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Real-World Efficacy of Luspatercept in Patients With Lower-risk Myelodysplastic Syndromes/ Neoplasms (LR-MDS); a Single-Center Study in a Heavily Pretreated Cohort

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INTRODUCTION

- Anemia is the most common cytopenia in patients with LR-MDS
- Anemia leads to transfusion dependence (TD) and inferior outcomes.
- Luspatercept has received regulatory approval to treat TD LR-MDS.

AIM

To evaluate the real-world efficacy and safety of luspatercept in LR-MDS and the impact of baseline characteristics and prior treatments on hematologic response (HI-E) per 2018 International Working Group Criteria (IWG)

METHOD

- Retrospective, single-institutional study, at an academic tertiary referral center
- Included patients treated with luspatercept for LR-MDS from 01/2020 through 12/2023
- Baseline characteristics extracted included prior therapies, serum erythropoietin (EPO) level, ring sideroblast (RS) status, karyotype, and gene mutations.
- Baseline transfusion burden (no=NTD, low=LTB, high=HTB) for all patients, HI-E in patients with ≥16 weeks of therapy were calculated
- Mann-Whitney U and Fisher Exact Tests were used to compare continuous and categorical variables, respectively.
- Leukemia-Free Overall Survival (OS) was calculated using the Kaplan-Meier method, and groups compared using log-rank testing.

RESULTS

Table I: Baseline Patient and Demographic Characteristics

Patient Characteristics	Total Data Set (N=37)	Responders (N= 18)	Non-responders (N= 13)
Demographic Characteristics			
Median Age at Start of Luspatercept (Range)-years	74 (58-93)	77 (58-86)	82 (65- 93)
Female sex, no. (% of N)	19 (51)	11 (61)	6 (46)
Patients with Therapy-Related MDS, no. (% of N)	6 (16)	5 (28)	1 (8)
Prior Treatments, no. (% of N)			
Prior ESA	34 (92)	17 (94)	13 (100)
Prior HMA	7 (19)	2 (11)	3 (23)
Prior Lenalidomide	5 (14)	1 (6)	3 (23)
Two or More Prior Therapies	8 (22)	2 (11)	4 (31)
Baseline Transfusion Requirements			
Median Baseline Transfusion Burden (Range) -units per 16 weeks prior to Tx	3 (0-11)	5 (1- 11)	3 (1-9)
HTB, no. (% of N)	15 (41)	8 (44)	5 (39)
LTB, no. (% of N)	15 (41)	7 (39)	7 (54)
NTD, n (% of N)	7 (19)	3 (17)	1 (8)
Baseline CBC Data			
Median Baseline Hb Level, (g/dL)	7.8	7.7	8.0
Median Baseline Plt Level, (10^{-9}/ L)	260	260	286
Median Baseline ANC Level, (cells/ µL)	2.87	2.45	2.83
Serum EPO Status, no. (% of N)			
<100 U/L	12 (32)	9 (50)	1 (8)
100-200 U/L	7 (19)	3 (17)	4 (31)
200-500 U/L	5 (14)	1 (6)	2 (15)
>500 U/L	11 (30)	3 (17)	6 (46)
No EPO Level Available	2 (5)	2 (11)	0 (0)

- Of 31 patients who were response evaluable, 52% had HI-E, and 48% of TD patients achieved ≥16 weeks of transfusion independence (TI).
- Median TI duration (48 weeks) did not differ between HTB and LTB responders.
- EPO <100 mU/ml significantly predicted response (*P*=.02).
- Patients achieved TI at equal rates for doses of 1.00, 1.33, and 1.75 mg/kg.
- TI was lost in 22% but restored following dose increases in 50% initially receiving <1.75 mg/kg.
- Adverse effects included shortness of breath, falls, fatigue, and hypertension and precipitated discontinuation in 8% of patients.
- Eleven percent progressed to HR-MDS or AML.
- Median leukemia-free OS was not reached and did not differ between responders and nonresponders (*p*=NS).

Table II: Baseline Morphologic, Cytogenetic, and Prognostic Characteristics

Baseline Characteristics	Total Data Set (N=37)	Responders (N= 18)	Non-responders (N= 13)
Ringed Sideroblasts, no. (% of N)			
Present	29 (78)	17 (94)	9 (69)
Absent	7 (19)	1 (6)	3 (23)
Aspirate Quality Too Poor for Morphology	1 (3)	0 (0)	1 (8)
SF3B1 Mutation Status, no. (% of N)			
Present	27 (73)	14 (78)	10 (77)
Absent	7 (19)	1 (6)	3 (23)
No NGS Data	3 (8)	3 (17)	0 (0)
Presence of High-Risk Mutations, no. (% of N)			
TP53, ASXL1, CBL, RUNX1, ETV6, or SRSF2	12 (32)	3 (17)	5 (39)
No NGS Data	3 (8)	3 (17)	0 (0)
Cytogenetic Abnormalities, no. (% of N)			
Any Cytogenetic Abnormality	13 (35)	4 (22)	7 (54)
Del5Q	3 (8)	0 (0)	3 (23)
Cytogenetic Abnormalities Other than Del5Q	11 (30)	4 (22)	5 (39)
IPSS-R, no. (% of N)			
Low	29 (78)	16 (89)	8 (62)
Intermediate ≤3.5	4 (11)	1 (6)	3 (23)
Intermediate ≥4.0	4 (11)	1 (6)	2 (15)
IPSS-M, no. % of N)			
Very Low, Low, or Moderate-Low (lower-risk)	27 (73)	13 (72)	9 (69)
Moderate-high, High, Very High (higher-risk)	7 (19)	2 (11)	4 (31)
Not Able to Calculate (no NGS Data)	3 (8)	3 (17)	0 (0)

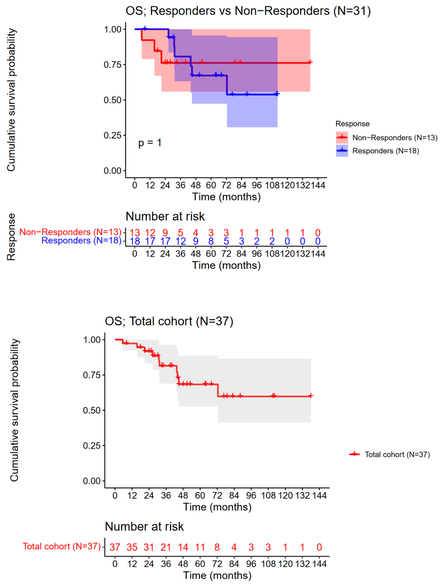


Figure I: Leukemia-free Survival for Total Data Set, Responders, and Non-responders

CONCLUSIONS

Luspatercept achieved high rates of durable TI in heavily pretreated LR-MDS patients. Dose escalation restored TI in 50% who lost response at submaximal dosages. Response was associated with EPO <100 mU/ml, but not with baseline transfusion burden. As luspatercept gains prominence as first-line therapy, further investigation is indicated to define predictors of response.

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