Efficacy of Ibrutinib, Ruxolitinib and/or Belumosudil without Concomitant Corticosteroids in the Treatment of Graft-Versus-Host Disease

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Introduction

Graft-versus-host disease is a debilitating and limiting complication following allogeneic hematopoietic stem cell transplant. Systemic corticosteroid therapy as first-line treatment achieves an initial response in only about 50% of cases. Currently there are three FDA approved agents for steroid-refractory GVHD: ibrutinib, ruxolitinib, and belumosudil. The best overall response rates for these agents were 69%, 76.4%, and 77% respectively. Patients may face numerous adverse effects to prolonged corticosteroid treatment or have underlying disease states that may limit prolonged steroid use. This study aims to assess the overall efficacy of ibrutinib, ruxolitinib, and belumosudil as *standalone* treatments for refractory GVHD.

Endpoints

The primary endpoint is overall response (complete response or partial response) per the treatment duration or up to 6 months, whichever occurred first. The secondary endpoints include overall survival, median duration of treatment, median duration of response, median time to response, incidence of change in systemic therapy and frequency of adverse events.

Methods

A single-center, retrospective cohort study was conducted. Data and patient demographics were extrapolated and evaluated from the hospital's electronic health record from August 1st, 2022 to July 8th, 2024. Adult patients receiving alloHSCT, developed GVHD, and treated with at least one dose of ibrutinib, ruxolitinib, or belumosudil without systemic corticosteroids were included. Concurrent treatment of novel agent with budesonide or beclomethasone was allowed. Statistical analysis for the primary and secondary endpoints included descriptive measures for continuous variables, alongside frequencies for categorical variables. Efficacy of novel oral agents used to treat GVHD without corticosteroids was summarized as response rates along with 95% confidence interval which was estimated using the binomial exact confidence interval (Clopper Pearson Method). The frequency of adverse events was determined.

Results

Table 1. Baseline Characteristics

Characteristic	N=16
Median age, *years (range)*	55 (34-69)
Male sex, *n (%)*	10 (63)
Novel agent used, *n (%)*	
Ruxolitinib	10 (63)
Belumosudil	6 (38)
Baseline disease, *n (%)*	
Acute myeloid leukemia	7 (44)
Myelodysplastic syndromes	4 (25)
Acute lymphoblastic leukemia	2 (13)
Other	3 (19)
GVHD type at novel treatment initiation, *n (%)*	
Chronic	13 (81)
Overlap	2 (13)
Acute	1 (6)
Steroid deferral reason, *n (%)*	
Recurrent symptoms	11 (69)
Infection	5 (31)
Adrenal insufficiency	2 (13)
Patient preference	2 (13)

Results (cont.)

Table 2. Transplant Characteristics

Transplant Characteristic	N=16
Donor source, *n (%)*	
Peripheral blood	13 (81)
Peripheral blood/umbilical cord	2 (13)
Umbilical cord	1 (6)
Match related, *n (%)*	4 (25)
Match unrelated, *n (%)*	9 (56)
Haploidentical, *n (%)*	3 (19)
Conditioning regimen, *n (%)*	
Fludarabine and busulfan	9 (56)
Other	7 (44)
GVHD prophylaxis, *n (%)*	
Tacrolimus/methotrexate/antithymocyte globulin	5 (31)
Tacrolimus/methotrexate	5 (31)
Tacrolimus/mycophenolate mofetil/antithymocyte globulin	3 (19)
Other	3 (19)

Figure 1. Response of Novel Agent

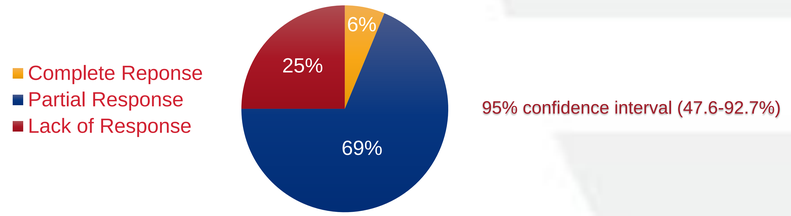

Figure 2. Swimmer Plot of Key Milestones in GVHD Management

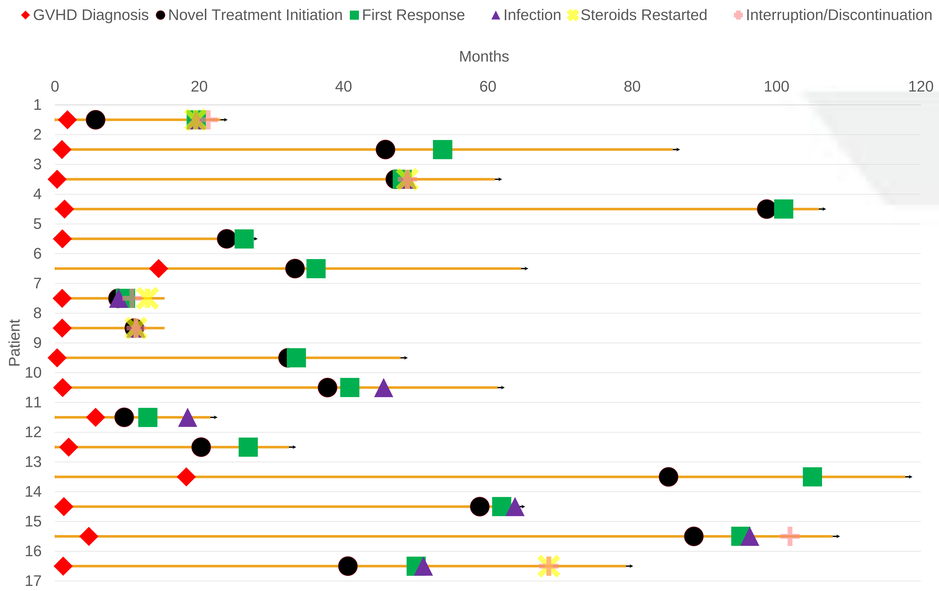

Figure 3. Frequency of Adverse Events, *n (%)*

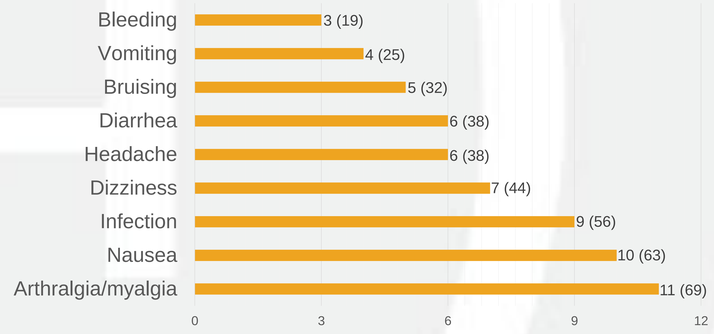

Table 3. Secondary Efficacy Endpoints

Outcomes	
Overall survival per treatment duration or up to 6 months, *(%)*	94
Median follow-up, *days (IQR)*	91 (61.2-227.5)
Median duration of treatment, *days (IQR)*	80 (52-325)
Median duration of response, *days (IQR)*	91 (71-195)
Median time to response, *days (IQR)*	93 (80.9 - 105.1)
Incidence of change in systemic therapy, *n (%)*	6 (38)

Conclusions

The use of novel agents, ruxolitinib and belumosudil, demonstrated high response rates in patients with acute and chronic GVHD, even in the absence of concomitant corticosteroids. Compared to the best overall response rates of the individual agents, a steroid-sparing strategy forges similar results. This suggests a potential alternative treatment strategy for a majority of patients who had recurrent symptoms, cannot tolerate long-term steroid-related adverse effects, or prefer to avoid prolonged steroid use. This study has several limitations, including a small sample size and retrospective design, a 6-month response window that may not capture longer-term effects, and that true treatment duration may be confounded by brief therapy interruptions given 60% of the number of patients who reinitiated steroids were due to treatment of pulmonary conditions and not necessarily for treatment of GVHD. Further investigational studies are needed to validate the efficacy and safety of this steroid-sparing approach in a larger patient population.

Disclosure/References

The authors of this study 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.

- Alina Hung: nothing to disclose
- Scott Heinemann: advisory board for Syndax Pharmaceuticals™
- Christina Luszcak: nothing to disclose
- Molly Gallogly: speakers bureau for Eli Lilly™ and advisory board for Incyte Corporation™

GVHD: graft versus host disease
FDA: Food and Drug Administration
alloHSCT: allogeneic hematopoietic stem cell transplant