TALKING

ALK-POSITIVE OPINIONS

with Nurse Practitioner,
Kayla Haines

What can ALUNBRIG® (brigatinib) offer patients with ALK+ mNSCLC in the first line?

"You may offer your next patient the chance for systemic and intracranial efficacy, and it's available as a once-daily oral therapy that is easy for patients to take, and tolerable over the long term."[1,2,a]

Kayla Haines, MSN, APRN, FNP-C
Florida Cancer Specialists & Research Institute

INDICATION

ALUNBRIG 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

ADVERSE REACTIONS

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

[a]Long-term tolerability is based on the median follow-up in the ALUNBRIG arm of ALTA 1L: 40.4 months.[3]
1L, first line; ALK, anaplastic lymphoma kinase; FDA, Food and Drug Administration; mNSCLC, metastatic non-small cell lung cancer.

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BRIGATINIB
180mg | 90mg | 30mg
TABLETS

Meet Kayla Haines, MSN, APRN, FNP-C

Florida Cancer Specialists & Research Institute

ALK+ mNSCLC QUICK FACTS

In the US, NSCLC is the most common type of lung cancer[4]

- ✓ Lung cancer is the leading cause of cancer death in the US[4]
- ✓ The 5-year relative survival rate for mNSCLC is as low as 9%[5]

ALK is an oncogenic driver of NSCLC

- ✓ NSCLC has a broad molecular profile with several genetic mutations known to cause the disease[6]
- ✓ Mutations and other clinical characteristics that trigger cellular growth and the development of cancer are called **oncogenic biomarkers**[7,8]
- ✓ **ALK** is an oncogenic biomarker[2]
- ✓ ALK rearrangements are usually mutually exclusive with other common biomarkers in NSCLC, such as EGFR and KRAS[9]
- ✓ Rearrangements in the ALK gene are found in 3%–5% of patients with NSCLC[10]
- ✓ ALK+ mNSCLC can be treated with TKIs, a class of therapy that may deliver positive outcomes to many patients[11,12]

What are some of the key challenges when treating a patient with ALK+ mNSCLC?

"Typically, I've seen that brain metastases are a particular challenge that ALK+ patients are susceptible to facing, and they can cause a multitude of issues that can be difficult to address."

How common are brain metastases for ALK+ patients?

"Brain metastases affect up to 35% of patients with ALK+ mNSCLC at the time of diagnosis. These pose many issues for patients, including psychological problems, like depression, anxiety, and cognitive issues as well as symptoms such as headaches and seizures."[13-19]

EGFR, epidermal growth factor receptor; KRAS, Kirsten rat sarcoma virus; TKI, tyrosine kinase inhibitor.

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What are the symptoms of brain metastases you've seen in your practice?

"Frequently, I see patients with brain metastases suffer from edema, which often requires treatment with corticosteroids. Dizziness and lack of coordination are also common. More severe symptoms like seizures may also occur, and management often requires an interdisciplinary approach involving neuro-oncologists, neurologists, and neurosurgeons."[17,20-22]

How do brain metastases affect patients?

"Brain metastases may affect a patient's ability to perform fundamental tasks—how they think, how they walk, and how they take in sensory information. Due to the severity of these symptoms, there's also a taxing psychological component that comes with a diagnosis of brain metastases."[17]

How can brain metastases impact a patient's psyche?

"Patients become anxious about how brain metastases may impact them in the future, and often question whether they'll still be able to walk and talk, or if they may experience mood changes over time. The prospect of having a seizure is also extremely daunting for patients and their care teams. This diagnosis alone brings a significant amount of anxiety and fear."[17]

What are some additional challenges faced by patients with ALK+ mNSCLC?

"With the advent of ALK TKIs, patient outcomes have improved in recent years. With patients spending more time on therapy, pill burden also becomes an increasingly important consideration when determining a therapy."[12,23]

How does pill burden affect patients?

"High pill burden can negatively impact adherence, and may contribute to poor quality of life. Additionally, patients may find it challenging to integrate multiple dosing schedules and accommodate the dietary requirements of other treatments, such as with food or on an empty stomach.[23,24]

From my experience, I've seen how important pill burden is, especially for my elderly patients. These patients may have difficulty swallowing or may be on other therapies, so having a low pill burden is important to them. Therefore, prioritizing treatment options with a lower pill burden may help optimize your patient's treatment journey."

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TABLETS

A PHASE 3 TRIAL DESIGNED TO ASSESS THE EFFICACY, SAFETY, AND TOLERABILITY OF ALUNBRIG® (brigatinib)[1,2]

ALTA 1L was a randomized (1:1), open-label, multicenter trial[1,2]

275 ADULT PATIENTS WITH LOCALLY ADVANCED OR METASTATIC ALK+ NSCLC[1]

- No prior treatment with an ALK inhibitor
- ≤1 regimen of prior systemic therapy in the locally advanced/metastatic setting

ALUNBRIG n=137 (ITT population)
180 mg orally once daily with a 7-day lead-in at 90 mg once daily

RANDOMIZED 1:1

STRATIFIED BY:
- Baseline brain metastases (present or absent)
- Prior chemotherapy in locally advanced/metastatic setting (yes or no)

Crizotinib n=138 (ITT population)
250 mg orally twice daily

Select exclusion criteria: Patients with a history of interstitial lung disease, drug-related pneumonitis, or radiation pneumonitis.[1]

Treatment was continued until disease progression or unacceptable toxicity.[2]

Crossover from crizotinib to ALUNBRIG was permitted after disease progression. After BIRC-assessed objective progression, 44% of patients taking crizotinib (n=61/138) crossed over to the ALUNBRIG arm.[2]

Major efficacy outcome measure: PFS according to RECIST v1.1 as evaluated by a BIRC.[1]

Additional efficacy outcome measures[a]: Confirmed ORR, DOR, intracranial ORR, intracranial DOR, and OS as evaluated by a BIRC.[1,2]

Median duration of follow-up: At the time of the second interim analysis, data cutoff was 22 months after the last patient was enrolled,[24] with a median follow-up of 24.9 months for ALUNBRIG and 15.2 months for crizotinib.[2,25]

Select efficacy data from the **final analysis** of the trial are included in this presentation. The median follow-up for ALUNBRIG was 40.4 months.[3]

HAINES EXPLAINS > The trial population and makeup of ALTA 1L

"ALTA 1L reflected real ALK+ metastatic NSCLC, as patients in the trial exhibited common, real-world characteristics like high rates of adenocarcinoma, presence of brain metastases at baseline, and a preponderance of patients in their 50s."[12,16,26]

[a]Nonpowered endpoints.
BIRC, Blinded Independent Review Committee; DOR, duration of response; ITT, intent to treat; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumors.

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 ALTA, ILD/pneumonitis occurred in 3.7% of patients in the 90 mg group (90 mg once daily) and 9.1% of patients in the 90→180 mg group (180 mg once daily with 7-day lead-in at 90 mg once daily).

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ITT POPULATION

ALUNBRIG (brigatinib) DEMONSTRATED POWERFUL SYSTEMIC EFFICACY IN ALTA 1L[1,3]

Systemic PFS With ALUNBRIG[1]

BIRC-assessed PFS (primary endpoint)[1]

24.0 months mPFS[1]

(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[a]

INV-assessed PFS (additional endpoint)[2,3]

30.8 months mPFS[3]

(95% CI: 21.3, 40.6) vs 9.2 months (95% CI: 7.4, 12.7) with crizotinib

- Based on the **final analysis** of ALTA 1L with a median follow-up of 40.4 months[3]
- INV-assessed PFS did not include a formal hypothesis test with Type I error control. In addition, ALTA 1L was an open-label trial, so there may be bias that contributed to the estimation of benefit from the INV-assessed PFS

Confirmed BIRC-assessed response rates[1]

In the ITT population, ALUNBRIG demonstrated[1]:
- ORR: 74% (95% CI: 66, 81) vs 62% (95% CI: 53, 70) with crizotinib; *P*=0.0342[a]
  - CR: 15% (95% CI: 9, 22) vs 9% (95% CI: 5, 15) with crizotinib
- mDOR: 33.1 months (95% CI: 22.0, NE) vs 13.8 months (95% CI: 10.4, 20.8) with crizotinib in the final analysis

[a]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]

CI, confidence interval; CR, complete response; ECOG, Eastern Cooperative Oncology Group; HR, hazard ratio; INV, investigator; mDOR, median duration of response; mPFS, median progression-free survival; NE, not estimable.

WARNINGS AND PRECAUTIONS (continued)

Interstitial Lung Disease (ILD)/Pneumonitis (continued)

Adverse reactions consistent with possible ILD/pneumonitis occurred within 9 days of initiation of ALUNBRIG (median onset was 2 days) in 6.4% of patients, with Grade 3 to 4 reactions occurring in 2.7% 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 resume ALUNBRIG with dose reduction according to Table 1 of the full Prescribing Information after recovery to baseline or permanently discontinue ALUNBRIG. Permanently discontinue ALUNBRIG for Grade 3 or 4 ILD/pneumonitis or recurrence of Grade 1 or 2 ILD/pneumonitis.

Hypertension

In ALTA 1L, hypertension was reported in 32% of patients receiving ALUNBRIG; 13% of patients experienced Grade 3 hypertension. In ALTA, hypertension was reported in 11% of patients in the 90 mg group and 21% of patients in the 90→180 mg group. Grade 3 hypertension occurred in 5.9% of patients overall. Control blood pressure prior to treatment with ALUNBRIG. Monitor blood pressure after 2 weeks and at least monthly thereafter during treatment with ALUNBRIG. Withhold ALUNBRIG for Grade 3 hypertension despite optimal antihypertensive therapy. Upon resolution or improvement to Grade 1, resume ALUNBRIG at the same dose. 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.

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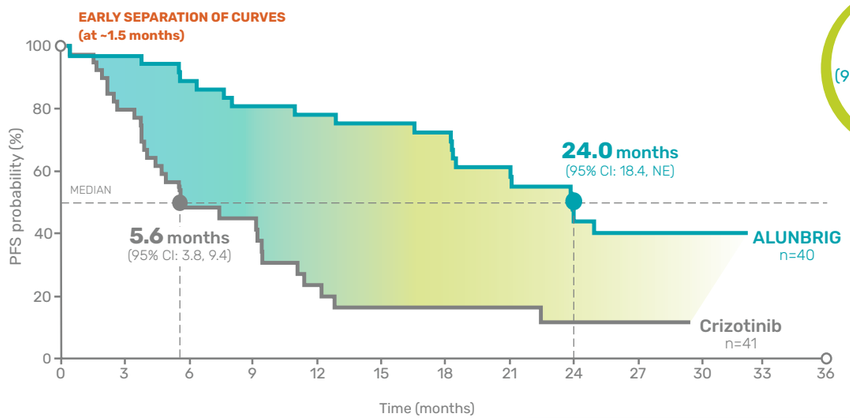
BRAIN METASTASES POPULATION (POST HOC SUBGROUP ANALYSIS)

75% REDUCTION IN RISK OF PROGRESSION OR DEATH vs CRIZOTINIB[2,25]

Systemic BIRC-Assessed PFS in Patients With Any Brain Metastases at Baseline[2,25]



Number at risk													
ALUNBRIG	40	36	32	29	28	26	25	21	11	4	2	0	0
Crizotinib	41	31	16	12	6	4	4	4	1	1	0	0	0

Study Limitation: ALTA 1L was not powered to detect differences across subgroups.

- **23% absolute risk reduction:** 50% event rate (n=20/40) for patients taking ALUNBRIG vs 73% event rate (n=30/41) for patients taking crizotinib[2]

HAINES EXPLAINS > The value of intracranial efficacy

"Ultimately, if a treatment option can deliver intracranial efficacy, you may avoid the need to administer additional therapy, like radiation.[17] By offering an option with intracranial efficacy, you may be able to provide some benefit to patients if their metastases go into remission.

One of the most valuable things you can potentially offer your patients is the opportunity to participate in important life events. Intracranial efficacy may make that possible."

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. In ALTA, heart rates less than 50 beats per minute (bpm) occurred in 5.7% of patients in the 90 mg group and 7.6% of patients in the 90→180 mg group. One patient (0.9%) in the 90 mg group experienced Grade 2 bradycardia. Monitor heart rate and blood pressure during treatment with ALUNBRIG. Monitor patients more frequently if concomitant use of drug known to cause bradycardia cannot be avoided. For symptomatic bradycardia, withhold ALUNBRIG and review concomitant medications for those known to cause bradycardia. If a concomitant medication known to cause bradycardia is identified and discontinued or dose adjusted, resume ALUNBRIG at the same dose following resolution of symptomatic bradycardia; otherwise, reduce the dose of ALUNBRIG following resolution of symptomatic bradycardia. Discontinue ALUNBRIG for life-threatening bradycardia if no contributing concomitant medication is identified.

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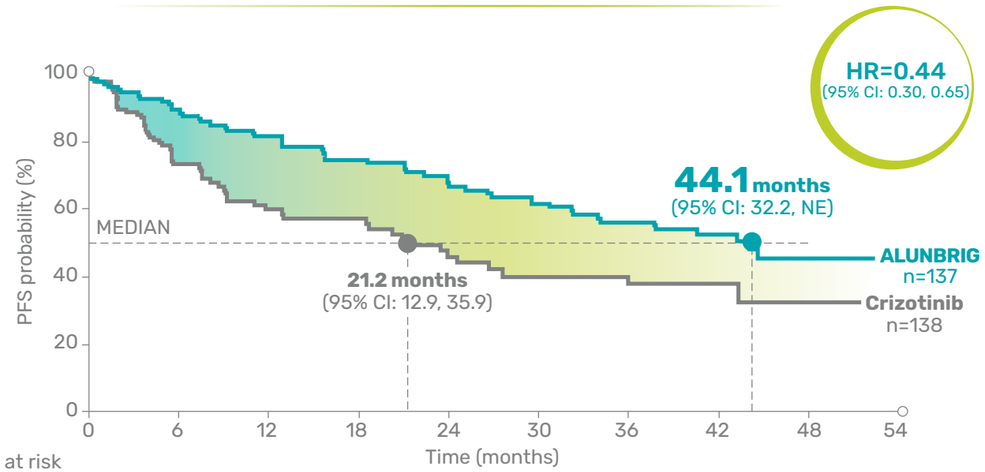
ITT POPULATION FINAL ANALYSIS WITH 40.4 MONTHS OF MEDIAN FOLLOW-UP

ALUNBRIG (brigatinib) DEMONSTRATED DURABLE INTRACRANIAL mPFS OF ~4 YEARS[3]

Intracranial PFS in the ITT Population[3]



Number at risk									
ALUNBRIG	137	103	89	76	66	59	53	31	2
Crizotinib	138	76	45	37	26	19	17	9	2

- **3-year intracranial PFS probability in the ITT population (BIRC-assessed): 56% for ALUNBRIG** (n=137) vs 38% for crizotinib (n=138)[3]
- In patients with any brain metastases at baseline, the intracranial mPFS was 24.0 months (95% CI: 12.9, 30.8) with ALUNBRIG vs 5.5 months (95% CI: 3.7, 7.5) with crizotinib[3]

Intracranial PFS was not part of the statistical testing hierarchy. The clinical relevance of these data is unknown, as only brain lesions were reviewed. Patients were counted as having an event if there was radiologic progression, radiotherapy to the brain, or death.[3]

Study Limitation: ALTA 1L was not powered to detect differences across subgroups; results are presented descriptively.

WARNINGS AND PRECAUTIONS (continued)

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 ALTA, adverse reactions leading to visual disturbance, including blurred vision, diplopia, and reduced visual acuity, were reported in 7.3% of patients treated with ALUNBRIG in the 90 mg group and 10% of patients in the 90→180 mg group. Grade 3 macular edema and cataract occurred in one patient each in the 90→180 mg group. 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 of Grade 2 or Grade 3 visual disturbances to Grade 1 severity or baseline, resume ALUNBRIG at a reduced dose. 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. In ALTA, CPK elevation occurred in 27% of patients receiving ALUNBRIG in the 90 mg group and 48% of patients in the 90→180 mg group. The incidence of Grade 3 to 4 CPK elevation was 2.8% in the 90 mg group and 12% in the 90→180 mg group. Dose reduction for CPK elevation occurred in 1.8% of patients in the 90 mg group and 4.5% of patients in the 90→180 mg group. Advise patients to report any unexplained muscle pain, tenderness, or weakness. Monitor CPK levels during ALUNBRIG treatment.

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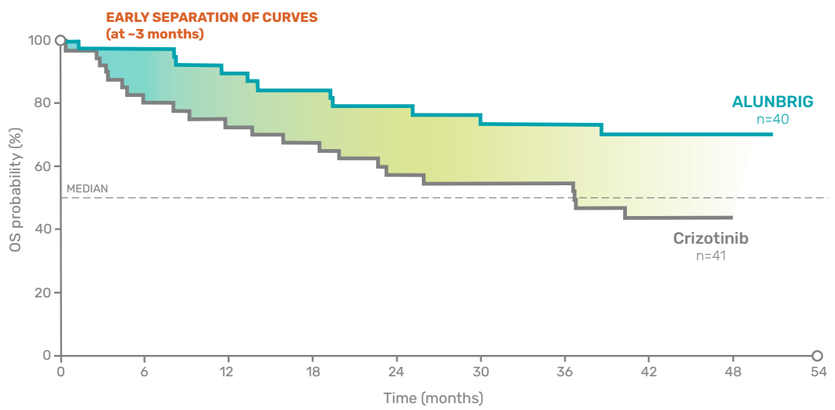
OS in the ITT population[1,3]

Based on the final analysis with 40.4 months of median follow-up, median OS was not reached for both arms; 30% of patients (n=41/137) died in the ALUNBRIG arm vs 37% of patients (n=51/138) in the crizotinib arm. The 3-year OS rate was 71% (95% CI: 62, 78) with ALUNBRIG and 68% (95% CI: 59, 75) with crizotinib (HR=0.81; 95% CI: 0.53, 1.22; *P*=0.331). 47% of patients (n=65) in the crizotinib arm had crossed over to receive ALUNBRIG.

BRAIN METASTASES POPULATION (POST HOC SUBGROUP ANALYSIS)

57% REDUCTION IN THE RISK OF DEATH vs CRIZOTINIB[3]

OS in Patients With Measurable Brain Metastases at Baseline[3]



Number at risk										
ALUNBRIG	40	38	35	32	29	26	26	16	4	0
Crizotinib	41	33	29	27	22	21	21	9	1	0

Study Limitation: ALTA 1L was not powered to detect differences across subgroups.

HAINES EXPLAINS > How important is intracranial efficacy to patients?

"As an experienced clinician, I know how brain metastases can take a toll on patients. I've seen the pain they cause, as well as the effects on behavior and mood.[17-19] I also know what intracranial efficacy can mean for patients. Remission of brain metastases can offer cathartic relief, giving cause for celebration."

WARNINGS AND PRECAUTIONS (continued)

Creatine Phosphokinase (CPK) Elevation (continued)

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 per Table 2 of the full Prescribing Information.

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. In ALTA, amylase elevation occurred in 27% of patients in the 90 mg group and 39% of patients in the 90→180 mg group. Lipase elevations occurred in 21% of patients in the 90 mg group and 45% of patients in the 90→180 mg group. Grade 3 or 4 amylase elevation occurred in 3.7% of patients in the 90 mg group and 2.7% of patients in the 90→180 mg group. Grade 3 or 4 lipase elevation occurred in 4.6% of patients in the 90 mg group and 5.5% of patients in the 90→180 mg

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A WELL-ESTABLISHED SAFETY PROFILE

Serious adverse reactions occurred in 33% of patients receiving ALUNBRIG[1]

- 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]
- 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]
- The most common adverse reactions (≥25%) with ALUNBRIG were diarrhea, fatigue, nausea, rash, cough, myalgia, headache, hypertension, vomiting, and dyspnea[1]
- In ALTA 1L, the most common laboratory abnormalities were increased creatine phosphokinase (81%), increased aspartate aminotransferase (72%), increased lipase (59%), hyperglycemia (56%), increased alanine aminotransferase (52%), and increased amylase (52%)[1]

Dose reductions occurred in 38% of patients receiving ALUNBRIG.[1] 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%).

Permanent discontinuation due to adverse reactions occurred in 13% of patients receiving ALUNBRIG.[1] The most frequent adverse reactions in ALTA 1L that led to discontinuation were ILD/pneumonitis (3.7%) and pneumonia (2.2%).

HAINES EXPLAINS > The value of long-term tolerability

"ALUNBRIG also demonstrated long-term tolerability in ALTA 1L, which is an important consideration in a treatment setting where patients frequently receive long-term[a] therapy."[1]

[a]Long-term tolerability is based on the median follow-up in the ALUNBRIG arm of ALTA 1L: 40.4 months.[3]
ILD, interstitial lung disease.

WARNINGS AND PRECAUTIONS (continued)

Pancreatic Enzyme Elevation (continued)

group. 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. In ALTA, AST elevations occurred in 38% of patients in the 90 mg group and 65% of patients in the 90→180 mg group. ALT elevations occurred in 34% of patients in the 90 mg group and 40% of patients in the 90→180 mg group. Grade 3 or 4 AST elevations occurred in 0.9% of patients in the 90 mg group and did not occur in any patients in the 90→180 mg group. Grade 3 or 4 ALT elevations did not occur in any patients in the 90 mg group and in 2.7% of patients in the 90→180 mg group. 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 per Table 2 of the full Prescribing Information. 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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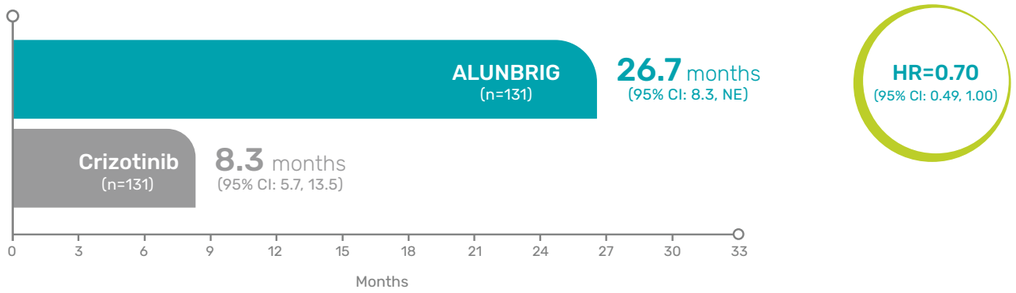
PATIENT-REPORTED QUALITY OF LIFE WITH ALUNBRIG (brigatinib)[2]

ALUNBRIG delayed time to worsening in Global Health Status (GHS)/Quality of Life (QoL) vs crizotinib[2]

Median Time to Worsening in GHS/QoL (≥10-Point Worsening in Score)[2,a]



Time to Worsening Was Assessed by[25]:

- ✓ Physical scales
- ✓ Emotional, cognitive, and social functioning scales
- ✓ Improvement of disease symptoms

Study Limitations: These patient-reported outcome endpoints were exploratory and not prespecified. The improvement in QoL scores and delay in worsening of GHS/QoL may be an overestimation, because patients were not blinded to treatment assignment. These differences in global QoL could reflect differences in efficacy on disease-related symptoms and in treatment-related adverse events.[2]

Among responders, the median duration of improvement in QoL had not been reached for ALUNBRIG vs 12 months for crizotinib.[2]

HAINES EXPLAINS > The importance of QoL

"Quality of life is crucial, especially for younger patients with metastatic disease who require long-term therapy. It's also important because metastatic NSCLC is a life-long disease. We want to make sure patients are living the best life that they can."[27,28]

[a]Patient-reported symptoms, functioning, and GHS/QoL were measured using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30) and supplemental QLQ-LC13 (Lung Cancer Module).[2]

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 ALTA, 43% of patients who received ALUNBRIG experienced new or worsening hyperglycemia. Grade 3 hyperglycemia, based on laboratory assessment of serum fasting glucose levels, occurred in 3.7% of patients. Two 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 dosage per Table 1 of the full Prescribing Information or permanently discontinuing ALUNBRIG.

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DOSING THAT FITS INTO PATIENTS' LIVES[1]

1 TABLET ONCE DAILY
WITH OR WITHOUT FOOD[1]

The recommended dosage for ALUNBRIG is 90 mg orally once daily for the first 7 days; then increase the dose to 180 mg orally once daily.[1]

- Administer ALUNBRIG until disease progression or unacceptable toxicity[1]
- If ALUNBRIG is interrupted for 14 days or longer for reasons other than adverse reactions, resume treatment at 90 mg once daily for 7 days before increasing to the previously tolerated dose[1]
- ALUNBRIG may be taken with or without food. Instruct patients to swallow tablets whole. Do not crush or chew tablets[1]
- Inform patients to avoid grapefruit or grapefruit juice while taking ALUNBRIG[1]
- If a dose of ALUNBRIG is missed or vomiting occurs after taking a dose, do not administer an additional dose and instruct patients to take the next dose of ALUNBRIG at the scheduled time[1]

HAINES EXPLAINS > What value does 1-tablet, once-daily dosing offer to patients?

"In my experience of treating ALK-positive metastatic NSCLC, I've seen that 1-tablet, once-daily dosing provides patients with a convenient option. The 90-mg and 180-mg doses each involve just 1 pill per day, making it easier to change the dosage if we need to, and for patients to adhere to their prescribed dosing schedule.[1] The ability to offer patients as few pills a day as possible can make a positive difference in their lives."

WARNINGS AND PRECAUTIONS (continued)

Photosensitivity

In ALTA 1L, 3.7% of patients who received ALUNBRIG experienced photosensitivity, with 0.7% of patients experiencing Grade 3 to 4 reactions. In ALTA, 0.9% of patients who received ALUNBRIG in the 90 mg group and 0.9% of patients in the 90→180 mg group experienced photosensitivity. Grade 3 to 4 photosensitivity was not reported in patients in the 90 mg group or in the 90→180 mg group. 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 a hat and protective clothing, and use a broad-spectrum Ultraviolet A (UVA)/Ultraviolet B (UVB) sunscreen and lip balm (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. Advise females of reproductive potential to use effective contraception during treatment with ALUNBRIG and for at least 4 months following the final dose. Advise males with female partners of reproductive potential to use effective contraception during treatment and for at least 3 months after the last dose of ALUNBRIG.

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.

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

*OFFER **SYSTEMIC EFFICACY** AND*

✓***BRAIN METS EFFICACY[2,a]***

✓***LONG-TERM TOLERABILITY[1,b]***

✓***ONCE-DAILY DOSING[1]***

"I've seen first-hand how intracranial efficacy can impact patients' lives. For example, when a patient learns that their brain metastases are in remission, it can be like a weight lifted off their shoulders, as they may no longer need to worry about the symptoms associated with brain metastases."

CHOOSE ALUNBRIG® (brigatinib) IN THE FIRST LINE

[a]Based on a post hoc subgroup analysis.

[b]Long-term tolerability is based on the median follow-up in the ALUNBRIG arm of ALTA 1L: 40.4 months.[3]

mets, metastases.

WARNINGS AND PRECAUTIONS (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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Please see Important Safety Information throughout and accompanying full Prescribing Information in pocket.

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