



Thoracic
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In This Issue:

Trial for Patients Doing Well on Nivolumab Expands to UCLA
Checkmate 384

Page 1

Pre-Surgical Immunotherapy Trial to open Mid-February
Genentech ML39236

Page 1

OncoTargets and Therapy Publication
A randomized phase II trial of the tumor vascular disrupting agent CA4P with carboplatin, paclitaxel, and bevacizumab in advanced NSCLC

Page 2

Cell Reports Publication
Targeted Inhibition of EGFR and Glutaminase Induces Metabolic Crisis in EGFR mutant lung cancer

Page 2

Trial for Patients Doing Well on Nivolumab Expands to UCLA

We are happy to announce that the Checkmate 384 study will be open tomorrow at UCLA sites in addition to the sites already open in the TRIO-US network. This study is a dose frequency optimization trial of nivolumab in patients with Stage IIIB or Stage IV squamous or non-squamous non-small cell lung cancer. The Checkmate 384 study will investigate whether or not progression-free survival at 6 months and at 1 year after receiving twice the dose of nivolumab half as frequently is inferior to nivolumab 240 mg every 2 weeks.

Patients must have received up to 12 months of nivolumab therapy at either 3mg/kg or 240 mg every 2 weeks with either complete response, partial response, or stable disease prior to enrollment. Patients will receive either 240 mg of nivolumab every 2 weeks or 480 mg nivolumab every 4 weeks and will continue treatment until disease progression or unacceptable toxicity for a maximum of 5 years.

The Checkmate 384 study is open to enrollment at UCLA Main campus, UCLA satellite sites in Alhambra, Burbank, Pasadena, Porter Ranch, Torrance, Valencia, and West Lake as well as sites in the TRIO-US network including Fullerton, Bakersfield, Santa Maria, Redondo Beach, Ft. Wayne, IN, Hollywood, FL, Wichita, KS, Paducah KY.

Pre-surgical Immunotherapy Trial to Open Mid-February

We are excited to announce the upcoming opening of a pre-surgical immunotherapy trial for patients with Stage IB, II, or IIIA non-small cell lung cancer. The Genentech ML39236 study will open on February 15th.

The Genentech ML39236 study is a phase II, open-label trial that will investigate atezolizumab as neoadjuvant (prior to surgery) and adjuvant (after surgery) therapy in patients with resectable and untreated non-small cell lung cancer. Atezolizumab is an antibody that inhibits the PD-L1 immune checkpoint pathway. Patients in Part 1 will receive neoadjuvant treatment with atezolizumab every three weeks for a maximum of two 21 day cycles. Following this initial therapy, patients will have their tumor surgically removed. In Part 2, interested patients can receive adjuvant treatment with atezolizumab every three weeks up to 12 months.

Eligible patients must have untreated Stage IB, II, or IIIA non-small cell lung cancer and eligible for surgical resection with curative intent. Interested patients must also be able to provide tissue for biomarker analysis prior to the start of treatment. The trial will open to enrollment at UCLA Main Campus.

Cell Reports Publication

An article discussing metabolic crisis in EGFR mutant lung cancer induced by targeted inhibition of EGFR and glutaminase was recently published in *Cell Reports*.

In order to keep up with the bioenergetics needs of proliferation, cancer cells use large amounts of nutrients, including glucose and glutamine. Glutaminase is a protein that plays a key role in cancer cell metabolism by converting glutamine into the amino acid glutamate. In an effort to suppress tumor growth by limiting the cancer cells' ability to utilize glucose and glutamine, researchers tested CB-839, an inhibitor of glutaminase, with erlotinib in EGFR mutant positive non-small cell lung cancer.

Tumor cells underwent metabolic crisis and cell death, leading to tumor regression in vivo in mouse non-small cell lung cancer models. In addition, PET imaging indicated a reduction in glucose and glutamine uptake in tumors treated with CB-839 and erlotinib.

Momeilovic M, Bailey ST, Lee JT, Fishbein MC, Magyar C, Braas D, Graeber T, Jackson NJ, Czernin J, Emberley E, Gross M, Janes J, Mackinnon A, Pan A, Rodriguez M, Works M, Zhang W, Parlati F, Demo S, Garon E, Krysan K, Walser TC, Dubinett SM, Sadeghi S, Christofk HR, Shackelford DB. Targeted inhibition of EGFR and glutaminase induces metabolic crisis in EGFR mutant lung cancer. *Cell Rep*. 2017 Jan 17;18(3):601-610. Doi:10.1016/j.celrep.2016.12.061

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OncoTargets and Therapy Publication

An article discussing the use of CA4P in combination with carboplatin, paclitaxel, and bevacizumab in patients with NSCLC was recently published in *OncoTargets and Therapy*.

Combretastatin A4-phosphate, fosbretabulin tromethamine (CA4P) is an agent designed to damage the blood vessels of tumors. In this study, patients with advanced, nonsquamous non-small cell lung cancer who were chemotherapy-naïve were treated with carboplatin, paclitaxel, and bevacizumab. Half of the patients were randomized to additionally receive CA4P.

Results showed that CA4P plus carboplatin, paclitaxel, and bevacizumab is a tolerable regimen with acceptable toxicity profile. The overall tumor response rate with CA4P was 50% versus 32% in controls.

Garon EB, Neidhart JD, Gabrail NY, de Oliveria MR, Balkissoon J, Kabbinnar F. A randomized phase II trial of the tumor vascular disrupting agent CA4P (fosbretabulin tromethamine) with carboplatin, paclitaxel, and bevacizumab in advanced nonsquamous non-small cell lung cancer. *Onco Targets Ther*. 2016 Nov 30;9:7275-7283. eCollection 2016.

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