Treatment of a JAK1 Positive Chronic Eosinophilic Leukemia with JAK 1/2 Inhibitor Ruxolitinib

Jane Van De Grift, PharmD, MPH, BCPS
Quincy Ostrem, PharmD, MBA
Jessie Modlin, PharmD, BCOP
Bobby Chawla, DO

Discussion

Patient response to ruxolitinib is promising over first month of treatment.

It is unclear if ruxolitinib would have a lasting effect on preventing transformation to AML, prolonging survival, or reducing eosinophil count.

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Background

- Chronic Eosinophilic Leukemia, not otherwise specified (CEL, NOS) is a rare leukemia under the umbrella of hypereosinophilias, associated with a high probability of transformation to acute myeloid leukemia (AML).[1-4]
- No guidance exists for first line therapy, however corticosteroids, hydroxyurea, PEG-interferon-alpha and imatinib have been used; these agents may elicit a response, but results are generally not long lasting.[2]
- One of the mediators involved in regulating cytokine response that leads to eosinophil proliferation is Janus kinase 1 (JAK1) (Figure 1).[5,6]
- JAK1 mutations in CEL, NOS are rare with only two cases identified in literature.[7,8]
- Ruxolitinib is a selective inhibitor of JAK1 and JAK2 currently FDA approved for myelofibrosis and polycythemia vera (Figure 2).[9]
- Ruxolitinib has impact on overall survival in the setting of myelofibrosis, however it is not a curative therapy. The duration of response in CEL, NOS is unknown.[10-12]

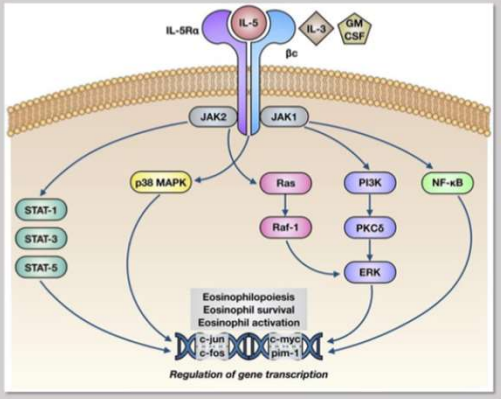

Figure 1: Eosinophil activation via the JAK1/2-STAT 1/3/5 pathway. Stimulation of this pathway leads to eosinophil maturation, activation, and survival.[13]

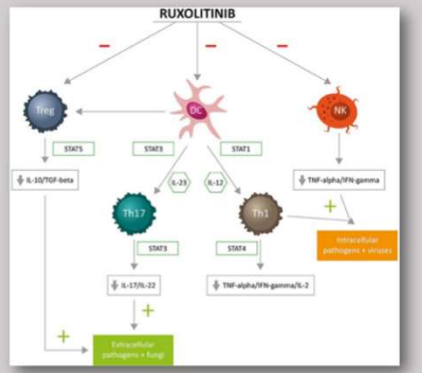

Figure 2: Ruxolitinib mechanism of action on innate and adaptive immunity. The inhibition of this pathway leads to a decrease in production of cytokines and chemokines, therefore inhibiting the inflammatory cascade.[14]

Case Description

- 81-year-old male, otherwise healthy, that presented to his primary care provider for a yearly check up with no complaints in January of 2024.
- CBC resulted with leukocytosis (36.6 k/mcL), significantly elevated eosinophils (26.42 k/mcL), platelets within normal limits at 221 k/mcL, and hemoglobin/hematocrit of 14.9 gm/dL /49.2%.
- At initial oncology consult, patient endorsed night sweats and slight fatigue as his only occasional symptoms; denied shortness of breath, chest pain, early satiety, unintentional weight loss, and pruritis/rash.
- Bone marrow biopsy demonstrated negative FISH panel results for PDGFRa/b, FGR1, CBFB, and BCR-ABL1; additional results included hypercellular marrow 60-70% without increased blasts, and megakaryocytic dysplasia without KIT mutation.
- NGS bone marrow results were positive for ASXL1, JAK1, and U2AF1 mutations. A diagnosis of CEL, NOS was made based on WHO criteria.
- The presence of a JAK1 mutation indicates activation of the JAK-STAT pathway and possible sensitivity to the JAK1/2 inhibitor ruxolitinib.
- Patient initiated treatment with ruxolitinib 10 mg twice daily with plans to titrate up to 20 mg twice daily.

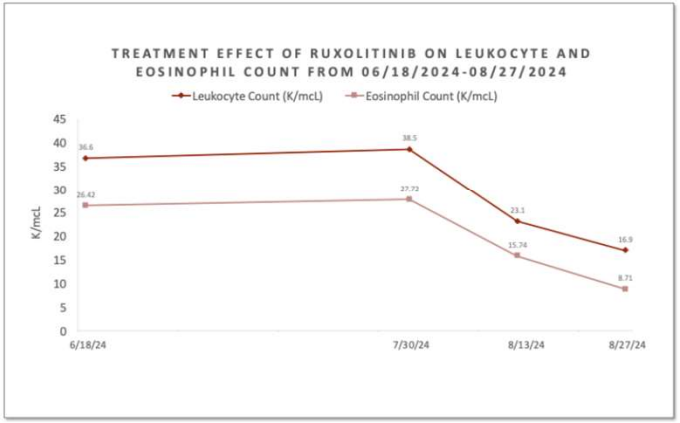

Figure 3: Treatment effect of ruxolitinib. This figure shows the dramatic decrease of both leukocyte and eosinophil counts during the first two months of treatment with ruxolitinib.

Results

- Patient started ruxolitinib 10 mg twice daily on 07/29/2024 with significantly elevated leukocytes and eosinophils.
- At oncology follow up visit on 08/27/2024 patient reported resolution of night sweats.
- There has been a >50% decrease in leukocyte and eosinophil values after approximately one month of treatment.

Authors have no conflicts of interest to disclose

Saint Alphonsus
PHARMACY BOISE, IDAHO