Simple Blood Marker for Predicting Luspatercept Response in Myelodyplastic Syndromes and Beta-Thalassemia

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INTRODUCTION

- **Ineffective erythropoiesis** is a key feature of both beta-thalassemia and myelodysplastic syndromes.
- **Luspatercept** enhances late-stage erythroid maturation and may reduce transfusion burden.
- **Clinical gap:** simple blood-based markers reflecting dynamic erythropoietic changes during treatment remain insufficiently characterized.

AIM

To evaluate the NRBC/WBC ratio as a potential dynamic marker of erythropoietic activity and biological changes during luspatercept therapy in BT and MDS, beyond hemoglobin and transfusion burden.

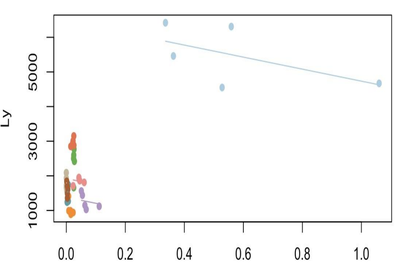
METHOD

- Retrospective observational study conducted between 2021-2026; longitudinal assessments at baseline and at 1,2,3,6 months after luspatercept initiation;
- **21 patients: 9 with BT (all phenotypes) + 12 with MDS (ring and non-ring sideroblast subtypes),** consecutively enrolled based on luspatercept treatment eligibility; all completed follow-up evaluations;
- Luspatercept was administered at standard dosing according to local guidelines over 6 months;
- **NRBC/WBC associations with erythropoiesis, inflammation, hemolysis, transfusion burden and MDS prognostic scores were analyzed using repeated-measures/ Spearman correlations, Kruskal-Wallis, and ROC analyses. P<0.05= significant.**

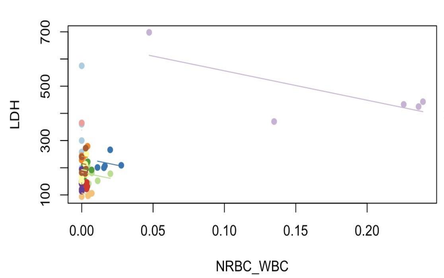
CONCLUSIONS

- NRBC/WBC demonstrated modest longitudinal associations with selected laboratory parameters during luspatercept therapy, without correlation with hemoglobin or transfusion burden.
- These findings suggest a role in capturing erythropoietic and inflammatory dynamics not reflected by conventional endpoints.
- Given the exploratory design, small sample size and heterogeneity, these findings require validation in larger prospective studies.

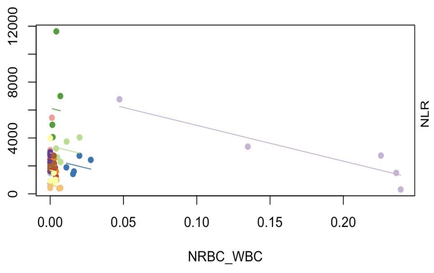
RESULTS



result	list [7] (S3: rmc)	List of length 7
r	double [1]	−0.4605243
df	integer [1]	35
p	double [1]	0.004127808
CI	double [2]	−0.683 −0.160
CI.level	double [1]	0.95
model	list [13] (S3: lm)	List of length 13
vars	character [3]	'PatientID' 'NRBC_WBC' 'Ly'



result	list [7] (S3: rmc)	List of length 7
r	double [1]	−0.3911101
df	integer [1]	47
p	double [1]	0.005457233
CI	double [2]	−0.606 −0.123
CI.level	double [1]	0.95
model	list [13] (S3: lm)	List of length 13
vars	character [3]	'PatientID' 'NRBC_WBC' 'LDH'



result	list [7] (S3: rmc)	List of length 7
r	double [1]	−0.4362233
df	integer [1]	47
p	double [1]	0.001728457
CI	double [2]	−0.639 −0.177
CI.level	double [1]	0.95
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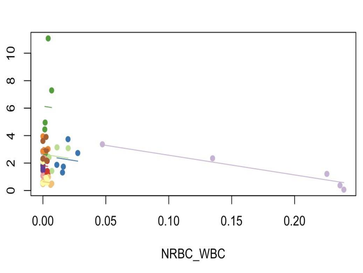
vars	character [3]	'PatientID' 'NRBC_WBC' 'Ne'



result	list [7] (S3: rmc)	List of length 7
r	double [1]	−0.3018629
df	integer [1]	47
p	double [1]	0.03503616
CI	double [2]	−0.5374 −0.0226
CI.level	double [1]	0.95
model	list [13] (S3: lm)	List of length 13
vars	character [3]	'PatientID' 'NRBC_WBC' 'NLR'

Legend: each color = individual patient; points = measurements at different timepoints

In BT- NRBC/WBC showed an inverse association with absolute lymphocyte count, without correlations with hemoglobin, LDH, ferritin, or transfusion burden.

In MDS- inverse associations were observed with LDH, neutrophil count and neutrophil-to-lymphocyte ratio, without other hematologic parameters, ferritin, transfusion burden, or prognostic scores.
Overall, correlations were modest (r=-0.30 to -0.46, 9-21% shared variance).
No significant temporal differences were detected (Kruskal-Wallis p=0.406) and ROC analysis showed no discriminatory performance.

KEY FINDINGS

- NRBC/WBC captured **selected erythropoietic and inflammatory dynamics** during luspatercept therapy;
- The observed associations were **modest** and **disease-specific**;
- NRBC/WBC was **not associated with hemoglobin or transfusion burden;**
- **No predictive performance** was demonstrated in this exploratory cohort.

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CONTACT INFORMATION

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