Cancer Management and Research

Dovepress
open access to scientific and medical research

Open Access Full Text Article

ORIGINAL RESEARCH

Anemia prevalence and treatment practice in patients with non-myeloid tumors receiving chemotherapy

This article was published in the following Dove Press journal:
Cancer Management and Research
1 August 2013
Number of times this article has been viewed

Laura Merlini[1]
Giacomo Cartenì[2]
Stefano Iacobelli[3]
Caterina Stelitano[4]
Mario Airoldi[5]
Peter Balcke[6]
Felix Keil[7]
Ferdinand Haslbauer[8]
Laura Belton[9]
Beatriz Pujol[10]

[1]Department of Medical Oncology, Ospedale Civile S, Bortolo, Vicenza, [2]Department of OncoHematology, Azienda Ospedaliera di Rilievo Nazionale "Antonio Cardarelli", Napoli, [3]Department of Medical Oncology, Ospedale Clinicizzato SS Annunziata, Chieti, [4]Department of Hematology, Azienda Ospedaliera "Bianchi Melacrino Morelli", Reggio Calabria, [5]Department of Medical Oncology, Azienda Ospedaliero Universitaria Le Molinette, Torino, Italy; [6]1st Medical Department, General Hospital St Pölten and Karl Landsteiner Institute of Oncology, St Pölten, [7]3rd Medical Department (Hematology and Oncology), Hanusch Krankenhaus der Wiener Gebietskrankenkasse, Vienna, [8]Department of Oncology, Landeskrankenhaus Vöcklabruck, Vöcklabruck, Austria; [9]Contract biostatistician, Amgen Ltd, Uxbridge, UK; [10]Research and Development Haematology/Oncology, Amgen Europe, Zug, Switzerland

Correspondence: Laura Merlini
Ospedale Civile S Bortolo,
Viale Rodolfi, 37, 36100 Vicenza, Italy
Tel +39 0444 753 906
Fax +39 0444 757 341
Email la.merlini@tiscali.it

Purpose: To describe the prevalence and management of anemia in cancer patients.

Methods: This cross-sectional, observational survey was conducted in Italy and Austria. Centers prespecified one day, during a 4-month enrollment window, to report specific data collected during normal clinical practice for patients with non-myeloid tumors attending for chemotherapy (±radiotherapy) treatment. The primary endpoint was the prevalence of anemia as determined using a prespecified algorithm: hemoglobin (Hb) ≤10 g/dL on/within 3 days prior to visit; ongoing anemia treatment; physician diagnosis of anemia, together with ≥1 anemia symptom.

Results: Between November 18, 2010 and March 18, 2011, data for 1412 patients were collected (Italy n = 1130; Austria n = 282). Most patients (n = 1136; 80%) had solid tumors; 809 (57%) had received ≤3 chemotherapy cycles. The prevalence of anemia was 32% (95% confidence interval: 29.4%–34.2%); 196 patients (14%) were deemed anemic based on Hb ≤10 g/dL, 131 (9%) on ongoing anemia treatment, and 121 (9%) on physician diagnosis/anemia symptom. Overall, 1153 patients (82%) had Hb data; mean (standard deviation [SD]) Hb levels were 11.7 (1.7) g/dL. In total, 456 patients (32%) had anemia symptoms: fatigue (n = 392; 28%), depression (n = 122; 9%), and dyspnea (n = 107; 8%) were most common. Fifty-one patients (4%) had had their current chemotherapy cycle delayed due to anemia. On visit day, or ≤28 days prior, 91 (6%), 188 (13%), and 81 patients (6%) had evidence of whole blood/red blood cell transfusion, erythropoiesis-stimulating agent use, or iron use, respectively.

Conclusion: On the prespecified study day, one-third of patients with non-myeloid tumors undergoing chemotherapy were found to be anemic and 13% had evidence of erythropoiesis-stimulating agent use then or in the 28 days prior.

Keywords: erythropoiesis-stimulating agent, hemoglobin, iron, management, transfusion

Introduction

Anemia is common in patients with cancer, especially in those undergoing myelosuppressive chemotherapy.[1] Anemia not only has detrimental effects on patient quality of life,[2] but also on survival, increasing overall mortality risk by up to 65% in some studies.[3–5] The chosen strategy for anemia management depends on the underlying cause, but treatment options may include use of an erythropoiesis-stimulating agent (ESA) in patients with non-myeloid tumors and chemotherapy-induced anemia (CIA),[6,7] iron supplementation (intravenous or oral, in absolute or functionally iron-deficient anemia),[6,8] and red blood cell or whole blood transfusions.[6,9] Despite this, anemia in cancer patients is frequently undermanaged or not managed at all.[6]

The European Cancer Anaemia Study (ECAS) was the first study to provide information on the prevalence, effects, and management of anemia in cancer patients in clinical practice.[1] At the time of this study, anemia was generally treated when patients had

hemoglobin levels <12 g/dL. Hemoglobin levels of <12 g/dL were frequently encountered in this study, with 39% of patients defined as anemic by this criterion at enrollment, and 67% of patients experiencing anemia at some point during their 6-month follow-up.[1] Using the more stringent definition of hemoglobin <10.0 g/dL, 10% of patients were found to be anemic at enrollment and 39% had anemia at some point during follow-up in the ECAS.[1]

Since the ECAS was conducted, updates have been made to both the prescribing information for ESAs and the guidelines for the treatment of anemia in cancer patients. Currently, prescribing information for ESAs recommends that treatment should be initiated in patients with symptoms of anemia who have hemoglobin levels ≤10 g/dL, with the aim of increasing levels to ≤12 g/dL.[10] Current treatment guidelines differ slightly from organization to organization and are also slightly different to the prescribing information above. For example, the European Organisation for Research and Treatment of Cancer (EORTC) recommends that ESAs should be considered in asymptomatic patients with hemoglobin levels ≤11.9 g/dL and that treatment should be initiated in symptomatic patients with hemoglobin between 9–11 g/dL.[6] In patients with hemoglobin levels <9 g/dL, the need for transfusion should be evaluated, and ESA treatment should also be considered.[6] By comparison, joint guidelines from the American Society of Clinical Oncology (ASCO) and the American Society of Hematology (ASH) recommend ESAs as a treatment option for patients with CIA and hemoglobin levels below or approaching 10 g/dL, in order to increase hemoglobin levels and decrease the need for transfusions.[11] For patients with hemoglobin levels <12 g/dL whose levels have never fallen near 10 g/dL, they state that the decision to use an ESA should be based on clinical circumstance.

Consequently, in view of these recent changes in product labeling and treatment guidelines,[6,10] there is a need to re-evaluate the prevalence and management of anemia in patients undergoing chemotherapy. Some country-specific survey data have been reported in the last few years,[12–15] but no data have been reported to date for Italy and Austria. Here we expand on these recent reports and provide information on the prevalence of anemia in patients undergoing chemotherapy in the clinical practice setting in Italy and Austria.

Patients and methods

Study design

This was a multicenter, observational, cross-sectional survey study conducted at clinics in Italy and Austria during a 4-month enrollment window. Clinics were asked to specify a single day within this window on which to participate and to report specific data collected as part of normal clinical practice. To help ensure the representativeness of the sample, centers were asked to enroll all eligible patients seen on the prespecified day and to include all types of centers (eg, oncology, hematology, gyneco-oncology). Participating centers were required to have knowledge of standard medical practices in their country and to be characteristic of centers normally treating the target group. The protocol received approval from the appropriate independent ethics committees (1 central committee for Austria and 37 local committees for Italy) and the study was conducted in accordance with the International Conference on Harmonisation Good Clinical Practice regulations and guidelines and the ethical standards laid down in the 1964 Declaration of Helsinki.

Objectives and endpoints

The primary objective was to estimate the prevalence of anemia in patients with non-myeloid tumors being treated with chemotherapy (±radiotherapy), as reported during a single office visit. The primary endpoint was the prevalence of anemia based on the full analysis set. A secondary objective was to describe the anemia management strategy as reported at a single office visit in this treatment setting. Other secondary endpoints included descriptions of the reasons for and type of visit (outpatient or hospitalized), patient demography, tumor type, type of chemotherapy, delays to chemotherapy due to anemia, hemoglobin levels, and consequences of anemia (including type[s] of treatment received for anemia on visit day, or in the 28 days prior to their visit).

Patients

This study included men and women aged ≥18 years, who had been diagnosed with non-myeloid tumors, were currently receiving systemic chemotherapy, and were seen at the participating center on the specified study day. Patients were excluded if they had been diagnosed with myelodysplastic syndrome, were hospitalized on the day of the study for reasons other than receipt of chemotherapy or related treatment (eg, transfusions), or were participating in a clinical trial with protocol-specified treatment for CIA (eg, an ESA or iron supplementation). Patients (or their representatives) provided informed consent where required by local regulations (informed consent was not required in Austria, but sites were given the option to use a consent form for data release).

Statistical methods

Analyses were descriptive in nature. The prevalence of anemia was determined using a predefined algorithm, which

defined a patient as anemic in a step-wise fashion, based on evidence of (1) hemoglobin ≤10 g/dL on or within 3 days prior to the office visit, (2) ongoing anemia treatment at the office visit, or (3) a physician diagnosis of anemia together with one or more anemia symptom at the office visit. Anemia symptoms included fatigue, headache, dyspnea, loss of libido, depression, dizziness, cold skin, palpitations, pulmonary edema, heart failure, severe impairment of cognitive function, or other symptoms possibly related to anemia.

Prevalence estimates of anemia were presented with their associated 95% confidence intervals (CIs), which were calculated using Wilson's method. All analyses were based on enrolled patients who met the study eligibility criteria; for some analyses, the full analysis set was further subdivided by country and by tumor type. Sensitivity analyses were performed to assess the prevalence of anemia based on the prespecified algorithm, by defining anemia using hemoglobin levels of ≤11 or ≤9 g/dL, respectively, as opposed to ≤10 g/dL.

Results

Patient demographics and disease characteristics

Overall results

All enrolled patients met the study eligibility criteria and were included in the full analysis set. Between November 18, 2010 and March 18, 2011, a total of 1412 patients were enrolled at 56 centers (Table 1). Overall, 689 patients (49%) were male, median age was 65 years, and most patients (n = 1136; 80%) had solid tumors, of which colorectal (n = 256; 23%), breast (n = 255; 22%), and lung (n = 197; 17%) cancers were the most common; although, 392 solid tumors (35%) were recorded as "other" (ie, tumor type unspecified). Overall, 809 patients (57%) had received three or fewer cycles of chemotherapy, and 477 (34%) were currently receiving platinum-containing regimens.

Results by country

Of the 1412 patients recruited, 80% were enrolled at 40 sites in Italy (n = 1130) and 20% (n = 282) at 16 sites in Austria (Table 1). Baseline demographics and disease characteristics were generally similar between countries, although the most common types of solid tumor in Italy were colorectal (n = 222; 20%) and breast (n = 188; 17%) cancers, while breast (n = 67; 24%), colorectal (n = 34; 12%), and lung (n = 35; 12%) cancers were most common in Austria.

Results by tumor type

Of the 1136 patients with solid tumors, 548 were male (48%), and the median age was 64 years (Table 2). Median age was highest in men with prostate cancer (73.5 years) and lowest for women with breast cancer (59 years). Overall, 640 patients

Table 1 Population summary by country (Italy, Austria, and overall)

	Italy (n = 1130)	Austria (n = 282)	Overall (n = 1412)
Male sex – n (%)	563 (50)	126 (45)	689 (49)
Age – median (Q1, Q3)	65.0 (56.0, 72.0)	65.0 (53.0, 71.0)	65.0 (55.0, 72.0)
Solid tumor – n (%)	914 (81)	222 (79)	1136 (80)
Breast	188 (17)	67 (24)	255 (18)
Lung	162 (14)	35 (12)	197 (14)
Prostate	32 (3)	4 (1)	36 (3)
Colorectal	222 (20)	34 (12)	256 (18)
Other solid tumor	310 (27)	82 (29)	392 (28)
Hematological malignancy – n (%)	216 (19)	60 (21)	276 (20)
Non-Hodgkin's lymphoma	108 (10)	31 (11)	139 (10)
Other hematological malignancy	108 (10)	29 (10)	137 (10)
Number of chemotherapy cycles completed since initiation – n (%)			
In first cycle	154 (14)	54 (19)	208 (15)
1–3	475 (42)	126 (45)	601 (43)
4–6	302 (27)	71 (25)	373 (26)
>6	199 (18)	31 (11)	230 (16)
Current chemotherapy regimen contains[a] – n (%)			
Platinum	386 (34)	91 (32)	477 (34)
Anthracycline	176 (16)	59 (21)	235 (17)
Taxane	158 (14)	58 (21)	216 (15)
Missing[b]	469 (42)	100 (35)	569 (40)
Currently undergoing radio-chemotherapy – n (%)	42 (4)	15 (5)	57 (4)

Notes: [a]Patients may be recorded in multiple chemotherapy type categories; [b]An unexpected number of patients had therapies other than those listed on the case report form and were therefore categorized as 'missing'.

Table 2 Population summary by tumor type (solid tumor or hematologic malignancy)

	Solid tumors (n = 1136)	Hematological malignancy (n = 276)
Male sex – n (%)	548 (48)	141 (51)
Age – median (Q1, Q3)	64.0 (55.0, 71.0)	68.0 (56.5, 74.0)
Number of chemotherapy cycles completed since initiation – n (%)		
In first cycle	163 (14)	45 (16)
1–3	477 (42)	124 (45)
4–6	304 (27)	69 (25)
>6	192 (17)	38 (14)
Current chemotherapy regimen contains[a] – n (%)		
Platinum	457 (40)	20 (7)
Anthracycline	134 (12)	101 (37)
Taxane	216 (19)	0 (0)
Missing[b]	414 (36)	155 (56)
Currently undergoing radio-chemotherapy – n (%)	54 (5)	3 (1)

Notes: [a]Patients may be recorded in multiple chemotherapy type categories; [b]An unexpected number of patients had therapies other than those listed on the case report form and were therefore categorized as 'missing'.

with solid tumors (56%) had received three or fewer cycles of chemotherapy. The proportion receiving platinum-containing regimens differed by tumor type, being highest in patients with lung cancer (122/197; 62%) and lowest in those with breast (22/255; 9%) or prostate (3/36; 8%) cancers. Overall, 414 patients with solid tumors (36%) had "missing" information regarding the type of chemotherapy they were receiving; it is likely that most of the patients with "missing" information here and in the analyses below were actually receiving a different type of chemotherapy than the available options (platinum, anthracycline, taxane) listed on the case report form.

Of the 276 patients with hematologic malignancies, 141 were male (51%), median age was 68 years, and most patients (n = 169; 61%) had received three or fewer cycles of chemotherapy (Table 2). Only 20 patients (7%) were receiving platinum-based therapy at that time; use of anthracycline-containing regimens was much more common, being used in 101 of these patients (37%). Overall, 155 patients with hematologic malignancies (56%) had "missing" information regarding the type of chemotherapy they were receiving.

Prevalence of anemia

Overall results

The overall prevalence of anemia was 32% (95% CI: 29.4%–34.2%); 196 patients (14%) were deemed anemic based on hemoglobin concentrations ≤10 g/dL, 131 (9%) were deemed anemic based on anemia treatment data, and 121 (9%) based on the physician's diagnosis of anemia along with the presence of at least one anemia symptom (Table 3). Overall, 456 patients (32%) reported symptoms of anemia, the most common of which were fatigue (n = 392; 28%), depression (n = 122; 9%) and dyspnea (n = 107; 8%). A total of 1153 patients (82%) had available hemoglobin data (on the day of visit or within 3 days prior to the visit) and among these, the mean (SD) hemoglobin level was 11.7 (1.7) g/dL. Only a small number of patients (n = 51; 4%) were found to have experienced delays in their current chemotherapy cycle due to anemia.

Table 3 Key primary and secondary outcome measures by country (Italy, Austria, and overall)

	Italy (n = 1130)	Austria (n = 282)	Overall (n = 1412)
Prevalence			
Anemic – n (%)	347 (31)	101 (36)	448 (32)
95% CI	28.1, 33.5	30.4, 41.6	29.4, 34.2
Type of visit – n (%)			
Outpatient	517 (46)	168 (60)	685 (49)
Hospitalized	613 (54)	114 (40)	727 (51)
Reason for visit[a] – n (%)			
Chemotherapy administration	698 (62)	193 (68)	891 (63)
Anemia treatment	43 (4)	9 (3)	52 (4)
Other cancer or chemotherapy-related reason	398 (35)	86 (30)	484 (34)
Other reason not related to cancer	14 (1)	6 (2)	20 (1)
Hemoglobin results			
n (%)	905 (80)	248 (88)	1153 (82)
Mean (SD) – g/dL	11.7 (1.7)	11.7 (1.7)	11.7 (1.7)
Hemoglobin category – n (%)			
≤10 g/dL	155 (17)	41 (17)	196 (17)
>10 g/dL	750 (83)	207 (83)	957 (83)
Physician's diagnosis of anemia – n (%)	419 (37)	135 (48)	554 (39)
Patients with anemia symptoms – n (%)	368 (33)	88 (31)	456 (32)
Type of symptom[a] – n (%)			
Fatigue	321 (28)	71 (25)	392 (28)
Headaches	53 (5)	8 (3)	61 (4)
Dyspnea	85 (8)	22 (8)	107 (8)
Loss of libido	45 (4)	6 (2)	51 (4)
Depression	112 (10)	10 (4)	122 (9)
Dizziness	31 (3)	11 (4)	42 (3)
Cold skin	66 (6)	10 (4)	76 (5)
Palpitations	59 (5)	3 (1)	62 (4)
Pulmonary edema	0 (0)	0 (0)	0 (0)
Heart failure	2 (<1)	2 (1)	4 (<1)
Severe impairment of cognitive function	10 (1)	2 (1)	12 (1)
Other symptoms possibly related to anemia	6 (1)	6 (2)	12 (1)
Current chemotherapy cycle delayed due to anemia – n (%)	37 (3)	14 (5)	51 (4)

Note: [a]Patients may be included in more than one category.
Abbreviations: CI, confidence interval; SD, standard deviation.

Sensitivity analyses determined the prevalence of anemia for the modified algorithms (hemoglobin levels of ≤11 or ≤9 g/dL) to be 39% (95% CI: 36.6%–41.7%) and 29% (95% CI: 26.7%–31.5%), respectively.

Results by country

The prevalence estimates of anemia were 31% (95% CI: 28.1%–33.5%) and 36% (95% CI: 30.4%–41.6%) for Italy and Austria, respectively; the respective proportions of patients with available hemoglobin data were 80% (n = 905) and 88% (n = 248) (Table 3). The most common anemia symptoms were fatigue (n = 321; 28%), depression (n = 112; 10%), and dyspnea (n = 85; 8%) in Italy, and were fatigue (n = 71; 25%), dyspnea (n = 22; 8%), and dizziness (n = 11; 4%) in Austria.

Results by tumor type

In patients with solid tumors, the overall prevalence of anemia was 31% (95% CI: 28.0%–33.4%); anemia was most common in patients with prostate cancer at 42% (95% CI: 27.1%–57.8%), and least common in those with colorectal cancer at 21% (95% CI: 16.9%–26.9%) (Table 4). Overall, 940 patients (83%) with solid tumors had available hemoglobin data and among these, the mean (SD) hemoglobin level was 11.8 (1.7) g/dL. Three hundred and eighty-seven patients (34%) with solid tumors had symptoms of anemia, with fatigue (n = 336; 30%), depression (n = 118; 10%) and dyspnea (n = 93; 8%) being most common. Forty-seven patients (4%) had had their current chemotherapy cycle delayed due to anemia.

In those with hematologic malignancies, the overall prevalence of anemia was 36% (95% CI: 30.8%–42.1%), and 213 patients (77%) had available hemoglobin data; among these, the mean (SD) hemoglobin level was 11.3 (1.8) g/dL (Table 4). Overall, 69 patients (25%) with hematologic malignancies had symptoms of anemia, with fatigue (n = 56; 20%) and dyspnea (n = 14; 5%) being most common. Four patients (1%) had had their current chemotherapy cycle delayed due to anemia.

Management of anemia

Overall results

Approximately half of patients overall were seen during an outpatient visit (n = 685; 49%), and the remainder (n = 727; 51%) were hospitalized (Table 3). The most common reason for their visit was chemotherapy administration (n = 891; 63%). At the time of clinic visit or within the 28 days prior, 91 patients (6%) had evidence of having received whole blood or red blood cell transfusion, 188 (13%) had evidence of having received an ESA, and 81 (6%) had evidence of having received iron supplementation (Table 5). It should be noted that evidence of any of these anemia treatments was reported for all patients and so there could be some overlap between these categories. ESA treatment was ongoing without change in 135 patients (10%) and had just been initiated in 43 patients (3%). ESA dose/schedule had been stopped or changed in 34 patients (2%), and the most common reason for stop or change was that the anemia had resolved (n = 18; 53% of cases).

Results by country

In Italy, broadly similar proportions of patients were seen during outpatient visits as were hospitalized (46% [n = 517] and 54% [n = 613]), whereas in Austria, proportionally more patients were evaluated as outpatients (60% [n = 168] and 40% [n = 114]) (Table 3). The most common reason for visits was chemotherapy administration in both Italy and Austria (n = 698; 62% and n = 193; 68%, respectively). In Italy and Austria, respectively, the proportion of patients having evidence of having received whole blood or red blood cell transfusion at the time of clinic visit or in the 28 days prior was 5% (n = 62) and 10% (n = 29), ESAs were 14% (n = 158) and 11% (n = 30), and iron supplementation was 7% (n = 74) and 2% (n = 7), respectively (Table 5).

Results by tumor type

Of those with solid tumors, 54 patients (5%) had evidence of having received whole blood or red blood cell transfusion, 144 (13%) had evidence of having received ESA, and 79 (7%) had evidence of having received iron supplementation at the time of clinic visit or within the 28 days prior (Table 6). Evidence of iron and ESA use were most common in patients with prostate cancer (11% [n = 4] and 22% [n = 8], respectively) and least common in patients with colorectal cancer (4% [n = 11] and 4% [n = 10], respectively). For those with hematologic malignancies, there was evidence of receiving whole blood or red blood cell transfusion in 37 patients (13%), ESA use in 44 (16%), and iron supplementation in only two (1%) patients at the time of clinic visit or within the 28 days prior.

Discussion

This study shows that anemia is commonly observed in Italian and Austrian patients undergoing myelosuppressive chemotherapy. The overall prevalence of anemia reported in this study was 32% (95% CI: 29.4%–34.2%) and the overall proportion

Table 4 Key primary and secondary outcome measures by tumor type (solid tumor or hematologic malignancy)

	Solid tumors						Hematological malignancy		
	Breast (n = 255)	Lung (n = 197)	Prostate (n = 36)	Colorectal (n = 256)	Other (n = 392)	Total (n = 1136)	NHL (n = 139)	Other (n = 137)	Total (n = 276)
Prevalence									
Anemic – n (%)	58 (23)	59 (30)	15 (42)	55 (21)	161 (41)	348 (31)	50 (36)	50 (36)	100 (36)
95% CI	18.0, 28.3	24.0, 36.7	27.1, 57.8	16.9, 26.9	36.3, 46.0	28.0, 33.4	28.5, 44.2	28.9, 44.8	30.8, 42.1
Type of visit – n (%)									
Outpatient	131 (51)	89 (45)	24 (67)	121 (47)	184 (47)	549 (48)	65 (47)	71 (52)	136 (49)
Hospitalized	124 (49)	108 (55)	12 (33)	135 (53)	208 (53)	587 (52)	74 (53)	66 (48)	140 (51)
Reason for visit[a] – n (%)									
Chemotherapy administration	155 (61)	142 (72)	24 (67)	180 (70)	248 (63)	749 (66)	70 (50)	72 (53)	142 (51)
Anemia treatment	5 (2)	8 (4)	2 (6)	2 (1)	26 (7)	43 (4)	1 (1)	8 (6)	9 (3)
Other cancer- or chemotherapy-related reason	96 (38)	50 (25)	10 (28)	73 (29)	128 (33)	357 (31)	68 (49)	59 (43)	127 (46)
Other reason not related to cancer	2 (1)	1 (1)	1 (3)	3 (1)	6 (2)	13 (1)	2 (1)	5 (4)	7 (3)
Hemoglobin results									
n (%)	214 (84)	171 (87)	30 (83)	205 (80)	320 (82)	940 (83)	105 (76)	108 (79)	213 (77)
Mean (SD) – g/dL	11.8 (1.4)	11.7 (1.8)	11.8 (1.9)	12.4 (1.7)	11.4 (1.6)	11.8 (1.7)	11.3 (1.6)	11.4 (1.9)	11.3 (1.8)
Hemoglobin category – n (%)									
≤10 g/dL	24 (11)	26 (15)	5 (17)	18 (9)	71 (22)	144 (15)	23 (22)	29 (27)	52 (24)
>10 g/dL	190 (89)	145 (85)	25 (83)	187 (91)	249 (78)	796 (85)	82 (78)	79 (73)	161 (76)
Physician's diagnosis of anemia	75 (29)	84 (43)	16 (44)	72 (28)	182 (46)	429 (38)	68 (49)	57 (42)	125 (45)
Patients with anemia symptoms – n (%)	74 (29)	68 (35)	16 (44)	70 (27)	159 (41)	387 (34)	33 (24)	36 (26)	69 (25)
Type of symptom[a] – n (%)									
Fatigue	64 (25)	57 (29)	15 (42)	62 (24)	138 (35)	336 (30)	27 (19)	29 (21)	56 (20)
Headaches	15 (6)	9 (5)	3 (8)	6 (2)	24 (6)	57 (5)	3 (2)	1 (1)	4 (1)
Dyspnea	17 (7)	31 (16)	4 (11)	9 (4)	32 (8)	93 (8)	5 (4)	9 (7)	14 (5)
Loss of libido	13 (5)	10 (5)	3 (8)	4 (2)	21 (5)	51 (5)	0 (0)	0 (0)	0 (0)
Depression	22 (9)	20 (10)	3 (8)	21 (8)	52 (13)	118 (10)	1 (1)	3 (2)	4 (1)
Dizziness	9 (4)	7 (4)	2 (6)	3 (1)	15 (4)	36 (3)	1 (1)	5 (4)	6 (2)
Cold skin	13 (5)	12 (6)	2 (6)	15 (6)	33 (8)	75 (7)	0 (0)	1 (1)	1 (<1)
Palpitations	14 (5)	11 (6)	3 (8)	7 (3)	22 (6)	57 (5)	2 (1)	3 (2)	5 (2)
Pulmonary edema	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Heart failure	1 (<1)	1 (<1)	0 (0)	0 (0)	1 (<1)	3 (<1)	0 (0)	1 (1)	1 (<1)
Severe impairment of cognitive function	1 (<1)	1 (<1)	0 (0)	3 (1)	6 (2)	11 (1)	0 (0)	1 (1)	1 (<1)
Other symptoms possibly related to anemia	1 (<1)	1 (<1)	1 (3)	1 (<1)	4 (1)	8 (1)	1 (1)	3 (2)	4 (1)
Current chemotherapy cycle delayed due to anemia – n (%)	9 (4)	10 (5)	4 (11)	5 (2)	19 (5)	47 (4)	1 (1)	3 (2)	4 (1)

Note: [a]Patients may be included in more than one category.
Abbreviations: CI, confidence interval; NHL, non-Hodgkin's lymphoma; SD, standard deviation.

of patients with hemoglobin levels ≤10 g/dL was 17%. It is worthwhile to note that the 95% CI were narrow, showing that the observed estimate of 32% is precise. Enrollment was higher than planned as more patients were seen at the study centers in a single (prespecified) day than expected. The fact that over 50% of patients in this study had received three or fewer cycles of chemotherapy showed that anemia can occur quite early on in a patient's treatment history.

A sensitivity analysis conducted in the present study found the prevalence of anemia defined by hemoglobin levels ≤11 g/dL gave very similar results to the most comparable analysis in the ECAS[1] (39% in each case). However, the sensitivity analysis

Table 5 Transfusions (red blood cell or whole blood), erythropoiesis-stimulating agent use and iron supplementation by country (Italy, Austria, and overall)

	Italy (n = 1130)	Austria (n = 282)	Overall (n = 1412)
Patients with evidence of transfusion at visit – n (%)	62 (5)	29 (10)	91 (6)
Transfusion data[a] – n (%)			
Within 28 days before visit	52 (5)	20 (7)	72 (5)
Ordered at visit	13 (1)	11 (4)	24 (2)
No transfusion/transfusion >28 days ago	1068 (95)	253 (90)	1321 (94)
Patients with evidence of ESA use at visit – n (%)	158 (14)	30 (11)	188 (13)
ESA data – n (%)			
No ESA prescribed	951 (84)	249 (88)	1200 (85)
Ongoing (without change)	115 (10)	20 (7)	135 (10)
Initiated at visit	35 (3)	8 (3)	43 (3)
Dose or schedule changed	4 (<1)	1 (<1)	5 (<1)
Stopped temporarily	19 (2)	2 (1)	21 (1)
Stopped permanently	6 (1)	2 (1)	8 (1)
Patients with ESA stop or change – n (%)	29 (3)	5 (2)	34 (2)
Reason for ESA stop or change – n (%)			
Anemic, but not responding	5 (<1)	2 (1)	7 (<1)
Anemic but experienced AE	3 (<1)	0 (0)	3 (<1)
Anemia resolved	16 (1)	2 (1)	18 (1)
Other	5 (<1)	1 (<1)	6 (<1)
Patients with evidence of iron (IV and/or oral) use at visit – n (%)	74 (7)	7 (2)	81 (6)
IV iron data – n (%)			
No iron prescribed	1048 (93)	275 (98)	1323 (94)
Ongoing (without change)	20 (2)	0 (0)	20 (1)
Initiated at visit	10 (1)	0 (0)	10 (1)
Dose or schedule changed	3 (<1)	0 (0)	3 (<1)
Stopped temporarily	2 (<1)	0 (0)	2 (<1)
Stopped permanently	0 (0)	0 (0)	0 (0)
Missing	47 (4)	7 (2)	54 (4)
Oral iron data – n (%)			
No iron prescribed	1048 (93)	275 (98)	1323 (94)
Ongoing (without change)	31 (3)	4 (1)	35 (2)
Initiated at visit	10 (1)	3 (1)	13 (1)
Dose or schedule changed	0 (0)	0 (0)	0 (0)
Stopped temporarily	3 (<1)	0 (0)	3 (<1)
Stopped permanently	0 (0)	0 (0)	0 (0)
Missing	38 (3)	0 (0)	38 (3)
Patients with iron (IV and/or oral) stop or change – n (%)	8 (1)	0 (0)	8 (1)
Reason for iron stop or change – n (%)			
Anemic, but not responding	3 (<1)	0 (0)	3 (<1)
Anemic but experienced AE	0 (0)	0 (0)	0 (0)
Anemia resolved	3 (<1)	0 (0)	3 (<1)
Other	2 (<1)	0 (0)	2 (<1)

Note: [a]Patients may be recorded in multiple categories.
Abbreviations: AE, adverse event; ESA, erythropoiesis-stimulating agent; IV, intravenous.

determining the prevalence of anemia defined by hemoglobin levels ≤9 g/dL in the present study gave a higher estimate than was observed in the ECAS (29% versus 10%, respectively).[1] The reason for this apparent difference may be due to differences in patient population hampering any descriptive comparisons between the two studies. For example, in the ECAS, prevalence estimates were assessed among all cancer patients, including those who did not receive any potentially myelotoxic chemotherapy treatment, whereas the present study only enrolled patients undergoing chemotherapy, with or without radiotherapy. However, when only the patients receiving chemotherapy at enrollment were considered in the ECAS, 50% of them were found to be anemic (hemoglobin <12 g/dL)[1] – a figure higher than observed here (39% were anemic based on hemoglobin levels ≤11 g/dL). Similarly, the prevalence of anemia, defined as hemoglobin levels <12 g/dL, was higher in the Belgian survey than in the present study (56% versus 39%).[14] However, the Belgian survey included patients with myelodysplasia, which was an exclusion criterion in the present study, and so increased reporting of anemia is to be expected in the former.

Although it is important to compare our data with previous observations in the literature, the differences in definitions of anemia that were used in these studies also make descriptive comparisons between studies difficult, and any apparent differences difficult to interpret. For example, in both the ECAS[1] and Belgian studies,[14] anemia was defined solely on the basis of hemoglobin levels, whereas in the present study, anemia definitions and the overall prevalence estimate included patients who were defined as anemic based on the presence of any of the following: hemoglobin levels, anemia treatment data, and anemia diagnosis data (including presence of anemia symptoms).

As anemia management data were also reported differently in each of these studies, it is difficult to draw conclusions regarding the impact of the changes in ESA prescribing information and anemia treatment guidelines over time. Overall, ESA use in the present study (13%) was similar to that noted in the Belgian study (14%),[14] whereas use of transfusions was higher (14% versus 6%) and iron supplementation lower (3% versus 6%) in the Belgian study than reported here. In comparison, in the ECAS, 17% of patients with anemia received epoetin, 15% received a transfusion, and 6% received iron supplementation.[1] In the Belgian study, the mean hemoglobin level at initiation of ESA treatment was 10.2 g/dL;[14] slightly higher than the level at which treatment was initiated in the ECAS (9.7 g/dL).[1]

Table 6 Transfusions (red blood cell or whole blood), ESA use and iron supplementation by tumor type (solid tumor or hematologic malignancy)

	Solid tumor						Hematological malignancy		
	Breast (n = 255)	Lung (n = 197)	Prostate (n = 36)	Colorectal (n = 256)	Other (n = 392)	Total (n = 1136)	NHL (n = 139)	Other (n = 137)	Total (n = 276)
Patients with evidence of transfusion at visit – n (%)	7 (3)	11 (6)	3 (8)	3 (1)	30 (8)	54 (5)	20 (14)	17 (12)	37 (13)
Transfusion data[a] – n (%)									
Within 28 days before visit	6 (2)	6 (3)	2 (6)	3 (1)	25 (6)	42 (4)	20 (14)	10 (7)	30 (11)
Ordered at visit	2 (1)	5 (3)	1 (3)	0 (0)	5 (1)	13 (1)	3 (2)	8 (6)	11 (4)
No transfusion/transfusion >28 days ago	248 (97)	186 (94)	33 (92)	362 (92)	362 (92)	1082 (95)	119 (86)	120 (88)	239 (87)
Patients with evidence of ESA use at visit – n (%)	20 (8)	34 (17)	8 (22)	10 (4)	72 (18)	144 (13)	22 (16)	22 (16)	44 (16)
ESA data – n (%)									
No ESA prescribed	231 (91)	160 (81)	27 (75)	243 (95)	312 (80)	973 (86)	113 (81)	114 (83)	227 (82)
Ongoing (without change)	15 (6)	19 (10)	4 (11)	6 (2)	53 (14)	97 (9)	18 (13)	20 (15)	38 (14)
Initiated at visit	4 (2)	11 (6)	2 (6)	3 (1)	17 (4)	37 (3)	4 (3)	2 (1)	6 (2)
Dose or schedule changed	2 (1)	1 (1)	0 (0)	1 (<1)	0 (0)	4 (<1)	1 (1)	0 (0)	1 (<1)
Stopped temporarily	2 (1)	4 (2)	2 (6)	3 (1)	6 (2)	17 (1)	3 (2)	1 (1)	4 (1)
Stopped permanently	1 (<1)	2 (1)	1 (3)	0 (0)	4 (1)	8 (1)	0 (0)	0 (0)	0 (0)
Patients with ESA stop or change – n (%)	5 (2)	7 (4)	3 (8)	4 (2)	10 (3)	29 (3)	4 (3)	1 (1)	5 (2)
Reason for ESA stop or change – n (%)									
Anemic, but not responding	1 (<1)	3 (2)	1 (3)	0 (0)	2 (1)	7 (1)	0 (0)	0 (0)	0 (0)
Anemic but experienced AE	0 (0)	1 (1)	1 (3)	1 (<1)	0 (0)	3 (<1)	0 (0)	0 (0)	0 (0)
Anemia resolved	3 (1)	0 (0)	1 (3)	3 (1)	7 (2)	14 (1)	3 (2)	1 (1)	4 (1)
Other	1 (<1)	3 (2)	0 (0)	0 (0)	1 (<1)	5 (<1)	1 (1)	0 (0)	1 (0)
Patients with evidence of iron (IV and/or oral) use at visit – n (%)	15 (6)	11 (6)	4 (11)	11 (4)	38 (10)	79 (7)	2 (1)	0 (0)	2 (1)
IV iron data – n (%)									
No iron prescribed	240 (94)	186 (94)	32 (89)	244 (95)	347 (89)	1049 (92)	137 (99)	137 (100)	274 (99)
Ongoing (without change)	2 (1)	5 (3)	3 (8)	0 (0)	10 (3)	20 (2)	0 (0)	0 (0)	0 (0)
Initiated at visit	0 (0)	2 (1)	0 (0)	3 (1)	5 (1)	10 (1)	0 (0)	0 (0)	0 (0)
Dose or schedule changed	2 (1)	1 (1)	0 (0)	0 (0)	0 (0)	3 (<1)	0 (0)	0 (0)	0 (0)
Stopped temporarily	0 (0)	0 (0)	0 (0)	0 (0)	2 (1)	2 (<1)	0 (0)	0 (0)	0 (0)
Stopped permanently	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Missing	11 (4)	3 (2)	1 (3)	9 (4)	28 (7)	52 (5)	2 (1)	0 (0)	2 (1)
Oral iron data – n (%)									
No iron prescribed	240 (94)	186 (94)	32 (89)	244 (95)	347 (89)	1049 (92)	137 (99)	137 (100)	274 (99)
Ongoing (without change)	7 (3)	3 (2)	0 (0)	5 (2)	19 (5)	34 (3)	1 (1)	0 (0)	1 (<1)
Initiated at visit	4 (2)	0 (0)	1 (3)	3 (1)	4 (1)	12 (1)	1 (1)	0 (0)	1 (<1)
Dose or schedule changed	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Stopped temporarily	0 (0)	0 (0)	0 (0)	1 (<1)	2 (1)	3 (<1)	0 (0)	0 (0)	0 (0)
Stopped permanently	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Missing	4 (2)	8 (4)	3 (8)	3 (1)	20 (5)	38 (3)	0 (0)	0 (0)	0 (0)
Patients with iron (IV and/or oral) stop or change – n (%)	2 (1)	1 (1)	0 (0)	1 (<1)	4 (1)	8 (1)	0 (0)	0 (0)	0 (0)
Reason for iron stop or change – n (%)	2 (1)	1 (1)	0 (0)	1 (<1)	4 (1)	8 (1)	0 (0)	0 (0)	0 (0)
Anemic, but not responding	2 (1)	1 (1)	0 (0)	0 (0)	0 (0)	3 (<1)	0 (0)	0 (0)	0 (0)
Anemic but experienced AE	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Anemia resolved	0 (0)	0 (0)	0 (0)	1 (<1)	2 (1)	3 (<1)	0 (0)	0 (0)	0 (0)
Other	0 (0)	0 (0)	0 (0)	0 (0)	2 (1)	2 (<1)	0 (0)	0 (0)	0 (0)

Note: [a]Patients may be recorded in multiple categories.

Abbreviations: AE, adverse event; ESA, erythropoiesis-stimulating agent; IV, intravenous; NHL, non-Hodgkin's lymphoma.

Nonetheless, both studies are in line with current EORTC guidelines, which state ESA treatment should be initiated at hemoglobin levels of 9–11 g/dL in patients undergoing chemotherapy or radiochemotherapy, based on anemia-related symptoms.[6] Information regarding the patient's hemoglobin levels at the start of treatment was not collected in the present study, but it is expected to be in line with the data reported previously.

Of note in the Belgian study, is that despite the potential deleterious impact on quality of life and prognosis, 53% of patients overall received no treatment for their anemia, including 15% of patients with hemoglobin levels <10 g/dL.[14] Similarly, 61% of anemic patients in the ECAS received no treatment.[1] Although the overall proportion of patients who did not receive treatment for anemia was not specifically collected in the present study, the proportions showing evidence of transfusion (6%), ESA use (13%) and iron supplementation (6%) suggest that many patients also did not receive any treatment for their anemia.

Conclusion

In this survey 32% of patients seen on the prespecified day were observed to be anemic, but there was only evidence of ESA use in approximately one-third of these. It is, however, possible that some patients with low hemoglobin levels may have had an ESA prescribed shortly after the office visit, which would not have been captured by the current study design. Nonetheless, these data suggest that, in line with previous studies, a significant proportion of patients with anemia, who could be treated with ESA according to EORTC or the ASCO and the ASH guidelines, may still not be receiving treatment.

Acknowledgments

This study was sponsored by Amgen Ltd. Medical writing support (funded by Amgen [Europe] GmbH) was provided by Dawn Batty from Bioscript Stirling Ltd. Mimma Rizzo (Azienda Ospedaliera di Rilievo Nazionale "Antonio Cardarelli", Napoli, Italy) is also acknowledged for reviewing the draft manuscript. The following study investigators are also acknowledged for collecting data and for providing care for study patients, Italy: R Addeo, F Angelini, A Ardizzoia, M Botta, C Buscarino, E Cammilluzzi, E Capochiani, E Cerqui, E Cortesi, N Di Renzo, F Gaion, R Ghio, G Giglio, P Giordani, M Giordano, C Ingrosso, V Lorusso, F Malorgio, R Mattioli, C Mulas, G Mustacchi, G Palmieri, C Pasquini, V Pavone, A Pelizzari, F Piantedosi, A Pisano, G Pisapia, I Romaniello, R Segati, G Battista Speranza, R Tassara, D Toniolo, F Vaira, P Varese; Austria: T Brodowicz, W Eisterer, A Georgoulopoulos, T Grünberger, M Hubalek, R Kolb, P Neumeister, A Petzer, TC Scholl, R Schramböck, C Singer, G Steger, E Ullsperger.

Disclosure

Laura Belton is a contract biostatistician for Amgen Ltd, and Beatriz Pujol is an employee of Amgen Europe. Ferdinand Haslbauer has received funding from Amgen GmbH. The other authors report no conflicts of interest in this work.

References

1. Ludwig H, Van Belle S, Barrett-Lee P, et al. The European Cancer Anaemia Survey (ECAS): a large, multinational, prospective survey defining the prevalence, incidence, and treatment of anaemia in cancer patients. *Eur J Cancer*. 2004;40(15):2293–2306.
2. Aapro MS, Cameron DA, Pettengell R, et al. EORTC guidelines for the use of granulocyte-colony stimulating factor to reduce the incidence of chemotherapy-induced febrile neutropenia in adult patients with lymphomas and solid tumours. *Eur J Cancer*. 2006;42(15): 2433–2453.
3. Caro JJ, Salas M, Ward A, Goss G. Anemia as an independent prognostic factor for survival in patients with cancer: a systemic, quantitative review. *Cancer*. 2001;91(12):2214–2221.
4. Harper P, Littlewood T. Anaemia of cancer: impact on patient fatigue and long-term outcome. *Oncology*. 2005;69 Suppl 2:2–7.
5. Calabrich A, Katz A. Management of anemia in cancer patients. *Future Oncol*. 2011;7(4):507–517.
6. Aapro MS, Link H. Sep 2007 update on EORTC guidelines and anemia management with erythropoiesis-stimulating agents. *Oncologist*. 2008;13 Suppl 3:33–36.
7. Schrijvers D, De Samblanx H, Roila F; for ESMO Guidelines Working Group. Erythropoiesis-stimulating agents in the treatment of anaemia in cancer patients: ESMO Clinical Practice Guidelines for use. *Ann Oncol*. 2010;21 Suppl 5:v244–v247.
8. Aapro M, Österborg A, Gascón P, Ludwig H, Beguin Y. Prevalence and management of cancer-related anaemia, iron deficiency and the specific role of i.v. iron. *Ann Oncol*. 2012;23(8):1954–1962.
9. Schrijvers D. Management of anemia in cancer patients: transfusions. *Oncologist*. 2011;16 Suppl 3:12–18.
10. Amgen Europe BV. Aranesp® *Annex I Summary of Product Characteristics*. The Netherlands: Amgen Europe BV; 2012. Available from: http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/000332/WC500026149.pdf. Accessed June 27, 2013.
11. Rizzo JD, Somerfield MR, Hagerty KL, et al. Use of epoetin and darbepoetin in patients with cancer: 2007 American Society of Clinical Oncology/American Society of Hematology clinical practice guideline update. *J Clin Oncol*. 2008;26(1):132–149.
12. Castaigne S, Tourani JM, Delaloge S, Hennequin C, Zureik M, Lemarié E. High prevalence of anaemia among French hospitalized cancer patients: A one-day cross-sectional survey. *Haematologica*. 2007;92 Suppl 2:28. Abstract 0077.
13. Schmitz S, Chatsiproios D, Sandermann A, Link H. High prevalence of anemia among cancer patients in outpatient clinics in Germany: A two-day cross-sectional survey. *Onkologie*. 2008;31 Suppl 4:220. Abstract.
14. Verbeke N, Beguin Y, Wildiers H, et al. High prevalence of anaemia and limited use of therapy in cancer patients: a Belgian survey (Anaemia Day 2008). *Support Care Cancer*. 2012;20(1):23–28.
15. Steegmann JL, Sánchez Torres JM, Colomer R, et al. Prevalence and management of anaemia in patients with non-myeloid cancer undergoing systemic therapy: a Spanish survey. *Clin Transl Oncol*. 2013;15(6):477–483.