Evaluation of Posaconazole in the Treatment of Severe Coccidioidomycosis

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BACKGROUND
- Coccidioidomycosis (also known as valley fever) affects more than 150,000 people in United States
- It is a fungal infection caused by the soil-dwelling Coccidioides immitis and Coccidioides posadasii
- It is prevalent in the Southwestern United States, Northern Mexico, Central and South America
- Most cases are self limiting and infections often are confined to the lungs.
- However, some patients may have severe coccidioidomycosis with miliary or extrapulmonary involvement. The disease can disseminate to the bone, soft tissue, and central nervous system in severe cases.
- The mainstay of treatment is intravenous amphotericin B and oral azole antifungal agents most commonly fluconazole
- Management of severe coccidioidomycosis can be challenging due to high rates of recurrence and patients are often refractory to standard treatment
- Posaconazole has been employed for severe coccidioidomycosis in refractory cases
- Nevertheless, no study has compared the effectiveness of posaconazole to fluconazole

STUDY OBJECTIVE
To compare the efficacy of posaconazole and fluconazole in the treatment of severe coccidioidomycosis

METHODS
Study Design: Retrospective chart review
Study Period: January 2013 to January 2014
Inclusion Criteria: older than 18 years old, taking posaconazole or fluconazole for severe coccidioidomycosis
Primary endpoint: Treatment improvement defined as >50% decrease in Mycosis Study Group (MSG) Score
Secondary endpoint: Overall change in MSG score and change in coccidioides complement fixation (CF) titers

RESULTS
46 patients with severe Coccidioidomycosis
23 patients posaconazole suspension 400mg twice daily
23 patients fluconazole 800mg-1200mg once daily

PRIMARY OUTCOMES
- Baseline Characteristics:
  - Age (yr):
  - Weight (kg):
  - Race:
  - Sex:
  - Hispanic:
  - African American:
  - White:
  - Other:
  - Disseminated diseases:
  - Bone:
  - Skin and soft tissue:
  - Central Nervous System:
- Past medical history:
  - Hypertension:
  - Diabetes:
  - Kidney disease:
  - HIV:
- Median MSG score:
  - At diagnosis:
  - At start of treatment:
  - At end of evaluation:

SECONDARY OUTCOMES
- Patients who received posaconazole had a greater overall decrease in MSG score than patients who received fluconazole (median decrease in MSG score 8 vs 5 respectively, P = 0.01)
- 19 out of 23 patients taking posaconazole and 18 out 23 patients taking fluconazole had decreased Coccidioides complement fixation titers

DISCUSSION
- Posaconazole appears to be an effective antifungal agent in the treatment of severe coccidioidomycosis
- The majority of the patients had >50% decrease in MSG score
- The number of patients that had >50% decrease in MSG score in posaconazole group were similar to those in the fluconazole group. There was no statistically significant difference in efficacy between the two groups.
- Because the study is a retrospective review, not all information was available to compute MSG scores. Complement fixation titers were used as secondary measures for treatment efficacy.
- The result of this study shows more than 75% of patients in both treatment groups had improvement in CF titers.
- Also, the result shows that patients continue to have disease control after they were transitioned from intravenous amphotericin B therapy to oral antifungal treatment
- There is a greater overall change in MSG score in patients taking posaconazole. These patients had more severe disease as demonstrated by a greater median MSG score at diagnosis. Prescriber bias is a factor leading to this result. There is a consensus among prescribers at Kern Medical Center to reserve posaconazole for patients with more severe disease.

LIMITATIONS
- Retrospective chart review
- Small sample size at a single center

CONCLUSION
Posaconazole is effective in the treatment of severe coccidioidomycosis. Its efficacy is similar to fluconazole. It can be considered as an alternative to fluconazole for maintenance therapy in the treatment of severe coccidioidomycosis.

REFERENCES