Real World Efficacy of Bezlotoxumab for Prevention of *Clostridioides difficile* Recurrence in Immunosuppressed Patients

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Background

- Bezlotoxumab has been shown to prevent recurrent episodes *of C. difficile* infection (CDI) in high risk patients.[1]
- Current studies define therapeutic efficacy of bezlotoxumab within the first 12 weeks when the risk of recurrence is greatest. However, the risk of recurrent CDI can occur beyond the 12-week window in the immunosuppressed population.[2,3]
- Given that bezlotoxumab has detectable serum levels for up to 24 weeks after infusion, the primary endpoint is to determine overall efficacy in immunosuppressed patients.[4]

Objectives

Primary Endpoint:
- Determine overall efficacy of bezlotuxumab in immunosuppressed patients by assessing the recurrence rate of CDI at 4 weeks, 12 weeks, and 24 weeks after initial infusion.

Secondary Endpoints:
- Risk factors for recurrent CDI, treatment of CDI, and antibiotics usage before and after bezlotoxumab.

Methods

- A single center, retrospective chart review of adult immunosuppressed patients at high risk for CDI recurrence who received bezlotoxumab at Yale New Haven Health between February 2017 and December 2019 was conducted utilizing the electronic medical record.
- Immunosuppressed patients were defined as a patient who received a solid or stem cell transplant requiring immunosuppression, oncology patients receiving cytotoxic chemotherapy, or biologic agents for non-oncology indications.
- High risk antibiotics included fluoroquinolones, beta-lactam/beta-lactamase inhibitors, third/fourth generation cephalosporins, carbapenems, and/or clindamycin.

Exclusion Criteria
Age < 18 years old
No follow-up appointments
C. difficile test neither positive or not tested

Patient Selection

Patients who received bezlotoxumab
February 2017 – December 2019
N = 48

Excluded Patients, n = 22
- Not immunosuppressed (18)
- No follow-up appointments (3)
- No positive *C. difficile* test (1)

Patients Included, n = 26
Number of bezlotoxumab doses, y = 27*

*1 patient had two doses of bezlotoxomab that was given 2 years apart

Results

Table 1: Baseline Demographics

	n = 26
Age, median (range)	65 (25-77)
Female, n (%)	15 (58)
Primary Diagnosis, n (%)	
Hematologic malignancy	17 (65)
Solid tumor malignancy	4 (15)
Status post kidney transplant	4 (15)
Rheumatoid arthritis	1 (5)
Stem Cell Transplantation, n (%)	13 (50)
Allogeneic	7
Autologous	6
Immunosuppression*, n (%)	12 (46)
Calcineurin inhibitor	10
Prednisone	10
Mycophenolate mofetil	2
Ruxolitinib	2
Azathioprine	1
Infliximab	1
Methotrexate	1

*Patients could be on one or more immunosuppressive agents

Results

Table 2: CDI Episodes

Number of CDI episodes prior to bezlotoxumab	
One episode	15 (55)
Two episodes	10 (37)
Three episodes	2 (8)
Total number of CDI episodes	41 episodes (%)
Receiving prophylactic/treatment antibiotics	17 (41)
High risk antibiotics	13 (32)
Received acid suppression^	19 (46)
Proton Pump Inhibitor	15 (36)
H2 Inhibitor	6 (15)
Evidence of colitis on CT scan	7 (17)
Median Zar score, (range)	1 (0-3)
Treatment of CDI episodes prior to bezlotoxumab, n (%)⁺	
Vancomycin oral	31 (76)
Vancomycin + Metronidazole	4 (10)
Vancomycin + Nitazoxanide	2 (5)
Vancomycin + Fidaxomicin	2 (5)
Metronidazole	1 (2)
Vancomycin + Metronidazole+ Fidaxomicin + Fecal transplant	1 (2)
Received additional vancomycin taper	15 (36)

^Some patients received both types of acid suppression
⁺Patients with multiple episodes received multiple treatment courses

Table 3: CDI Recurrences after Bezlotuxumab

	0-4 week recurrence y = 27	5-12 week recurrence y = 26	13-24 week recurrence y = 26
Recurrence, n	1*	2†	1^
Receiving prophylaxis/treatment abx	1	0	1
High risk antibiotics	1	0	1
No Recurrence, n	26	24	25
Receiving prophylaxis/treatment abx	12	9	9
High risk antibiotics	0	7	9
Evidence of colitis on CT scan	0	0	0
Median Zar score	0	1	1
Treatment			
Vancomycin only	1	0	1
Vancomycin and Metronidazole	0	0	0
Fidaxomicin	0	2	0
Vancomycin taper	1	0	1

*Kidney Transplant. † Rheumotoid Arthritis & Kidney Transplant/Rectal Cancer, No Recurrence at 4 weeks ^ AML, No Recurrence at 4 & 12 weeks, received antibiotics through both

Results

- Of the 26 patients who received bezlotoxumab, only 4 (15%) had CDI recurrence within 24 weeks-
- Additionally all CDI recurrences were mild to moderate in disease severity due to:
  - No evidence of colitis was seen on CT scan
  - Median Zar score of 1 (range 0-1) due to age >60 years
- High risk antibiotics were given in 2/4 (50%) of the CDIs recurrences and 22/75 (29%) in the non-recurrence group.(p=0.5)

Discussion

- Bezlotoxumab is an effective strategy to prevent recurrence in this high risk immunosuppressed patient population even with the additional risk factor of exposure to high risk antibiotics.
- Despite a large portion of patients receiving high risk antibiotics, bezlotoxumab exhibited additional protection up to 24 weeks in this immunosuppressed population.
- This benefit was demonstrated up to 24 weeks which is beyond the initially reported 12 week benefit. It is unknown whether repeated doses after this time period are warranted in this patient population which remains to be evaluated.

Conclusion

In immunosuppressed patients with CDI, bezlotoxumab is effective at reducing CDI episodes up to 24 weeks even in this highly antibiotic exposed population.

References

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Disclosure: The authors of this presentation have the following to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation: All Authors: Nothing to disclose.