MEET GREG

A REAL PATIENT LIVING WITH ALK+ mNSCLC

Medical, Family, and Social History:

- CrossFit athlete and fitness trainer who enjoys being outdoors and leads an active lifestyle
- Loves spending time with his wife, family, and dog, Ruby
- Smoked socially for 2 years in high school (<5 cigarettes per day)
- Family history of cancer
- Board member of a non-profit lung cancer organization

LEARN ABOUT GREG'S TREATMENT JOURNEY INSIDE.

INDICATION

ALUNBRIG® (brigatinib) is indicated for the treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive metastatic non-small cell lung cancer (NSCLC) as detected by an FDA-approved test.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Interstitial Lung Disease (ILD)/Pneumonitis

Severe, life-threatening, and fatal pulmonary adverse reactions consistent with interstitial lung disease (ILD)/pneumonitis have occurred with ALUNBRIG. In ALTA 1L, ILD/pneumonitis occurred in 5.1% of patients receiving ALUNBRIG. ILD/pneumonitis occurred within 8 days of initiation of ALUNBRIG in 2.9% of patients, with Grade 3 to 4 reactions occurring in 2.2% of patients. In the ALTA study, at the approved dose (90→180 mg), ILD/pneumonitis occurred in 9.1% of patients. Monitor for new or worsening respiratory symptoms (dyspnea, cough, etc.), particularly during the first week of initiating ALUNBRIG. Withhold ALUNBRIG in any patient with new or worsening respiratory symptoms, and promptly evaluate for ILD/pneumonitis or other causes of respiratory symptoms (e.g., pulmonary embolism, tumor progression, and infectious pneumonia). For Grade 1 or 2 ILD/pneumonitis, either dose reduce or permanently discontinue ALUNBRIG. Permanently discontinue ALUNBRIG for Grade 3 or 4 ILD/pneumonitis or recurrence of Grade 1 or 2 ILD/pneumonitis.

ALK, anaplastic lymphoma kinase; mNSCLC, metastatic non-small cell lung cancer.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information in the pocket.

ALUNBRIG®
BRIGATINIB
180mg | 90mg | 30mg
TABLETS

GREG'S DIAGNOSIS AND TREATMENT JOURNEY

Diagnosis of ALK+ mNSCLC:

- In May of 2021, Greg noticed an increased time to recovery after his usual workouts and, a few weeks later, developed swelling of lymph nodes.
- A month later, the lymph node swelling worsened, followed by persistent and worsening cough. He was treated for pneumonia with antibiotics and an inhaler following a chest X-ray.
- As his symptoms did not improve, he was referred to a pulmonologist and treated with high-dose steroids for sarcoidosis.
- Greg's cough worsened and he developed cognitive issues on the third day.
- On the fourth day, he had a bout of hemoptysis and went to the emergency room. A CT scan revealed pulmonary embolism. Anticoagulation therapy was initiated, and steroids were discontinued.
- A few days later, Greg developed aphasia and loss of motor skills. A consultation with a neurologist and an MRI of the brain revealed 13 lesions.
- After bronchoscopy with bronchoalveolar lavage, pleural biopsy, and next-generation sequencing, Greg was diagnosed with ALK+ mNSCLC at 40 years of age, in early September of 2021.

Initial Treatment

- Radiation therapy for symptomatic brain metastases was initiated followed by treatment with a TKI.
- After three weeks of TKI therapy, Greg developed bilateral DVT, hypercholesterolemia, hypoxia, and was suspected of developing interstitial lung disease.

HOW WOULD YOU TREAT A PATIENT LIKE GREG?

Trial Design[a]: ALTA 1L was a Phase 3, open-label, multicenter trial that evaluated adult patients with advanced ALK+ NSCLC who had not previously received an ALK-targeted therapy. Patients were randomized (1:1) to receive ALUNBRIG 180 mg orally once daily with a 7-day lead-in at 90 mg once daily (n=137) or crizotinib 250 mg orally twice daily (n=138). Patients with a history of interstitial lung disease, drug-related pneumonitis, or radiation pneumonitis were excluded.[1,2]

Primary Endpoint[1]: BIRC-assessed mPFS[b] with ALUNBRIG was 24.0 months (95% CI: 18.5, NE) vs 11.0 months (95% CI: 9.2, 12.9) with crizotinib. HR=0.49 (95% CI: 0.35, 0.68); *P*<0.0001.[c]

Confirmed BIRC-Assessed Response Rates (ITT Population)[1,3]: ALUNBRIG (n=101/137) and crizotinib (n=85/138).

- ORR: 74% (95% CI: 66, 81) vs 62% (95% CI: 53, 70) with crizotinib; *P*=0.0342[c]
  - CR: 15% (95% CI: 9, 22) vs 9% (95% CI: 5, 15) with crizotinib
  - PR: 59% (95% CI: 50, 67) vs 53% (95% CI: 44, 61) with crizotinib

[a]Baseline characteristics were balanced across trial arms: the median age was 59 years, 55% of patients were female, and 96% had an ECOG status of 0 or 1; 29% of patients had brain metastases at baseline, 27% had received prior chemotherapy, and 13% had received prior radiotherapy to the brain. Eligible patients were allowed to have up to 1 prior regimen of chemotherapy in the locally advanced or metastatic setting and were required to have an ECOG Performance Status of 0-2.[1,3]

[b]According to RECIST v1.1.

[c]Stratified by presence of brain metastases at baseline and prior chemotherapy for locally advanced or metastatic disease for log-rank test and Cochran-Mantel-Haenszel test, respectively.[1]

ALK, anaplastic lymphoma kinase; BIRC, Blinded Independent Review Committee; CI, confidence interval; CR, complete response; CT, computerized tomography; DVT, deep vein thrombosis; ECOG, Eastern Cooperative Oncology Group; HR, hazard ratio; ITT, intent to treat; mNSCLC, metastatic non-small cell lung cancer; mPFS, median progression-free survival; MRI, magnetic resonance imaging; NE, not estimable; ORR, overall response rate; PR, partial response; RECIST, Response Evaluation Criteria In Solid Tumors; TKI, tyrosine kinase inhibitor.

WARNINGS AND PRECAUTIONS (continued)

Hypertension

In ALTA 1L, hypertension was reported in 32% of patients receiving ALUNBRIG; 13% of patients experienced Grade 3 hypertension. Control blood pressure prior to treatment with ALUNBRIG. Monitor blood pressure and withhold ALUNBRIG for Grade 3 hypertension despite optimal antihypertensive therapy.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information in the pocket.

GREG'S TREATMENT GOALS

- An option with strong systemic efficacy
- Due to his brain metastases, he wanted a treatment with strong intracranial efficacy and an acceptable safety profile
- Continue an active lifestyle, spend quality time with his wife and family, and maintain his quality of life with a treatment option that is well tolerated

*It was **important that ALUNBRIG has the ability to impact brain metastases.** My wife and I discussed ALUNBRIG and felt like the side effect profile could be manageable for me. We also appreciated that it was one pill a day.*[1]

— Greg

ALUNBRIG was initiated at 90 mg once daily for the first 7 days, then the dose was increased to 180 mg once daily[1]

SEE GREG'S RESULTS ON THE BACK COVER.

- **Serious adverse reactions occurred in 33% of patients receiving ALUNBRIG.** The most common serious adverse reactions in ALTA 1L were pneumonia (4.4%), ILD/pneumonitis (3.7%), pyrexia (2.9%), dyspnea (2.2%), pulmonary embolism (2.2%), and asthenia (2.2%). Fatal adverse reactions occurred in 2.9% of patients and included pneumonia (1.5%), cerebrovascular accident (0.7%), and multiple organ dysfunction syndrome (0.7%)[1]
- **13% of patients permanently discontinued ALUNBRIG due to adverse reactions.** Dose reductions occurred in 38% of patients receiving ALUNBRIG. The most common adverse reactions in ALTA 1L that led to dose reduction were increased creatine phosphokinase (15%), increased lipase (6.6%), increased amylase (4.4%), increased aspartate aminotransferase (2.2%), ILD/pneumonitis (2.2%), and hypertension (2.2%)[1]

ILD, interstitial lung disease

WARNINGS AND PRECAUTIONS (continued)

Hypertension (continued)

Consider permanent discontinuation of treatment with ALUNBRIG for Grade 4 hypertension or recurrence of Grade 3 hypertension. Use caution when administering ALUNBRIG in combination with antihypertensive agents that cause bradycardia.

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

Bradycardia

In ALTA 1L, heart rates less than 50 beats per minute (bpm) occurred in 8.1% of patients receiving ALUNBRIG; one patient (0.7%) experienced Grade 3 bradycardia. Monitor heart rate and blood pressure during treatment with ALUNBRIG. For symptomatic bradycardia, withhold ALUNBRIG and review concomitant medications for those known to cause bradycardia; dose reduce concomitant medication or ALUNBRIG as appropriate. Discontinue ALUNBRIG for life-threatening bradycardia if no contributing concomitant medication is identified.

Visual Disturbance

In ALTA 1L, Grade 1 or 2 adverse reactions leading to visual disturbance, including blurred vision, photophobia, photopsia, and reduced visual acuity, were reported in 7.4% of patients receiving ALUNBRIG. In the ALTA study, at the approved dose (90→180 mg), Grade 3 macular edema and cataract occurred in one patient each. Advise patients to report any visual symptoms. Withhold ALUNBRIG and obtain an ophthalmologic evaluation in patients with new or worsening visual symptoms of Grade 2 or greater severity; upon recovery, dose reduce as appropriate. Permanently discontinue treatment with ALUNBRIG for Grade 4 visual disturbances.

Creatine Phosphokinase (CPK) Elevation

In ALTA 1L, creatine phosphokinase (CPK) elevation occurred in 81% of patients who received ALUNBRIG. The incidence of Grade 3 or 4 CPK elevation was 24%. Dose reduction for CPK elevation occurred in 15% of patients. Advise patients to report any unexplained muscle pain, tenderness, or weakness. Monitor CPK levels during ALUNBRIG treatment. Withhold ALUNBRIG for Grade 3 or 4 CPK elevation with Grade 2 or higher muscle pain or weakness. Upon resolution or recovery to Grade 1 CPK elevation or baseline, resume ALUNBRIG at the same dose or at a reduced dose.

Pancreatic Enzyme Elevation

In ALTA 1L, amylase elevation occurred in 52% of patients, and Grade 3 or 4 amylase elevation occurred in 6.8% of patients who received ALUNBRIG. Lipase elevations occurred in 59% of patients, and Grade 3 or 4 lipase elevation occurred in 17% of patients. Monitor lipase and amylase during treatment with ALUNBRIG. Withhold ALUNBRIG for Grade 3 or 4 pancreatic enzyme elevation. Upon resolution or recovery to Grade 1 or baseline, resume ALUNBRIG at the same dose or at a reduced dose.

Hepatotoxicity

In ALTA 1L, aspartate aminotransferase (AST) elevations occurred in 72% of patients, and Grade 3 or 4 AST elevations occurred in 4.5% of patients who received ALUNBRIG. Alanine aminotransferase (ALT) elevations occurred in 52% of patients, and Grade 3 or 4 ALT elevations occurred in 5.2% of patients. One patient (0.7%) had a serious adverse reaction of hepatocellular injury. Monitor AST, ALT, and total bilirubin during treatment with ALUNBRIG, especially during the first 3 months. Withhold ALUNBRIG for Grade 3 or 4 hepatic enzyme elevation with bilirubin less than or equal to 2 × ULN. Upon resolution or recovery to Grade 1 or less (less than or equal to 3 × ULN) or to baseline, resume ALUNBRIG at a next lower dose. Permanently discontinue ALUNBRIG for Grade 2 to 4 hepatic enzyme elevation with concurrent total bilirubin elevation greater than 2 times the ULN in the absence of cholestasis or hemolysis.

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WARNINGS AND PRECAUTIONS (continued)

Hyperglycemia

In ALTA 1L, 56% of patients who received ALUNBRIG experienced new or worsening hyperglycemia.Grade 3 hyperglycemia, based on laboratory assessment of serum fasting glucose levels, occurred in 7.5% of patients. In the ALTA study, 2 of 20 (10%) patients with diabetes or glucose intolerance at baseline required initiation of insulin while receiving ALUNBRIG. Assess fasting serum glucose prior to initiation of ALUNBRIG and monitor periodically thereafter. Initiate or optimize anti-hyperglycemic medications as needed. If adequate hyperglycemic control cannot be achieved with optimal medical management, withhold ALUNBRIG until adequate hyperglycemic control is achieved and consider reducing the dose of ALUNBRIG.

Photosensitivity

In ALTA 1L, 3.7% of patients who received ALUNBRIG experienced photosensitivity, with 0.7% of patients experiencing Grade 3 to 4 reactions. Advise patients to limit sun exposure while taking ALUNBRIG, and for at least 5 days after discontinuation of treatment. Advise patients, when outdoors, to wear protective clothing and use a broad-spectrum sunscreen (SPF ≥30) to help protect against sunburn. Based on the severity, withhold ALUNBRIG, then resume at the same dose, or reduce the dose, or permanently discontinue.

Embryo-Fetal Toxicity

Based on its mechanism of action and findings in animals, ALUNBRIG can cause fetal harm when administered to pregnant women. There are no clinical data on the use of ALUNBRIG in pregnant women. Advise women of the potential risk to a fetus.

ADVERSE REACTIONS

The most common adverse reactions (≥25%) with ALUNBRIG were diarrhea, fatigue, nausea, rash, cough, myalgia, headache, hypertension, vomiting, and dyspnea.

DRUG INTERACTIONS

CYP3A Inhibitors: Avoid coadministration of ALUNBRIG with strong or moderate CYP3A inhibitors. If coadministration of a strong or moderate CYP3A inhibitor is unavoidable, reduce the dose of ALUNBRIG.

CYP3A Inducers: Avoid coadministration of ALUNBRIG with strong or moderate CYP3A inducers. If coadministration of a moderate CYP3A inducer is unavoidable, increase the dose of ALUNBRIG.

References:

1. Alunbrig. Prescribing information. Takeda Pharmaceuticals America, Inc; 2024.
2. Camidge DR, Kim HR, Ahn MJ, et al. Brigatinib versus crizotinib in advanced ALK inhibitor–naive ALK-positive non–small cell lung cancer: second interim analysis of the phase III ALTA-1L trial. *J Clin Oncol*. 2020;38(31):3592-3603.
3. Camidge DR, Kim HR, Ahn MJ, et al. Brigatinib versus crizotinib in ALK-positive non-small-cell lung cancer. *N Engl J Med*. 2018;379(21):2027-2039.

GREG EXPERIENCED A MEANINGFUL RESPONSE WITH ALUNBRIG

Greg Achieved a Response in his Lungs and Brain

- Treatment with ALUNBRIG was started in October of 2021 and is ongoing
- Greg continues to receive radiation therapy to the brain approximately every 12 months
- He has shown no evidence of disease below the cervical region since January 2022

Greg Tolerated ALUNBRIG well

- He has not experienced any side effects since initiating ALUNBRIG
- Treatment with ALUNBRIG once daily has helped Greg focus on his active lifestyle

In clinical trials of ALUNBRIG, the most common adverse reactions (≥25%) were diarrhea, fatigue, nausea, rash, cough, myalgia, hypertension, and dyspnea.[1]

As of August 2025:

- Greg continues as a CrossFit coach and pursues activities he is passionate about
- He spends quality time with his wife, family, and dog

This is Greg's experience with ALUNBRIG. Individual results may vary.

WILL YOU CONSIDER ALUNBRIG FOR YOUR NEXT PATIENT LIKE GREG?

IMPORTANT SAFETY INFORMATION (continued)

USE IN SPECIFIC POPULATIONS

Females and Males of Reproductive Potential
Verify pregnancy status in females of reproductive potential prior to initiating ALUNBRIG. Advise females of reproductive potential to use effective contraception during treatment with ALUNBRIG and for at least 4 months after the final dose. Advise males with female partners of reproductive potential to use effective contraception during treatment with ALUNBRIG and for at least 3 months after the final dose. ALUNBRIG may cause reduced fertility in males.

Lactation: Advise patients not to breastfeed.

Hepatic Impairment: Reduce the dose of ALUNBRIG for patients with severe hepatic impairment.

Renal Impairment: Reduce the dose of ALUNBRIG for patients with severe renal impairment.

To report SUSPECTED ADVERSE REACTIONS, contact Takeda Pharmaceuticals U.S.A., Inc. at 1-844-217-6468 or the FDA at 1-800-FDA-1088 or **www.fda.gov/medwatch**.

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BRIGATINIB
180mg | 90mg | 30mg
TABLETS