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Total Patients Enrolled Patients Who Receive

### INTRODUCTION

- Patients with cancer who are treated with myelosuppressive chemotherapy often develop chemotherapy-induced anemia (CIA)<sup>1-3</sup>
- CIA often leads to the need for intervention; one possible intervention is blood transfusion
- Transfusion with packed red blood cells (PRBCs) is a key supportive measure in the care of patients with CIA,<sup>2</sup> offering the benefit of rapid correction of anemia in these patients
- The decision to prescribe a PRBC transfusion in patients with CIA includes assessment of clinical features such as the patient's cancer type and treatment regimen, severity of signs and symptoms of anemia, and consideration of comorbidities
- Current guidelines from the National Comprehensive Cancer Network (NCCN) are restrictive on transfusions, supporting transfusions to achieve a hemoglobin (Hb)  $\geq$  7 g/dL only when patients exhibit anemia symptoms or when patients have comorbidities such as cardiac disease, chronic pulmonary disease, or cerebrovascular disease<sup>2</sup>
- There is a lack of data regarding clinical factors that form the basis for making decisions on when to transfuse patients with CIA;2,4 therefore, a study evaluating the clinical factors used in making decisions for prescribing transfusions for patients with CIA can inform practitioners on current practice patterns
- Here, we sought to examine contemporary transfusion practices in patients with nonmyeloid cancer

### **OBJECTIVE**

• To evaluate physician-assessed primary clinical considerations for prescribing PRBC transfusions in patients with nonmyeloid cancer and CIA and who had baseline Hb concentration ≤ 10.0 g/dL

## **METHODS**

### Study Design

- This was a multi-center, prospective, observational study
- Patients with an order or prescription for PRBC transfusion were identified by site staff, and those who met the eligibility criteria were enrolled into the study
- No study drug was administered as part of this study

#### **Patient Eligibility**

- Key inclusion criteria:
- ≥ 18 years of age
- Diagnosis of nonmyeloid cancer
- Receiving first- or second-line myelosuppressive chemotherapy
- Baseline Hb ≤ 10.0 g/dL
- Planned to receive ≥ 1 PRBC transfusion.
- Key exclusion criteria:
- Receipt of an erythropoiesis-stimulating agent (ESA) within 8 weeks prior to screening
- Diagnosis of chronic renal insufficiency

## **Data Sources**

- Medical records of patients were evaluated to obtain information on sex, age, cancer type, cancer stage at initial diagnosis, date of initial cancer diagnosis, date and regimen of myelosuppressive chemotherapy received, and comorbidities
- Most recent laboratory reports were evaluated to obtain last Hb concentration before a PRBC
- Questionnaires completed by physicians/providers were evaluated to determine considerations for
- Physicians selected the "most important (primary) consideration", "second-most important consideration", or "least important consideration" from the list of 3 considerations of anemia symptoms, Hb value, or medical history (including comorbidities)
- Physicians also recorded the signs and symptoms of anemia affecting the decision to prescribe a PRBC transfusion
- Physicians were also asked if they used ESAs or not

### Study Outcomes and Data Assessment

- The proportions of patients with specific signs and symptoms of anemia were determined
- Signs and symptoms of anemia affecting the decision to prescribe a PRBC transfusion were also evaluated
- The overall and stratified proportion of patients for each primary clinical consideration leading to a PRBC transfusion were determined and 95% exact binomial confidence intervals (CIs) estimated. Baseline covariate strata included sex (male vs female), age (<65 years vs ≥65 years), primary tumor type, chemotherapy type (platinum vs non-platinum), chemotherapy line (first- vs second line), and site type (academic vs nonacademic)

# RESULTS

# Study Period and Enrollment

- The recruitment period was from 30 September 2014 to 31 October 2015, with the last visit of the last patient in October 2015
- A total of 154 patients were enrolled at 18 sites in the United States, out of the 25 recruited sites
- Database lock was on 7 January 2016

### Study Site Characteristics

Characteristics of study sites are shown in Table 1

### Table 1 Characteristics of Study Sites

Characteristic	Recruited Study Sites N = 25 n (%)	Study Sites That Enrolled Patients N = 18 n (%)
Location of site		
Urban	11 (44.0)	10 (55.6)
Suburban	10 (40.0)	4 (22.2)
Rural	4 (16.0)	4 (22.2)
Site type		
Academic	2 (8.0)	2 (11.1)
Nonacademic	23 (92.0)	16 (88.9)
Transfusion center on site		
Yes	9 (36.0)	8 (44.4)
No	16 (64.0)	10 (55.6)
Routine usage of erythropoiesis-stimulating agents		
Yes	18 (72.0)	12 (66.7)
No	7 (28.0)	6 (33.3)

### PRBC Transfusion and Last Hb Value Prior to PRBC Transfusion

- PRBC transfusion and last Hb value prior to PRBC transfusion are shown in Table 2 - Of the 154 patients enrolled, 147 (95.5%) received a PRBC transfusion
- Mean [95% CI] last Hb value before PRBC transfusion was 8.1 [8.0, 8.3] g/dL
- 140 (95.9%) patients received a transfusion at Hb ≥ 7.0 g/dL and 70 (47.9%) patients received a transfusion at Hb ≥ 8.0 g/dL

### Table 2. PRBC Transfusion and Last Hb Value Prior to PRBC Transfusion

	Total Patients Enrolled in the Study N = 154
PRBC transfusion, n (%)	
Received a PRBC transfusion	147 (95.5)
Did not receive a PRBC transfusion	7 (4.5)
Last Hb value prior to PRBC transfusion	
n	146a
Mean (range), g/dL	8.1 (4.9–9.9)
Hb category, n (%)	
< 7.0 g/dL	6 (4.1)
≥ 7.0 g/dL	140 (95.9)
< 8.0 g/dL	76 (52.1)
≥ 8.0 g/dL	70 (47.9)

<sup>a</sup>One patient was excluded as the Hb concentration was measured after a PRBC transfusion. Hb = hemoglobin; PRBC = packed red blood cell.

### Patient Demographics

- Baseline demographics and clinical characteristics of total patients enrolled in the study and patients who received a PRBC transfusion are shown in Table 3
- Of the patients who received a PRBC transfusion, most (100 [68.0%] patients) were female and over half (81 [55.1%] patients) were ≥65 years of age
- Most patients (106 [72.1%]) did not present with comorbidities relevant to the anemia. In the 41 (27.9%) patients who did, the most common comorbidity was chronic pulmonary disease (22 [15.0%] patients). Only 9 (6.1%) patients had underlying cardiovascular disease

### **RESULTS (Continued)**

Table 3. Baseline Demographics and Clinical Characteristics

Characteristic	in the Study  N = 154	a PRBC Transfusion N = 147
Sex, n (%)		
Female	107 (69.5)	100 (68.0)
Male	47 (30.5)	47 (32.0)
Age, mean (SD), years	65.3 (9.8)	65.3 (9.9)
<65 years, n (%)	70 (45.5)	66 (44.9)
≥65 years, n (%)	84 (54.5)	81 (55.1)
Primary tumor type, n (%)		
Gynecological cancer	43 (27.9)	38 (25.9)
Non-small cell lung cancer	32 (20.8)	32 (21.8)
Small cell lung cancer	25 (16.2)	24 (16.3)
Gastrointestinal cancer	19 (12.3)	18 (12.2)
Breast cancer	14 (9.1)	14 (9.5)
Urogenital cancer	7 (4.5)	7 (4.8)
Hematological malignancies	7 (4.5)	7 (4.8)
Othera	7 (4.5)	7 (4.8)
Chemotherapy type, n (%)	,	,
Platinum	113 (73.4)	107 (72.8)
Non-platinum	41 (26.6)	40 (27.2)
Chemotherapy line, n (%)	,	,
First	100 (64.9)	95 (64.6)
Second	54 (35.1)	52 (35.4)
Signs and symptoms of anemia, n (%)	,	, ,
Yes	137 (89.0)	133 (90.5)
No	17 (11.0)	14 (9.5)
Comorbidities relevant to the anemia, n (%)	· ·	· ·
Yes	_	41 (27.9)
Chronic pulmonary disease	-	22 (15.0)
Congestive heart failure or coronary heart dis	sease –	9 (6.1)
Cerebral vascular disease	-	2 (1.4)
Other	_	17 (11.6)
No	-	106 (72.1)

Includes bone/sarcoma, brain, head and neck, skin, and thyroid cancers. PRBC = packed red blood cell; SD = standard deviation.

#### Signs and Symptoms of Anemia

- Proportions of patients with specific signs and symptoms of anemia are shown in Table 4
- In patients who received a PRBC transfusion, fatigue was the most common sign and symptom of anemia (127 [86.4%] patients), followed by dyspnea on exertion (58 [39.5%] patients)

Table 4. Proportion of Patients With Specific Signs and Symptoms of Anemia

Signs and Symptoms of Anemia <sup>a</sup>	Total Patients Enrolled in the Study N = 154 n (%)	Patients Who Received a PRBC Transfusion N = 147 n (%)
Fatigue	130 (84.4)	127 (86.4)
Dyspnea on exertion	60 (39.0)	58 (39.5)
Pallor	41 (26.6)	40 (27.2)
Lightheadedness	40 (26.0)	38 (25.9)
Sustained tachycardia	12 (7.8)	10 (6.8)
Other	11 (7.1)	11 (7.5)
Postural hypotension	9 (5.8)	8 (5.4)
Tachypnea	7 (4.5)	6 (4.1)
Syncope	5 (3.2)	5 (3.4)
Chest pain/pectoral angina	2 (1.3)	2 (1.4)

<sup>a</sup>Patients could be included in > 1 symptom category but were included only once within each category. PRBC = packed red blood cell.

#### Signs and Symptoms of Anemia Affecting the Decision to Prescribe a PRBC **Transfusion**

- Signs and symptoms affecting the physician's decision to prescribe a PRBC transfusion are shown in Table 5
- The most common signs and symptoms affecting the decision to prescribe a PRBC transfusion were fatigue (101 [69.2%] patients) and dyspnea on exertion (49 [33.6%] patients)

#### Table 5. Signs and Symptoms of Anemia Affecting the Decision to Prescribe a **PRBC Transfusion**

	Patients Who Received a PRBC Transfusion N = 146 <sup>b</sup>
Signs and Symptoms of Anemia <sup>a</sup>	n (%)
Fatigue	101 (69.2)
Dyspnea on exertion	49 (33.6)
Pallor	33 (22.6)
Lightheadedness	31 (21.2)
Sustained tachycardia	9 (6.2)
Other	6 (4.1)
Postural hypotension	5 (3.4)
Tachypnea	4 (2.7)
Syncope	4 (2.7)
Chest pain/angina	2 (1.4)

<sup>a</sup>Patients could be included in > 1 symptom category but were included only once within each category. bOne patient was excluded as the Hb concentration was measured after a PRBC transfusion Hb = hemoglobin; PRBC = packed red blood cell.

### Primary Clinical Considerations for Prescribing a PRBC Transfusion

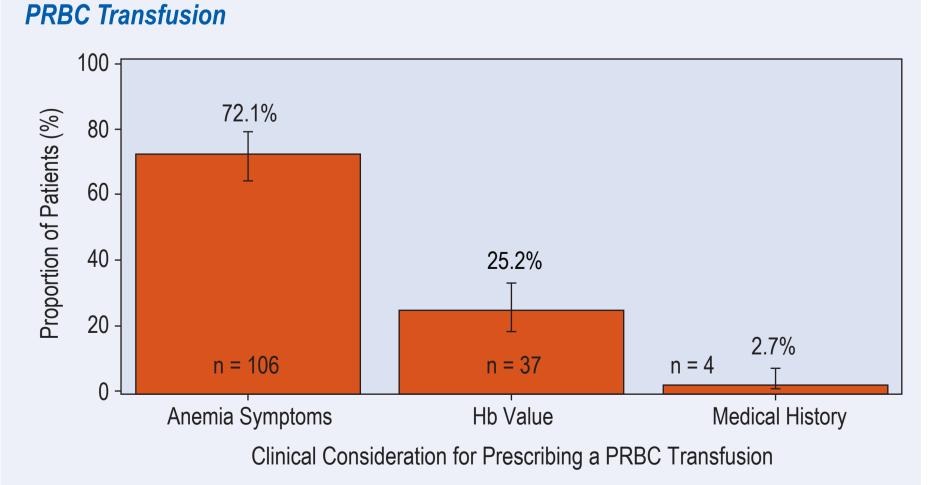
• Physician-reported clinical considerations for prescribing a PRBC transfusion are shown in Table 6 and Figure 1

### Table 6. Primary Clinical Considerations for Prescribing a PRBC Transfusion

	Patients Who Received a PRBC Transfusion N = 147
Anemia symptoms, n (%)	106 (72.1)
Mean (range) last Hb value prior to a PRBC transfusion, g/dL	8.1 (6.2–9.9)
Hb value, n (%)	37 (25.2)
Mean (range) last Hb value prior to a PRBC transfusion, g/dL	8.1 (4.9–9.9)
Medical history, n (%)	4 (2.7)
Mean (range) last Hb value prior to a PRBC transfusion, g/dL	8.5 (7.8–9.8)

Physicians selected the "most important (primary) consideration", "second-most important consideration", or "least important consideration" from the list of 3 considerations of anemia symptoms, Hb value, or medical history (including comorbidities). Hb = hemoglobin; PRBC = packed red blood cell.

### Figure 1. Physician-Assessed Primary Clinical Considerations for Prescribing a



Error bars are 95% exact binomial confidence intervals. Hb = hemoglobin; PRBC = packed red blood cell.

- The most frequently reported primary clinical consideration for prescribing a PRBC transfusion was anemia symptoms (106 patients; 72.1%, 95% CI: 64.1%, 79.2%), followed by Hb value (37 patients; 25.2%, 95% CI: 18.4%, 33.0%) and medical history (4 patients; 2.7%, 95% CI: 0.7%, 6.8%) (Table 6, Figure 1)
- Mean [95% CI] last Hb value before a PRBC transfusion was 8.1 [7.9, 8.3] g/dL for patients who received a transfusion for anemia symptoms, 8.1 [7.8, 8.5] g/dL for Hb value, and 8.5 [7.0, 9.9] g/dL for medical history (Table 6)

#### Primary Clinical Considerations for Prescribing a PRBC Transfusion Stratified by **Baseline Covariates**

- Clinical considerations for prescribing a PRBC transfusion stratified by baseline covariates are shown in Tables 7 to 10
- Sex (male vs female) and age (<65 years vs ≥65 years) (Table 7)</li> Primary tumor type (Table 8)
- Chemotherapy type (platinum vs non-platinum) and chemotherapy line (first vs second) (Table 9)
- Site type (academic vs nonacademic) (Table 10)
- When stratified by age, approximately twice the number of patients ≥65 years of age received a PRBC transfusion based on Hb value: 25 (30.9%) patients who were ≥65 years old vs 12 (18.2%) patients who were <65 years old (Table 7)
  - Primary tumor type, chemotherapy type, or chemotherapy line did not influence the decision to transfuse above and beyond anemia symptoms (Tables 8 to 10)

#### Table 7. Primary Clinical Considerations for Prescribing a PRBC Transfusion by Sex and Age

Baseline Covariate / Primary Clinical	Patients Who Received a PRBC Transfusion N = 147	
Consideration for PRBC Transfusion	n (%)	95% CI
Sex		
Female	n =	= 100
Anemia symptoms	76 (76.0)	66.4, 84.0
Hb value	23 (23.0)	15.2, 32.5
Medical history	1 (1.0)	0.0, 5.4
Male	n	= 47
Anemia symptoms	30 (63.8)	48.5, 77.3
Hb value	14 (29.8)	17.3, 44.9
Medical history	3 (6.4)	1.3, 17.5
Age		
<65 years	n	= 66
Anemia symptoms	53 (80.3)	68.7, 89.1
Hb value	12 (18.2)	9.8, 29.6
Medical history	1 (1.5)	0.0, 8.2
≥65 years	n	= 81
Anemia symptoms	53 (65.4)	54.0, 75.7
Hb value	25 (30.9)	21.1, 42.1
Medical history	3 (3.7)	0.8, 10.4

rnysicians selected the important (primary) consideration", "second-most important consideration", or "least important consideration" from the list of 3 considerations of anemia symptoms, Hb value, or medical history (including comorbidities). CI = confidence interval; Hb = hemoglobin; PRBC = packed red blood cell.

#### Table 8. Primary Clinical Considerations for Prescribing a PRBC Transfusion by **Primary Tumor Type**

**Patients Who Received a PRBC Transfusion** 

aseline Covariate / Primary Clinical	N = 147		
Consideration for PRBC Transfusion	n (%)		95% CI
Primary tumor type			
Gynecological cancer		n = 37	
Anemia symptoms	26 (70.3)		53.0, 84.1
Hb value	10 (27.0)		13.8, 44.1
Medical history	1 (2.7)		0.1, 14.2
Non-small cell lung cancer	,	n = 30	
Anemia symptoms	23 (76.7)		57.7, 90.1
Hb value	7 (23.3)		9.9, 42.3
Medical history	0		
Small cell lung cancer		n = 24	
Anemia symptoms	18 (75.0)		53.3, 90.2
Hb value	5 (20.8)		7.1, 42.2
Medical history	1 (4.2)		0.1, 21.1
Gastrointestinal cancer	, ,	n = 10	
Anemia symptoms	9 (90.0)		55.5, 99.7
Hb value	1 (10.0)		0.3, 44.5
Medical history	0		
Breast cancer		n = 14	
Anemia symptoms	9 (64.3)		35.1, 87.2
Hb value	5 (35.7)		12.8, 64.9
Medical history	0		
Urogenital cancer		n = 7	
Anemia symptoms	6 (85.7)		42.1, 99.6
Hb value	0		
Medical history	1 (14.3)		0.4, 57.9
Othera	· ·	n = 25	
Anemia symptoms	15 (60.0)		38.7, 78.9
Hb value	9 (36.0)		18.0, 57.5
Medical history	1 (4.0)		0.1, 20.4

consideration" from the list of 3 considerations of anemia symptoms, Hb value, or medical history (including comorbidities). <sup>a</sup>Includes bone/sarcoma, brain, head and neck, skin, thyroid, hematological cancers, other gastrointestinal cancers, and missing CI = confidence interval; Hb = hemoglobin; PRBC = packed red blood cell.

### Table 9. Primary Clinical Considerations for Prescribing a PRBC Transfusion by Chemotherapy Type and Line

Baseline Covariate / Primary Clinical	Patients Who Received a PRBC Transfusion N = 147	
Consideration for PRBC Transfusion	n (%)	95% CI
Chemotherapy type		
Platinum		n = 107
Anemia symptoms	79 (73.8)	64.4, 81.9
Hb value	25 (23.4)	15.7, 32.5
Medical history	3 (2.8)	0.6, 8.0
Non-platinum		n = 40
Anemia symptoms	27 (67.5)	50.9, 81.4
Hb value	12 (30.0)	16.6, 46.5
Medical history	1 (2.5)	0.1, 13.2
Chemotherapy line	·	
First line		n = 95
Anemia symptoms	67 (70.5)	60.3, 79.4
Hb value	26 (27.4)	18.7, 37.5
Medical history	2 (2.1)	0.3, 7.4
Second line	,	n = 52
Anemia symptoms	39 (75.0)	61.1, 86.0
Hb value	11 (21.2)	11.1, 34.7
Medical history	2 (3.8)	0.5, 13.2

Physicians selected the "most important (primary) consideration", "second-most important consideration", or "least important consideration" from the list of 3 considerations of anemia symptoms, Hb value, or medical history (including comorbidities). CI = confidence interval; Hb = hemoglobin; PRBC = packed red blood cell.

#### Table 10. Primary Clinical Considerations for Prescribing a PRBC Transfusion by Site Type

Baseline Covariate / Primary Clinical	Patients Who Received a PRBC Transfusion N = 147	
Consideration for PRBC Transfusion	n (%)	95% CI
Site type		
Academic		n = 40
Anemia symptoms	30 (75.0)	58.8, 87.3
Hb value	8 (20.0)	9.1, 35.6
Medical history	2 (5.0)	0.6, 16.9
Nonacademic		n = 107
Anemia symptoms	76 (71.0)	61.5, 79.4
Hb value	29 (27.1)	19.0, 36.6
Medical history	2 (1.9)	0.2.66

Physicians selected the "most important (primary) consideration", "second-most important consideration", or "least important consideration" from the list of 3 considerations of anemia symptoms, Hb value, or medical history (including comorbidities). CI = confidence interval; Hb = hemoglobin; PRBC = packed red blood cell.

# STUDY STRENGTH AND LIMITATIONS

- The major strength of the study is that it was prospectively designed with pre-defined outcome measures that enabled the evaluation of transfusion patterns in patients with anemia who are receiving chemotherapy in real-world settings (not clinical trials)
- However, a number of limitations have to be noted:
- The study relied on questionnaires completed by the physicians to determine considerations for transfusions and, as such, data analyzed were limited to the information obtained in answer to the questions included in the survey. For example, physicians were not queried as to how they might integrate the use of ESAs into the transfusion algorithm
- Although anemia symptoms was one of the major outcome measures for the study, this was not defined by a threshold of a severity scale, grade of fatigue, or other standardized measure, for consistency across the study sites
- Physicians were not queried as to whether the decision to transfuse had any relationship to anticipated number of chemotherapy cycles with respect to the potential effects of cumulative myelotoxicity

### CONCLUSIONS

- In this prospective, multi-center, observational study of transfusion practices in patients with CIA, the primary consideration for prescribing a PRBC transfusion was anemia symptoms in 72.1% of patients, with absolute Hb value responsible for the decision to transfuse in only 25.2% of patients. 47.9% of patients received a transfusion at an Hb level of ≥ 8 g/dL
- The decision to transfuse was independent of sex, medical comorbidities, cancer type, or chemotherapy regimen
- In this unique patient population receiving myelosuppressive chemotherapy, clinical judgment and individual patient symptoms and not solely the Hb value impacted significantly on the decision to transfuse
- Future research could include correlative analysis of cancer fatigue and how it relates to transfusion therapy or the use of hematopoietic growth factors in transfusion algorithms in patients receiving chemotherapy

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- Sejal Badre was an employee of Amgen Inc. at the time of the study and owns/may have owned stock in Amgen Inc. • Chet Bohac was an employee of Amgen Inc. at the time of the study and owns/may have owned stock in Amgen Inc.; he is currently an employee of and owns stock in Immune Design
- Cisio De Oliveira Brandao is an employee of and owns stock in Amgen Inc. • Sharon Hunter, who previously consulted for Amgen Inc., provided statistical support for many of the analyses Medical writing support was provided by Martha Mutomba (on behalf of Amgen Inc.) and Susanna Mac from Amgen Inc. • The authors thank the patients and families who participated in this study and the investigators and study staffs who contributed