers often have undruggable mutations in tumor suppressor genes, and our lab has been focused on exploiting the survival pathways in these cancers to find new drug targets," said Dr. Burtness, who is also a professor of medicine (medical oncology) at Yale Cancer Center.

In this study, researchers evaluated treatment with the AURKA inhibitor alisertib (MLN8237) and the WEE1 inhibitor adavosertib (AZD1775), alone, or in combination. The results support further evaluation of combined AURKA and WEE1 inhibition as a novel and effective treatment for patients with HNSCC or lung cancer with elevated AURKA expression.

Dr. Burtness said, "We previously showed that when the tumor suppressor p53 is mutated, cells are susceptible to treatment with an

inhibitor of Aurora kinase A, and that the combination of the Aurora kinase A inhibitor with a WEE1 inhibitor was synergistic. We have now uncovered a new mechanism for this synergy, demonstrating that Aurora kinase A inhibition impairs replication fork progression, increasing dependence on WEE1 and making WEE1 an important target for combination therapy. We hope to advance this combination into clinical trials."

Additional Yale authors include Jong Woo Lee, Wendell Yarbrough, Erica Golemis, Ja Seok Koo, Elizabeth Perry, and Jeffrey Townsend. The research team at Yale Cancer Center collaborated with scientists at Johns Hopkins School of Medicine in Baltimore, Maryland on the study.

Provided by Yale Cancer Center/Smilow Cancer Hospital

Citation: New findings support novel combination treatment for head and neck cancers (2023, April 5) retrieved 5 May 2024 from https://medicalxpress.com/news/2023-04-combination-treatment-neck-cancers.html