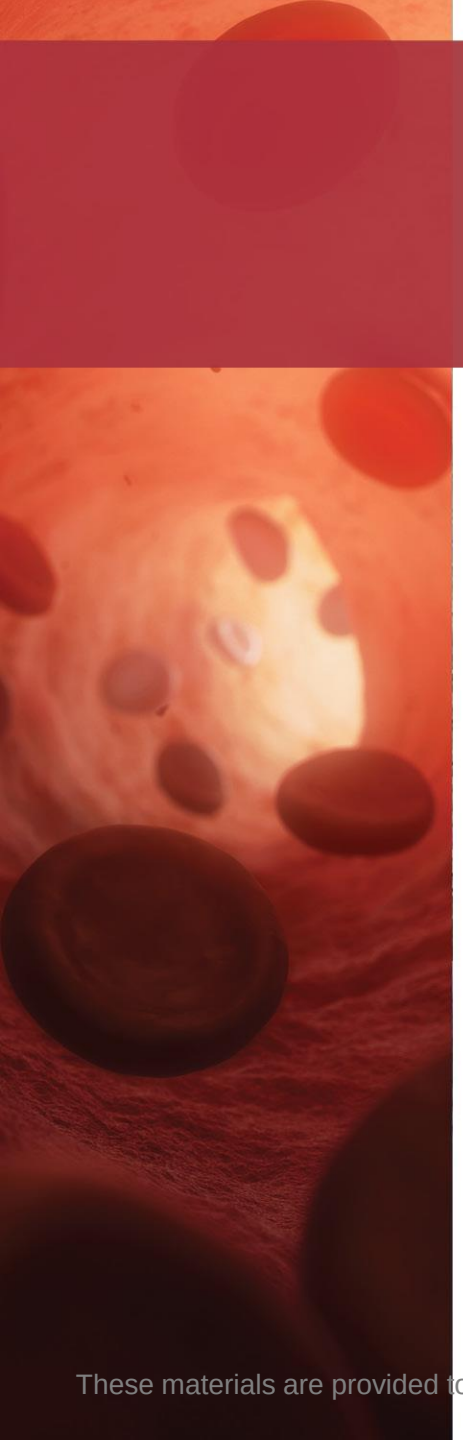
Anemia Management in Lower-Risk Myelodysplastic Syndromes

Current and Emerging Treatment Options

These slides are meant to be used as an accompaniment to the presentation for note taking purposes, they are not intended as a standalone reference.



This educational activity is sponsored by Postgraduate Healthcare Education, LLC and supported by an educational grant from Bristol Myers Squibb.

Faculty

Christopher A. Fausel, PharmD, MHA

Senior Pharmacist, Oncology Precision Genomics
Department of Pharmacy
Indiana University Simon Comprehensive Cancer Center
Indianapolis, IN

Dr. Fausel is a Senior Pharmacist for Oncology Precision Genomics at the Indiana University, Simon Comprehensive Cancer Center in Indianapolis, Indiana. He also serves as Chairman of the Board of the Hoosier Cancer Research Network, a non-profit organization that conducts clinical trials and translational research in cancer and serves as the administrative headquarters for the Big Ten Cancer Research Consortium.
Dr. Fausel is the Chair of a biomedical Institutional Review Board (IRB) and serves on the IRB Executive Committee for Indiana University.

Disclosures

Dr. Fausel has disclosed that he has no relevant affiliations or financial relationships with a commercial interest to disclose.

The clinical reviewer, Lisa Holle, PharmD, has disclosed that she has served as a consultant for McGraw-Hill Education and Postgraduate Healthcare Education; and has received honoraria from Pharmacy Times Continuing Education, Postgraduate Healthcare Education, AXIS Medical Education, HOPA, HMP CME and ISOPP.

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UAN: 0430-0000-21-052-H01-P
Credits: 1.0 hour (0.1 CEU)
Type of Activity: Application

Learning Objectives

- Describe the varying presentations and prognoses of myelodysplastic syndromes (MDS)
- Discuss supportive care options for anemia in lower-risk MDS, including limitations of such therapies
- Explain new and emerging management options for anemia in lower-risk MDS
- Formulate approaches to provide optimal management of patients with anemia in MDS

Myelodysplastic Syndrome (MDS)

- Clonal hematopoietic stem cell disorder
  - ineffective hematopoiesis
  - progressive cytopenia(s)
  - risk of progression to acute myeloid leukemia (AML)
- Chromosomal deletions drive hypoplastic marrow function and subsequent progression to AML
- Cytogenetics correlated with prognosis
- Median Age: 70 years
- Incidence: 4 to 5 cases per 100,000 persons
  - Increases with age – may be as high as 75 per 100,000 in age > 70 years

Cazzola M. *N Engl J Med.* 2020;383(14):1358-1374.

Clinical Presentation

Diagnostic Test(s)	Finding Consistent with MDS
Complete blood count	Persistent and otherwise clinically unexplained cytopenia(s)
Bone marrow biopsy – high-quality material for morphologic analysis; review of peripheral blood smear and bone marrow aspirate	Significant morphologic dysplasia of hematopoietic elements*
Conventional bone marrow karyotype, molecular genetic testing, and flow cytometry immunophenotyping	Cytogenetic and/or molecular genetic evidence of clonal hematopoiesis

*exception of cases bearing certain qualifying cytogenetic aberrations

Hasserjian RP. *Pathobiology.* 2019;86(1):7-13.

2016 WHO Classification of MDS

Subtype	Cytopenia	BM/PB
MDS with single lineage dysplasia (MDS-SLD)*	1 or 2 lineages	BM < 5%, PB < 1%, no Auer rods
MDS with multilineage dysplasia (MDS-MLD)*	1 to 3 lineages	BM < 5%, PB < 1%, no Auer rods
MDS with ring sideroblasts (MDS-RS) with single lineage dysplasia*	1 or 2 lineages	BM < 5%, PB < 1%, no Auer rods
MDS-RS with multilineage dysplasia*	1 to 3 lineages	BM < 5%, PB < 1%, no Auer rods
MDS with isolated del(5q)	1 or 2 lineages	BM < 5%, PB < 1%, no Auer rods
MDS with excess blasts-1 (MDS-EB-1)	1 to 3 lineages	BM 5%-9%, PB 2%-4%, no Auer rods
MDS with excess blasts-2 (MDS-EB-2)	1 to 3 lineages	BM 10%-19%, PB 5%-19%, or (+) Auer rods
MDS, unclassifiable (MDS-U)	1 to 3 lineages	BM < 5%, PB < 1%, no Auer rods

BM = bone marrow; PB = peripheral blood blasts; WHO = World Health Organization

Arber DA, et al. *Blood.* 2016;127(20):2391-2405.

*Contains ringed sideroblasts as % of marrow erythroid elements

International Prognostic Scoring System (IPSS)

Blasts

< 5%: Score 0

5% - 10%: Score 0.5

11% - 20%: Score 1.5

21% - 30%: Score 2

Karyotype

Favorable [normal, -Y, del(5q), del (20q)]:	Score 0
Intermediate [other abnormalities]:	Score 0.5
Unfavorable [≥ 3 or Ch 7 abnormalities]:	Score 1

Cytopenias

≤ 1: Score 0

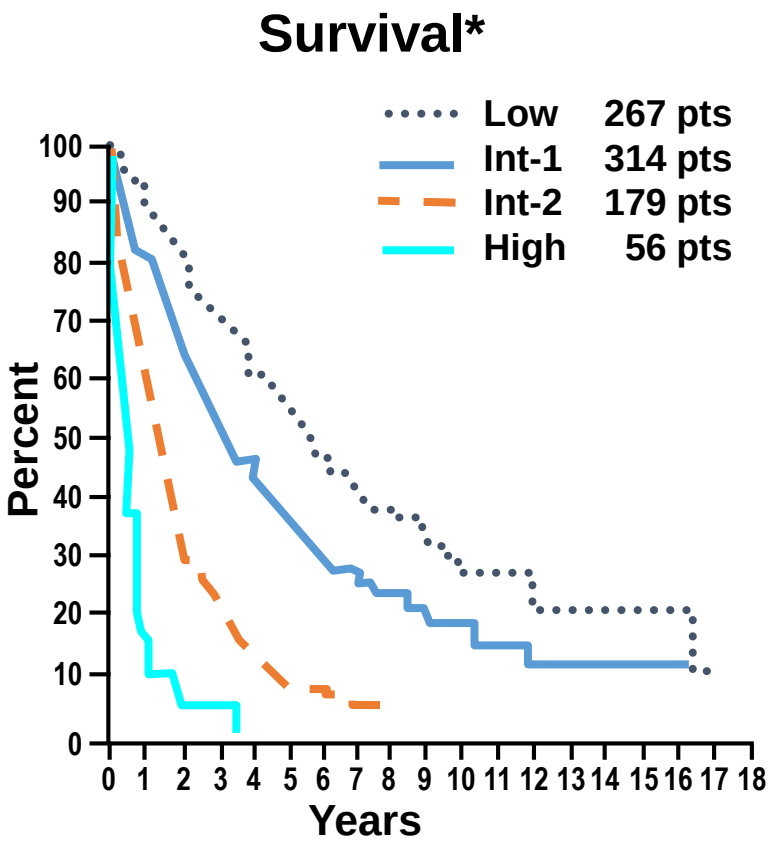
≥ 2: Score 0.5

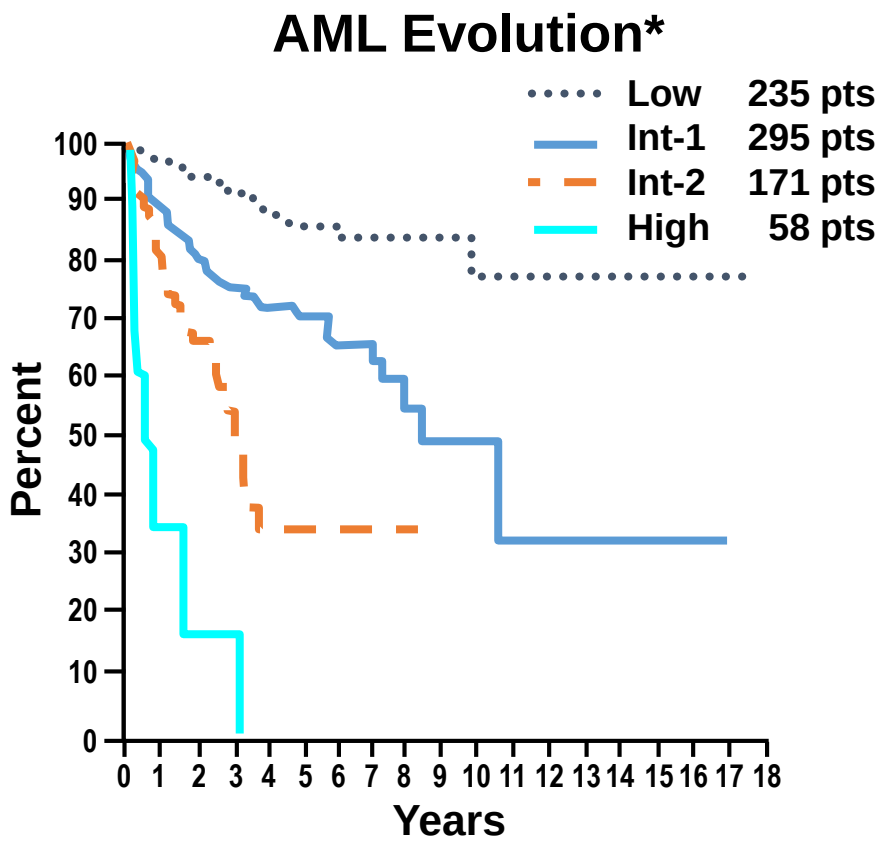
Risk groups:

Score 0:	Low
Score ≤1:	Int-1
Score 1.5–2:	Int-2
Score ≥ 2.5:	High

Greenberg P, et al. *Blood*. 1997;89(6):2079-2088.

Survival and AML Evolution by IPSS





*From diagnosis in untreated patients.

Greenberg P, et al. *Blood*. 1997;89(6):2079-2088.

Revised IPSS (IPSS-R): Prognostic Scoring Values

Prognostic Variable	0	0.5	1	1.5	2	3	4
Cytogenetics	Very Good	--	Good	--	Intermediate	Poor	Very Poor
Bone Marrow Blasts (%)	≤ 2	--	> 2 – < 5	--	5 – 10	> 10	--
Hemoglobin (g/dL)	≥ 10	--	8 – 9.9	< 8	--	--	--
Platelets (mm^3)	≥ 100,000	50 – 99,999	< 50,000	--	--	--	--
ANC (mm^3)	≥ 800	< 800	--	--	--	--	--

ANC = absolute neutrophil count

Greenberg PL, et al. *Blood*. 2012;120(12):2454-2465.

IPSS-R Prognostic Risk Categories

Risk Category	Risk Score
Very Low	≤ 1.5
Low	> 1.5 – 3
Intermediate	> 3 – 4.5
High	> 4.5 – 6
Very High	> 6

Greenberg PL, et al. *Blood*. 2012;120(12):2454-2465.

Cytogenetic Abnormalities

Risk Category	Very Good (3%)	Good (66%)	Intermediate (21%)	Poor (4%)	Very Poor (7%)
Karyotype	Single: del(11q) -Y	Single: Normal der(1;7) del(5q) del(12p) del(20q) Double: del 5q (included)	Single: -7/7q- +8 iso(17q) +19 +21 Any other independent clones Double: Any other double	Single: der(3)(q21)/ der(3)(q26) Double: -7/7q- (included) Complex: 3 abnormalities	Complex: > 3 abnormalities
Median OS	61 months	49 months	25 months	15 months	6 months

Garcia-Manero G, et al. *Am J Hematol.* 2020;95(11):1399-1420.

OS = overall survival

Common Genetic Aberrations in MDS

Gene	Frequency	Location	Function
SF3B1	28%	2q33	Splicing factor
TET2	21%	4q24	Cytosine hydroxymethylation
ASXL1	14%	20q11	Epigenetic regulator
SRSF2	12%	17q25	Splicing factor
RUNX1	9%	21q22	Transcription factor
TP53	8%	17p13	Transcription factor
U2AF1	7%	21q22	Splicing factor
EZH2	6%	7q36	Polycomb group protein
NRAS	4%	1p13	Signal transduction
JAK2	3%	9p24	Tyrosine kinase
ETV6	3%	12p13	Transcription factor

Garcia-Manero G, et al. *Am J Hematol.* 2020;95(11):1399-1420.

Low-Risk vs. High-Risk MDS

Low-Risk	High-Risk
IPSS: Low, INT-1 IPSS-R: Very low, Low, Intermediate Bone marrow blasts: < 10%	IPSS: INT-2, High IPSS-R: Intermediate, High, Very High Bone marrow blasts: ≥ 10%

INT = intermediate

Garcia-Manero G, et al. *Am J Hematol.* 2020;95(11):1399-1420.

Goals of Treatment

- Hemoglobin (Hgb) level improvement
- Transfusion independence
- Minimizing infection/bleeding risk
- Maintenance or improvement in quality of life
- Halting or slowing progression to AML

Treatment Options: Lower-Risk MDS

- Active surveillance
- Erythropoiesis stimulating agent (ESA) therapy (± GCSF)
- Lenalidomide in MDS with isolated 5q-
- Luspatercept in MDS with ringed sideroblasts
- Immunosuppressive therapy in hypoplastic MDS
- Red blood cell (RBC) transfusion
- Iron chelation therapy

Cazzola M. *N Engl J Med.* 2020;383(14):1358-1374.

GCSF = granulocyte colony-stimulating factor

Transfusion Support

- Most patients receive transfusions during their clinical course
- Effective to achieve hemoglobin >10 g/dL
- Frequent transfusions (> 20-30 units) associated with risk of iron overload
- Iron chelation therapy considered
- Infectious complications
- Decreased survival reported in transfusion-dependent MDS

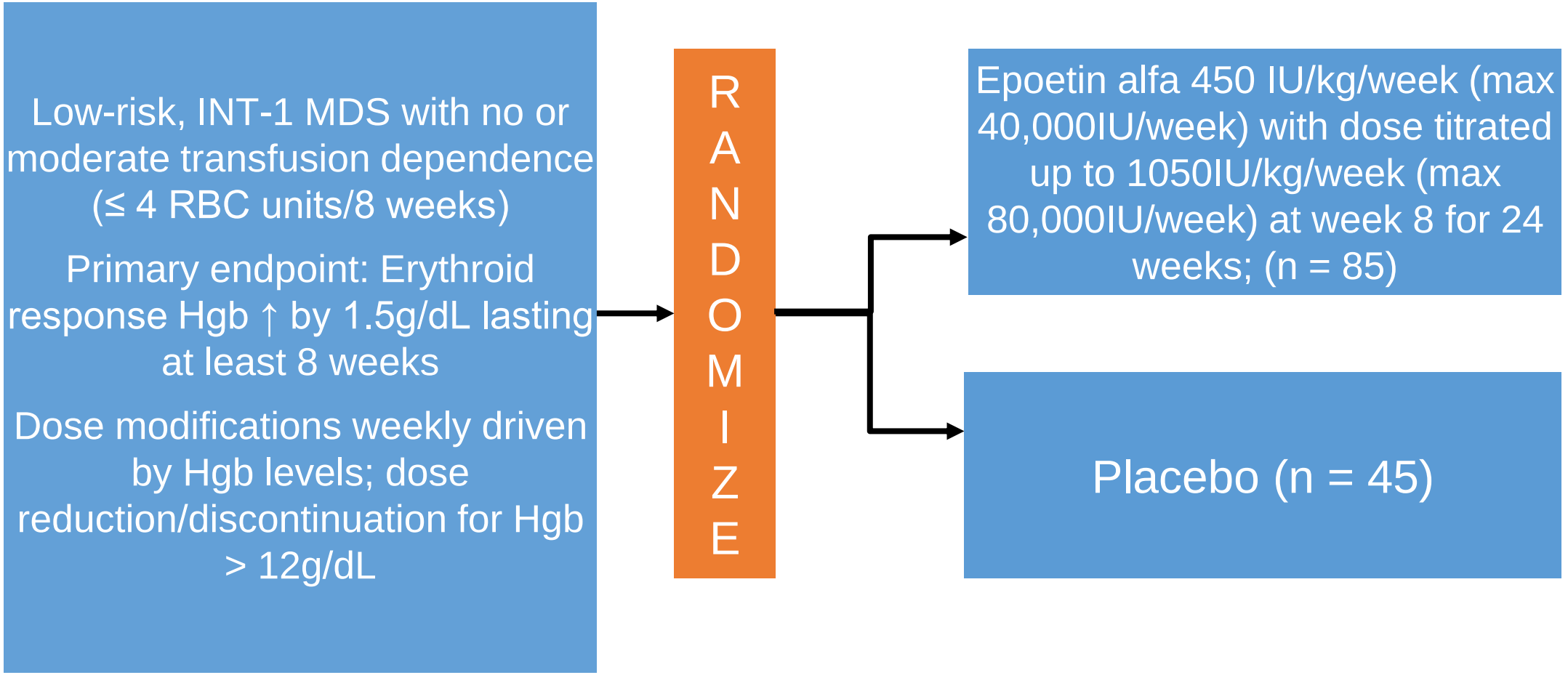
Fenaux P, et al. *Br J Haematol.* 2020;189(6):1016-1027.

ASCO/ASH Guidelines: ESAs

- **Recommendation:** ESAs may be offered to patients with lower-risk MDS and serum erythropoietin (EPO) ≤ 500 IU/L
- **Clinical Interpretation:** In patients with MDS, some studies suggest patients with baseline EPO > 500 IU/L are unlikely to respond to ESAs
  - Recent data suggests EPO levels < 200 IU/L have a better Hgb response
  - Lower pretreatment transfusion dependence (< 2 units per month) is associated with higher likelihood of ESA response
  - ESA may provide benefit in avoiding hemochromatosis

Bohlius J, et al. *J Clin Oncol.* 2019;37(15):1336-1351. ASCO = American Society of Clinical Oncology; ASH = American Society of Hematology

Epoetin alfa in low-risk MDS: Phase III



Fenaux P, et al. *Leukemia.* 2018;32(12):2648-2658.

Efficacy: Modified Intent to Treat Analysis

Parameter	Epoetin alfa (n = 85)	Placebo (n = 45)
ER at ANY time during 24-week study interval	31.8%	4.4%
ER, **no** transfusions, and EPO < 200 mU/mL	50%	4.8%
ER, transfusion requirement, and serum EPO < 200 mU/mL	22.6%	5.6%
ER, **no** transfusions, and serum EPO ≥ 200 mU/mL	0	0
ER, transfusion requirement, and serum EPO ≥ 200 mU/mL	0	0
ER, Low (0) IPSS risk category	45.7%	8.7%
ER, INT-1 (0.5–1) IPSS risk category	20.4%	0

EPO = erythropoietin; ER = erythroid response

Fenaux P, et al. *Leukemia.* 2018;32(12):2648-2658.

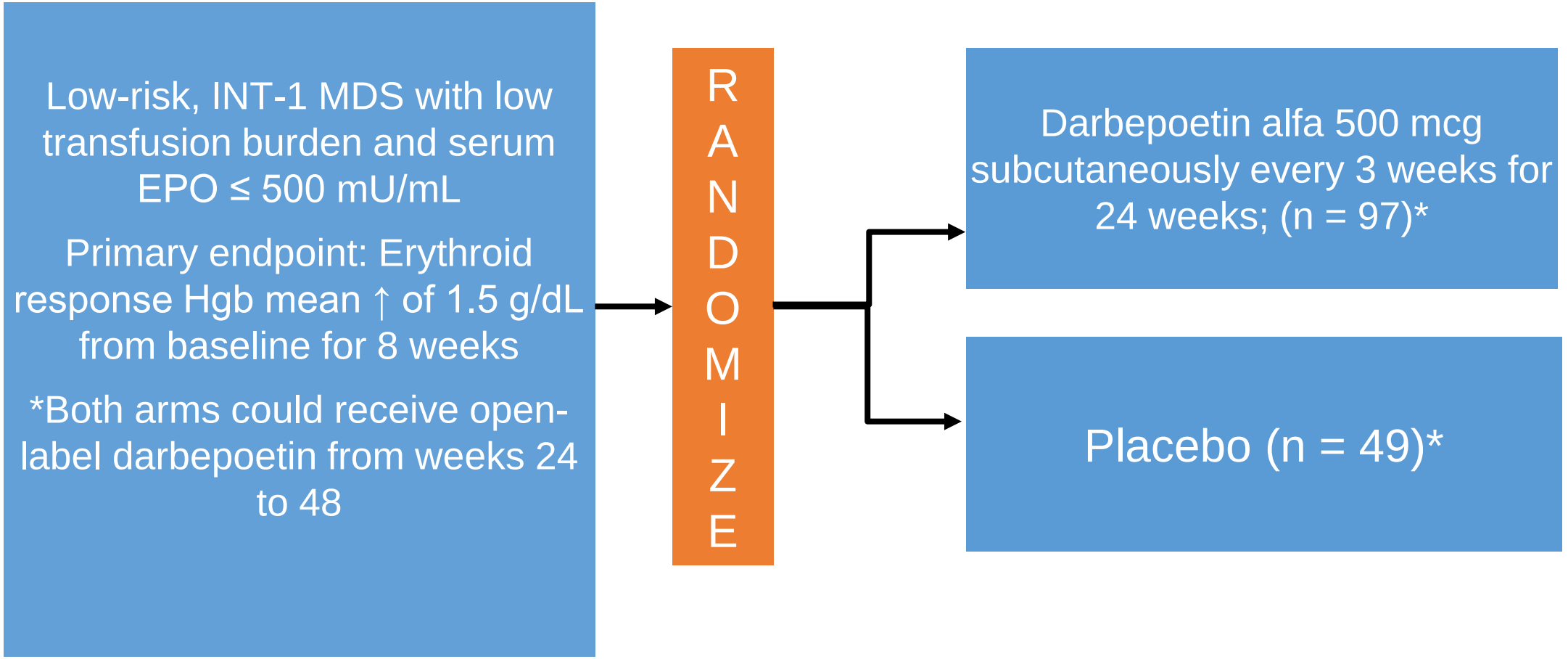
Toxicity: Key Safety Findings During 24-Week Study Interval

Parameter	Epoetin Alfa (n = 85)	Placebo (n = 45)
≥ 1 treatment emergent AE	77.6%	88.9%
≥ 1 serious treatment-emergent AE	25.9%	17.8%
≥ 1 treatment-emergent Grade III/IV AE	25.9%	26.7%
≥ 1 treatment-emergent AE leading to study discontinuation	10.6%	13.3%
Death	4.7%	2.2%
≥ 1 thrombotic vascular event	4.7%	0
Disease progression*	12.9%	8.9%
Progression to AML	3.5%	4.4%

Fenaux P, et al. *Leukemia.* 2018;32(12):2648-2658.

AE = adverse event; *includes progression to AML

Darbepoetin alfa in low-risk MDS: Phase III



Platzbecker U, et al. *Leukemia.* 2017;31(9):1944-1950.

Efficacy

Parameter	Darbepoetin alfa (n = 97)	Placebo (n = 49)
Hematologic improvement – erythroid	23.6%	4.2%
Transfusion incidence (weeks 5 – 24)	36.1%	59.2%
Transfusion incidence (open-label weeks 24 – 48)	26.4%	28.9%
Doses withheld for Hgb > 12 g/dL	11%	0

Platzbecker U, et al. *Leukemia.* 2017;31(9):1944-1950.

Toxicity During 24-Week Study Interval

Parameter	Darbepoetin (n = 98)	Placebo (n = 48)
AE leading to study drug discontinuation	3.1%	4.2%
≥ Grade III	15.3%	27.1%
≥ Grade IV	5.1%	12.5%
Fatal AEs (none treatment related)	1%	4.2%
Serious AEs	11.2%	16.7%
Treatment-related serious AEs	1%	0
Thrombovascular events	1%	0
Progression to AML	2.1%	2.2%

AE = adverse event

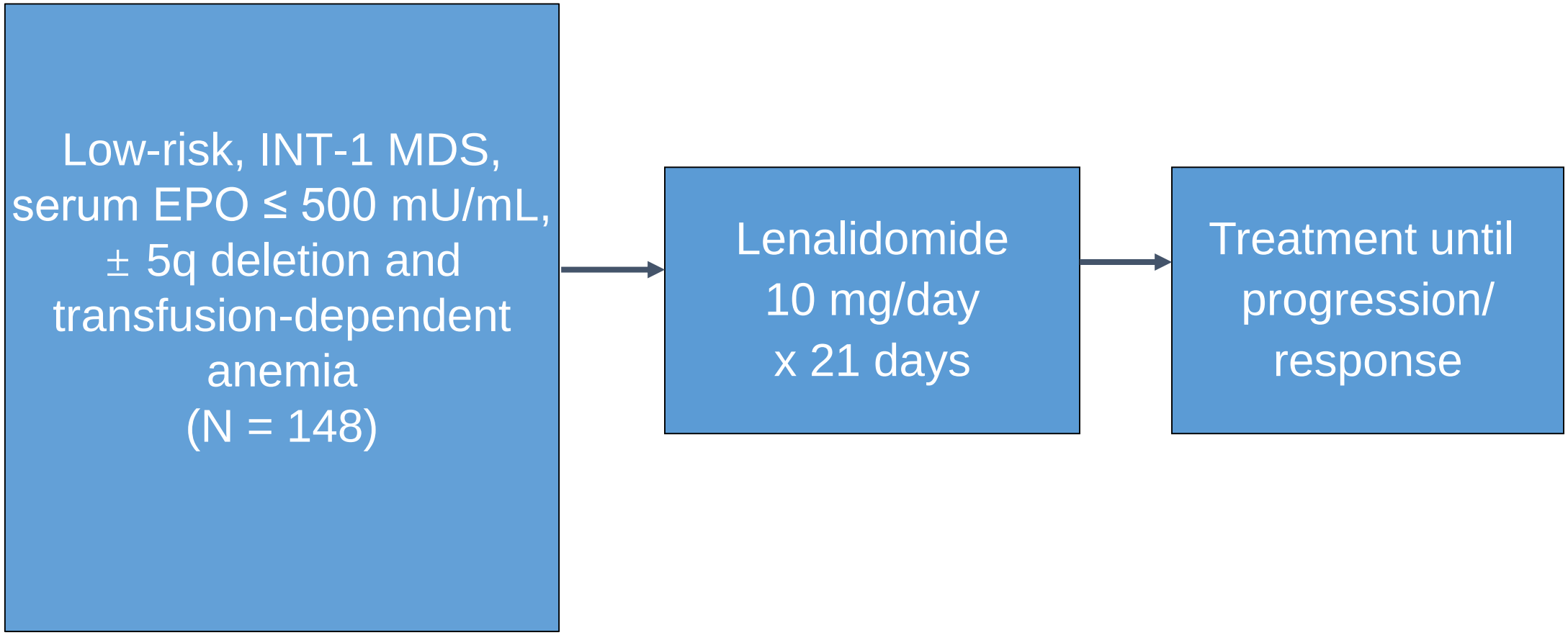
Platzbecker U, et al. *Leukemia.* 2017;31(9):1944-1950.

5q- Syndrome

- Defined by isolated 5q-, < 5% blasts
- IPSS low or INT-1
- Characteristics:
  - Majority female
  - Symptomatic, macrocytic severe anemia
  - Up to 20% have splenomegaly
  - Median survival 53 to 146 months
    - 5% to 16% evolve to AML
  - Poor response to ESAs (6% to 14%)

List A, et al. *Leukemia.* 2018;32(7):1493-1499.

Lenalidomide: 5q- Syndrome



List A, et al. *Leukemia. N Engl J Med.* 2006;355(14):1456-1465.; Raza A, et al. *Blood.* 2008;111(1):86-93.

Efficacy

Parameter	5q- Patients (n = 148)	All Cytogenetic Abnormalities (n = 214)
Transfusion independence	67%	26%
Time to response (median)	4.6 weeks	4.8 weeks
Median Hgb ↑	5.4 g/dL	3.2 g/dL
Complete cytogenetic response	45%	9%
Partial cytogenetic response	28%	11%

List A, et al. *Leukemia. N Engl J Med.* 2006;355(14):1456-1465.; Raza A, et al. *Blood.* 2008;111(1):86-93.

Toxicity

Parameter	All Grades (n = 214)	Grades ≥ III (n = 214)
Neutropenia	28%	25%
Thrombocytopenia	26%	20%
Rash	22%	4%
Pruritus	21%	1%
Fatigue	15%	4%
Diarrhea	15%	1%
Thromboembolism	1%	1%

Raza A, et al. *Blood.* 2008;111(1):86-93.

Luspatercept

- **FDA-approved indications:**
  - Anemia failing an ESA and requiring 2 or more RBC units over an 8 week period in adult patients with very low- to intermediate-risk MDS-RS or with MDS/MPN-RS-T
  - Anemia in adult patients with beta-thalassemia requiring regular RBC transfusions
  - Not a substitution for RBC transfusion for patients in need of immediate correction of anemia
- **Dosing:**
  - 1mg/kg subcutaneously every 21 days
- **Common toxicities:**
  - Abdominal pain, arthralgia, cough, diarrhea, dizziness, dyspnea, fatigue, hypertension, headache, hypersensitivity, musculoskeletal pain, injection-site reactions, thromboembolism

MDS/MPN-RS-T = myelodysplastic/myeloproliferative neoplasm with ring sideroblasts and thrombocytosis

Reblozyl [prescribing information]. Celgene Corporation; 2020.

Luspatercept: Upward Dose Titration

Dosing Criteria	Dose Adjustment
Not RBC transfusion-free after at least 2 consecutive doses (6 weeks) at 1 mg/kg starting dose	Increase to 1.33 mg/kg every 3 weeks
Not RBC transfusion-free after at least 2 consecutive doses (6 weeks) at 1.33 mg/kg	Increase to 1.75 mg/kg every 3 weeks
No reduction in RBC transfusion burden after at least 3 consecutive doses (9 weeks) at 1.75 mg/kg	Discontinue treatment

Reblozyl [prescribing information]. Celgene Corporation; 2020.

Luspatercept: Downward Dose Titration

Dosing Criteria	Dose Adjustment
Pre-dose Hgb ≥ 11.5 g/dL in the absence of transfusions	• Interrupt treatment • Restart when Hgb ≤ 11 g/dL
Hgb increase > 2 g/dL within 3 weeks in the absence of transfusions and • Current dose is 1.75 mg/kg • Current dose is 1.33 mg/kg • Current dose is 1 mg/kg • Current dose is 0.8 mg/kg • Current dose is 0.6 mg/kg	 • Reduce dose to 1.33 mg/kg • Reduced dose to 1 mg/kg • Reduce dose to 0.8 mg/kg • Reduce dose to 0.6 mg/kg • Discontinue treatment

Reblozyl [prescribing information]. Celgene Corporation; 2020.

Luspatercept: Dose Modifications for Toxicity

Event	Dosing Recommendation
Grade III or IV hypersensitivity reactions	**Discontinue** treatment
Other Grade III or IV adverse reactions	• **Interrupt** treatment • When the adverse reaction resolves to no more than Grade I, restart treatment at the next lower dose level • If dose delay is >12 consecutive weeks, discontinue treatment

Reblozyl [prescribing information]. Celgene Corporation; 2020.

Lupatercept: Phase II in MDS

Low-risk, INT-1 MDS or non-proliferative CMML per IPSS-R who are low (< 4 units per 8 weeks and Hgb < 10 g/dL) or high RBC transfusion dependent (≥ 4 units per 8 weeks) (n = 229)

Primary endpoint: HI-E – Hgb improvement of 1.5 g/dL from baseline for ≥ 14 days and a reduction in RBC transfusion of 4 or more units or ≥ 50% reduction RBC units in 8 weeks post-treatment

(n = 58)

→ ENROLL →

Dose-Finding: Luspatercept 0.125 to 1.75 mg/kg subcutaneously every 3 weeks x 5 doses (max. 12 weeks)

Expansion: Luspatercept 1 mg/kg subcutaneously every 3 weeks; dose may be increased to 1.75 mg/kg

CMML = chronic myelomonocytic leukemia; HI-E = hematologic improvement-erythroid

Platzbecker U, et al. *Lancet Oncol*. 2017;18(10):1338-1347.

Baseline Transfusion Requirements

Base Study

Parameter	(n = 58)
No Transfusion Burden	19%
Low Transfusion Burden (1 – 3 units in last 8 weeks)	14%
High Transfusion Burden (>4 units in last 8 weeks)	67%

Extension Study

Parameter	(n = 32)
Low Transfusion Burden (1 – 3 units in last 8 weeks)	41%
High Transfusion Burden (>4 units in last 8 weeks)	59%

Platzbecker U, et al. *Lancet Oncol*. 2017;18(10):1338-1347.

Efficacy Results

Parameter	IWG HI-E	RBC-TI
Low/No Transfusion Burden	65%	75%
High Transfusion Burden	62%	29%
Previous Use of ESAs	62%	38%
Serum EPO (<200IU/L)	76%	53%
Serum EPO (200 – 500 IU/L)	58%	44%
Serum EPO (>500IU/L)	43%	14%
IPSS-R Classification Very Low to Low	65%	48%
IPSS-R Classification Intermediate	59%	31%
IPSS-R Classification High to Very High	67%	0

IWG HI-E: 1.5g/dL or high increase in Hgb over 8 weeks
RBC-TI: Red blood cell transfusion independence

Platzbecker U, et al. *Lancet Oncol*. 2017;18(10):1338-1347.

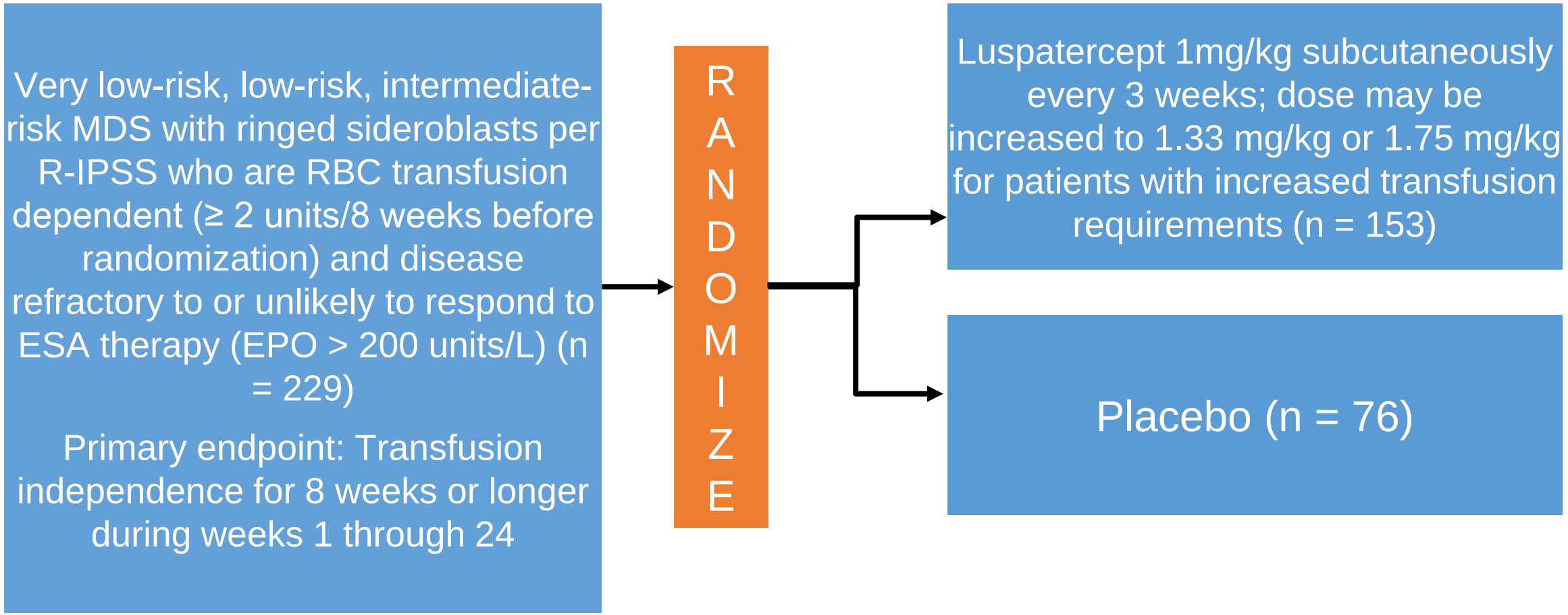
Toxicity: Grade ≥ III

Event	Frequency* (n = 58)
General physical health deterioration	2%
Increased blast count	2%
Myalgia	2%

Platzbecker U, et al. *Lancet Oncol*. 2017;18(10):1338-1347.

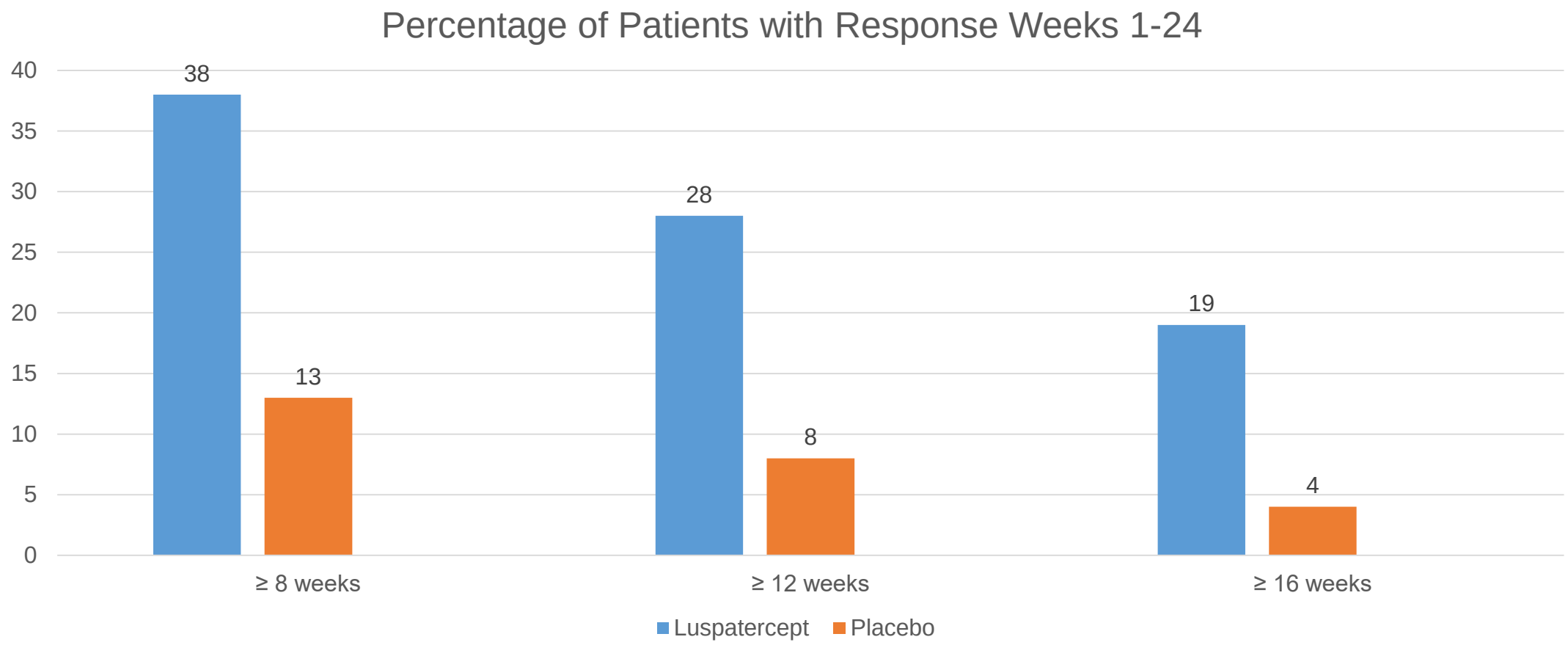
*No Grade I/II toxicities exceeded 10%

Luspatercept: Phase III Trial



Fenaux P, et al. *N Engl J Med*. 2020;382(2):140-151.

Independence from Red-Cell Transfusion



Fenaux P, et al. *N Engl J Med*. 2020;382(2):140-151.

Secondary Endpoints

Parameter	Luspatercept (n = 153)	Placebo (n = 76)
Median duration of transfusion independence (in patients meeting primary endpoint)	30.6 weeks	13.6 weeks
Erythroid response (weeks 1-24)	53%	12%
Mean Hgb increase ≥ 1.5g/dL (weeks 1-24)	63%	5%
Reduction of ≥ 4 red-cell units/8 weeks (weeks 1-24)	49%	14%
Erythroid Response (weeks 1-48)	59%	17%
Mean Hgb increase ≥ 1.5 g/dL (weeks 1-48)	70%	5%
Reduction of ≥ 4 red-cell units/8 weeks (weeks 1-48)	54%	21%

Fenaux P, et al. *N Engl J Med*. 2020;382(2):140-151.

Toxicity (Grade ≥ III)

Event*	Luspatercept (N = 153)	Placebo (N = 76)
Fatigue	5%	3%
Injury, poisoning, or procedural complication: fall	5%	3%
Asthenia	3%	0%
Back pain	2%	0%
Bronchitis	1%	0%
Arthralgia	1%	3%
Headache	1%	0%
Nausea	1%	0%
Urinary tract infection	1%	4%

*No patients discontinued luspatercept treatment for hypertension or thrombosis

Fenaux P, et al. *N Engl J Med*. 2020;382(2):140-151.

Treatment Options for Refractory/Advancing MDS

- Hypomethylating agents:
  - Azacitidine, decitabine, decitabine/cedazuridine
- Immunosuppressive therapy (hypocellular MDS):
  - Antithymocyte globulin + cyclosporine
- Intensive chemotherapy
- Hematopoietic stem cell transplant (allogeneic)

Decitabine/Cedazuridine

- **Mechanisms of action:**
  - Decitabine: nucleoside metabolic inhibitor
  - Cedazuridine: cytidine deaminase inhibitor
- **FDA-approved indications:**
  - Adult patients with MDS, including previously treated and untreated, de novo and secondary MDS with the following French-American-British subtypes (refractory anemia, refractory anemia with ringed sideroblasts, refractory anemia with excess blasts, and CMML) and INT-1, INT-2, and high-risk IPPS groups
- **Dosing:**
  - 1 tablet (decitabine 35mg/cedazuridine 100mg) by mouth daily on days 1 through 5 every 28 days on an empty stomach
- **Common toxicities:**
  - Anorexia, arthralgia, constipation, cough, diarrhea, dizziness, dyspnea, edema, fatigue, febrile neutropenia, headache, hemorrhage, mucositis, myalgia, myelosuppression, nausea, pneumonia, rash, transaminitis, upper respiratory tract infection

Inqovi [prescribing information]. Taiho Oncology, Inc.; 2020.

Decitabine/Cedazuridine: Phase II Pharmacodynamic/ Pharmacokinetic Crossover Trial

INT-1 or -2 MDS or CMML per IPSS who are RBC transfusion dependent < 4 units per 8 weeks and Hgb < 10 g/dL (n=229)

Primary endpoints: Mean decitabine systemic exposure (5-day AUC), DNA demethylation for oral cedazuridine/decitabine vs. IV decitabine, and ORR (IWG 2006 criteria)

RANDOMIZE

Note: All patients received oral decitabine/cedazuridine as a single arm following Cycle 2

Oral decitabine 35mg/ cedazuridine 100mg

Decitabine 20 mg/m^2 IV

Decitabine 20 mg/m^2 IV

Oral decitabine 35mg/ cedazuridine 100mg

Median follow- up 24.3 months

Garcia-Manero G, et al. *Blood.* 2020;136(6):674-683.

AUC = area under the curve; DNA = deoxyribonucleic acid; IV = intravenous; IWG = International Working Group; ORR = overall response rate

Pharmacokinetic Analysis

Parameter: Primary paired population 5 day AUC_{last} (ng x hr/mL)	IV Geometric LSM	Oral Geometric LSM	LSM Ratio (Oral/IV)	80% CI
DC cohort (n = 40)	802.81	750.82	93.52	82.10 – 106.5
FDC cohort (n = 24)	745.26	727.29	97.59	80.48 – 118.3

Garcia-Manero G, et al. *Blood.* 2020;136(6):674-683.

Pharmacodynamic Analysis

Phase 2 Overall Stage Cycle	Patients	Treatment	Mean Baseline	LSM[b]	95% CI[b]	Estimate[c]	95% CI[c]
1	40 38	Oral C/D[a] IV decitabine	79.349 79.119	10.726 11.805	9.2 - 12.3 10.2 – 13.4	-1.079	-3.3 – 1.2
2	31 33	Oral C/D IV decitabine	77.626 77.298	9.340 9.357	7.4 – 11.3 7.5 – 11.2	-0.017	-2.73 – 2.70

a. C/D – decitabine/cedazuridine
b. Maximum % LINE-1 demethylation change from baseline
c. Difference (oral-IV) in mean maximum % LINE 1 demethylation

Garcia-Manero G, et al. *Blood.* 2020;136(6):674-683.

Efficacy – Clinical Response

Parameter	Phase II Overall (n = 80)
CR	21%
PR	0
mCR	22%
mCR with HI	7%
Overall Response	60%
No Response	40%
Median Duration of Response	13.3 months
Median Overall Survival	18.3 months
Median Time to AML or Death	12.1 months

Garcia-Manero G, et al. *Blood.* 2020;136(6):674-683.

Toxicity

Parameter	All oral cedazuridine/ decitabine cycles (n = 78)
Neutropenia	46%
Thrombocytopenia	38%
Febrile neutropenia	29%
Leukopenia	27%
Anemia	24%
Pneumonia	13%
Sepsis	10%

Garcia-Manero G, et al. *Blood.* 2020;136(6):674-683.

Ongoing MDS Clinical Trials

Agent(s)	Treatment Setting	Phase	NCT #
Luspatercept/Lenalidomide	Lower-risk MDS non-del(5q)	Ib/II	04539236
Luspatercept vs. Epoetin alfa	IPSS-R very low-, low- or intermediate-risk MDS in ESA-naive patients (RBC transfusion dependent)	III	03682536
ASTX727 (cedazuridine/ decitabine) – low dose	Lower-risk MDS	I - II	03502668
Roxadustat (FG-4592)	Lower-risk MDS	III	03263091
Imetelstat (GRN163L)	IPSS low- or INT-1-risk MDS	II/III	02598661

www.clinicaltrials.gov Accessed May 25, 2021.

Role of the Pharmacist

- Supportive care management
  - Iron overload management
  - Dose titration
    - ESAs (assess appropriateness of biosimilars)
    - Myeloid colony-simulating factors (assess appropriateness of biosimilars)
    - Luspatercept
  - Anti-infective management
- Patient counseling
- Toxicity management (e.g., hypertension and thromboembolism with ESAs)
- Drug procurement (lenalidomide, decitabine/cedazuridine)

Iron Overload: MDS Foundation Consensus Guidelines

- Hgb transfusion threshold: 10 g/dL
- Monitor serum ferritin and transferrin saturation to detect iron overload
  - Liver imaging is not considered essential and should be further investigated
- Number of individual patient transfusions aids clinicians in determining whether to initiate iron chelation therapy (ICT)
  - A standardized methodology to document transfusions will facilitate decision-making

Bennett JM. *Am J Hematol.* 2008;83(11):858-861.

Iron Overload: MDS Foundation Consensus Guidelines

- Assess body iron stores at MDS diagnosis and at regular intervals thereafter
  - Monitor transfusion-dependent patients every 3 to 4 months
  - Chelation therapy monitoring after ICT initiation
- Initiate ICT when:
  - Serum ferritin reaches 1000 mg/L
  - Transfusions at 2 units/month for at least 1 year
  - Need to preserve organ function
- Other patients who are likely to benefit:
  - Low-risk MDS
  - Life expectancy > 1 year without comorbidities that limit prognosis
  - Allogeneic stem cell transplant candidates

Bennett JM. *Am J Hematol.* 2008;83(11):858-861.

Iron Overload: MDS Foundation Consensus Guidelines

- Consider ICT for patients with idiopathic myelofibrosis who are allogeneic stem cell transplant (SCT) candidates
- MDS patients are likely to benefit from ICT
  - Agent choice is at physician discretion
  - Variation exists with respect to agent availability and reimbursement
- ICT should continue as long as patient requires transfusions and iron overload remains clinically relevant

Bennett JM. *Am J Hematol.* 2008;83(11):858-861.

Questions & Answers