

A Risk Model for Thrombocytopenia Requiring Platelet Transfusion After Cytotoxic Chemotherapy

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Severe thrombocytopenia is a rare but life-threatening side effect of cytotoxic chemotherapy for which risk factors are not well known. Our objective was to delineate a risk model for chemotherapy-induced thrombocytopenia requiring platelet transfusions in cancer patients. Univariate and multivariate analysis of risk factors for chemotherapy-induced thrombocytopenia requiring platelet transfusions were performed on the cohort of the 1,051 patients (CLB 1996) treated with chemotherapy in the Department of Medicine of the Centre Léon Bérard (CLB) in 1996. In univariate analysis, performance status (PS) greater than 1, platelet count less than 150,000/ μ L at day 1 (d1) before the initiation of chemotherapy, d1 lymphocyte count \leq 700/ μ L, d1 polymorphonuclear leukocyte count less than 1,500/ μ L, and the type of chemotherapy (high risk v others) were significantly associated ($P < .01$) with an increased risk of severe thrombocytopenia requiring platelet transfusions. Using logistic regression, d1 platelet count less than 150,000/ μ L (odds ratio [OR], 4.3; 95% confidence interval [CI], 1.9 to 9.6), d1 lymphocyte counts

SEVERE THROMBOCYTOPENIA is a rare but life-threatening side effect of cytotoxic chemotherapy.^{1,2} Until now, the management of severe thrombocytopenia has been curative, relying on platelet transfusions when platelet counts are less than 20,000/ μ L and/or in case of bleeding.^{3,4} There are several drawbacks for platelet transfusions, in particular the risk of viral transmission and resistance to platelet transfusions that occurs in 0% to 24% of patients requiring frequent platelet transfusions.⁵⁻⁷

Interleukin-11 (IL-11), thrombopoietin/megakaryocyte growth and development factor (MGDF), IL-1, IL-3, and IL-6 have been reported to be capable of increasing platelet count, reducing platelet nadir, or decreasing the duration of platelet transfusions, therefore opening the possibility of a prophylaxis of severe thrombocytopenia in the near future.⁸⁻¹⁴ However, the incidence of platelet transfusions is low in a general population of cancer patients treated with conventional chemotherapy.² It would therefore be useful to identify risk factors for platelet transfusions to select candidate patients for the prophylactic administration of thrombopoietic growth factors.

We report here a retrospective study of risk factors for chemotherapy-induced thrombocytopenia requiring platelet transfusions in the cohort of cancer patients treated in the Department of Medicine of the Centre Léon Bérard in 1996. A risk model for platelet transfusions was delineated and then validated in 3 distinct series of patients.

PATIENTS AND METHODS

Criteria for patients selection. The method used in this study was to delineate a risk index for severe thrombocytopenia requiring platelet transfusions in a retrospective series and to validate this index in 3 distinct series of patients. Four distinct cohorts of patients are thus considered in this study.

In all 4 series, the selection criteria for the patients were identical and as follows. Patients were to be more than 17 years of age. Patients with leukemia, in particular chronic lymphocytic leukemia, were excluded, because of the possible contamination of peripheral blood by malignant

\leq 700/ μ L (OR, 3.37; 95% CI, 1.77 to 6.4), the type of chemotherapy (OR, 3.38; 95% CI, 1.77 to 6.4), and PS greater than 1 (OR, 2.23; 95% CI, 1.22 to 4.1) were identified as independent risk factors for platelet transfusions. The observed incidences of platelet transfusions were 45%, 13%, 7%, and 1.5% for patients with \geq 3, 2, 1, or 0 risk factors, respectively. This model was then tested in 3 groups of patients treated with chemotherapy used as validation samples: (1) the series of 340 patients treated in the CLB in the first 6 months of 1997, (2) the prospective multicentric cohort of 321 patients of the ELYPSE 1 study, and (3) the series of 149 patients with non-Hodgkin's lymphoma treated in the CLB within prospective phase III trials (1987 to 1995). In these 3 groups, the observed incidences of platelet transfusions in the above-defined risk groups did not differ significantly ($P > .1$) from those calculated in the model. This risk index could be useful to identify patients at high risk for chemotherapy-induced thrombocytopenia requiring platelet transfusions.

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cells. Patients receiving chemotherapy regimens administered daily were excluded. Patients were not to be treated concomitantly with cytokines (ie, interferon, IL-2, or others). Massive chemotherapy regimens, ie, regimens requiring bone marrow or peripheral blood stem cell reinjection, were excluded. Each patient was analyzed for only 1 course of chemotherapy in the 4 series.

The retrospective group of 1996 (CLB 1996) comprised all patients treated with chemotherapy in the Department of Medicine of the Centre Léon Bérard in 1996. That year, 3,223 courses of chemotherapy were administered to 1,116 patients matching the inclusion criteria. Every patient was analyzed only for his first course of chemotherapy administered in the Centre Léon Bérard in 1996. Histology, primary tumor site, chemotherapy regimen, sex, age, performance status (PS), blood cell count at day 1 (d1) just before the administration of chemotherapy, as well as platelet transfusions after the studied course were collected. Patients with missing blood cell count at day 1 ($n = 65$) were excluded. Of the 1,116 patients, 1,051 (94%) were therefore analyzed (Table 1). The risk model was established in this retrospective series.

The risk model was then tested in 3 groups used as validation samples. The first group (CLB 1997) is the retrospective series of 340 patients treated in the Centre Léon Bérard during the first 6 months of 1997 and who had not received chemotherapy in the Department of

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Medicine of the Centre Léon Bérard in 1996. Every patient was analyzed only for his first course of chemotherapy administered in the Centre Léon Bérard in 1997. Only 312 of the 340 patients (92%) were included in the analysis because of missing data on blood cell count at day 1 (n = 28).

The second group (ELYPSE 1) is a multicentric prospective series of 321 patients treated with conventional chemotherapy in both general hospital (n = 13) and comprehensive cancer centers (n = 5): 84 patients (26%) were treated in cancer centers and 237 (74%) in general hospitals. Every participating physician had to include all his consecutive patients for 1 month between November 1995 and September 1996.

Only 295 of the 321 patients (92%) were analyzed because of missing data for performance status (n = 24) or blood cell count at day 1 (n = 2). This series has been recently reported.¹⁵

The third group (NHL-CLB) is the cohort of 149 non-pretreated patients with intermediate- or high-grade non-Hodgkin's lymphoma included in prospective multicentric phase III of the GELA group who received a first course of conventional chemotherapy regimen in the Centre Léon Bérard between 1987 and 1995. There were no missing data in this series and all patients were evaluated.

The characteristics of the patients in the 4 series are listed in the Table 1.

Table 1. Characteristics of Patients

	CLB 1996 (n = 1,051)		CLB 1997 (n = 312)		ELYPSE 1 (n = 295)		CLB-NHL (n = 149)		Total (n = 1,807)	
	No. of Patients	%	No. of Patients	%	No. of Patients	%	No. of Patients	%	No.	%
Median age (range)	55 (18-86)		56 (18-85)		58 (18-86)		70 (27-93)			
Age (yr)										
<60	655	62	179	57	167*	57	37	25	1,038	58
≥60	396	38	133	43	123*	43	112	75	764	42
Sex										
F	567	54	161	52	178	60	68	46	974	54
M	484	46	151	48	117	40	81	54	833	46
Diagnostic										
Carcinoma										
Breast	247	24	78	25	99	34	0	0	424	23
Colon-rectum	96	9	16	5	50	17	0	0	162	9
Ovary	90	9	14	5	32	11	0	0	136	8
Head and neck	103	10	20	6	20	7	0	0	143	8
Other gastrointestinal	112	11	18	5	11	4	0	0	141	8
Lung cancer	61	6	22	7	8	3	0	0	91	5
Lymphoma	93	9	37	12	21	7	149	100	300	17
Bone and soft tissue sarcoma	68	7	17	5	13	4	0	0	98	5
Germ cells tumors	32	3	15	5	7	2	0	0	54	3
Others	149	14	75	25	34	10	0	0	258	14
High-risk chemotherapy†										
Yes	105	10	92	29	24	8	74	50	295	16
No	946	90	220	71	271	92	75	50	1,512	84
Chemotherapy regimens										
ACVBP/ECVBP	14	1	14	4	4	1	74	50	106	6
ADRIAMYCINE alone	27	3	13	4	0	0	0	0	40	2
CDDP-5FU	85	8	15	5	16	5	0	0	116	6
CDDP-NAV/CDDP-VP16	55	5	22	7	7	2	0	0	84	5
DHAP	24	2	7	2	0	0	0	0	31	2
FAC/FEC/AC	115	11	44	14	90	28	0	0	249	14
FUFOL/LV5FU2	71	7	14	5	47	15	0	0	132	7
MAID	11	1	7	2	2	1	0	0	20	1
mBACOD	0	0	0	0	0	0	15	10	15	1
TAXANES	124	12	29	9	29	9	0	0	182	10
CHOP	25	2	12	4	9	3	53	36	99	5
BEP/EP	30	3	17	5	7	2	0	0	54	3
NAVELBINE alone	74	7	15	5	0	0	0	0	89	5
CAP/CEP/CP	34	3	2	1	22	7	0	0	58	3
Other	362	34	101	36	71	24	7	5	541	30
No. of chemotherapy course										
1	766‡	78	306	98	130	44	149	100	1,351	78
≥2	213‡	22	6	2	165	56	0	0	384	21
Performance status										
0-1	881	84	250	80	252	85	103	69	1,486	82
>1	170	16	62	20	43	15	46	31	321	18

*Missing data: n = 5.

†See the Patients and Methods.

‡Missing data: n = 72.

Indications of platelet transfusions. Platelet transfusions administered for chemotherapy-induced thrombocytopenia within the 28 days after the course of chemotherapy was chosen as the end-point for this study. Criteria for platelet transfusions in the Centre Léon Bérard as well as for the physicians who participated to the ELYPSE 1 series were platelet count less than 20,000/ μ L or thrombocytopenia less than 50,000/ μ L with coagulation disorders and/or heparin therapy and/or with bleeding complications. Within the database, 4 patients with the above-described inclusion criteria (all in the CLB 1996 series) were not transfused with platelets, although they had platelet counts less than 20,000/ μ L. In all 4 cases, this decision was made by the physician because a rapid (<48 hours) death due to tumor progression was expected (and indeed occurred). The model presented here was not modified when these patients are considered as having had an event.

Chemotherapy regimens. The chemotherapy regimens were separated in 2 subgroups according to the doses and the type of drugs administered. The criteria high-risk chemotherapy has been previously reported and refers to regimens containing either greater than 90 mg/m² doxorubicin, greater than 90 mg/m² epirubicin, greater than 100 mg/m² cisplatin, greater than 9 g/m² ifosfamide, greater than 1 g/m² cyclophosphamide, greater than 500 mg/m² etoposide, or greater than 1 g/m² cytarabine per course.^{15,16} The other subgroup of regimens included all other chemotherapy regimens.

Statistical analysis. Risk factors for platelet transfusions were tested in univariate and multivariate analysis using the procedures of the SPSS 6.01 program (1994; SPSS, Inc, Chicago, IL). The correlation between a clinical or a biological parameter and the incidence of chemotherapy-induced thrombocytopenia requiring platelet transfusions was performed using the χ^2 test or Fisher's exact test. A logistic regression including the parameters studied in the univariate analysis was performed using logistic program of SPSS. The forward regression procedure was used with a *P* value less than .05 for entry. Risk factors (eg, PS >1) and end-point (ie, platelet transfusions) were considered 0 if absent and 1 if present. This multivariate analysis was performed in the 1,051 patients of the CLB 1996 series. A risk model was established using the independent risk factors identified in this multivariate analysis. This risk model was then tested on the 3 distinct cohorts of patients.

RESULTS

Univariate analysis. Fifty-six of the 1,051 patients (5.3%) of the CLB 1996 series received platelet transfusions because of severe thrombocytopenia within the 28 days after the administration of the course of cytotoxic chemotherapy. In univariate analysis, platelet count less than 150,000/ μ L immediately before the initiation of chemotherapy (d1), d1 polymorphonuclear leukocyte (PMN) count less than 1,500/ μ L, d1 lymphocyte count \leq 700/ μ L, PS greater than 1, and the type of chemotherapy regimen (high risk *v* others) as previously defined (Patients and Methods) were found to be significantly correlated to the risk of platelet transfusions (Table 2). In contrast, age less than 60 years, sex, and number of previous courses of chemotherapy were not significantly correlated to the incidence of platelet transfusions (Table 2).

Multivariate analysis. A logistic regression to identify independent risk factors for platelet transfusions was performed among all the parameters tested in univariate analysis. The parameters identified as independent risk factors for platelet transfusions were PS greater than 1 (odds ratio [OR], 2.23; 95% confidence interval [CI], 1.22 to 4.11), d1 platelet count less than 150,000/ μ L (OR, 4.30; 95% CI, 1.93 to 9.61), d1 lymphocyte count \leq 700/ μ L (OR, 3.37; 95% CI, 1.77 to 6.44), and

Table 2. Risk Factors for Thrombocytopenia Requiring Platelet Transfusions

	No. of Patients (%)	Platelet Transfusions		<i>P</i>
		N	%	
Age (yr)				
\leq 60	655 (62)	37	5.6	
>60	396 (38)	19	4.8	.32
Sex				
F	567 (54)	32	5.6	
M	484 (46)	24	5	.36
No. of chemotherapy courses*				
1	766 (78)	43	5.6	
2-6	185 (18)	6	3.2	
\geq 7	28 (4)	0	0	.19
High-risk chemotherapy†				
Yes	105 (10)	11	10.5	
No	946 (90)	45	4.8	.01
Performance status				
0-1	881 (84)	36	4.1	
>1	170 (16)	20	11.8	<.01
d1 platelet count				
<150,000/ μ L	100 (9)	19	19.2	
\geq 150,000/ μ L	951 (91)	37	3.9	<.01
d1 lymphocyte count				
\leq 700/ μ L	234 (22)	29	12.4	
>700/ μ L	817 (78)	27	3.3	<.01
d1 PMN count				
<1,500/ μ L	26 (2)	5	19.2	
\geq 1,500/ μ L	1025 (98)	51	5	.009

*Missing data (n = 72).

†See the Patients and Methods.

high-risk chemotherapy regimens (OR, 3.38; 95% CI, 1.77 to 6.46; Table 3).

Risk model. To construct a simple algorithm for calculating the expected risk of platelet transfusions for each patient, the parameters PS greater than 1, high-risk chemotherapy, d1 lymphocyte count \leq 700/ μ L, and d1 platelet count less than 150,000/ μ L were all given an arbitrary risk coefficient of 1. The risk index for a given patient was obtained by summing the coefficients of these 4 risk factors and therefore ranged from 0 to 4. For example, a patient with PS equal to 1, receiving a non-high-risk chemotherapy regimen with d1 lymphocyte count \leq 700/ μ L and d1 platelet count less than 150,000/ μ L, has a risk index of 2. Because patients with 4 risk factors represented only 0.17% of these patients (3 of 1,807), patients with 3 and 4 risk factors were pooled; 4 risk groups of patients were thus defined (Table 4). The calculated probability of platelet transfusions was 44.5% (95% CI, 37.3% to 51.8%) in patients with 3 or 4 risk factors, 13% (95% CI, 10.1% to 16.8%) for

Table 3. Logistic Regression of Risk Factors for Platelet Transfusions

	β	SE	χ^2	<i>P</i>	OR	95% CI
Platelet transfusions						
Intercept	3.94	.24	252	<.001	—	
High-risk chemotherapy*	1.21	.38	10.1	.001	3.38	1.77-6.46
d1 lymphocyte count \leq 700/ μ L	1.21	.30	156.1	.001	3.37	1.77-6.44
PS >1	0.80	.31	6.6	.01	2.23	1.22-4.11
d1 platelet count <150,000/ μ L	1.46	.32	20.3	<.001	4.30	1.93-9.61

*See the Patients and Methods.

Table 4. Incidence of Platelet Transfusions in the 4 Groups According to the Risk Model

	Calculated Incidence (%; 95% CI)	Observed Incidence									
		Validation Series									
		CLB 1996		CLB 1997		ELYPSE 1		CLB-NHL		Total	
No.	% (95% CI)	No.	% (95% CI)	No.	% (95% CI)	No.	% (95% CI)	No.	% (95% CI)		
≥3 risk factors	44.5 (37-52)	9/20	45 (23-67)	4/12	33.3 (6-60)	0/2	0	4/8	50 (15-85)	17/42*	40 (25-55)
2 risk factors	13 (10-17)	14/109	12.8 (7-19)	4/41	9.8 (1-19)	3/18	17 (0-34)	5/29	17 (3-31)	26/197	13 (8-18)
1 risk factor	7 (5-10)	24/330	7.3 (5-10)	3/122	2.5 (0-5)	5/73	7 (1-13)	2/75	3 (0-7)	34/600	5.3 (3.5-7)
No risk factor	1.5 (1-2)	9/592	1.5 (0.5-2.5)	2/137	1.5 (0-3.5)	2/202	1 (0-2)	0/37	0	13/968	1.3 (0.5-2)

The observed incidences of differences in platelet transfusions in risk groups ≥3, 2, 1, or 0 risk factors were not statistically different among the 4 series ($\chi^2 = 2.09$, $P = .55$ for comparison of patients with 3 or all risk factors; $\chi^2 = 1.04$, $P = .79$ for comparison of patients with 2 risk factors; $\chi^2 = 5.77$, $P = .12$ for comparison of patients with 1 risk factor; and $\chi^2 = 0.85$, $P = .83$ for comparison of patients with no risk factors).

*Including 3 patients with 4 risk factors.

patients with 2 risk factors, 7% (95% CI, 4.9% to 9.9%) for patients with 1 risk factor only, and 1.5% (95% CI, 1.1% to 2.2%) for patients with none of these risk factors (Table 4).

Validation of the model. This model was then tested in the 3 series of patients used as validation samples (Table 4).

In the CLB 1997 series, 4.2% (13 of 312) of the patients received platelet transfusions. The observed incidence of platelet transfusions was significantly different ($P < 10^{-5}$) in patients with ≥3, 2, 1, or 0 risk factors (33.3%, 9.8%, 2.5%, and 1.5%, respectively; Table 4). A single patient had 4 risk factors and received platelet transfusions.

In the ELYPSE 1 series, 3.3% (10 of 295) of the patients received platelet transfusions. The observed incidence of platelet transfusions was significantly different ($P = .001$) in patients with ≥3, 2, 1, or 0 risk factors (0%, 17%, 7%, and 1%, respectively; Table 4). Of note, although none of the 2 patients with ≥3 risk factors were transfused with platelets, their nadir of platelets were 25,000/ μ L and 35,000/ μ L, respectively.

In the CLB-NHL series, 7.4% (11 of 149) of the patients received platelet transfusions. The observed incidence of platelet transfusions was significantly different ($P < 10^{-5}$) in patients with ≥3, 2, 1, or 0 risk factors (50%, 17%, 3%, and 0%, respectively; Table 4).

The observed incidence of platelet transfusions in the 4 cohorts of patients studied were not significantly different (56 of 1,051, v 13 of 312, v 10 of 295, v 11 of 149; $\chi^2 = 4.01$, $P = .25$). The observed incidences of platelet transfusions in risk group ≥3, 2, 1, or 0 were not significantly different among the 4 series ($\chi^2 = 2.09$, $P = .55$ for patients with ≥3 risk factors; $\chi^2 = 1.04$, $P = .79$ for patients with 2 risk factors; $\chi^2 = 5.77$, $P = .12$ for patients with 1 risk factor; and $\chi^2 = 0.85$, $P = .83$ for patients with no risk factor; Table 4).

Risk factors for patients not receiving high-risk chemotherapy. Because it is well established that the risk of thrombocytopenia correlates to the dose of chemotherapy, we asked whether this model could be useful in the subgroup of patients who did not receive high-risk chemotherapy as defined in this study. This subgroup represented, respectively, 946, 220, 271, and 75 of the patients in the CLB 1996, CLB 1997, Elypse 1, and NHL-CLB series. Forty-five patients (4.7%) of the CLB 1996 series (4.7%) received platelet transfusions because of severe thrombocytopenia. A multivariate analysis was performed on this subgroup of 946 patients to identify independent

risk factors for severe thrombocytopenia requiring platelet transfusion in these patients. Logistic regression again identified the same 3 independent risk factors for platelet transfusion: PS greater than 1 (OR, 2.14; 95% CI, 0.87 to 5.3), d1 platelet count less than 150,000/ μ L (OR, 4.3; 95% CI, 0.6 to 30), and d1 lymphocyte count \leq 700/ μ L (OR, 3.15; 95% CI, 0.8 to 13). The observed incidences of platelet transfusions in patients with 0, 1, 2, and 3 of these risk factors (PS, lymphocyte counts, and platelet counts) were 1.5%, 8%, 13%, and 36%, respectively, in the CLB 1996 series. The observed incidences of platelet transfusions in risk group 3, 2, 1, or 0 were not significantly different among the 4 series ($\chi^2 = 1.5$, $P = .46$ for patients with 3 risk factors; $\chi^2 = 1.92$, $P = .58$ for patients with 2 risk factors; $\chi^2 = 1.56$, $P = .66$ for patients with 1 risk factor; and $\chi^2 = 0.81$, $P = .84$ for patients with no risk factor). These results confirm that the general model described in Table 4 is also efficient for patients not receiving high-risk chemotherapy.

DISCUSSION

Severe thrombocytopenia induced by cytotoxic chemotherapy is associated with a potential risk of toxic death due to bleeding and may require to delay the administration of chemotherapy. The objective of the present study was to identify risk factors for chemotherapy-induced thrombocytopenia requiring platelet transfusions. The number of platelet transfusions was chosen as the most relevant end-point, because these patients could benefit the most of a prophylactic treatment capable to prevent or reduce the incidence of severe thrombocytopenia.

Little is known on the risk factors for platelet transfusions after conventional chemotherapy. A search on the electronic database (Medline) using the MESH terms platelet transfusions, thrombocytopenia, chemotherapy, toxicity, and risk factors identified no report devoted to the analysis of individual risk factors for severe thrombocytopenia induced by conventional cytotoxic chemotherapy. Therefore, it was chosen to select clinical and biological factors that were potentially correlated to the incidence of hematological toxicity of chemotherapy according to our previous studies (age, sex, PS, number of previous courses, and blood cell counts).^{15,16} Day-5 lymphocyte count \leq 700/ μ L, a major risk factor for febrile neutropenia, was not available in most patients; hence, the day-1 lymphocyte count

$\leq 700/\mu\text{L}$, which was less strongly correlated to hematological toxicity in previous studies, was therefore tested.¹⁶

The risk model for chemotherapy-induced thrombocytopenia requiring platelet transfusions was established on the retrospective cohort of patients treated in the Department of Medicine of the Centre Léon Bérard in 1996. Each patient was analyzed only for his first course during the year. As expected, the incidence of platelet transfusions was low in this series of patients treated with conventional chemotherapy regimens ($n = 56$ [5.3%]). Four parameters were found to have an independent prognostic value for platelet transfusions, ie, platelet count less than $150,000/\mu\text{L}$ at d1, lymphocyte count less than $700/\mu\text{L}$ at d1, high-risk chemotherapy regimens, and PS greater than 1. It is noteworthy that, when a logistic regression was applied to all 3,223 chemotherapy courses administered in the Department of Medicine of the CLB in 1996, the same independent risk factors with a similar weight were identified, supporting the validity of this model (data not shown). These results show that 2 categories of parameters influence the incidence of chemotherapy-induced thrombocytopenia requiring platelet transfusions: (1) parameters reflecting clinical and biological status of patient (ie, PS and day-1 platelet and lymphocyte count) and (2) the type of chemotherapy regimen (high-risk chemotherapy as defined in our previous study).^{15,16} The relative weight of the independent risk factors being not significantly different, a simple risk model was established that delineates 4 risk groups with 0, 1, 2, and ≥ 3 of these risk factors. Importantly, this model also proved to be efficient to identify patients at high risk for severe thrombocytopenia requiring platelet transfusion among the subgroup of patients not receiving high-risk chemotherapy. Twenty-nine percent (5 of 17 among the 4 series) of patients not receiving high-risk chemotherapy but with all 3 other risk factors experienced severe thrombocytopenia requiring platelet transfusion, a notably high incidence for patients receiving conventional chemotherapy.

The cohort of high-risk patients (≥ 3 risk factors) represented less than 3% of all patients in these 4 series and comprised 19% (17 of 90) of the patients who required platelet transfusions in the 4 series. The intermediate-risk group (2 risk factors) with a 13% calculated incidence of platelet transfusions comprised 29% (26 of 90) of the patients transfused with platelets in the 4 series. Patients with a risk index ranging from 2 to 4 included, therefore, 48% (43 of 90) of the patients who require platelet transfusions after chemotherapy administration in the 1,807 patients of the 4 series, although they represented only 13% (239 of 1,807) of all patients.

A potential limit of this study is the heterogeneity of these series in terms of disease types and chemotherapy regimens. Indeed, the CLB 1996 and CLB 1997 series included patients with similar clinical characteristics. In contrast, the CLB-NHL series comprised only patients with non-Hodgkin's lymphoma receiving their first course of chemotherapy, and the ELYPSE 1 series was a multicentric prospective cohort of patients. Despite the differences in the characteristics of patients, the risk index proved efficient to distinguish patients with a high risk of platelet transfusions. The reproducibility of the results in the 3 groups used as validation samples as well as the large number of patients analyzed ($n = 1,807$) suggest that the risk model may

be useful to identify patients at high risk for chemotherapy-induced thrombocytopenia requiring platelet transfusions in the general population of patients treated with conventional chemotherapy.

This model could distinguish a cohort of patients with such a high risk of platelet transfusions that a prophylactic administration of a platelet growth factor, such as MGDF or IL-11, could be both clinically justified and cost-effective.^{13,14} Randomized phase III studies could focus on the subgroup of high-risk patients (with or without the subgroup of 2 risk factors) to evaluate the prophylactic use of these platelet growth factors versus placebo.

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APPENDIX

Investigator List for the ELYPSE 1 Study

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