Adlai Nortye

Adlai Nortye Announces the Publication of the Biomarker Analysis From BERIL-1

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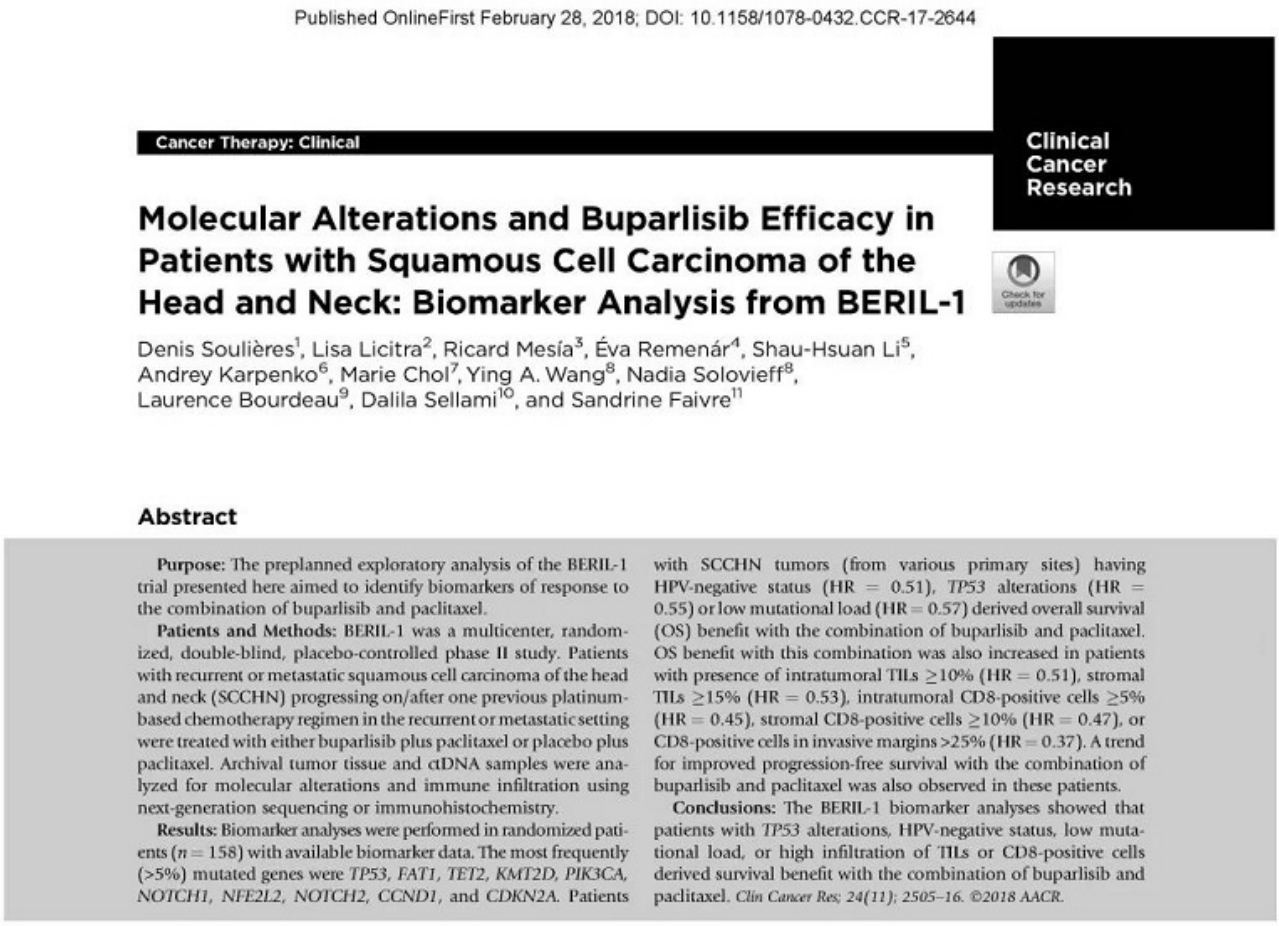
HANGZHOU, China, July 30, 2018, Adlai Nortye Corporation, a leading biotech company in China, today announced a biomarker analysis publication by the investigators from the phase II study BERIL-1 Buparlisib/Paclitaxel vs Paclitaxel in 2nd Line HNSCC. The study was published by Clinical Cancer Research, June 2018, volume 24, issue 11, titled "Molecular Alterations and Buparlisib Efficacy in Patients With Squamous Cell Carcinoma of the Head and Neck: Biomarker Analysis From BERIL-1".



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Cancer Therapy: Clinical

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Molecular Alterations and Buparlisib Efficacy in Patients with Squamous Cell Carcinoma of the Head and Neck: Biomarker Analysis from BERIL-1

Denis Soulières[1], Lisa Licitra[2], Ricard Mesía[3], Éva Remenár[4], Shau-Hsuan Li[5], Andrey Karpenko[6], Marie Chol[7], Ying A. Wang[8], Nadia Solovieff[8], Laurence Bourdeau[9], Dalila Sellami[10], and Sandrine Faivre[11]

Abstract

Purpose: The preplanned exploratory analysis of the BERIL-1 trial presented here aimed to identify biomarkers of response to the combination of buparlisib and paclitaxel.

Patients and Methods: BERIL-1 was a multicenter, randomized, double-blind, placebo-controlled phase II study. Patients with recurrent or metastatic squamous cell carcinoma of the head and neck (SCCHN) progressing on/after one previous platinum-based chemotherapy regimen in the recurrent or metastatic setting were treated with either buparlisib plus paclitaxel or placebo plus paclitaxel. Archival tumor tissue and ctDNA samples were analyzed for molecular alterations and immune infiltration using next-generation sequencing or immunohistochemistry.

Results: Biomarker analyses were performed in randomized patients ($n = 158$) with available biomarker data. The most frequently (>5%) mutated genes were *TP53, FAT1, TET2, KMT2D, PIK3CA, NOTCH1, NFE2L2, NOTCH2, CCND1,* and *CDKN2A*. Patients with SCCHN tumors (from various primary sites) having HPV-negative status (HR = 0.51), *TP53* alterations (HR = 0.55) or low mutational load (HR = 0.57) derived overall survival (OS) benefit with the combination of buparlisib and paclitaxel. OS benefit with this combination was also increased in patients with presence of intratumoral TILs ≥10% (HR = 0.51), stromal TILs ≥15% (HR = 0.53), intratumoral CD8-positive cells ≥5% (HR = 0.45), stromal CD8-positive cells ≥10% (HR = 0.47), or CD8-positive cells in invasive margins >25% (HR = 0.37). A trend for improved progression-free survival with the combination of buparlisib and paclitaxel was also observed in these patients.

Conclusions: The BERIL-1 biomarker analyses showed that patients with *TP53* alterations, HPV-negative status, low mutational load, or high infiltration of TILs or CD8-positive cells derived survival benefit with the combination of buparlisib and paclitaxel. *Clin Cancer Res; 24(11); 2505–16. ©2018 AACR.*

The paper contains the analysis results of tumor tissue and ctDNA samples collected in the phase II study, and concluded that the BERIL-1 biomarker analyses showed that patients with TP53 alterations, HPV-negative status, low mutational load or above-threshold infiltration of TILs or CD8-positive cells derived survival benefit with the combination of buparlisib and paclitaxel. Early last year, the full phase II study data were also published on The Lancet Oncology Jan. 27, 2017: http://dx.doi.org/10.1016/S1470-2045(17)30064-5

Mr. Yang Lu, the CEO of Adlai Nortye stated, "We are firmly committed to bringing Buparlisib to the market for the treatment of HNSCC and the findings in this study provide important direction for the future Buparlisib program (AN2025) in HNSCC. This is in line with Adlai Nortye's strong commitment to developing unique therapeutic options for cancer patients."

Dr. Denis Soulières, medical oncologist at Centre Hospitalier de l'Université de Montréal, Montréal, Canada, principal investigator on BERIL-1 and leading author of the publication, commented, "As investigators and treating physicians we are very excited to see the Buparlisib (AN2025) development moving forward in the HNSCC indication. HNSCC are the 6th most common cancers worldwide and 3rd most common cancers in the developing world. They account for about 5% of all malignancies worldwide and constitute a very important unmet medical need. Buparlisib (AN2025) showed strong results in a randomized trial in the second line setting of HNSCC and could become an important asset for the treatment of these patients."

About Buparlisib (AN2025)

Buparlisib (BKM120) is an oral pan-PI3K inhibitor that targets all class 1 PI3K isoforms and is active in both hematologic malignancies and solid tumors. It has shown promising efficacy in combination with paclitaxel in head and neck squamous cell carcinoma (HNSCC) and has received a Fast-Track designation from the FDA. Combination of buparlisib and paclitaxel demonstrated improved clinical efficacy with a manageable safety profile in patients with HNSCC compared to paclitaxel alone.