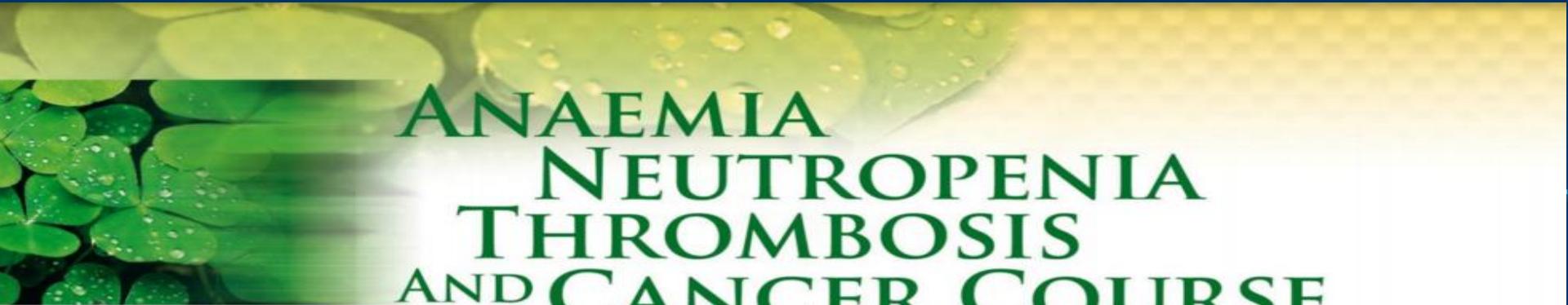




TRANSATLANTIQUES EN ONCOLOGIE



ANAEMIA NEUTROOPENIA THROMBOSIS AND CANCER COURSE

Invitation to

**15th Annual Course
“Anaemia, Neutropenia, Thrombosis and Cancer”**

Vienna, Austria - April 8th / 9th , 2016

**Implications of anemia and neutropenia
in the elderly patient**

Dr.D.KAMIONER

Hôpital Privé Ouest Parisien

TRAPPES - F

09h00-09h45

Salle 1

BLANCS SUR ROUGES, SI ÇA BOUGE : LE POINT SUR LES TOXICITÉS HÉMATOLOGIQUES DES TRAITEMENTS ANTI-CANCÉREUX

Intervenant : Matti AAPRO (Genolier, Suisse)



Disclosures



CLINIQUE DE GENOLIER

- Collaborations in this field:
Teva, Sandoz, Hospira/Pfizer,
Amgen, Kyowa Hakko Kirin,
Dr Reed



Prophylaxie de la Neutropénie Fébrile (NF)

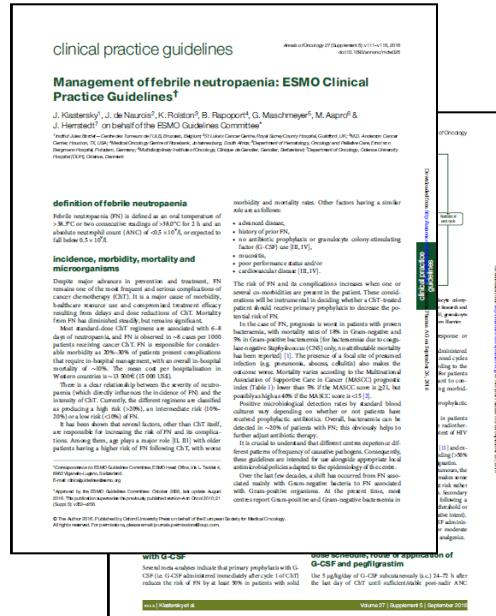
REFERENTIEL AFSOS

Date : 14/07/2014

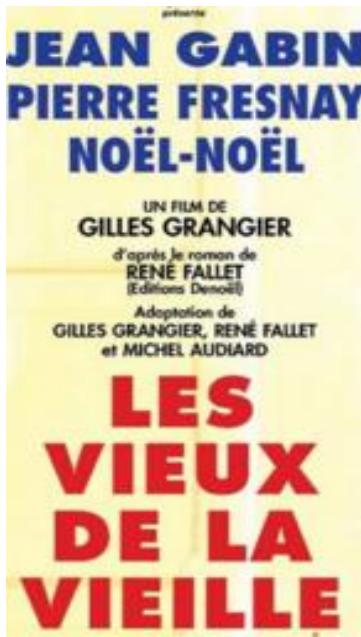
New ESMO Clinical Practice Guidelines on Management of Febrile Neutropenia

Klastersky J, et al. *Management of febrile neutropaenia: ESMO Clinical Practice Guidelines*. Ann Oncol. 2016;27(suppl 5):v111–v118.

- A significant update since the last version is the inclusion of information regarding primary prophylaxis with granulocyte colony-stimulating factors (G-CSF)
- The updated guidelines generally reflect recommendations made in other published guidelines (ASCO 2015, EORTC 2010, NCCN 2016) including



- G-CSF should be administered prophylactically if the risk of FN is >20% for planned chemotherapy cycles [level of evidence: I, grade of recommendation: A]
- For patients with an intermediate risk (10%–20%), it is important to consider other risk factors
- Primary prophylaxis should be recommended for patients at risk; but secondary prophylaxis is indicated if a dose reduction below threshold or a delay of chemotherapy is not desirable



Les vieux de la vieille, is an adaptation of the novel "The Old Guard" of René Fallet. The movie was directed by Gilles Grangier in 1960.

To resume the theme :

Even if you are older you can love drinking, eating, singing, joking etc...

Someone can be old with fantastic mental & physical conditions

Another one can be young with poor mental & physical conditions

So, it is important to realize an evaluation of the patient before deciding:
"what is good for him"

Myelosuppression and medical cancer treatment (in older patients)

Complications	Cause	Possible Prevention/ Treatment
Myelosuppression	Disease itself Chemotherapy Select forms of targeted therapy (palbociclib, idelalisib, rituximab, ibrutinib, lenalidomide, TKI [chronic myeloid leukemia])	Dose reductions Prophylactic use of myeloid growth factors (cytotoxic chemotherapy alone) Blood transfusions Erythropoiesis-stimulating agents (cytotoxic chemotherapy alone) Platelet transfusions

- La neutropénie fébrile (NF) est associée à :
 - Une morbidité et une mortalité importantes → annexe 1
 - Un coût élevé pour la société
- Pour le patient
 - Hospitalisation, antibiothérapie
 - Retard de traitement (chimiothérapie), diminution de dose
 - Accroissement de la mortalité

Importance de la prophylaxie de la neutropénie fébrile

Utilisation des G-CSF = méthode validée

N.B. :

- le traitement curatif de la NF n'est pas abordé ici (Cf. référentiel)
- la chimiothérapie intensifiée n'est pas abordée ici

CASE ANNA

- Anna is a healthy 68 years old patient with a history of recurrent urinary tract infections. She is diagnosed with G2 ductal invasive « luminal B » ER60 PgR 60 Ki67 25% T1c N1(1/10)MO breast cancer. Adjuvant therapy with docetaxel / cyclophosphamide is planned. What do you suggest?
 1. (li)pegfilgrastim prophylaxis of FN
 2. Filgrastim/lenograstim prophylaxis
 3. Either one combined with a fluoroquinolone
 4. No primary prophylaxis
 5. Other choice

UN DOMAINE MAL EXPLORE:

G-CSF ET ASTHENIE, MUCITE, DIARHEE.....

	Febrile neutropenia	Grade 3–4 asthenia	Grade 3–4 mucositis	Grade 3–4 diarrhoea
NO	23.9%	21.1%	6.4%	6.4%
YES	3.5% ↓	3.5% ↓	2.6% ↓	0.9% ↓

Prophylactic G-CSF

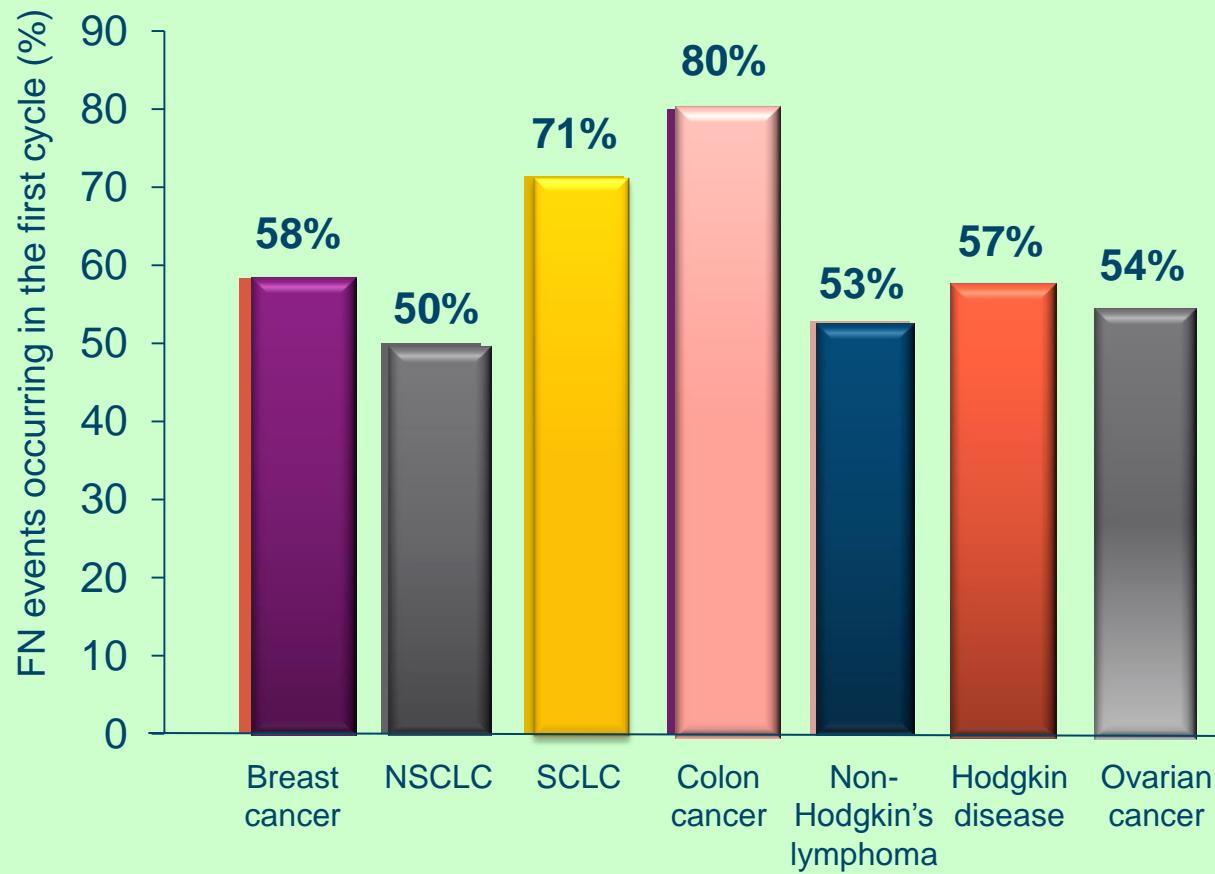
Les types de prophylaxies

Les types de prophylaxies

- Prophylaxie primaire
 - Attitude ayant pour but de diminuer les risques de NF **dès le 1^{er} cycle** de chimiothérapie
- Prophylaxie secondaire
 - Attitude ayant pour but de diminuer les risques de NF après un événement neutropénique (**≥ 2^{ème} cycle** de chimiothérapie)

COMMENT JUSTIFIER UNE “PROPHYLAXIE” SECONDAIRE CHEZ UN PATIENT A RISQUE?

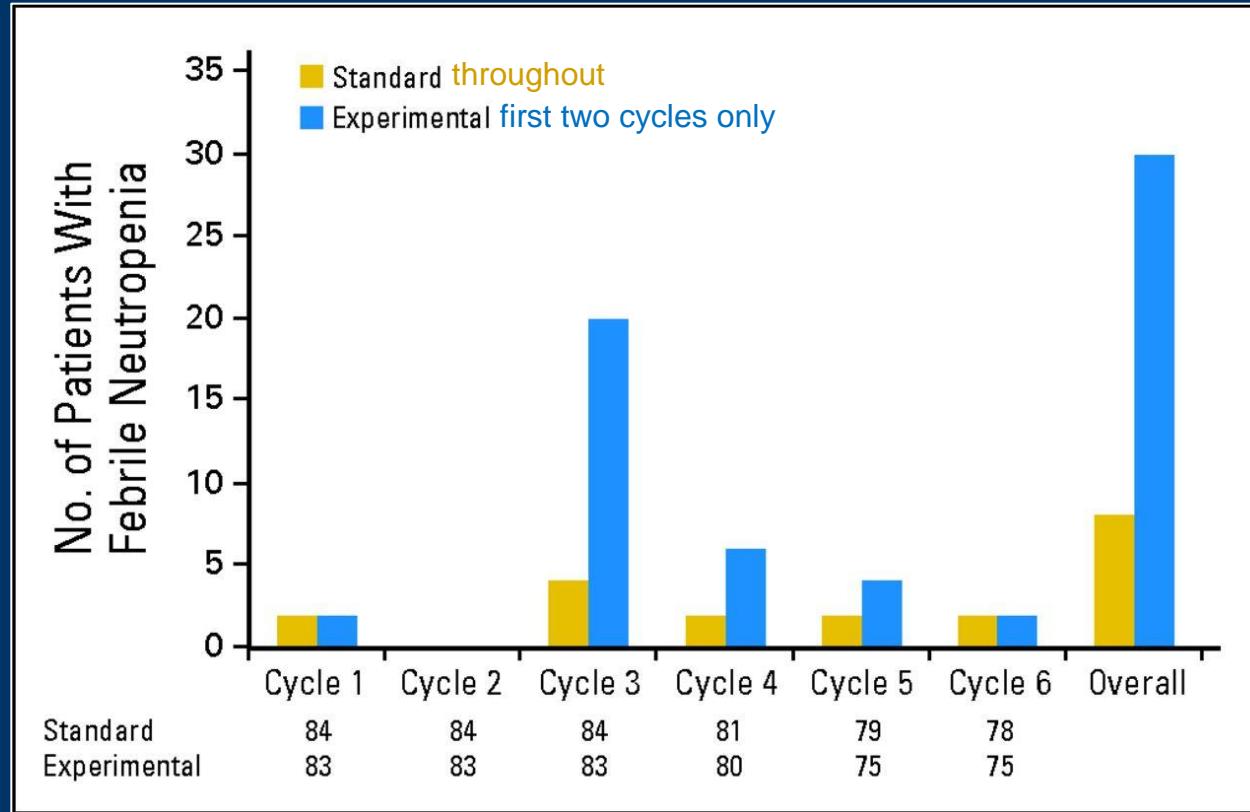
First course : the most difficult





Primary G-CSF prophylaxis in patients with breast cancer at risk of FN

Incidence of febrile neutropenia per treatment arm

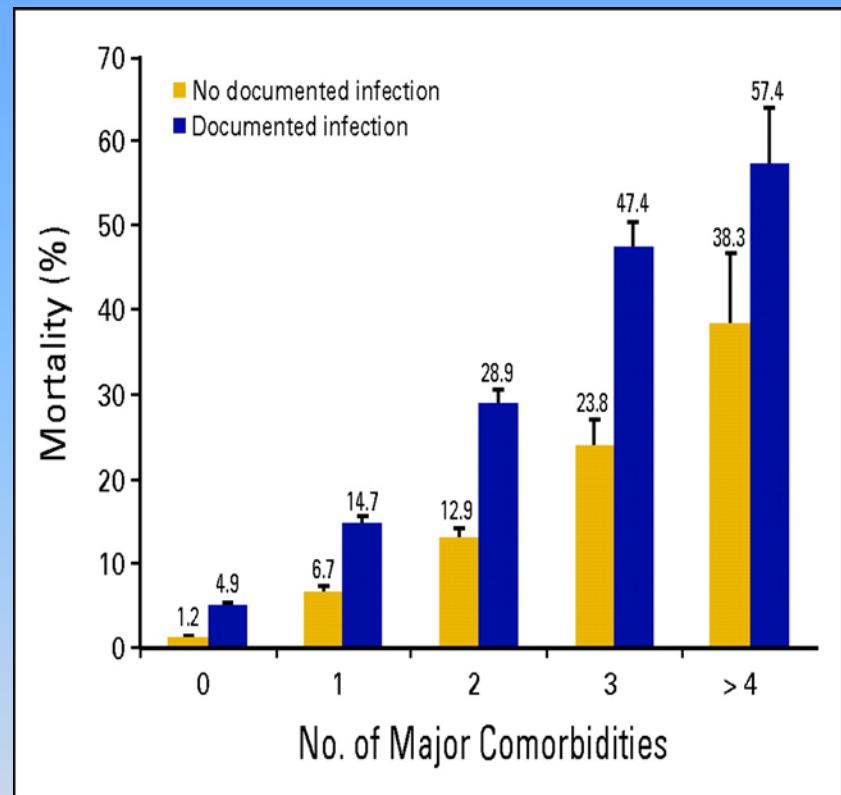


- Primary G-CSF prophylaxis was provided during the first two cycles only or throughout all cycles in patients with breast cancer at risk of FN

G-CSF = granulocyte-colony stimulating factor; FN = febrile neutropenia
Aarts M, et al. *J Clin Oncol* 2013;31:4290–6.

Solid and Nonsolid Tumours: Major Comorbidities and Infections Significantly Increase Mortality

- US retrospective database analysis of cancer patients hospitalised with FN ($n = 41,779$)
 - Solid and nonsolid tumours
- Major comorbid illnesses in addition to cancer and FN were reported in 48.8% of patients
 - In total, 19.1% reported 2 or more major comorbidities



In patients with FN, comorbid conditions and infectious complications were significantly associated with increased mortality

Solid and Nonsolid Tumours: Primary G-CSF Prophylaxis Reduces Mortality

- Systematic review and meta-analysis of 59 RCTs
- Relative risk (RR) with G-CSF support for all-cause mortality across all RCTs was 0.93 (0.90–0.96; $P<.001$)

Relative Risk and Absolute Risk Decrease for All-Cause Mortality with G-CSF vs No G-CSF by Cancer Type

Cancer Type	N	RR	95% CLs	ARD (%)	95% CLs (%)
Breast	20	0.954	0.898, 1.013	-1.5*	-2.9, -0.2
Genitourinary	7	0.946	0.884, 1.013	-4.2*	-7.8, -0.7
Lung	16	0.930**	0.882, 0.980	-5.6***	-8.5, -2.7
Lymphoma	16	0.895***	0.841, 0.952	-4.8***	-7.1, -2.4
Other	2	0.867	0.630, 1.193	-8.3	-18.0, 1.4

CLs, confidence limits; N, number of trials; * $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$.

Lyman GH, et al. *Ann Oncol.* 2013;24:2475-2484.

Les moyens prophylactiques

G-CSF disponibles en France

Formes à injection quotidienne		
Nom Commercial	DCI	Dosages disponibles
Granocyte®	Lénograstim (P)	13 et 34 MUI
Neupogen®	Filgrastim (P)	30 et 48 MUI
Nivestim®	Filgrastim (BS)	12, 30 et 48 MUI
Ratiograstim®	Filgrastim (BS)	30 et 48 MUI
Tevagrastim®	Filgrastim (BS)	30 et 48 MUI
Zarzio®	Filgrastim (BS)	30 et 48 MUI
Forme à injection unique		
Nom commercial	DCI	Dosage disponible
Neulasta®	Pegfilgrastim (P)	6 mg

Si traitement initié avec molécule princeps (P) ou biosimilaire (BS) : poursuivre le traitement avec le même produit pdt la ligne de traitement.

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Nivestim		
Ratiogran		
Tevagrasfim	Filgrastim (BS)	30 et 48 MUI
Zarzio®	Filgrastim (BS)	30 et 48 MUI

Et le lipegfilgrastim?....

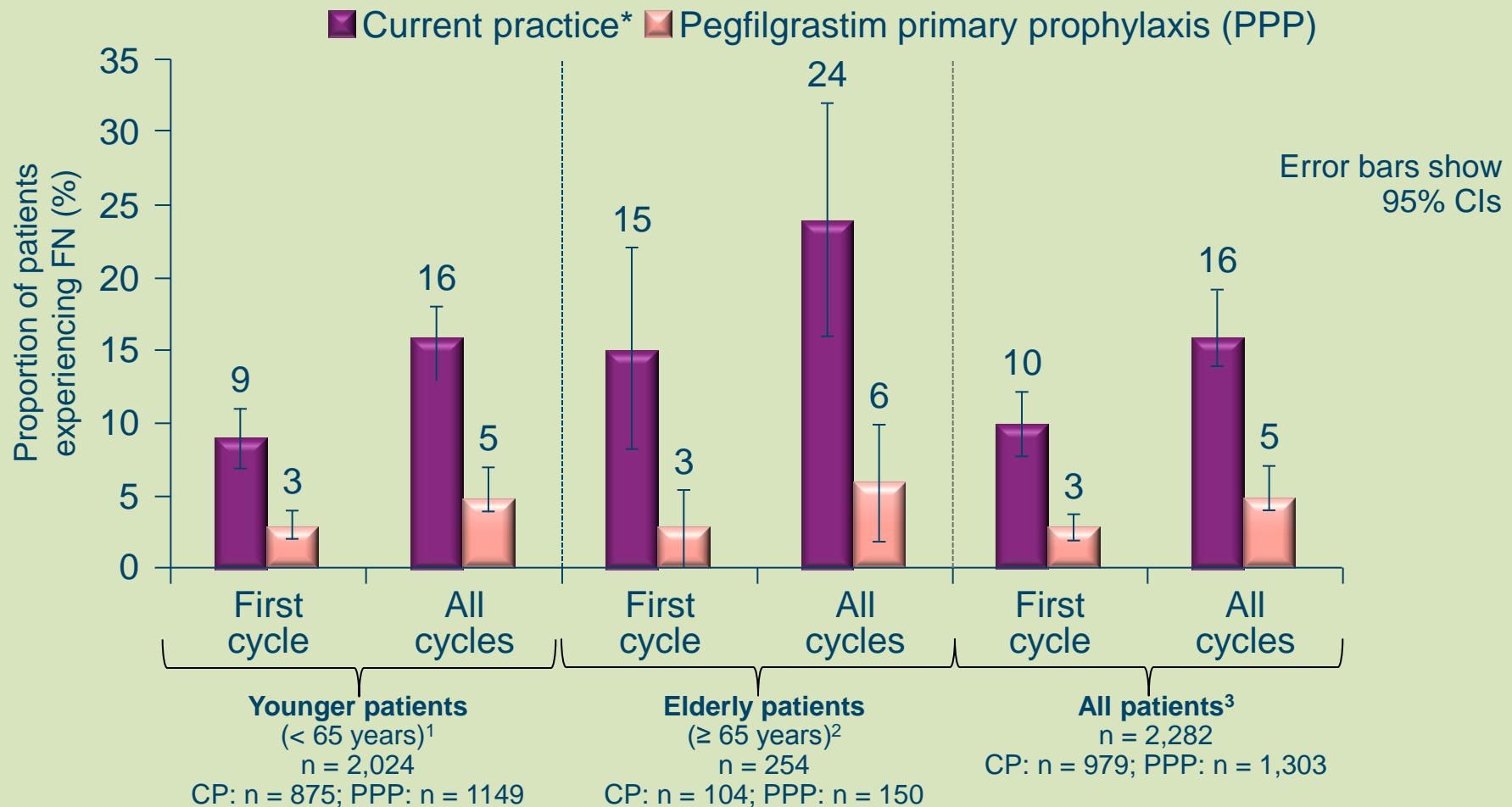
Forme à injection unique

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LES G-CSFs
SONT-ILS TOUS LES MÊMES?

Short acting G-CSF versus long acting...



*Current practice neutropenia management = any current strategy, including no G-CSF, or daily G-CSF or pegfilgrastim in any cycle

Adapted from: ¹Schwenkglenks et al. EJC Supplements 2008;6:68(Abstract); ²Aapro M, et al. Crit Rev Oncol Hematol. 2010;74:203–10;

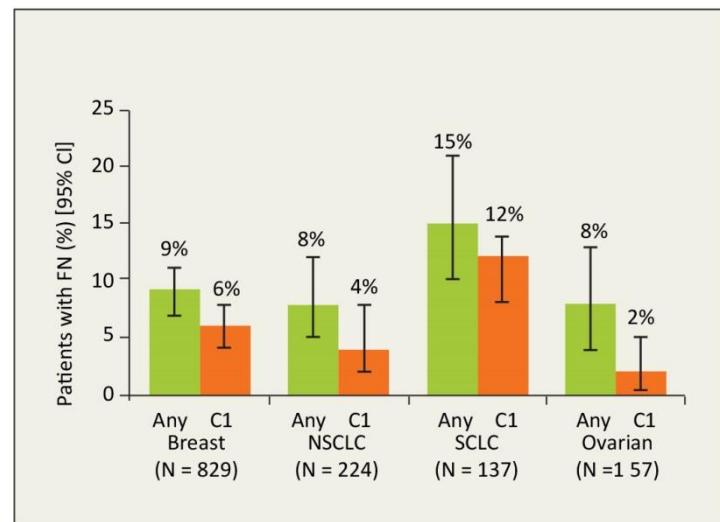
³von Minckwitz G, et al. Eur J Cancer. 2009;45:608–17.

MAIS....
QUE FONT LES CANCEROLOGUES

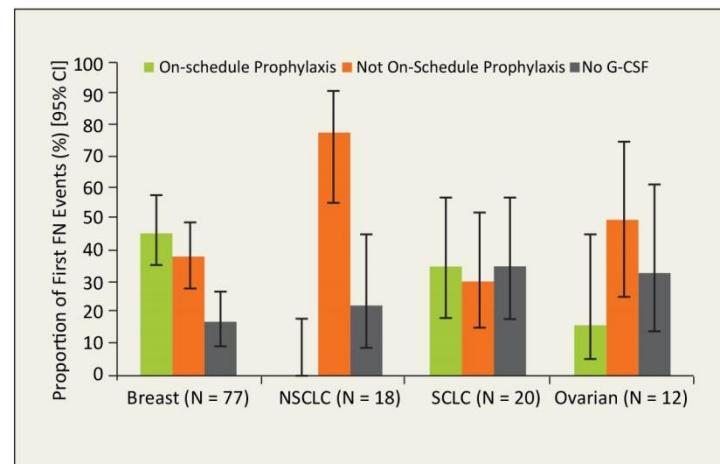
SOLID TUMOURS: ADHERENCE TO CLINICAL GUIDELINES IS POOR AND PATIENTS ARE UNDERTREATED WITH G-CSF

- Patients with breast cancer, NSCLC, SCLC, or ovarian cancer receiving chemotherapy regimens with high ($\geq 20\%$) risk of FN (n = 1,347)
 - Multicentre, international, observational study; majority were public or university hospitals
- FN occurred in 127 patients overall; incidence was highest in SCLC
 - G-CSF was either pegfilgrastim or a daily G-CSF
 - Pegfilgrastim was the most commonly prescribed G-CSF in patients given PP, administered to 82% of patients receiving PP
 - Daily G-CSF was given to 16% of patients who received PP
- **45%–80% of all patients did not receive G-CSF PP according to recommendations**

Incidence of FN in Cycles 1-8 (Any) and in Cycle 1 (C1)



G-CSF Use at the Time of the First FN Event

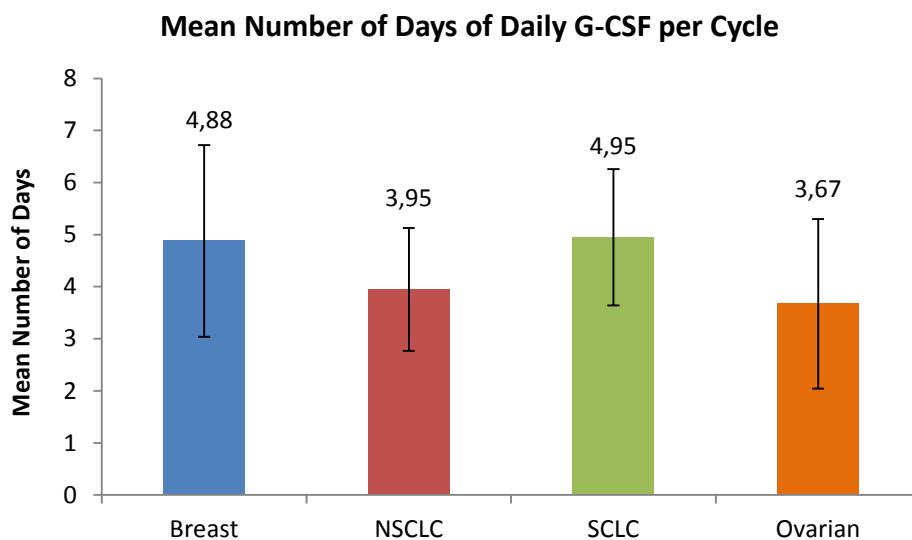


PP, primary prophylaxis.

Krzemieniecki K, et al. *Support Care Cancer*. 2014;22(3):667-677.

SOLID TUMOURS: ADHERENCE TO CLINICAL GUIDELINES IS POOR AND PATIENTS ARE UNDERTREATED WITH G-CSF

- In breast cancer, pegfilgrastim PP was maintained for a greater number of continuous cycles than daily G-CSF PP
 - Pegfilgrastim PP was maintained until the fourth cycle in 95% of patients and until the sixth cycle in 89% of patients
 - Daily G-CSF PP was maintained until the fourth cycle in 62% of patients and until the sixth cycle in 56% of patients
- Post-hoc analysis: 39% of the 127 patients who experienced FN were not given on-schedule G-CSF prophylaxis in the cycle after the first FN event occurred



FN risk assessment was predominantly based on clinical judgment and individual risk factors; guidelines for patients at high FN risk were not consistently followed



And on the other side of the ocean?

- Only **17%** of patients treated with high-risk CT regimens received CSFs, compared with 18% and 10% of patients treated with intermediate- (10%-20% risk of FN) and low-risk (<10% risk of FN) CT regimens, respectively
- Overall, **96%** of CSFs were administered in scenarios where CSF therapy is not recommended by evidence-based guidelines

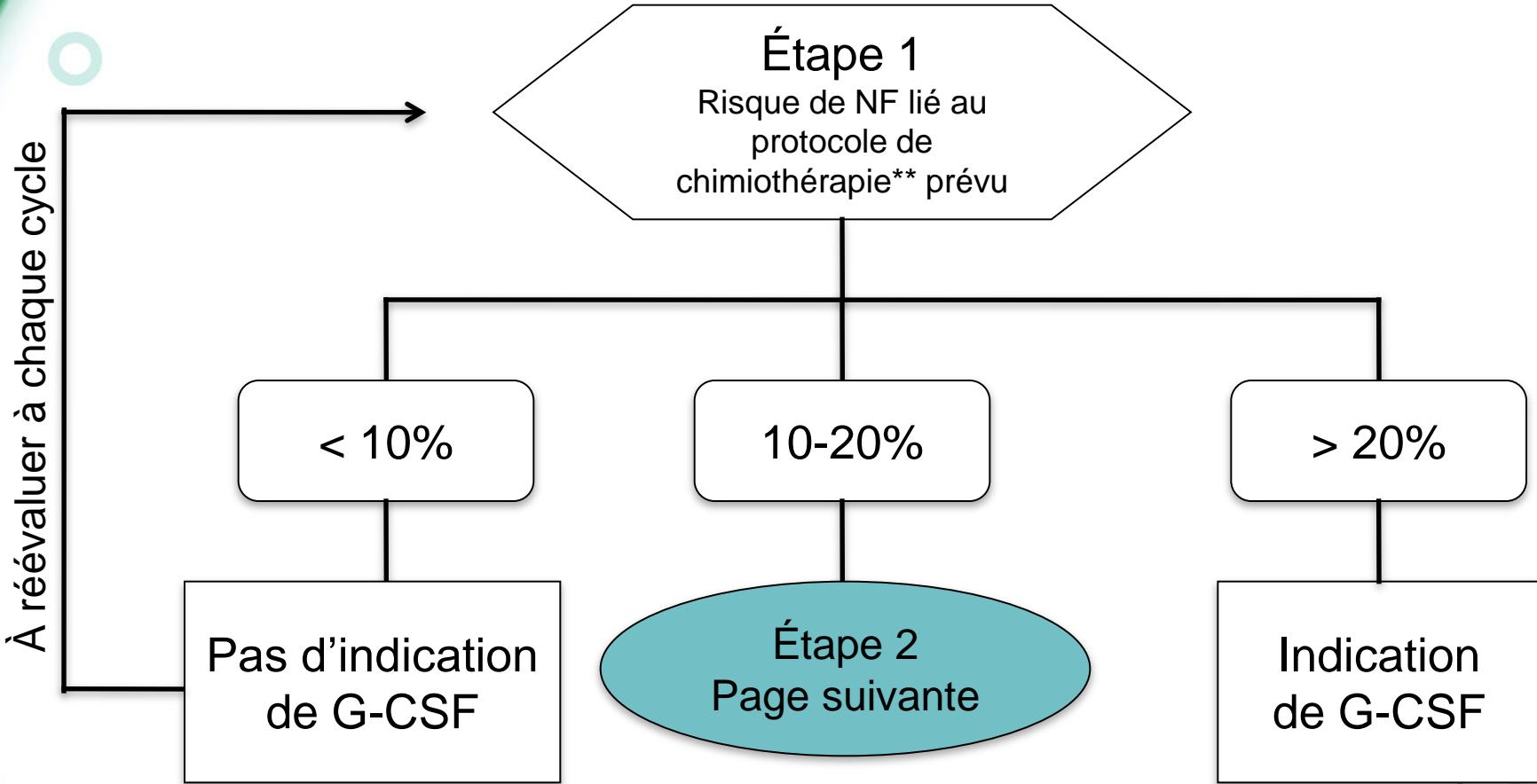
ASCO TOP FIVE

- Avoid administering colony stimulating factors (CSFs) to patients undergoing chemotherapy who have less than a 20 percent risk for febrile neutropenia ASCO guidelines recommend these treatments only when the risk of febrile neutropenia from chemotherapy is greater than 20 percent and when effective alternatives to high risk therapy are unavailable. However, some exceptions exist, such as for patients at higher risk for chemotherapy-related febrile neutropenia because of other complications (including age, medical history, or disease characteristics).

Mise en œuvre des G-CSF

**Prophylaxie Primaire
Prophylaxie secondaire**

Quelle que soit l'indication : curatif ou palliatif :
Néo-adjuvant, adjuvant ou métastatique*



* : Si palliatif, faire le choix (si possible) d'un traitement non neutropéniant`

** : liste des protocoles : NCCN ou EORTC ou ASCO (liens en annexe 2 p36)

Étape 2

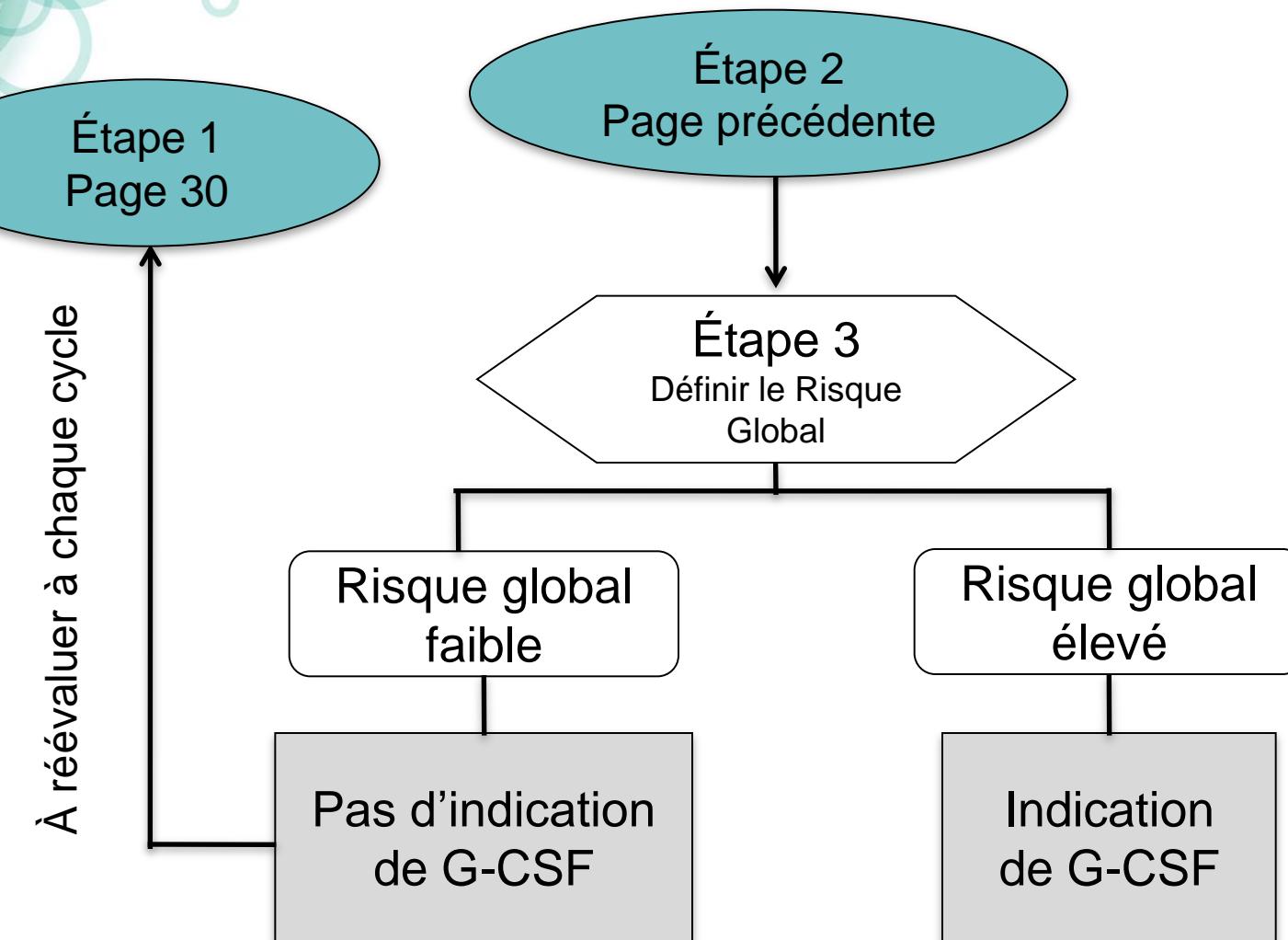
Facteurs de risques individuels de NF ?

Évaluation des facteurs ↗ risque de NF

Risque important	Age > 65 ans
Qui ↗ le risque	Maladie avancée
	Antécédent de NF
	Ni ATB, ni G-CSF
Autres facteurs	Karnofsky bas et/ou dénutrition
	Sexe féminin
	Insuffisance hépatique, rénale
	Maladie cardiovasculaire
	Hb < 12 g/dl

Étape 3
page suivante

Prophylaxie Primaire



CONCLUSIONS en BLANC

LE REFERENTIEL AFSOS DEVRAIT PERMETTRE
UN EMPLOI RATIONNEL DES G-CSF
et UNE MEILLEURE PREVENTION DE LA NF

S'IL ETAIT APPLIQUE...

COMME TOUT REFERENTIEL IL DEMANDE A ETRE REVU
ET CORRIGE REGULIEREMENT
...comme pour les rouges...

Supportive Care:

Updates on Anemia Management



DR. MATTI S. AAPRO

Dean, Genolier Cancer Center,
Switzerland

Member European Society for Medical Oncology (ESMO) Supportive Care Faculty
Past President of the Multinational Association for Supportive Care in Cancer (MASCC)
And Honorary President of AFSOS
(French-speaking Association for Supportive Care)
And Consultant to JASCC (Japanese Association for Supportive Care in Cancer)



Disclosures



Collaborations in this field: Teva, Sandoz, Celgene, Roche, Novartis, JnJ, Hospira/pfizer, Amgen, DRL, Pierre Fabre



**2017 VERSION OF THESE GUIDELINES
SHOULD BE AVAILABLE SOON. THERE WILL
BE NO FUNDAMENTAL CHANGE**

Erythropoiesis-Stimulating Agents in the
Treatment of Anaemia in Cancer Patients:



European Society for Medical Oncology

Clinical Practice Guidelines

for Use

Anémie et cancer

Date : 26/03/2012

Anemia in the Elderly

- Anemia in the elderly has been properly defined as the silent epidemic, representing 3 millions people in the United States aged 65 years and older.
- Anemia is associated with reduced survival, increased risk of functional dependence and hospitalization, increased risk of congestive heart failure and renal disease and cognitive disorders.
- Approximately 70 percent of anemia in older individuals is reversible.
- 2/3 of anemia in the elderly can be attributed to 2 major causes:
 - Nutritional deficiencies
 - Anemia of chronic disease

Lodovico Balducci, Springer-Verlag New York Inc 2008

K. G. Prakash Sch. J. App. Med. Sci., 2015; 3(3C):1266-1270

Lodovico Balducci, Springer-Verlag New York Inc 2008

Guidelines for the Treatment of Anemia in Patients With Cancer

- Additional causes of anemia should be corrected prior to erythropoietic protein therapy....

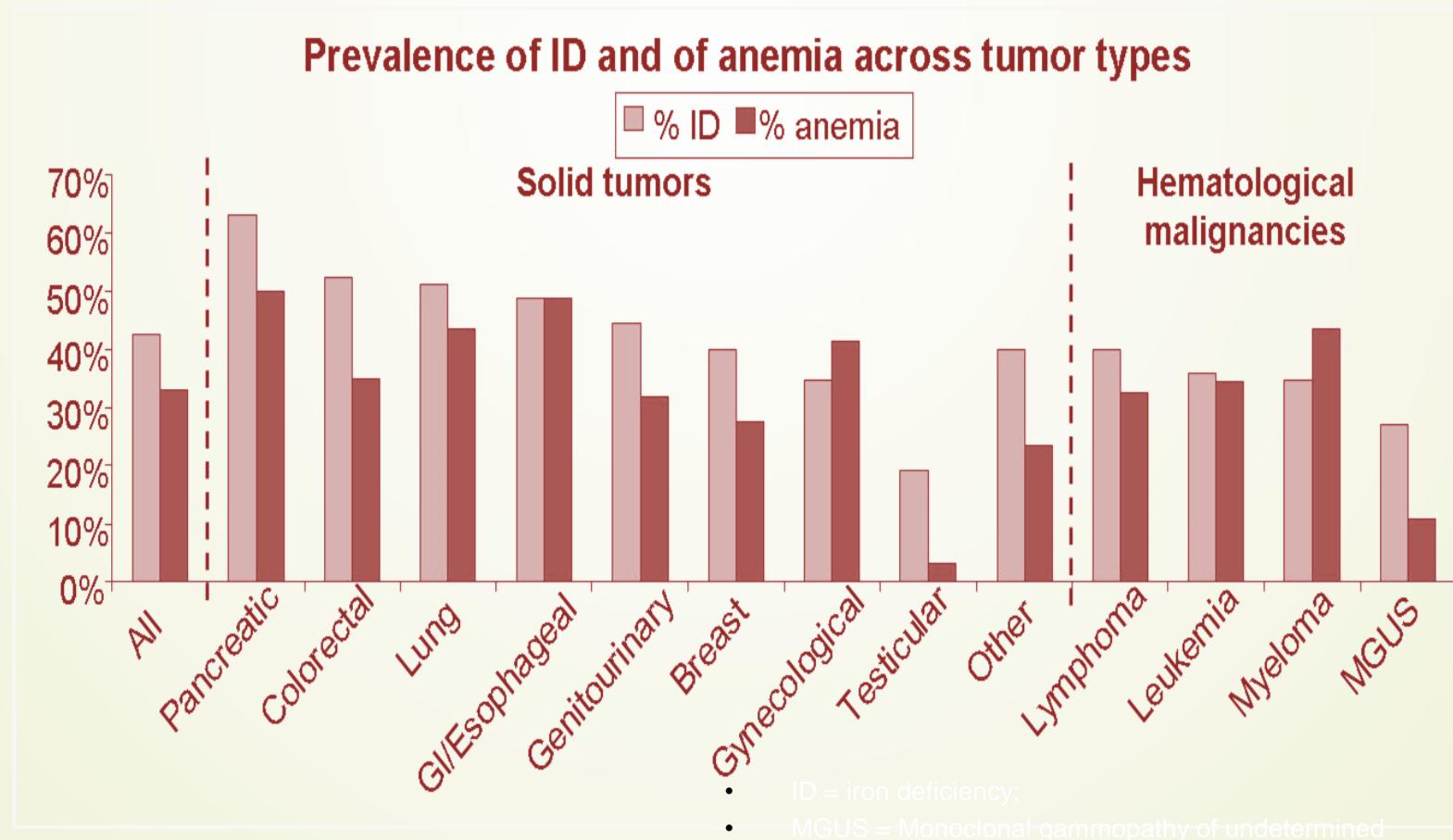
- Schrijvers D, et al. Ann Oncol. 2010;21(suppl 5):v244-v247.
- Aapro et al new ESMO guidelines in preparation.

Guidelines for the Treatment of Anemia in Patients With Cancer

- Additional causes of anemia should be corrected prior to erythropoietic protein therapy
- iron deficiency (absolute or functional), bleeding, vitamin B12 or folate deficiency, nutritional defects or hemolysis

- Schrijvers D, et al. Ann Oncol. 2010;21(suppl 5):v244-v247.
- Aapro et al new ESMO guidelines in preparation.

Prevalence of Iron Deficiency and Anemia in 1513 Consecutive Patients Seen at a Cancer Center



- Ludwig H, et al. Ann Oncol. 2013;24:1886-1892.

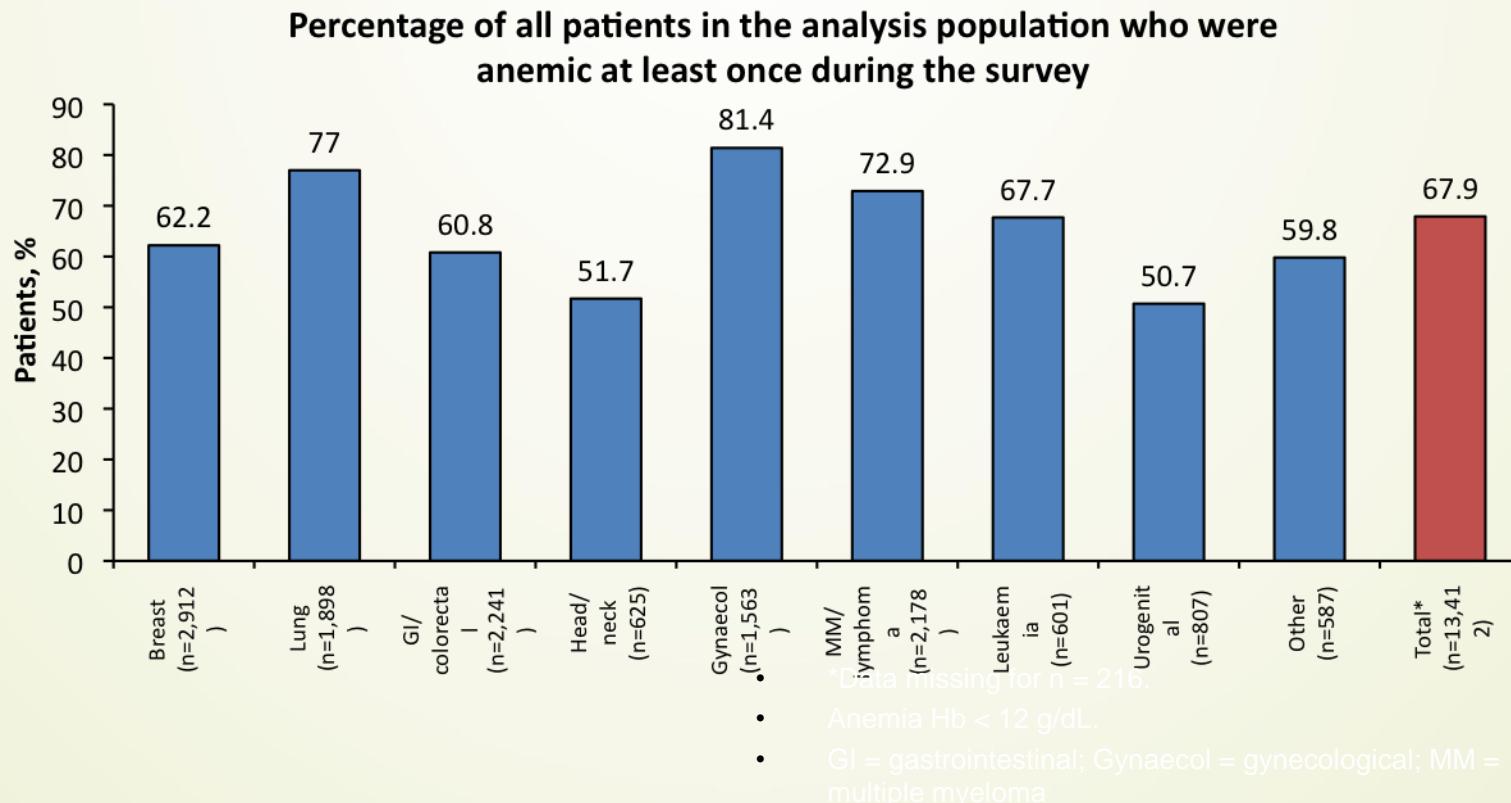
Why Does Anemia Need to Be Treated?

- Anemia is associated with poor prognosis in patients with cancer¹
- The ability to complete chemotherapy regimens on time and with full dose might be compromised²
- A significant association ($P<.001$) between chemotherapy dose delays/reductions and anemia has been observed²
- Low Hb levels affect patients' quality of life (QOL)³

- Caro JJ, et al. Cancer. 2001;91:2214-2221.
- Repetto L, et al. Crit Rev Oncol Hematol. 2009;72:170-179.
- Ludwig H, et al. Eur J Cancer. 2004;40:2293-2306.

Anemia is Very Common in Patients with Cancer

- Data from the European Cancer Anemia Survey (ECAS)
 - Total of 15,367 patients enrolled; analysis population = 13,628



- Ludwig H, et al. Eur J Cancer. 2004;40:2293-2306.

ESAs: Therapy Objectives

- The aim is to . . .
 - Prevent RBC transfusions and their possible complications
 - Iron overload
 - Transmission of infection
 - Immune suppression related to transfusions
- And improve HRQOL

. . . by increasing the Hb level

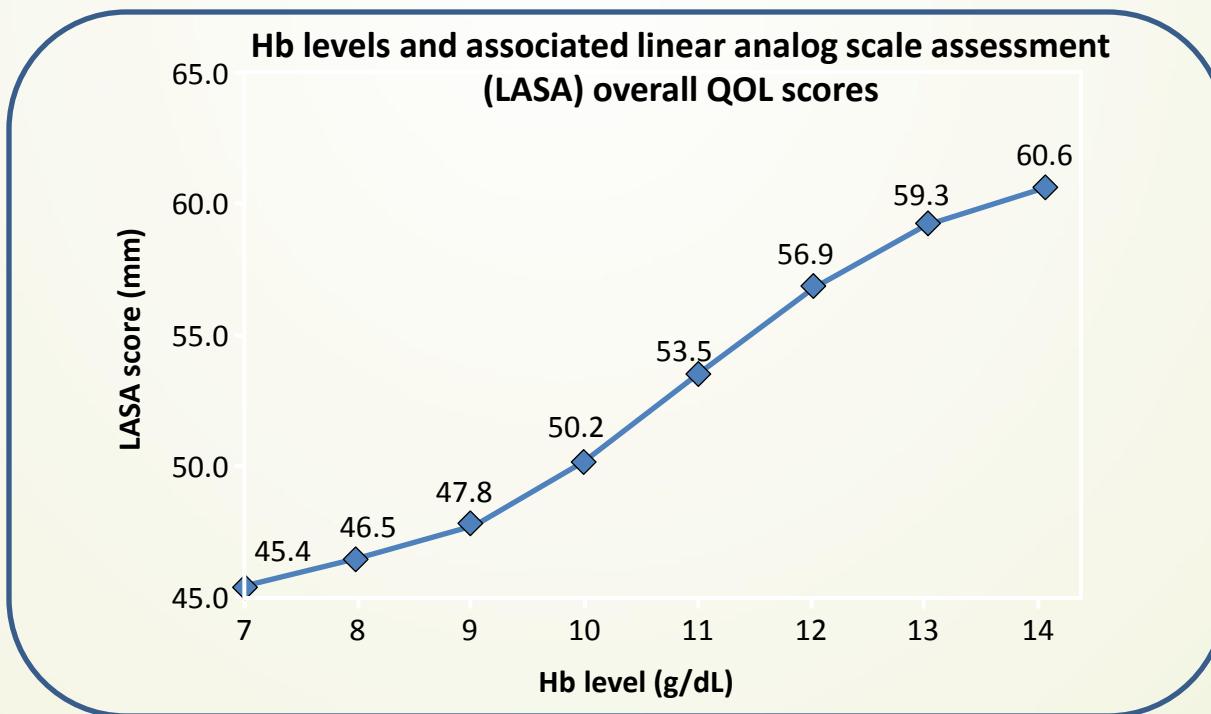
- HRQOL = health-related quality of life; RBC = red blood cell
- Schrijvers D, et al. Ann Oncol. 2010;21(suppl 5):v244-v247.

Impact of Erythropoietin or Darbepoetin on Quality of Life

- Overall, there is a statistically significant difference between patients treated with ESAs and controls when combining QOL parameters and fatigue- and anemia-related symptoms, which is however, most likely not clinically important.
- Tonia T, et al. Cochrane Database Syst Rev. 2012;12:CD003407.

Relationship Between Hb Level and QOL

- US open-label, community-based trial of epoetin alfa therapy in anemic cancer patients receiving chemotherapy (N = 2352)



A direct relationship exists between Hb increases and corresponding QOL improvements in cancer patients receiving chemotherapy across the clinically relevant Hb range of 8-14 g/dL

- Crawford J, et al. Cancer. 2002;95:888-895.

Keypad Question



Before treating anaemia you obviously want to have a diagnosis...so in a patient with Hb of 9.5 you order...

1. Iron status
2. B12 and folates
3. Reticulocytes, LDH, possibly haptoglobin and a Coombs
4. All 3
5. 1 and 2 and sometimes 3
6. Completely different tests

Guidelines for the Treatment of Anemia in Patients With Cancer

- Additional causes of anemia should be corrected prior to erythropoietic protein therapy
- iron deficiency (absolute or functional), bleeding, vitamin B12 or folate deficiency, nutritional defects or hemolysis

- Schrijvers D, et al. Ann Oncol. 2010;21(suppl 5):v244-v247.
- Aapro et al new ESMO guidelines in preparation.

From ESMO 2010 Guidelines



- The European Medicines Agency (EMEA) labels the use of ESAs as follows:
- In patients treated with chemotherapy and an Hb level of ≤ 10 g/dL, treatment with ESAs might be considered to increase Hb to ≤ 12 g/dL or to prevent further decline in Hb [II, A]
- **In patients treated with curative intent, ESAs should be used with caution [D]**
- Treatment recommendations according to label can be followed if there is no suspicion of functional iron deficiency (ferritin > 100 ng/mL and TFS saturation $< 20\%$)
 - TFS = transferring saturation
- Schrijvers D, et al. Ann Oncol. 2010;21(suppl 5):v244-v247.

Guidelines for the Treatment of Anemia in Patients With Cancer

Prevalence and Management of Cancer-Related Anaemia, Iron Deficiency and the Specific Role of IV Iron¹

Epidemiological and Nonclinical Studies Investigating Effects of Iron in Carcinogenesis— A Critical Review²

- Aapro M, et al. Ann Oncol. 2012;23:1954-1962.
- Beguin Y, et al. Crit Rev Oncol Hematol. 2014;89:1-15.

Risks and Benefits of RBC Transfusions

RBC Transfusions	
Risks	<ul style="list-style-type: none">■ Transfusion reactions (eg, hemolytic, febrile, nonhemolytic, lung injury)■ Transfusion-associated circulatory overload■ Virus transmission (eg, hepatitis, HIV)■ Bacterial contamination■ Iron overload■ <i>Increased thrombotic events</i>■ <i>Possible decreased survival</i>
Benefits	<ul style="list-style-type: none">■ Rapid increase in Hb and hematocrit levels■ Rapid improvement in anemia-related symptoms

- NCCN Clinical Practice Guidelines in Oncology. Cancer- and chemotherapy-induced anemia. Version 2. 2015.

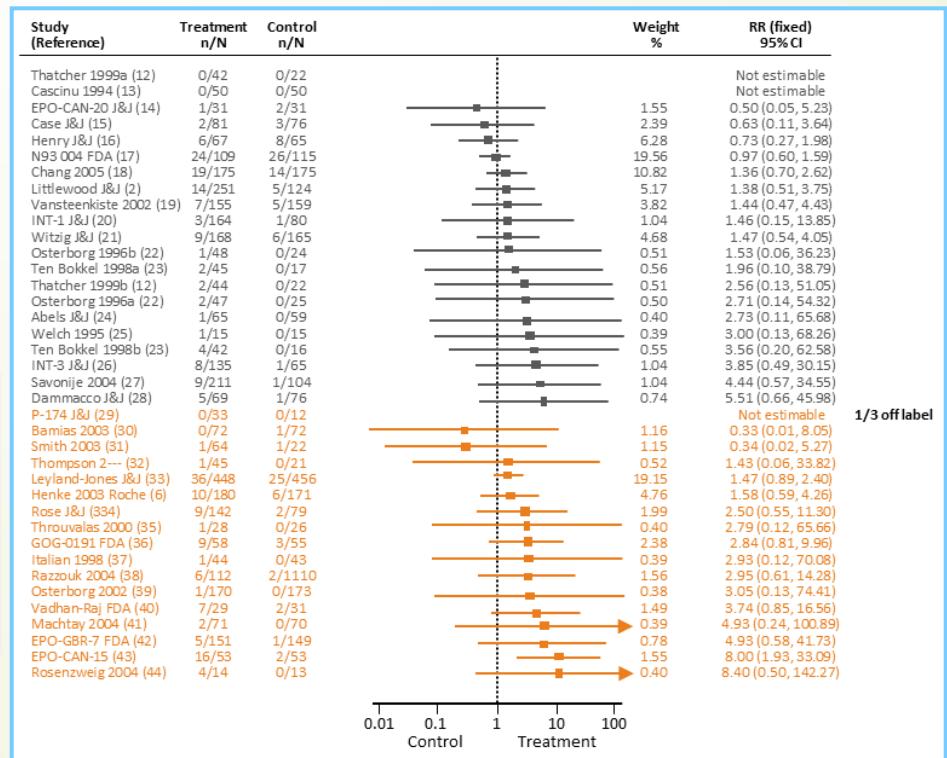
• REMS = risk evaluation
and mitigation strategy

Safety of ESAs

Thromboembolic Events

- VTEs are frequent in patients with cancer because of the effects of malignant disease, its treatment and associated comorbidities, and TRANSFUSIONS¹

Forest plot analysis of RR for thromboembolic complications in patients with cancer receiving ESAs or standard care¹



CI = confidence interval; RR = relative risk; VTE = venous thromboembolic event

- Dicato M. Oncologist. 2008;13(suppl 3):11-15.
- Tonia T, et al. Cochrane Database Syst Rev. 2012;12:CD003407.

NO ACTIVE RECEPTORS NO TUMOR PROGRESSION IN CIA PATIENTS

Effects of Erythropoietin Receptors and
Erythropoiesis-Stimulating Agents on Disease
Progression in Cancer

Keypad Question

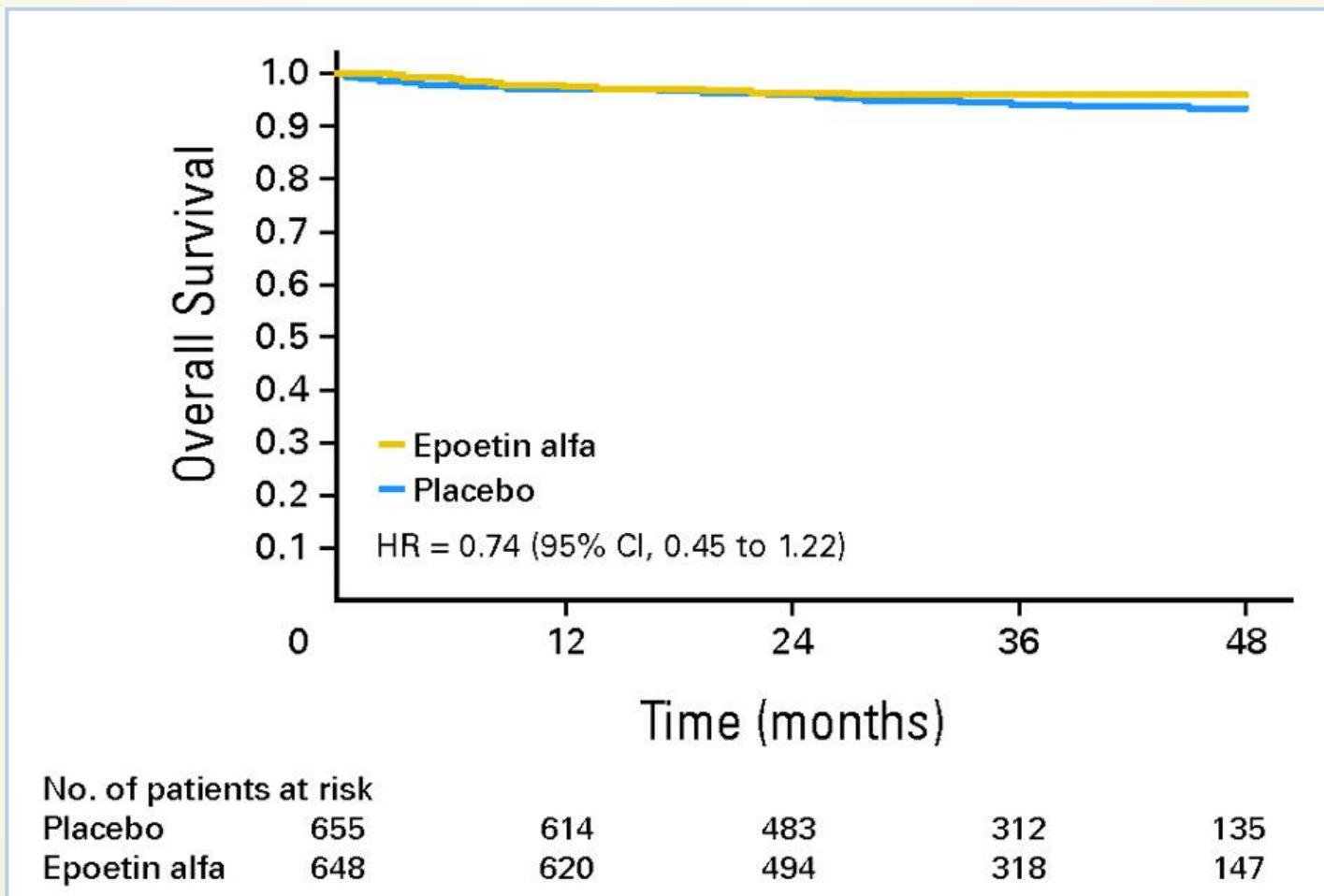


DO YOU HAVE CONCERNS ABOUT CURATIVE
TREATMENT IN ONCOLOGY and USE OF ESAs?

1. YES
2. NO
3. I have not seen the final publication of key studies

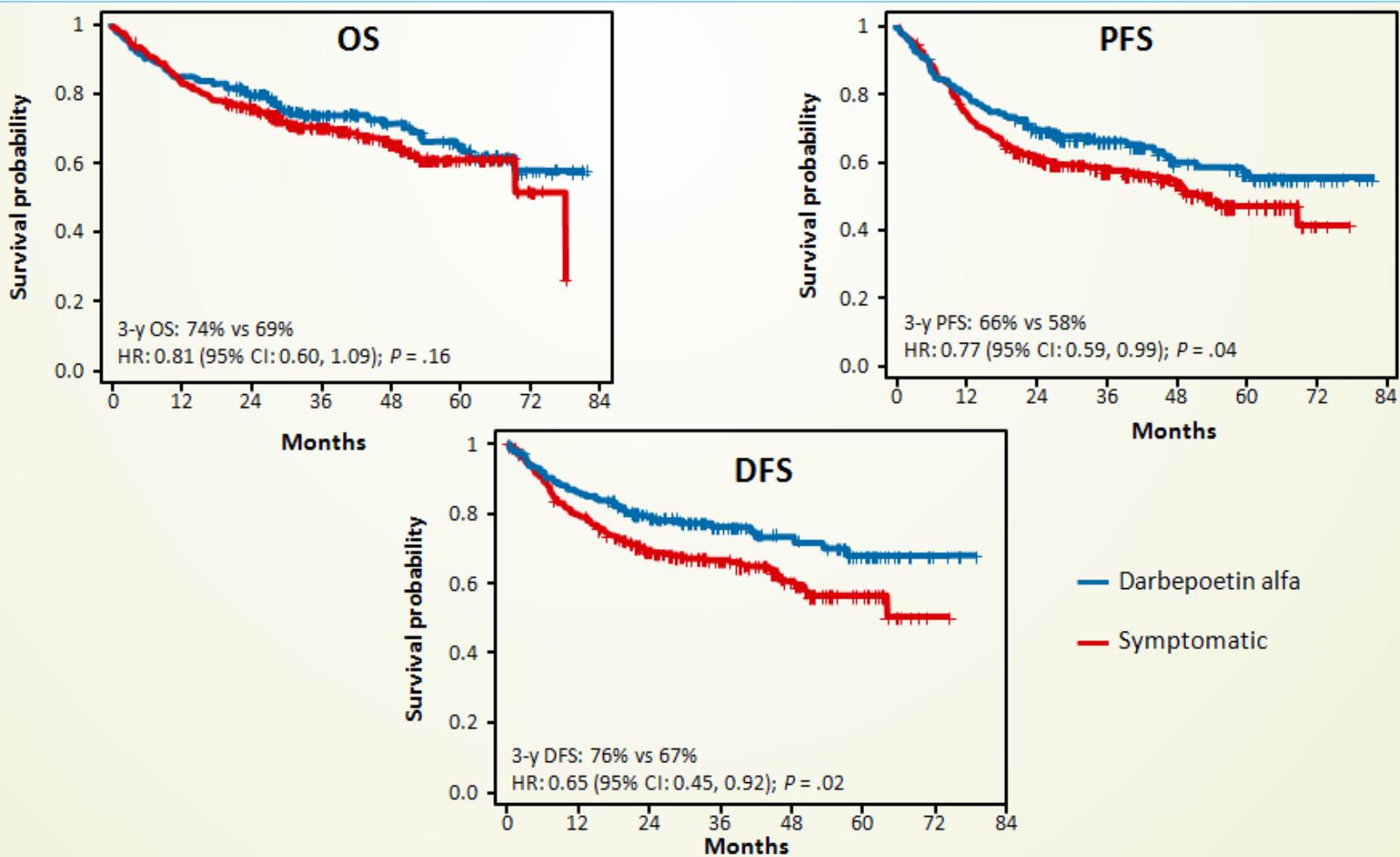
Hodgkin's Disease

GHSG HD15-EPO Trial: OS



- Engert A, et al. J Clin Oncol. 2010;28:2239-2245.

LNH03-6B Study: Erythropoietins in Patients With Diffuse Large B-Cell Lymphoma



- Delarue R, et al. J Clin Oncol. 2011;29(suppl):Abstract 9048 and Poster.

Safety and Efficacy Outcomes With Erythropoiesis-Stimulating Agents in Patients With Breast Cancer: A Meta-analysis

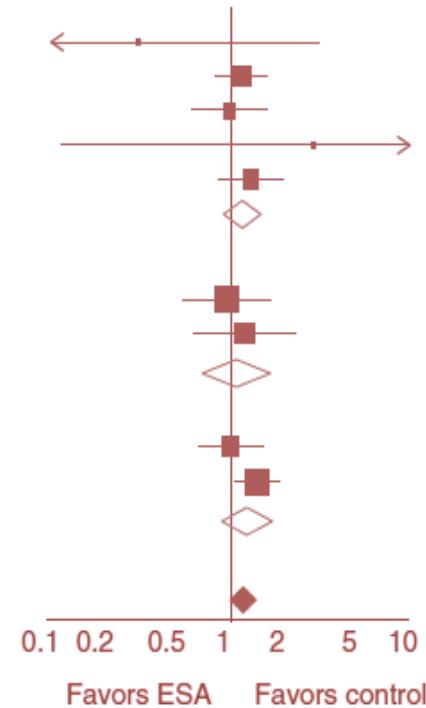
Aapro M, et al. Ann Oncol. 2015;26:688-695.

Survival

B Stratified analysis

Category	Study name	95% CI		
		Odds ratio	Lower limit	Upper limit
Adjuvant / Neoadjuvant	Del Mastro 1997	0.31	0.03	3.17
	Moebus 2012	1.17	0.84	1.63
	Nitz 2013	1.00	0.62	1.62
	O'Shaughnessy 2005	2.94	0.12	73.93
	Untch 2008	1.33	0.88	2.00
Adjuvant /Neoadjuvant: Random effect model		1.17	0.93	1.46
Mixed Therapy Stages	Chang 2005	0.97	0.55	1.73
	Pronzato 2002	1.23	0.63	2.39
	Mixed Therapy Stages: Random effect model	1.07	0.69	1.66
Metastatic	Aapro 2008	1.02	0.67	1.53
	Leyland-Jones 2005	1.42	1.07	1.90
Metastatic Tumors: Random effects model		1.24	0.90	1.72
Overall		1.17	0.99	1.39

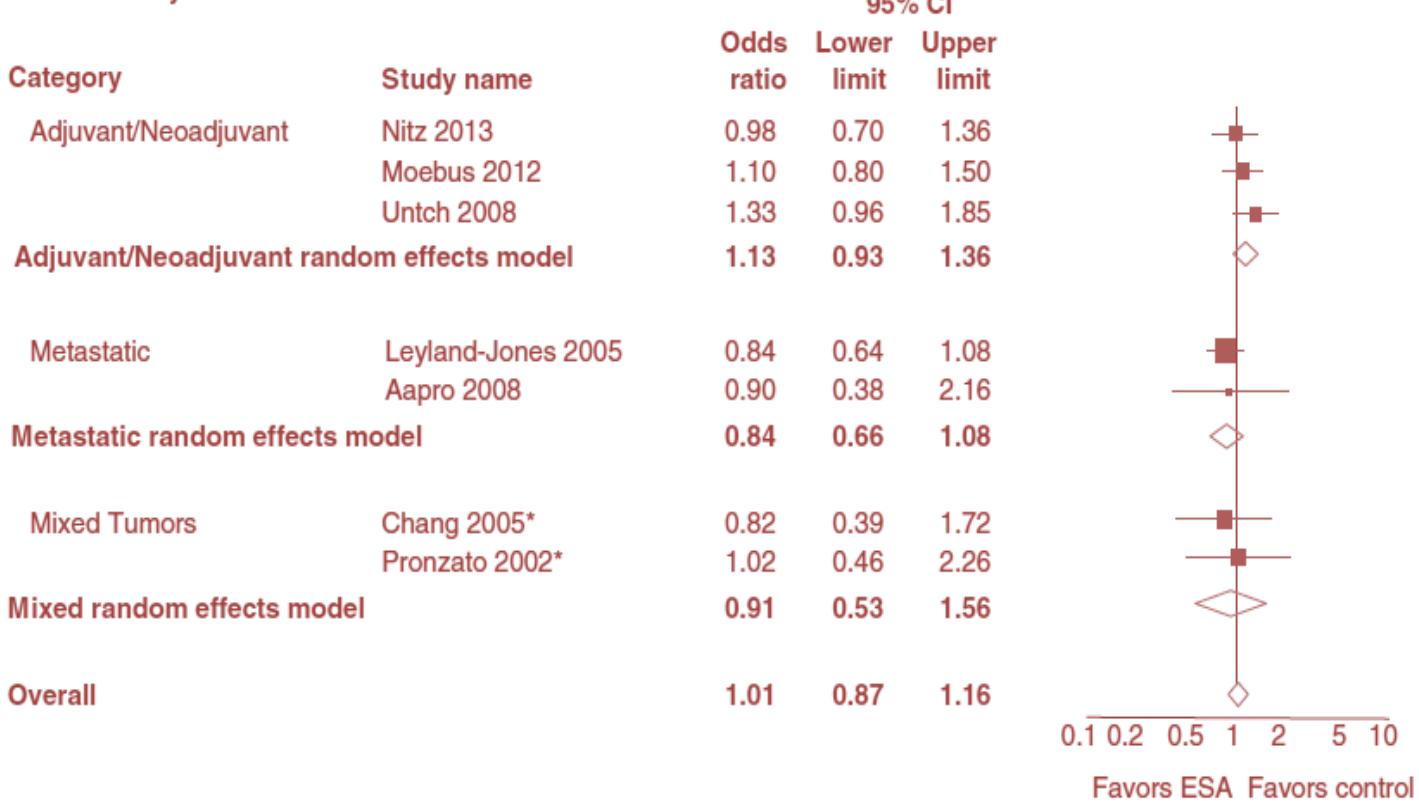
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- Aapro M, et al. Ann Oncol. 2015;26:688-695.

Disease Progression

B Stratified analysis



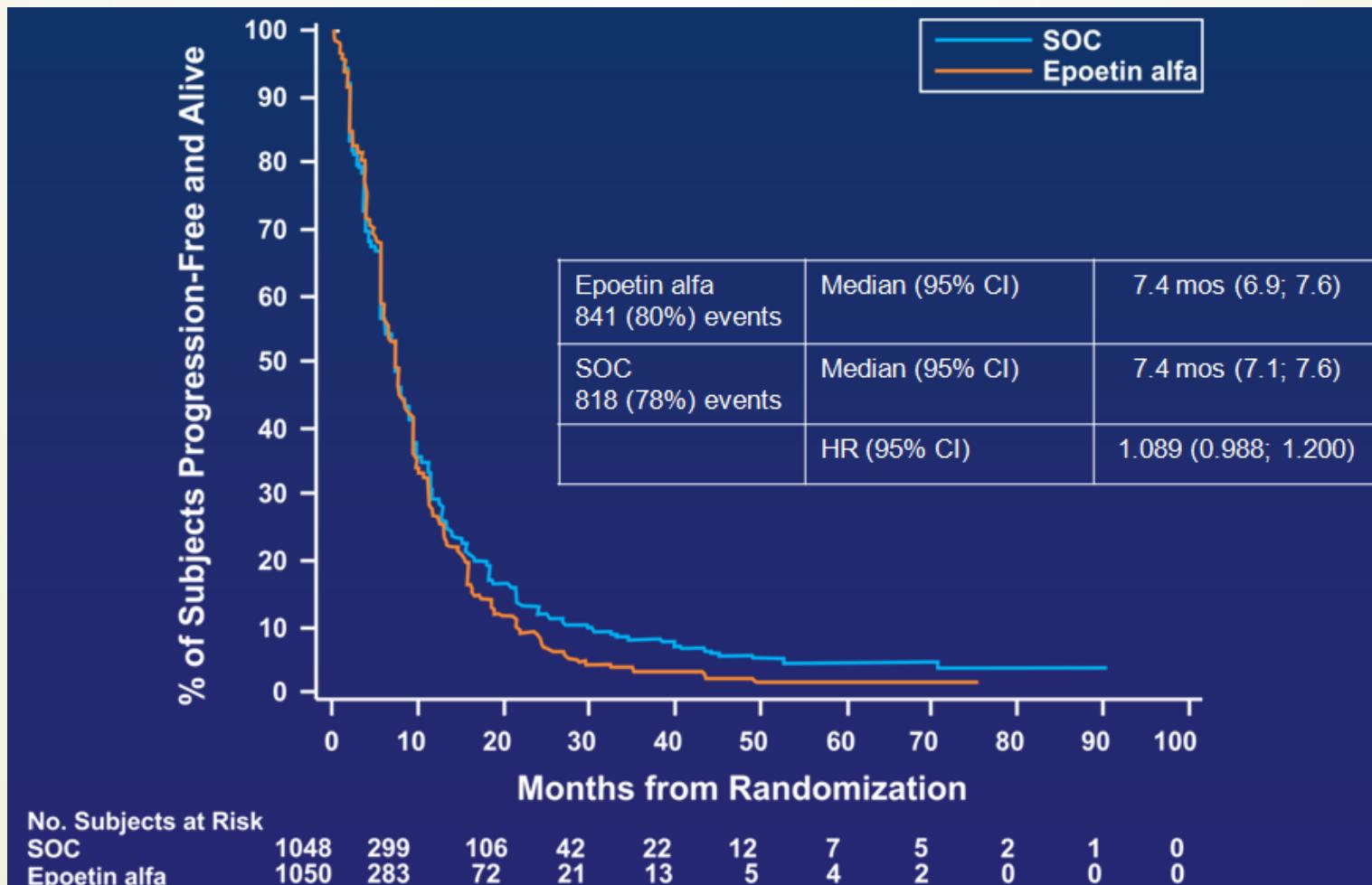
- Aapro M, et al. Ann Oncol. 2015;26:688-695.

A randomized, phase 3 study of epoetin alfa plus standard supportive care versus standard supportive care in anemic patients with metastatic breast cancer receiving standard chemotherapy

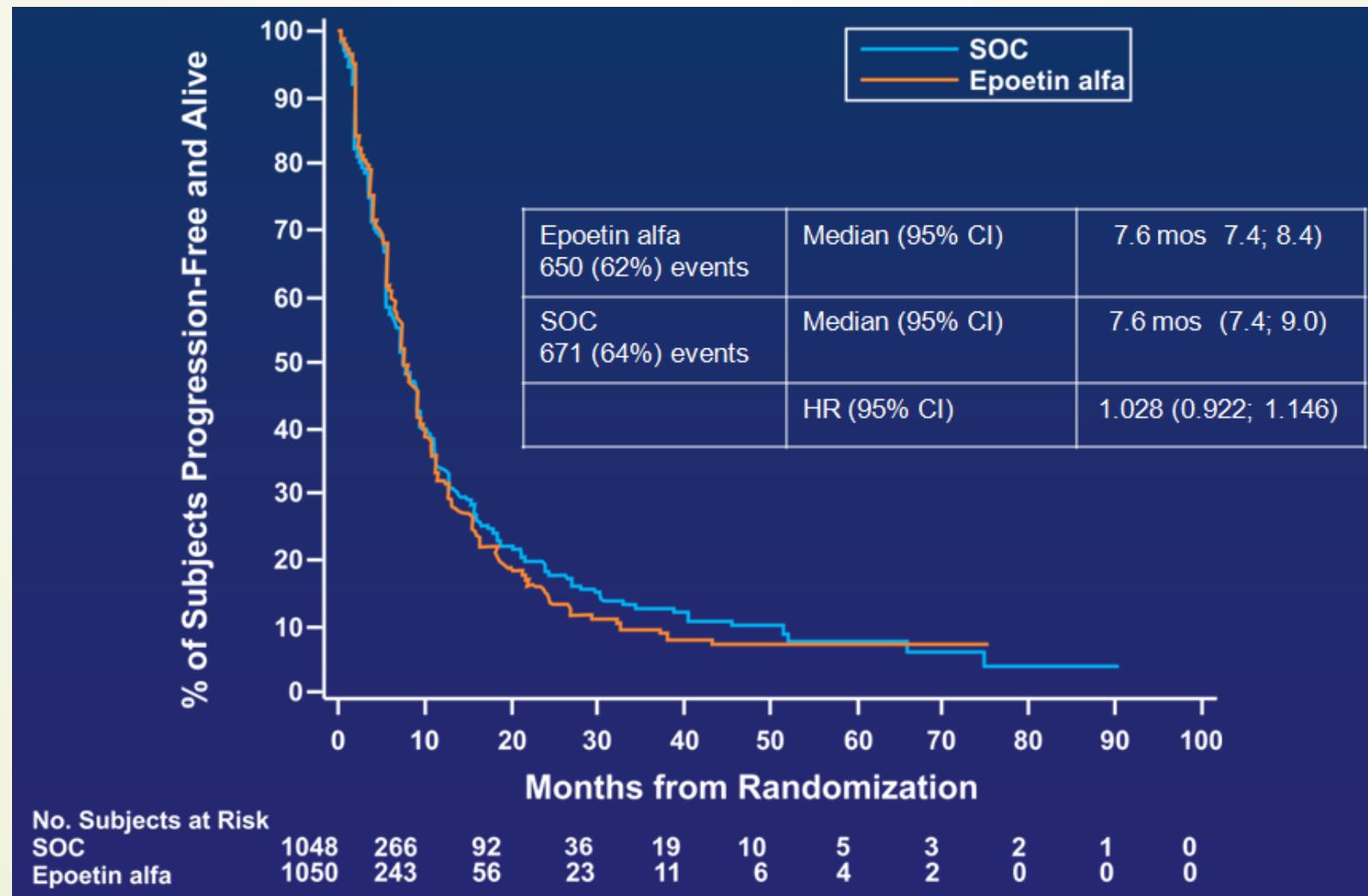
1Brian Leyland-Jones, 2Igor Bondarenko, 3Gia Nemsadze, 4Vitaliy Smirnov, 5Iryna Litvin, 6Irakli Kokhreidze, 7Lia Abshilava, 8Mikheil Janjalia, 9Rubi Li, 10KC Lakshmaiah, 11Beka Samkharadze, 12Oksana Tarasova, 13Ranjan Kumar Mohapatra, 14Yaroslav Sparyk, 15Sergey Polenkov, 16Vladimir Vladimirov, 17Liang Xiu, 17Bruce Kimelblatt, 17Kris DePrince, 17Ilya Safonov, 17Els Vercammen, 17Peter Bowers for the EPO-ANE-3010 trial investigators

1Avera Cancer Institute, Sioux Falls, SD; 2Dnepropetrovsk Medical Academy, Dnepropetrovsk, Ukraine; 3Institute of Clinical Oncology (LTD. K. Madichi Mammological Center), Tbilisi, Georgia; 4Donetsk Regional Anticancer Center, Donetsk, Ukraine; 5Dnepropetrovsk Regional Oncological Dispensary, Dnepropetrovsk, Ukraine; 6Martin D. Abeloff Laboratory Cancer Research Center, Tbilisi, Georgia; 7Chemotherapy and Immunotherapy Clinic MEDULLA, Tbilisi, Georgia; 8Tbilisi Cancer Center, Tbilisi, Georgia; 9St. Luke's Medical Center, Quezon City, Philippines; 10Kidwai Memorial Institute of Oncology, Bangalore, India; 11Research Institute of Clinical Medicine, Tbilisi, Georgia; 12Institute of Medical Radiology, Kharkiv, Ukraine; 13Apollo Specialty Hospital, Chennai, India; 14Lviv State Oncology Regional Treatment and Diagnostic Centre, Lviv, Ukraine; 15Chernigov Regional Oncology Center, Chernigov, Ukraine; 16Pyatigorsk Oncology Dispensary, Pyatigorsk, Russian Federation; 17Janssen R&D

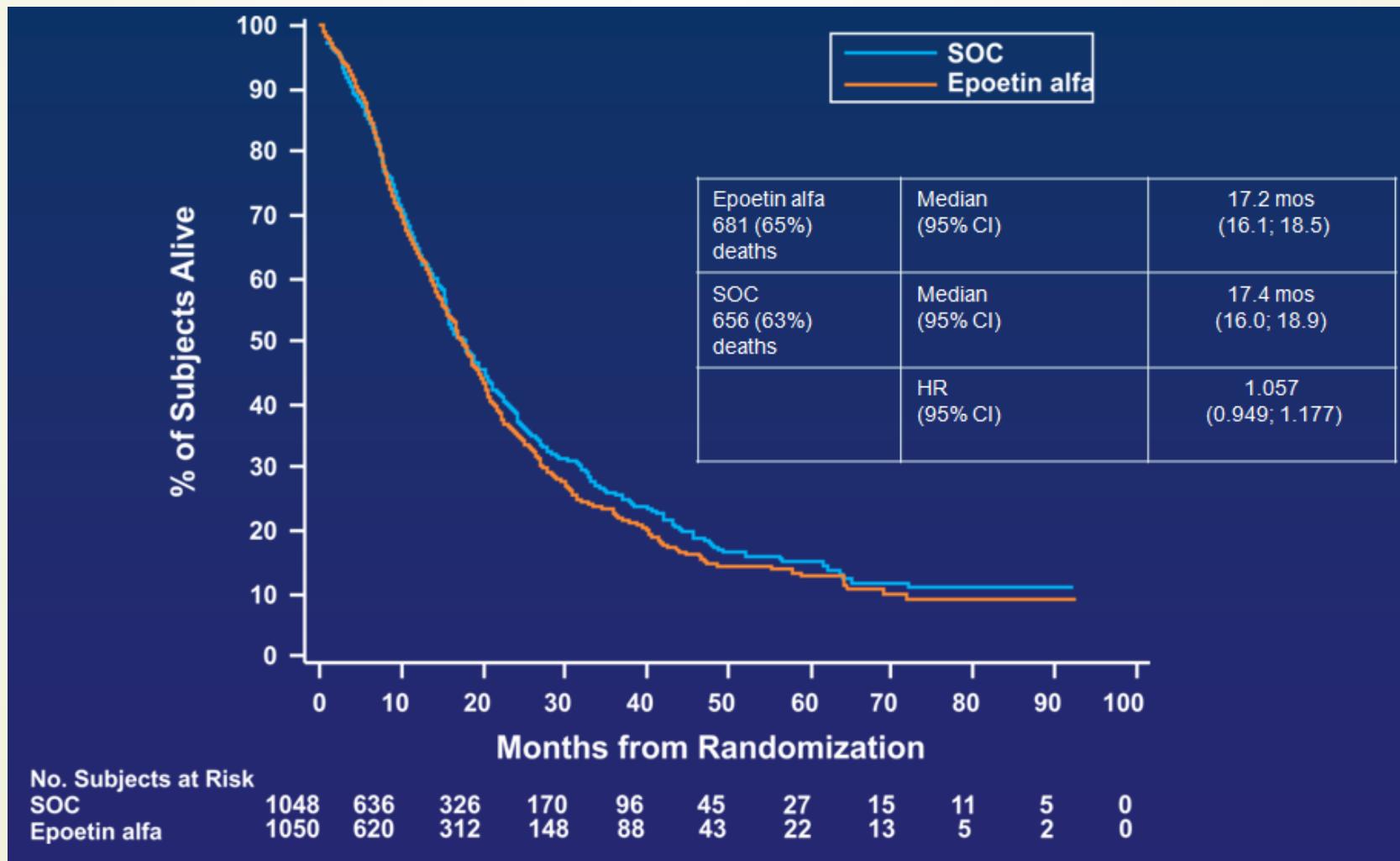
Primary Endpoint: Progression-Free Survival per Investigator-Determined PD



PFS: IRC-Determined PD



Overall Survival at Clinical Cut-off*



*Current analysis includes 1337 deaths, final analysis will include 1650 deaths

Pooled Analysis of Individual Patient-Level Data From All Randomized, Double-blind, Placebo-Controlled Trials of Darbepoetin Alfa in the Treatment of Patients With Chemotherapy-Induced Anemia

To Conclude

- Anemia in patients with cancer has multiple causes
- Treatment of anemia in cancer depends on these causes
- Iron should be used IV in patients with active cancer
- For patients receiving chemotherapy, ESAs should be used according to guidelines
- x

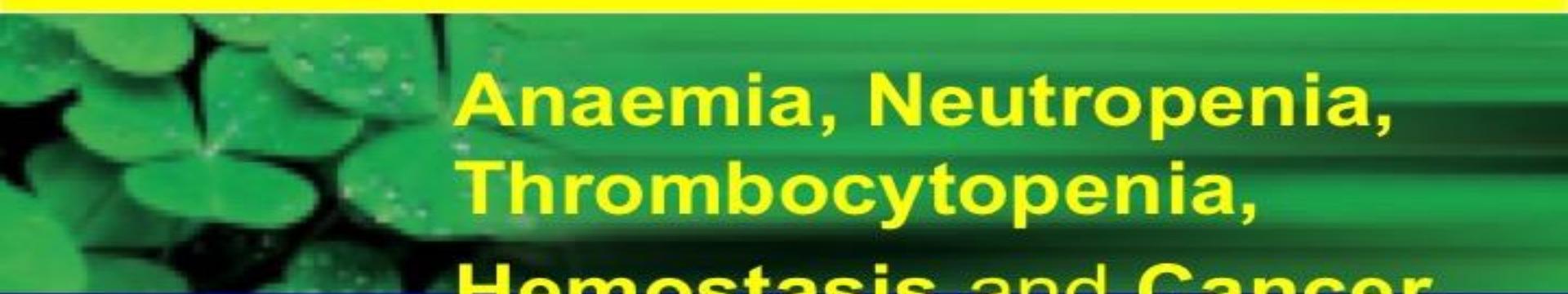
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