CLINICAL CASE PRESENTATION

64-YEAR-OLD MALE WITH STAGE IV NON-SMALL CELL LUNG CANCER WITH AGGRESSIVE DISEASE*

Clinical Case Presentation By:
Mark A. Socinski, MD
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*Aggressive disease is defined by those patients who were primary platinum refractory (patients whose best response was progressive disease) or patients with rapidly progressing disease (time-to-progression within 9 or 12 weeks) after starting initial platinum-based treatment.1,2

INDICATION
CYRAMZA, in combination with docetaxel, is indicated for the treatment of patients with metastatic non-small cell lung cancer (NSCLC) with disease progression on or after platinum-based chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving CYRAMZA.

SELECT IMPORTANT SAFETY INFORMATION

WARNING: HEMORRHAGE, GASTROINTESTINAL PERFORATION, AND IMPAIRED WOUND HEALING

Hemorrhage: CYRAMZA increased the risk of hemorrhage and gastrointestinal hemorrhage, including severe and sometimes fatal hemorrhagic events. Permanently discontinue CYRAMZA in patients who experience severe bleeding.

Gastrointestinal Perforation: CYRAMZA can increase the risk of gastrointestinal perforation, a potentially fatal event. Permanently discontinue CYRAMZA in patients who experience a gastrointestinal perforation.

Impaired Wound Healing: Impaired wound healing can occur with antibodies inhibiting the VEGF pathway. Discontinue CYRAMZA therapy in patients with impaired wound healing. Withhold CYRAMZA prior to surgery and discontinue CYRAMZA if a patient develops wound healing complications.

Please see Important Safety Information, including a Boxed Warning for hemorrhage, gastrointestinal perforation, and impaired wound healing, on pages 6-7 and accompanying full Prescribing Information for CYRAMZA.
History of present illness

- The patient is a 64-year-old male who presented with increasing dyspnea as well as low grade fever.
- On initial evaluation, a chest X-ray showed a 4-cm left upper lobe mass with mediastinal widening and blunting of the left costophrenic angle.
- Pertinent findings related to his physical exam included decreased breath sounds at the left lung base and mild hepatomegaly and trace lower extremity edema.
- Chest/abdominal CT confirmed the 4-cm left upper lobe mass without evidence of vessel invasion. There were four hypodense lesions in the liver as well as a 5-cm right adrenal mass consistent with metastases.
- A core biopsy as well as several FNAs of the right adrenal mass revealed squamous cell carcinoma.
- Brain MRI and bone scan showed no evidence of either brain or bone metastases.
- PD-L1 IHC staining was negative (TPS score of <1%).
- The diagnosis was made as stage IV (T2N2M1b) and his ECOG PS was 1.

Past Medical History

- Mild COPD and diet controlled diabetes.
- Ulcerative colitis inactive for “several years” but he had several flares requiring steroid therapy in the past.
- One PPD for 45 years, quitting at age 60.

Social History

- Married with three children as well as four grandchildren.
- Wife accompanies him to each office visit and often accompanied by his daughter who is a nurse.
- Retired only one year ago after 30 years of civil service.

Initial Treatment

- Treated with platinum plus a taxane.
- Following two cycles of treatment he had no improvement of his symptoms and the concern was progression.

Physical Exam/Review of Symptoms at Progression

- He had slight tenderness over his liver on exam.
- He was complaining of slight worsening of his dyspnea.

Response Assessment/Follow-Up Imaging

- A repeat CT scan after two cycles showed a worsened pleural effusion and progression of the liver metastases.

Patient Attitude/Characteristics

- Patient was devastated by the CT showing worsening of his cancer.
- He is motivated to attend his grandson’s college graduation, who is graduating from the patient’s alma mater.
- He is enthusiastic about starting treatment with the hopes a treatment could shrink his tumor and/or help him live longer.

Treatment Plan

- A variety of treatment options were discussed, and the patient’s history of ulcerative colitis was taken into consideration for the treatment decision.
- Considering his complete medical profile, he elected to receive ramucirumab plus docetaxel every 21 days.

Dr. Socinski Presents a Challenging Clinical Case of a Patient with Aggressive Disease

Why adding CYRAMZA may be appropriate

- Patient presents with aggressive disease†
- ECOG PS 1
- He has aggressive disease and is both determined and focused on exhausting his options.
- Patient is hopeful for response and a chance to live longer.
- In light of the patient’s poor prognosis, a discussion was had with the patient regarding the risk of side effects as well as potential benefits of treatment.

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Hemorrhage

- CYRAMZA increased the risk of hemorrhage and gastrointestinal hemorrhage, including severe and sometimes fatal hemorrhagic events. In study 3, which evaluated CYRAMZA plus docetaxel in metastatic non-small cell lung cancer (NSCLC), the incidence of severe bleeding was 2.4% for CYRAMZA plus docetaxel and 2.3% for placebo plus docetaxel. Patients with NSCLC receiving therapeutic anticoagulation or chronic therapy with NSAIDs or other antiplatelet therapy other than once-daily aspirin or with radiographic evidence of major airway or blood vessel invasion or intratumor cavitation were excluded from study 3; therefore, the risk of pulmonary hemorrhage in these groups of patients is unknown. Permanently discontinue CYRAMZA in patients who experience severe bleeding.

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With Consistent Results in Patients With Aggressive Disease

**REVEL Trial**

The REVEL trial evaluated the efficacy and safety of CYRAMZA plus docetaxel vs placebo plus docetaxel in patients with metastatic NSCLC with disease progression on or after platinum-based chemotherapy. Major efficacy outcome measures were OS, PFS, and ORR. Supportive efficacy outcome measures were PFS and ORR. All patients were required to have Eastern Cooperative Oncology Group performance status 0 or 1. Patients were randomized 1:1 to receive either CYRAMZA 10 mg/kg plus docetaxel or placebo plus docetaxel, respectively. Safety analyses were performed on both subsets of patients from the safety population, defined as all patients who received at least one dose of study drug.

### REVEL Trial Design (N=1253)

The phase III REVEL trial evaluated the efficacy and safety of CYRAMZA plus docetaxel vs placebo plus docetaxel in patients with metastatic NSCLC with disease progression on or after platinum-based chemotherapy. Major efficacy outcome measures were OS, PFS, and ORR. All patients were required to have Eastern Cooperative Oncology Group performance status 0 or 1. Patients were randomized 1:1 to receive either CYRAMZA 10 mg/kg (n=628) or placebo (n=625), in combination with docetaxel at 75 mg/m² every 21 days.

### REVEL EXPLORATORY ANALYSES

The REVEL trial was not powered for subgroup analyses, nor were any such analyses error-controlled. The primary platinum-refractory population (n=360/N=1253) was a pre-specified subgroup in the REVEL trial; however, the subgroup of patients with limited time on initial platinum-based therapy (≤8 or ≤12 weeks; n=200/N=1253 and n=448/N=1253, respectively) was not pre-specified. Each subgroup analysis presented was exploratory. Kaplan-Meier estimates and Cox regression analyses of OS and PFS were performed for all subgroups. Safety analyses were performed on both subsets of patients from the safety population, defined as all patients who had received at least one dose of study drug.

### SELECT IMPORTANT SAFETY INFORMATION

- **The labeling for CYRAMZA contains a Boxed Warning for: hemorrhage, including severe and sometimes fatal events; gastrointestinal (GI) perforation, a potentially fatal event; and impaired wound healing. CYRAMZA should be permanently discontinued in patients who experience severe bleeding or a GI perforation. CYRAMZA contains additional Warnings and Precautions for arterial thromboembolic events, which are sometimes fatal, hypertension, infusion-related reactions, clinical deterioration in patients with Child-Pugh B or C cirrhosis; reversible posterior leukoencephalopathy syndrome; proteinuria including nephrotic syndrome; thoracic syndrome; and embryofetal toxicity. The most commonly reported adverse reactions (all grades; grade 3/4) occurring in ≥5% of patients receiving CYRAMZA plus docetaxel and ≤2% higher than placebo plus docetaxel in study 3 were neutropenia (85% vs 46%; 49% vs 40%), fatigue/asthenia (85% vs 50%; 14% vs 11%), stomatitis/mucosal inflammation (37% vs 19%; 7% vs 2%), epistaxis (19% vs 7%; <1% vs <1%), febrile neutropenia (16% vs 10%; 16% vs 10%), peripheral edema (16% vs 9%; 0% vs <1%), thrombocytopenia (13% vs 5%; 3% vs <1%), lactic acidosis increased (13% vs 5%; <1% vs 0%), and hypertension (11% vs 5%; 6% vs 2%). The most common serious adverse events with CYRAMZA plus docetaxel in study 3 were febrile neutropenia (14%), pneumonia (6%), and neutropenia (5%). The use of granulocyte colony-stimulating factors was 42% in CYRAMZA plus docetaxel-treated patients versus 37% in patients who received placebo plus docetaxel.**

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### CONSIDER CYRAMZA PLUS DOCETAXEL FOR PATIENTS WITH AGGRESSIVE DISEASE

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- **The percentage of patients with limited time on initial platinum-based therapy (≤8 or ≤12 weeks; n=200/N=1253 and n=448/N=1253, respectively) was not pre-specified. Each subgroup analysis presented was exploratory. Kaplan-Meier estimates and Cox regression analyses of OS and PFS were performed for all subgroups. Safety analyses were performed on both subsets of patients from the safety population, defined as all patients who had received at least one dose of study drug.**
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Warnings and Precautions

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ABOUT THE PRESENTER

MARK A. SOCINSKI, MD

Dr. Mark A. Socinski is a board-certified, fellowship-trained medical oncologist, specializing in all thoracic malignancies, including small cell and non-small cell lung cancers and mesothelioma. He is an internationally recognized expert in the development of novel chemotherapy agents and treatment strategies for advanced non-small cell lung cancer and small-cell lung cancer. His research has focused on incorporating personalized medicine and molecular biomarkers in the treatment of lung cancer. Dr. Socinski received a medical degree from the University of Vermont in Burlington. He completed an internship and residency at Beth Israel Deaconess Medical Center, Harvard Medical School, in Boston, Massachusetts, and fellowships in medical oncology and clinical medicine at the Dana-Farber Cancer Institute in Boston.

He is a member of several professional organizations, including the American College of Physicians, American Society of Clinical Oncology, Cancer and Leukemia Group B, International Association for the Study of Lung Cancer, and the American College of Chest Physicians. He serves as co-Chair of the Thoracic Malignancies Steering Committee for the National Cancer Institute. Dr. Socinski serves on the Respiratory Core Committee of the Cancer and Leukemia Group B (Alliance) and has been instrumental in the development of many cooperative clinical trials. He is also co-Chair of the Winter Lung Cancer Annual Conference, now in its 14th year.