Incidence and Outcomes of Outpatient Surveillance Cultures in Graft Versus Host Disease (GvHD) on High Dose ≥0.5 mg/kg/day (HD) and Low Dose <0.5 mg/kg/day (LD) Steroid Therapy in Hematopoietic Stem Cell Transplantation (HSCT) Patients

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Background

- Graft versus Host Disease (GvHD) is generally treated with high dose steroids which increase the risk of developing an infection.
- The use of steroids for GvHD add additional immunosuppression due to inhibition of cytokine production, limiting the ability to produce systemic symptoms in the setting of an infection. This can potentially delay diagnosis of an infection, which can result in serious complications like sepsis, ICU admission, and death.[1,2]
- Outpatient surveillance blood cultures in asymptomatic patients with GvHD being treated with high doses (HD), ≥0.5 mg/kg/day of steroids has demonstrated a blood stream infections (BSI) incidence of 3.5%, with CoNS being the most common organism.[3]
- Treatment for acute and chronic GvHD can require patients to be on long term steroids at doses ≥ and < 0.5 mg/kg/day. At Yale New Haven Hospital (YNHH), patients on HD and LD steroids for GvHD receive weekly outpatient surveillance blood cultures if a central line is present.

Objectives

Primary Endpoint:

- Assess the incidence of bacterial infections from outpatient surveillance cultures in afebrile/asymptomatic GvHD patients with a central line during steroid therapy.

Secondary Endpoints:

- Identify number of patients requiring treatment, hospitalization, 30 day mortality due to infection, and BSI organisms isolated.

Methods

- A single center, retrospective chart review of adult allogeneic HSCT patients at YNHH between January 2013 and May 2019 was conducted utilizing the electronic medical record.
- GvHD was defined by established international criteria[4]
- Blood culture definition

Exclusion Criteria

- No signs and symptoms of GvHD
- Treatment with steroids for any indication other than GvHD
- Patients with GvHD and no central line
- Surveillance cultures were excluded if patients were receiving antibiotics for a bacteremia or a concurrent infection.

Patient Selection

Patients who underwent an Allogeneic HSCT between January 2013 – May 2019
N = 343

Excluded Patients, (272)
- No signs and symptoms of GvHD or treatment with steroids for any indication other than GvHD (165)
- Patients with GvHD and no central line (107)

Excluded Surveillance Cultures, (113)

Included Patients, n = 71
Surveillance Cultures, y = 901

Results

Baseline Demographics	n = 71
Age, median (range)	58 (22-76)
Male, n (%)	41 (58)
Type of Conditioning Regimen, n (%)	
Reduced intensity	47 (67)
Myeloablative	24 (33)
Type of Donor Match, n (%)	
Matched related donor, 10/10	25 (35)
Matched related donor, 8/10	1 (1)
Matched unrelated donor, 10/10	31 (44)
Matched unrelated donor, 9/10	7 (10)
Haploidentical	7 (10)
Acute GvHD grade*, n (%)	
Grade I	8 (11)
Grade II	22 (31)
Grade III	9 (12)
Grade IV	17 (24)
Chronic GvHD grade*, n (%)	
Mild	15 (21)
Moderate	20 (28)
Severe	8 (11)

Results

Baseline Demographics cont.	
Initial glucocorticoid dose*, n (%)	
HD	56 (79)
LD	65 (92)
Time to initiation of steroids	
Transplant to starting HD, median days (range)	164 (13-1364)
From 0 - 29 days post transplant, n, median days (range) From 30 - 99 days post transplant Greater than 100 days post transplant	4, 13, (13-20) 17, 50 (35-92) 50, 199 (106-1364)
Transplant to starting LD, median days (range)	215 (22-1461)
From 0 - 29 days post transplant, n, median days (range) From 30 - 99 days post transplant Greater than 100 days post transplant	3, 27 (22-29) 12, 69 (46-99) 63, 245 (104-1461)
Duration of HD steroids, median days (range)	41 (2-510)
Duration of LD steroids, median days (range)	150.5 (5-2121)
Additional agents for GvHD+ Ruxolitinib Basiliximab Infliximab Ibrutinib Rituximab Vedolizumab Imatinib	 32 21 8 2 1 1 1

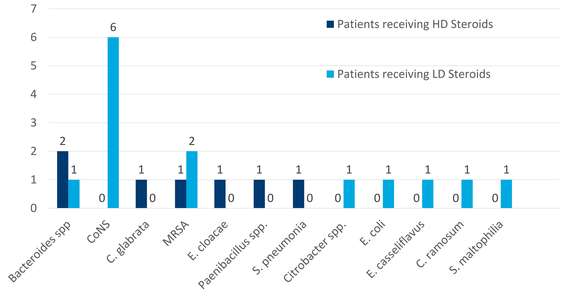
*Multiple patients were on included in both HD and LD dose of steroids.
+Multiple patients received multiple additional agents for GvHD

Blood Culture Results	HD Patients* n=56, y=296	LD Patients* n=65, y=605
Number of positive cultures, n (%), y (%)	8 (14), 12 (4)	16 (25), 22 (4)
Patients treated for positive culture, n (%)^	6 (75)	12 (75)
Patients admitted for treatment, n (%)	4 (24)	10 (83)
30 day mortality from infection, (%)	0	1 (8)
Duration of steroids, median (range)	93 (46-150)	236 (21-1143)
Median dose of steroids (mg/kg/day)	1 (0.6-2)	0.165 (0.05 – 0.33)
GvHD, n Acute, Grade 4 Involvement skin, GI, liver Chronic	 6, 3 6, 4, 4 6	 11, 4 11, 9, 6 6
Number of positive/per 100 days	0.11	0.05
Number of positive/per 1000 days£	1.189	0.517

*Multiple patients were on included in both HD and LD dose of steroids. ^p = 0.45. £ RR 2.2

Results

Culture Documented Treated Organisms Requiring Treatment



Discussion

- To our knowledge, this is the largest study evaluating surveillance cultures in patients with GvHD receiving HD steroids compared to LD steroids.
- The relative risk of positive cultures per 1000 days were two fold higher in patients receiving HD steroids.
- Patients receiving LD steroids interesting had a higher rate of infections requiring treatment likely attributed to the longer duration of steroids.
- Although CoNS is usually a contamination, in the LD group it was the most common BSI requiring treatment.

Conclusion

Although the relative risk of positive surveillance blood cultures in HD patients compared to LD was twofold higher, there were clinically significant infections identified in the LD group.

References

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