GLI EFFETTI COLLATERALI DELLE TERAPIE IN ONCOLOGIA GERIATRICA

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SIGG Torino 28-11-2013

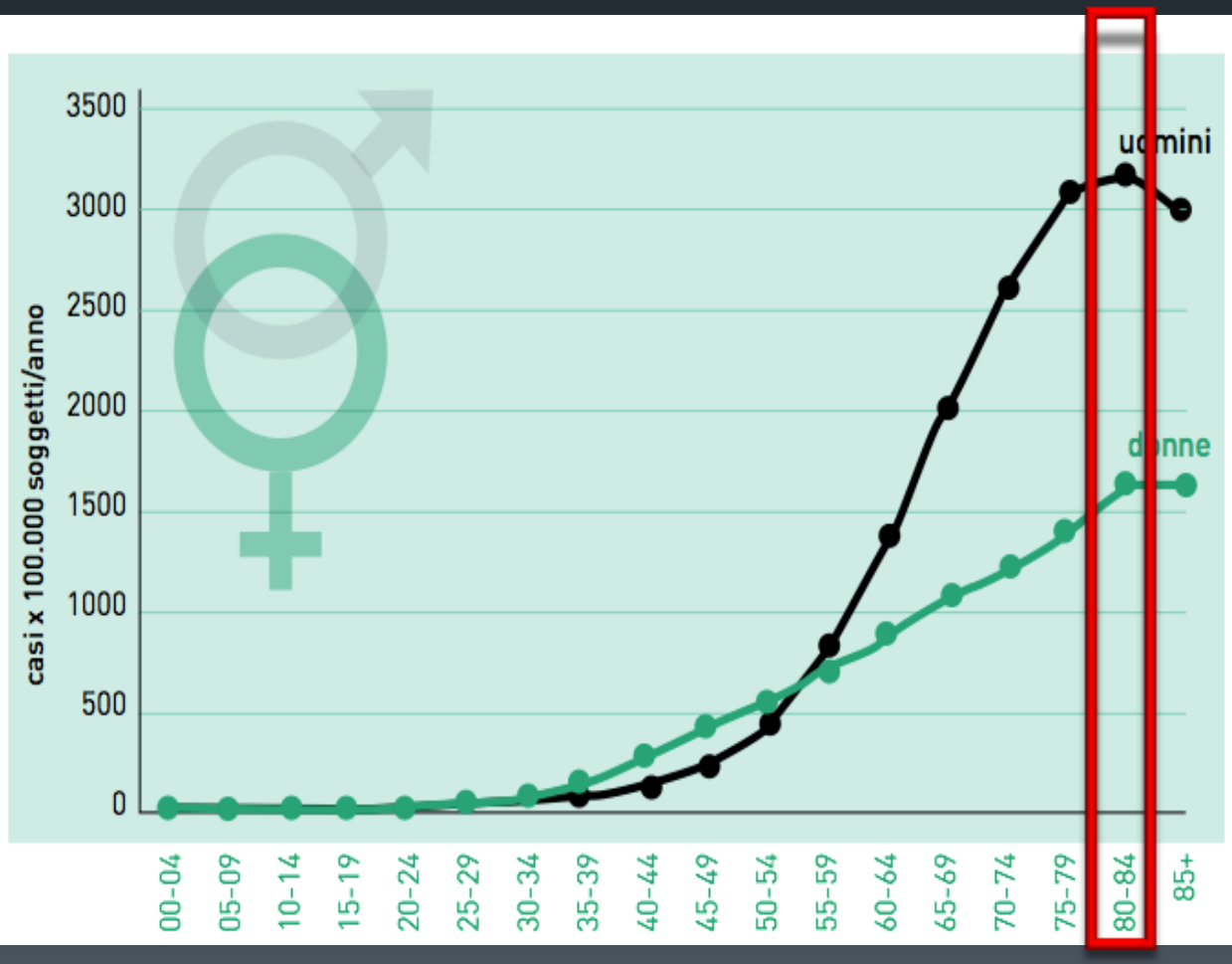


FIGURA 1.
AIRTUM 2006-2009. Tassi età-specifici (x 100.000) per sesso. Tutti i tumori esclusi carcinomi della cute.

	Maschi - Età			Femmine - Età		
Rango	0-49	50-69	70+	0-49	50-69	70+
1°	Testicolo (11%)	Prostata (23%)	Prostata (21%)	Mammella (41%)	Mammella (36%)	Mammella (21%)
2°	Linfoma non-Hodgkin (9%)	Colon-retto (15%)	Polmone (17%)	Tiroide (14%)	Colon-retto (13%)	Colon-retto (17%)
3°	Cute (melanomi) (8%)	Polmone (14%)	Colon-retto (15%)	Cute (melanomi) (7%)	Utero corpo (7%)	Polmone (7%)
4°	Colon-retto (8%)	Vescica* (10%)	Vescica* (11%)	Colon-retto (5%)	Polmone (6%)	Stomaco (6%)
5°	Tiroide (7%)	Vie aerodigestive superiori (5%)	Stomaco (6%)	Utero cervice (4%)	Tiroide (5%)	Pancreas (5%)

TABELLA 9. Primi cinque tumori in termini di frequenza e proporzione sul totale dei tumori incidenti (esclusi i carcinomi della cute) per sesso e fascia di età. Pool Airtum 2006-2009.

* comprende sia tumori infiltranti che non infiltranti.

	Maschi			Femmine		
Rango	anni 0-49	anni 50-69	anni 70+	anni 0-49	anni 50-69	anni 70+
1°	Polmone (16%)	Polmone (30%)	Polmone (25%)	Mammella (28%)	Mammella (21%)	Mammella (14%)
2°	Sist. nervoso centrale (11%)	Colon-retto (10%)	Colon-retto (11%)	Polmone (11%)	Polmone (14%)	Colon-retto (13%)
3°	Colon-retto (8%)	Fegato (8%)	Prostata (11%)	Colon-retto (7%)	Colon retto (10%)	Polmone (10%)
4°	Vie aerodigestive superiori (7%)	Pancreas (7%)	Stomaco (7%)	Sist. nervoso centrale (7%)	Pancreas (7%)	Pancreas (8%)
5°	Stomaco (7%)	Stomaco (6%)	Fegato (7%)	Leucemie (6%)	Ovaio (7%)	Stomaco (7%)

TABELLA 6. Prime cinque cause di morte oncologica e proporzione sul totale dei decessi per tumore per sesso e fascia di età. Pool Airtum 2006-2009.

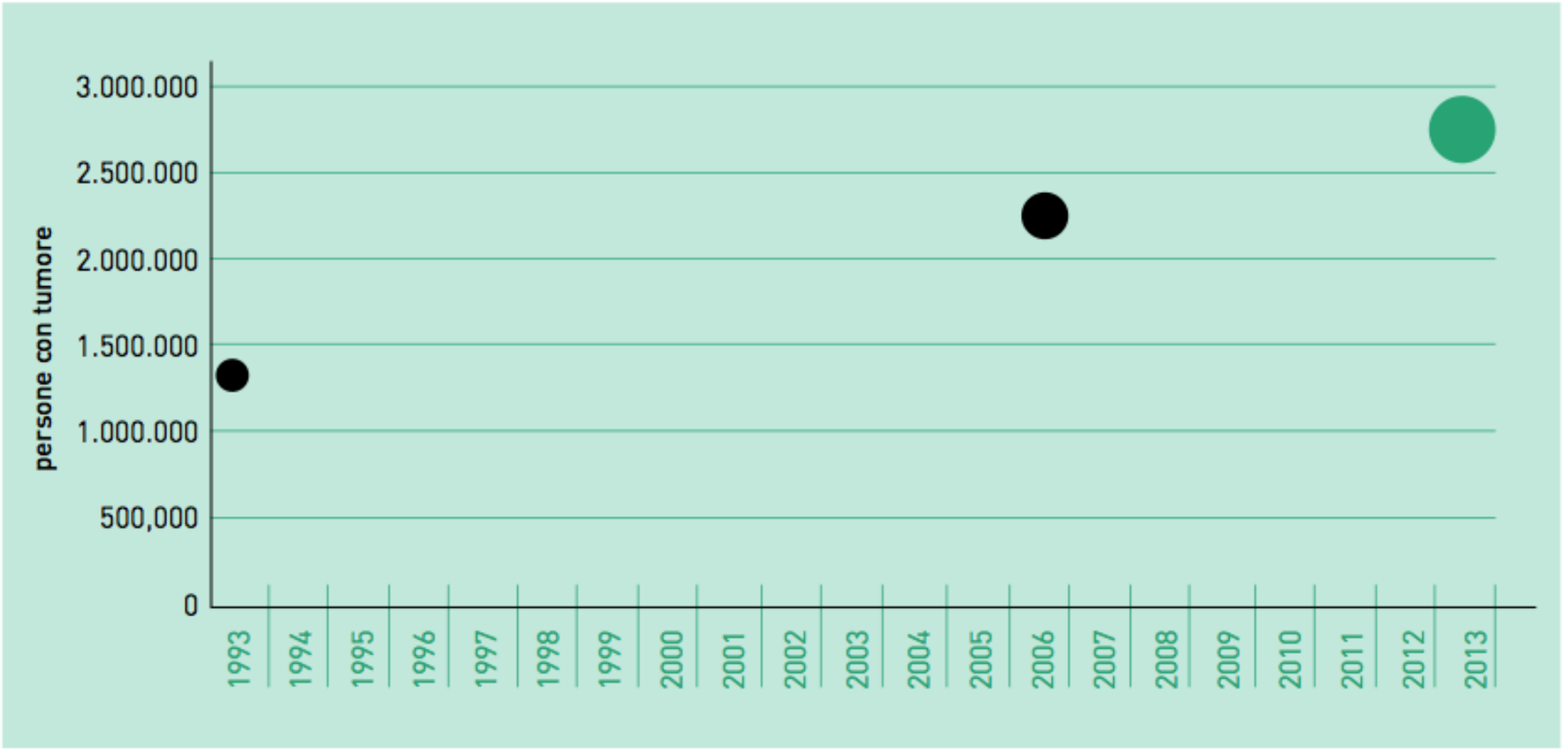
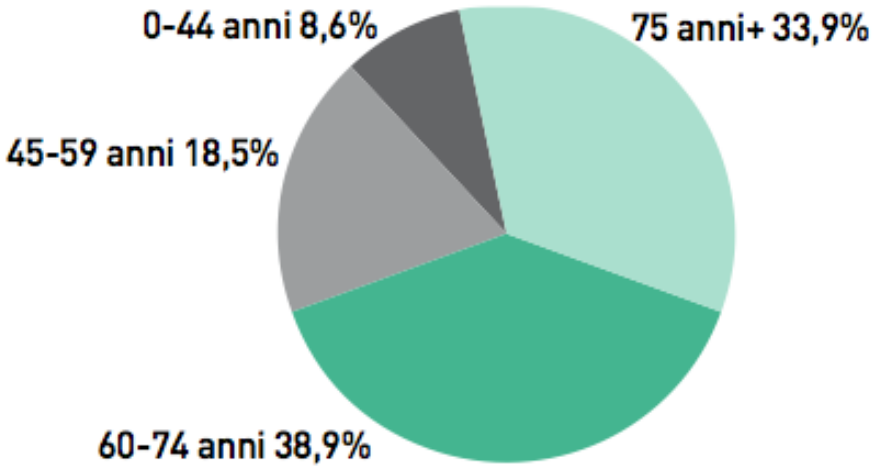


FIGURA 8. Persone viventi dopo una diagnosi di tumore in Italia: numeri stimati nel 1992 e nel 2006 (•) e previsti per il 2013 (•).



Tutti i tumori*	%	Pazienti in vita
Età (anni)		
0-44	8,6%	194.062
45-59	18,5%	415.960
60-74	38,9%	872.146
75+	33,9%	761.785

*eccetto tumori cutanei non melanomatosi

FIGURA 4. Numero di italiani con precedente diagnosi di tumore, divisi per fascia di età.

Il 39% (quasi 900.000 soggetti) ha un'età compresa tra 60 e 74 aa, il 34% (oltre 750.000 soggetti) un'età ≥ a 75 aa.
In quest'ultima fascia di età, la proporzione di soggetti che convivono con una diagnosi di tumore è particolarmente elevata (il 19% degli uomini ed 13% delle donne oltre i 75 aa ha avuto un tumore o convive con una diagnosi di tumore)

Several retrospective studies have reported that the toxicity of chemotherapy is not more severe or prolonged in persons older than 70 years. However, the results of these studies cannot be generalized for the following reasons:

- Only a few pts were 80 years or older; therefore, minimal information is available on the oldest pts
- The older pts involved in these studies were highly selected by the eligibility criteria of the cooperative group protocols and were not representative of the general older population, because they were probably healthier than most older pts
- Many of the treatment regimens used in these trials had lower dose intensity than those in current use
- Nevertheless, these studies are important, because they demonstrate that age, by itself, is not a contraindication to cancer chemotherapy. Therefore, pt selection is extremely important to maximize the benefits of adjuvant chemotherapy in older pts with breast cancer, colon cancer, ovarian cancer and lung cancer
- Increased age has been associated with changes in the pharmacokinetic and pharmacodynamics of cancer therapy and increased susceptibility of normal tissues to toxic complications. In general, all of these changes increase the risks of chemotherapy

Pharmacology of CT in the older pts

- **Absorption** (↓ oral drug absorption may reduce the effectiveness of oral agents) ↓ **Adherence**
- **Volume of distribution (Vd)** is a function of body composition (↑ body fat and ↓ body water), serum albumin and Hgb (the majority of antineoplastic agents are bound to red blood cells). A ↓ in the concentration of Hgb may result in ↑ serum concentration of free drug and ↑ toxicity
- **Hepatic drug metabolism** (↓ liver volume and hepatic blood flow, polypharmacy)
- **Renal excretion** (GFR ↓ consistently with age. Compounds excreted through the bile may give origin to active and toxic metabolites excreted through the kidney. Thus, renal insufficiency may ↑ the toxicity of drugs that are primarily eliminated with bile)

PHARMACODYNAMICS

- The ability of aging cells to catabolize drugs or to buffer the toxic effects of drugs may become more limited than in young cells
- Age may also be associated with tumors that are resistant to chemotherapy (↑ MDR-1, anoxia of neoplastic cells and reduced cell proliferation may also reduce the effectiveness of cycle-active drugs)

Principio Attivo	Segnalazioni
Oxaliplatino	156
Erlotinib	136
Acido acetilsalicilico	132
Warfarin	131
Sunitinib	87
Levofloxacina	72
Ticlopidina	69
Lenalidomide	64
Cetuximab	61
Exenatide	59
Sorafenib	59
Bevacizumab	58
Amoxicillina più acido clavulanico	56
Ceftriaxone	56
Iomeprolo	54
Lansoprazolo	52

Tabella 12: Segnalazioni di reazioni avverse da farmaci negli anziani per principio attivo pervenute nel 2008 (D.L. 8/4/2003 n. 95)

E' raccomandabile estrema prudenza nell'uso di dosaggi standard normalmente riferiti ai soggetti non anziani specificatamente per farmaci con caratteristiche di seguito riportate:

- ***Ad alta estrazione epatica***
- ***Ad elevato legame proteico***
- ***Eliminati prevalentemente inalterati dal rene o i cui metaboliti eliminati dal rene siano ancora attivi***
- ***Con basso indice terapeutico***

ELSEVIER

Critical Reviews in Oncology/Hematology 78 (2011) 220–226

CRITICAL REVIEWS IN
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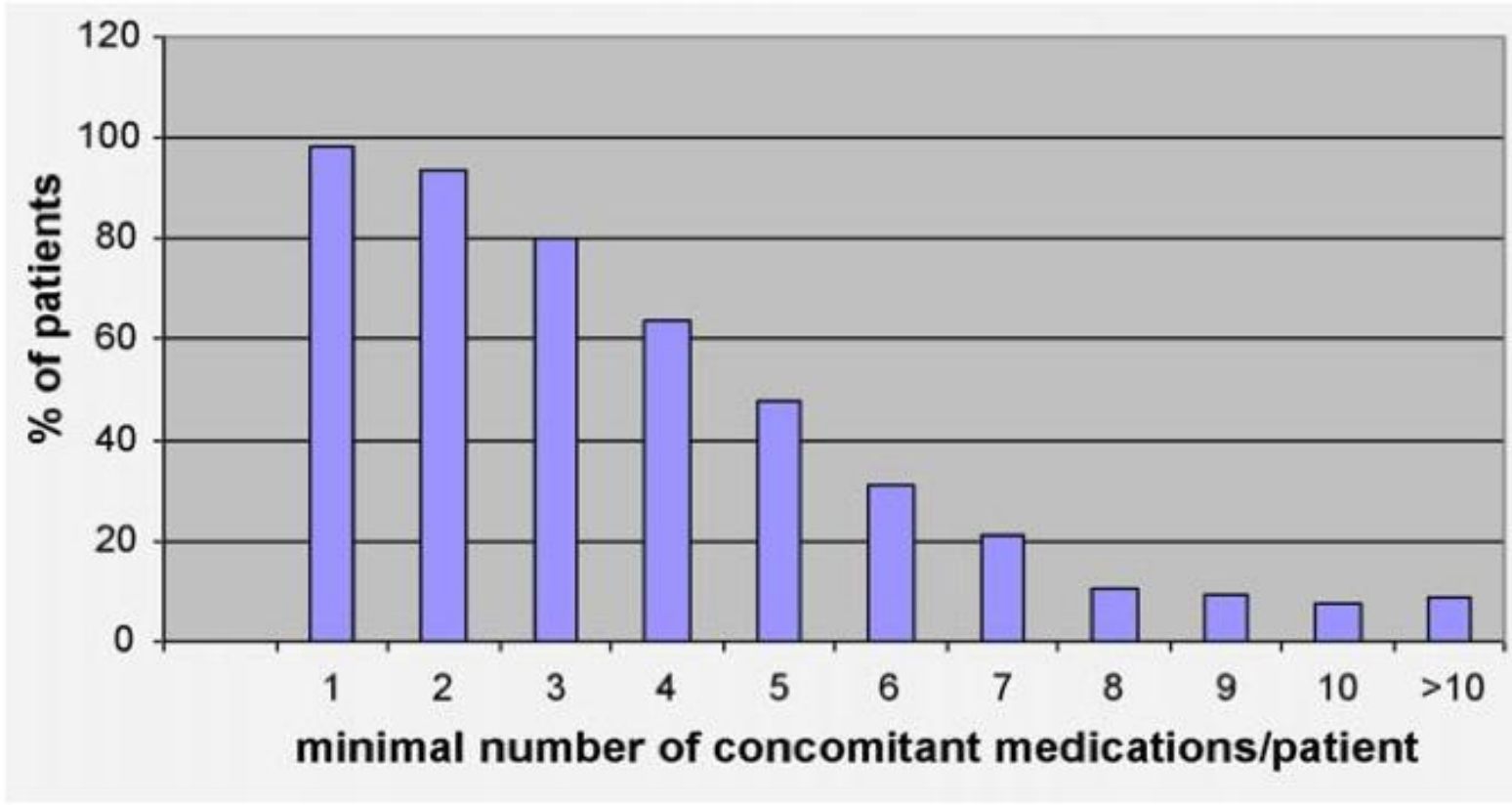
www.elsevier.com/locate/critrevonc

Potential drug interactions in elderly cancer patients

V. Girre [a,*,1], H. Arkoub [a,1], M.T.E. Puts [b,1], C. Vantelon [a,c,1], F. Blanchard [d,1], J.P. Droz [e,1], L. Mignot [a,1]

Number of concomitant medications per patient.



Top 10 pharmacotherapeutic groups used.

Rank	% of prescriptions	Pharmacotherapeutic groups
1	29.1	Level II opioid analgesics
2	26.2	Benzodiazepines
3	21.4	Hypnotic Benzodiazepines and others
4	18.4	Beta-blockers Proton pump inhibitors
5	17.5	HMG-CoA reductase inhibitor lipid-lowering drugs
6	16.5	Non-opioid analgesic Diuretics
7	13.6	Platelet aggregation inhibitors Antineoplastic, endocrine therapy and similar Bisphosphonates Minerals
8	12.6	Cytotoxic drugs Calcium channel blockers
9	11.6	Other antianginal drugs Serotonin reuptake inhibitor antidepressants Thyroid hormones
10	10.7	Level III opioid analgesics H2 antihistamine antisecretory agents Angiotensin-converting enzyme inhibitors Vasoconstrictors

Top 5 therapeutic fields.

Therapeutic fields	Number of medications prescribed (% of all drug prescriptions)
Cardiovascular	149 (28.7)
Analgesics and anti-inflammatory	71 (13.7)
Psychotropic medications	68 (13.1)
Gastrointestinal medications	47 (9.1)
Antineoplastic medications	43 (8.2)

MEDICATION-RELATED PROBLEMS ASSOCIATED WITH POLYPHARMACY

- Adverse drug reactions
- Duplication of therapy
- Adverse drug-drug interactions
- Adverse drug-disease interactions
- Adherence to treatment
- Cost

DRUG-DRUG INTERACTIONS: MAJOR RISKS

1. Respiratory distress, and sedation in the case of overdose
2. Bleeding
3. Cardiac side effects
4. Masking hypoglycemia
5. Serotoninergic syndrome and/or seizures
6. Hypotension and orthostatic hypotension
7. Ulcer and GI bleeding
8. Decreased absorption of H2 antihistamines

USEFUL QUESTIONS

- Is there a proper indication for each medication?
- Is the medication achieving the desired effect (e.g. for a pain medication, is the pain controlled?)
- Does the pt present with nonspecific symptoms (for example fatigue, impaired cognition) that may ascribed to some of medications?
- Are the medications prescribed at an appropriate dose?
- Is there potential for clinically important drug-drug interactions?
- May some of the drugs interfere with antineoplastic treatment?
- What is the risk of drug-tumor interactions?
- Does the pt adhere to the treatment plan?
- Are there conditions that need treatment and at present are left untreated?

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SPECIAL CONSIDERATIONS FOR PATIENTS ABLE TO TOLERATE TREATMENT[h,i]

Surgery

- In general, age is not the primary consideration for surgical risk.
- Emergency surgery carries increased risk of complications.
- Assess physiologic status.
- American Geriatrics Society (AGS) Task Force and American College of Surgeons provided general guidelines for older adults undergoing surgery.[1] These guidelines can be applied to older cancer patients undergoing surgery.
- There are data to suggest that an increased need for functional assistance pre-surgery (measured by ADL, IADL, and PS) predicts postoperative complications, extended hospital stay, and 6-month mortality in older patients undergoing cancer surgery.[2-4]
- Impaired cognitive status is a risk factor for postoperative complications, prolonged length of stay, and 6-month overall mortality postoperatively.[2,5]
- In patients undergoing general surgery
  - Older age is a risk factor for postoperative delirium.[6]
  - Delirium is a risk factor for functional decline.[7] See Assessment of Cognition (SAO-E)
- Preventive measures exist for delirium
  - Yale Delirium Prevention Trial and Hospitalized Elder Life Program (HELP): http://info.med.yale.edu/intmed/elp/print_version/background_print.htm
  - National Institute for Health and Clinical Excellence (NICE) Guideline for Prevention of Delirium: http://publications.nice.org.uk/delirium-cg103

Radiation Therapy

- Use caution with concurrent chemoradiation therapy; dose modification of chemotherapy may be necessary.
- Nutritional support and pain control are needed if radiation therapy-induced mucositis is present.

Systemic Therapy

- Chemotherapy toxicity risk can be predicted by parameters that are typically included in a Comprehensive Geriatric Assessment (CGA). These tools are awaiting additional validation.
  - Chemotherapy Risk Assessment Scale for High-Age Patients (CRASH) score (http://eforms.moffitt.org/crashScore.aspx)
  - Cancer and Aging Research Group (CARG) Chemo Toxicity Calculator (http://www.mycarg.org)

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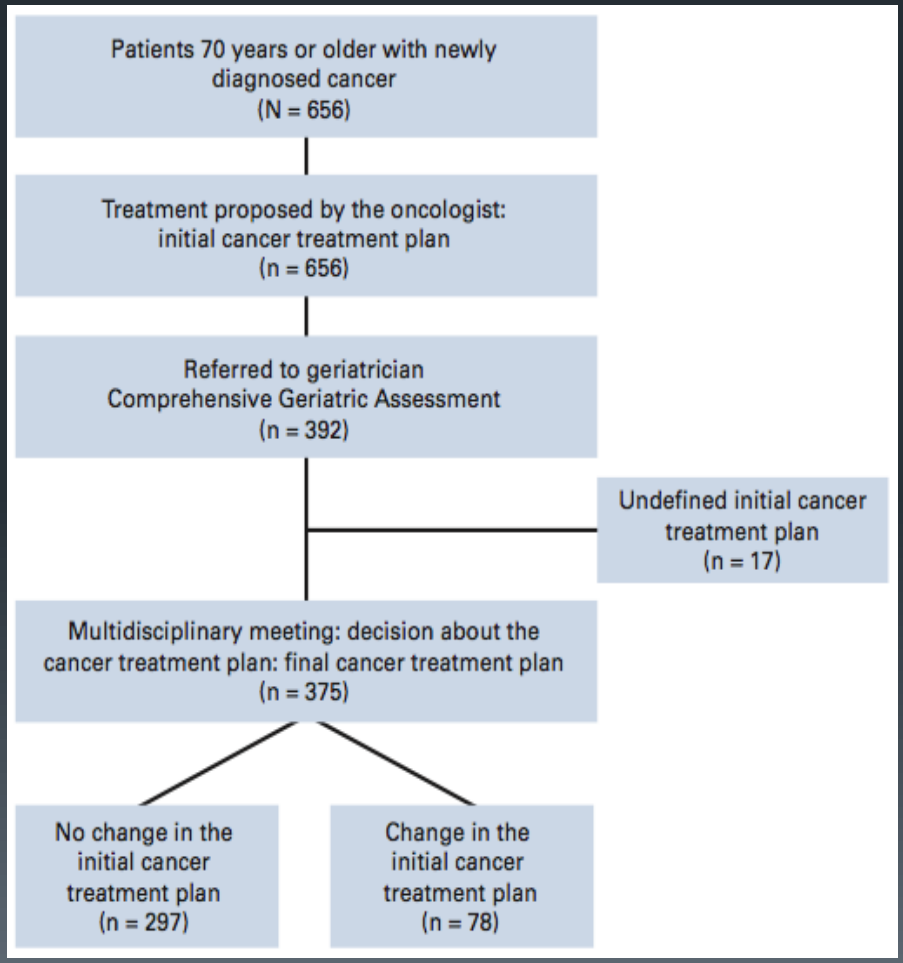
JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Comprehensive Geriatric Assessment in the Decision-Making Process in Elderly Patients With Cancer: ELCAPA Study

Philippe Caillet, Florence Canoui-Poitrine, Johanna Vouriot, Muriel Berle, Nicoleta Reinald, Sebastien Krypciak, Sylvie Bastuji-Garin, Stephane Culine, and Elena Paillaud



DISCUSSION

- In our elderly population with cancer, nearly 21% of pts had changes made to their initial cancer treatment plan on the basis of the CGA results
- The most common change was a switch from CT to SC
- Two factors were indipendently associated with changing the initial cancer treatment: functional impairment (defined as an at least 0.5-point ADL score decrease) and malnutrition

Predicting the Risk of Chemotherapy Toxicity in Older Patients: The Chemotherapy Risk Assessment Scale for High-Age Patients (CRASH) Score

Cancer 2012;118:3377-86

Martine Extermann, MD[1]; Ivette Boler, ARNP[1]; Richard R. Reich, PhD[1,2]; Gary H. Lyman, MD[3]; Richard H. Brown, MD[4]; Joseph DeFelice, MD[5†]; Richard M. Levine, MD[6]; Eric T. Lubiner, MD[7]; Pablo Reyes, MD[8]; Frederic J. Schreiber III, MD[9]; and Lodovico Balducci, MD[1]

Table 4. The Chemotherapy Risk Assessment Scale for High-Age Patients (CRASH) Score

	Points		
Predictors	**0**	**1**	**2**
Hematologic score[a]			
Diastolic BP	≤72	>72	
IADL	26-29	10-25	
LDH (if ULN 618 U/L; otherwise, 0.74 /L*ULN)	0-459		>459
Chemotox[b]	0-0.44	0.45- 0.57	>0.57
Nonhematologic score[a]			
ECOG PS	0	1-2	3-4
MMS	30		<30
MNA	28-30		<28
Chemotox[b]	0-0.44	0.45-0.57	>0.57

Abbreviations: BP, blood pressure; Chemotox, toxicity of the chemotherapy regimen (for details, see text); ECOG PS, Eastern Cooperative Oncology Group performance status; IALD, Instrumental Activities of Daily Living; LDH, lactate dehydrogenase; MMS, Mini Mental Health Status; MNA, Mini Nutritional Assessment; ULN, upper limit of normal.

Table 6. Example of Toxicity of the Chemotherapy Regimen (Chemotox) Values for Various Chemotherapy Regimens[a]

CRASH Points[b]		
0	1	2
Capecitabine 2g	Capecitabine 2.5 g	5-FU/LV (Roswell-Park)
Cisplatin/pemetrexed	Carboplatin/gemcitabine AUC 4-6/1 g d1,d8	5-FU/LV (Mayo)
Dacarbazine	Carboplatin/pemetrexed	5-FU/LV and bevacizumab
Docetaxel weekly	Carboplatin/paclitaxel q3w	CAF
FOLFIRI	Cisplatin/gemcitabine d1,d8	Carboplatin/docetaxel q3w
Gemcitabine 1 g 3/4 wk	ECF	CHOP
Gemcitabine 1.25 g 3/4 wk	Fludarabine	Cisplatin/docetaxel 75/75
Paclitaxel weekly	FOLFOX 85 mg	Cisplatin/etoposide
Pemetrexed	Gemcitabine 7/8 wk then 3/4 wk	Cisplatin/gemcitabine d1,d8,d15
	Gemcitabine/irinotecan	Cisplatin/paclitaxel 135-24 h q3w
	PEG doxorubicin 50 mg q4w	CMF classic
	Topotecan weekly	Doxorubicin q3w
	XELOX	FOLFOX 100-130 mg
		Gemcitabine/pemetrexed d8
		Irinotecan q3w
		Paclitaxel q3w
		Docetaxel q3w
		Topotecan monthly

Abbreviations: 5-FU, 5-fluorouracil; AUC, area under the concentration-time curve; CAF, cyclophosphamide, doxorubicin, and 5-fluorouracil; CHOP, cyclophosphamide, doxorubicin, vincristine, and prednisone; CMF, cyclophosphamide, methotrexate, and 5-fluorouracil; CRASH, Chemotherapy Risk Assessment Scale for High-Age Patients; ECF, epirubicin, cisplatin and 5-fluorouracil; FOLFIRI, irinotecan, leucovorin, and 5-fluorouracil; FOLFOX, folinic acid, 5-fluorouracil, and oxaliplatin; LV, leucovorin; PEG, pegylated; q3w, every 3 weeks; q4w, every 4 weeks; XELOX, capecitabine and oxaliplatin.

PREDICTORS

- Severe toxicity was observed in 64% of pts. The CRASH score was constructed along 2 subscores: H(ematologic) toxicity and NH toxicity.
- Predictors of H toxicity were: lymphocytes, AST level, IADL score, LDH level, DBP, and chemotox (the MAX2 index). The best model included the 4 latter predictors (risk categories: low 7%, medium-low 23%, medium-high 54%, and high 100%, respectively; P_{trend} <.001)
- Predictors of NH toxicity were: Hgb, CrCl, Albumin, self-rated health, ECOG PS, MMS, MNA, and chemotox

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JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Predicting Chemotherapy Toxicity in Older Adults With Cancer: A Prospective Multicenter Study

Arti Hurria, Kayo Togawa, Supriya G. Mohile, Cynthia Owusu, Heidi D. Klepin, Cary P. Gross, Stuart M. Lichtman, Ajeet Gajra, Smita Bhatia, Vani Katheria, Shira Klapper, Kurt Hansen, Rupal Ramani, Mark Lachs, F. Lennie Wong, and William P. Tew

Table 5. Predictive Model

Risk Factor	Prevalence No.	Prevalence %	Grades 3 to 5 Toxicity No.	Grades 3 to 5 Toxicity %	OR	95% CI	Score
Age ≥ 72 years	270	54	163	60	1.85	1.22 to 2.8	2
Cancer type GI or GU	185	37	120	65	2.13	1.39 to 3.2	2
Chemotherapy dosing, standard dose	380	76	204	54	2.13	1.29 to 3.5	2
No. of chemotherapy drugs, polychemotherapy	351	70	192	55	1.69	1.08 to 2.6	2
Hemoglobin < 11 g/dL (male), < 10 g/dL (female)	62	12	46	74	2.31	1.15 to 4.6	3
Creatinine clearance (Jelliffe, ideal weight) < 34 mL/min	44	9	34	77	2.46	1.11 to 5.4	3
Hearing, fair or worse	123	25	76	62	1.67	1.04 to 2.6	2
No. of falls in last 6 months, 1 or more	91	18	61	67	2.47	1.43 to 4.2	3
IADL: Taking medications, with some help/unable	39	8	28	72	1.50	0.66 to 3.3	1
MOS: Walking 1 block, somewhat limited/limited a lot	109	22	69	63	1.71	1.02 to 2.8	2
MOS: Decreased social activity because of physical/emotional health, limited at least sometimes	218	44	126	58	1.36	0.90 to 2.0	1

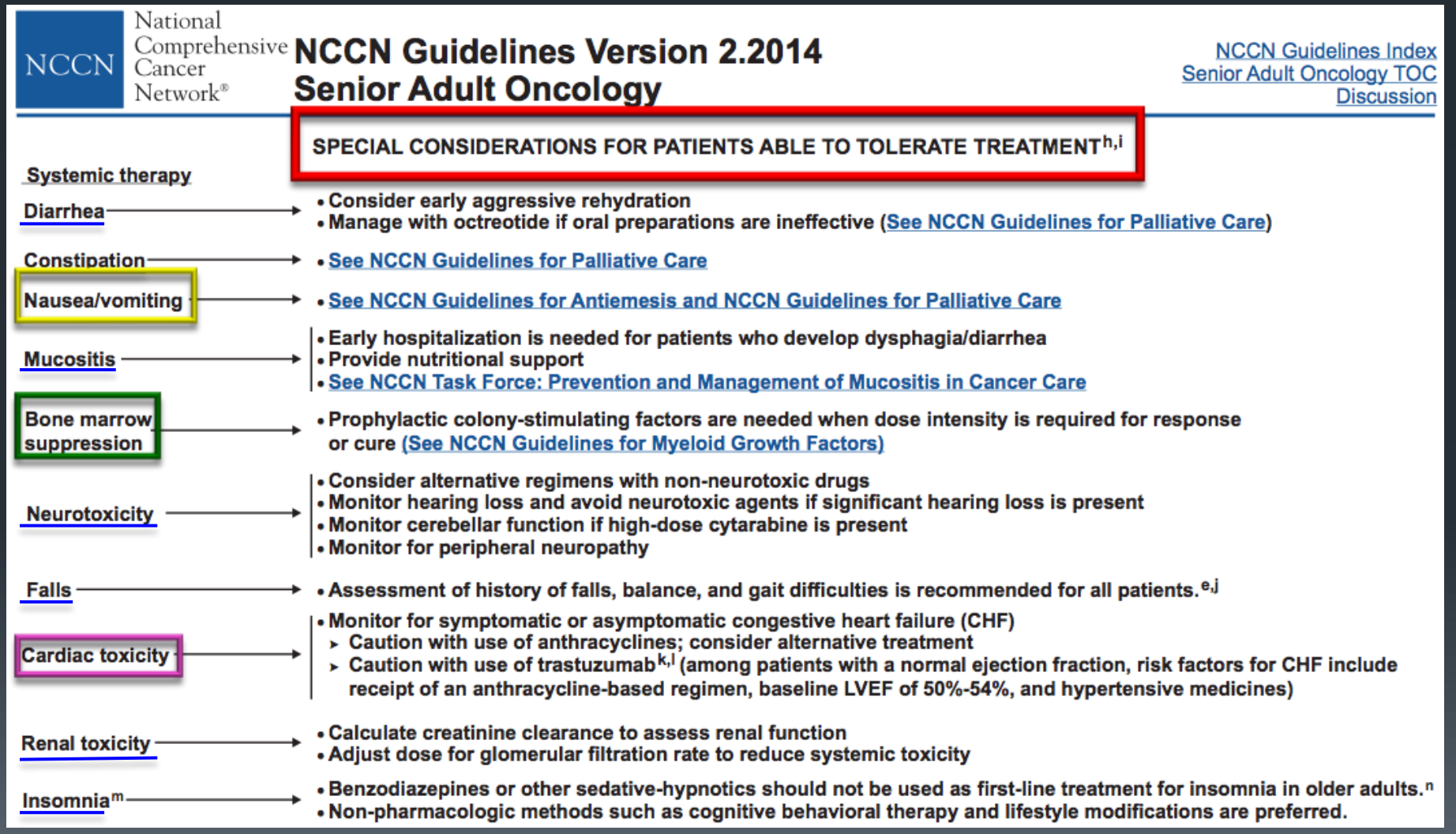
Abbreviations: GU, genitourinary; IADL, instrumental activities of daily living; MOS, Medical Outcomes Study; OR, odds ratio.

Table 6. Ability of Risk Score Versus Physician-Rated KPS to Predict Chemotherapy Toxicity

Risk Strata	No Toxicity No.	No Toxicity %	Toxicity No.	Toxicity %	Total	*P*	ROC
By total score						< .001	0.72*
0-5 (low)	89	70	39	30	128		
6-9 (mid)	110	48	117	52	227		
10-19 (high)	19	17	90	83	109		
By physician-rated KPS (%)						.19	0.53*
90-100	125	49	128	51	253		
80	73	49	76	51	149		
≤ 70	33	38	53	62	86		

Abbreviations: KPS, Karnofsky performance status; ROC, receiver operating characteristic.

*Risk score and physician-rated KPS were treated as continuous to calculate the ROC.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SPECIAL CONSIDERATIONS FOR PATIENTS ABLE TO TOLERATE TREATMENT[h,i]
Systemic therapy
Diarrhea
• Consider early aggressive rehydration
• Manage with octreotide if oral preparations are ineffective (See NCCN Guidelines for Palliative Care)
Constipation
• See NCCN Guidelines for Palliative Care
Nausea/vomiting
• See NCCN Guidelines for Antiemesis and NCCN Guidelines for Palliative Care
Mucositis
• Early hospitalization is needed for patients who develop dysphagia/diarrhea
• Provide nutritional support
• See NCCN Task Force: Prevention and Management of Mucositis in Cancer Care
Bone marrow suppression
• Prophylactic colony-stimulating factors are needed when dose intensity is required for response or cure (See NCCN Guidelines for Myeloid Growth Factors)
Neurotoxicity
• Consider alternative regimens with non-neurotoxic drugs
• Monitor hearing loss and avoid neurotoxic agents if significant hearing loss is present
• Monitor cerebellar function if high-dose cytarabine is present
• Monitor for peripheral neuropathy
Falls
• Assessment of history of falls, balance, and gait difficulties is recommended for all patients.[e,j]
Cardiac toxicity
• Monitor for symptomatic or asymptomatic congestive heart failure (CHF)
▸ Caution with use of anthracyclines; consider alternative treatment
▸ Caution with use of trastuzumab[k,l] (among patients with a normal ejection fraction, risk factors for CHF include receipt of an anthracycline-based regimen, baseline LVEF of 50%-54%, and hypertensive medicines)
Renal toxicity
• Calculate creatinine clearance to assess renal function
• Adjust dose for glomerular filtration rate to reduce systemic toxicity
Insomnia[m]
• Benzodiazepines or other sedative-hypnotics should not be used as first-line treatment for insomnia in older adults.[n]
• Non-pharmacologic methods such as cognitive behavioral therapy and lifestyle modifications are preferred.

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Cancer- and Chemotherapy-Induced Anemia

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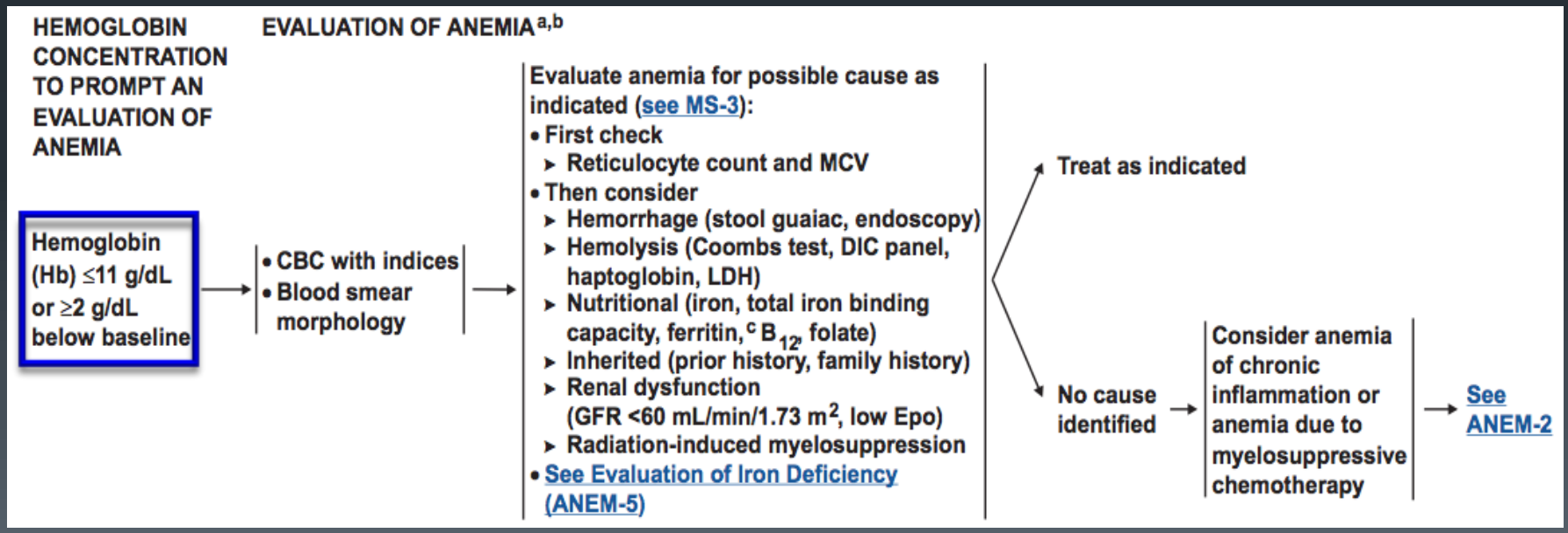

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Cancer- and Chemotherapy-Induced Anemia

INDICATIONS FOR RED BLOOD CELL TRANSFUSION IN CANCER PATIENTS[a,b]

Goal: Prevent or treat deficit of oxygen-carrying capacity

Asymptomatic Anemia

- **Hemodynamically stable chronic anemia without acute coronary syndrome:**
  - **Transfusion goal to maintain Hb 7-9 g/dL**

Symptomatic Anemia

- **Acute hemorrhage with evidence of hemodynamic instability or inadequate oxygen delivery:**
  - **Transfuse to correct hemodynamic instability and maintain adequate oxygen delivery**
- **Symptomatic (including tachycardia, tachypnea, postural hypotension) anemia (Hb <10 g/dL):**
  - **Transfusion goal to maintain Hb 8-10 g/dL as needed for prevention of symptoms**
- **Anemia in setting of acute coronary syndromes or acute myocardial infarction:**
  - **Transfusion goal to maintain Hb ≥10 g/dL**

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Cancer- and Chemotherapy-Induced Anemia

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ERYTHROPOIETIC THERAPY - DOSING AND TITRATION (1 of 5)[1-4]

INITIAL DOSING	TITRATION FOR NO RESPONSE
Epoetin alfa 150 units/kg 3 times wk by subcutaneous injection	Increase dose of epoetin alfa to 300 units/kg 3 times wk by subcutaneous injection
or	
Epoetin alfa 40,000 units every wk by subcutaneous injection	Increase dose of epoetin alfa to 60,000 units every wk by subcutaneous injection
or	
Darbepoetin alfa 2.25 mcg/kg every wk by subcutaneous injection	Increase darbepoetin alfa to up to 4.5 mcg/kg every wk by subcutaneous injection
or	
Darbepoetin alfa 500 mcg every 3 wks by subcutaneous injection	

TITRATION FOR RESPONSE

- **The dose should be adjusted for each patient to maintain the lowest Hb level sufficient to avoid RBC transfusion.**
- **If Hb reaches a level needed to avoid transfusion or increases >1 g/dL in any 2-week period, reduce dose by 25% for epoetin alfa and by 40% for darbepoetin alfa.**

COMPARISON OF RISKS AND BENEFITS OF ESA USE VERSUS RED BLOOD CELL TRANSFUSION[9]

If anemia is not due to absolute or functional iron deficiency, there are currently only two proven methods of improving Hb - ESAs and red blood cell transfusion. Listed below are risks and benefits of each method.

	ESA in the Cancer Setting	Red Blood Cell Transfusion
Risks	• Increased thrombotic events • Possible decreased survival • Time to tumor progression shortened	• Transfusion reactions (eg, hemolytic, febrile, non-hemolytic, lung injury) • Congestive heart failure • Virus transmission (eg, hepatitis, HIV) • Bacterial contamination • Iron overload • Increased thrombotic events • Possible decreased survival
Benefits	• Transfusion avoidance • Gradual improvement in fatigue	• Rapid increase of Hb and hematocrit levels • Rapid improvement in fatigue

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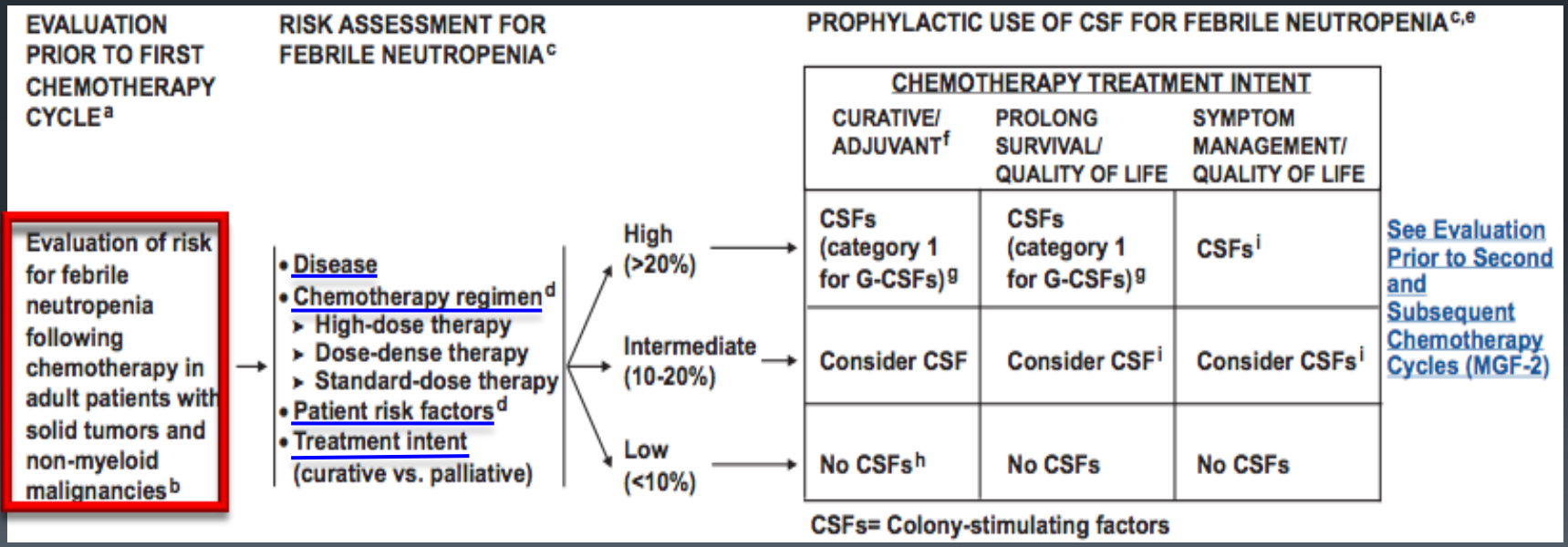
Myeloid Growth Factors

Version 2.2013

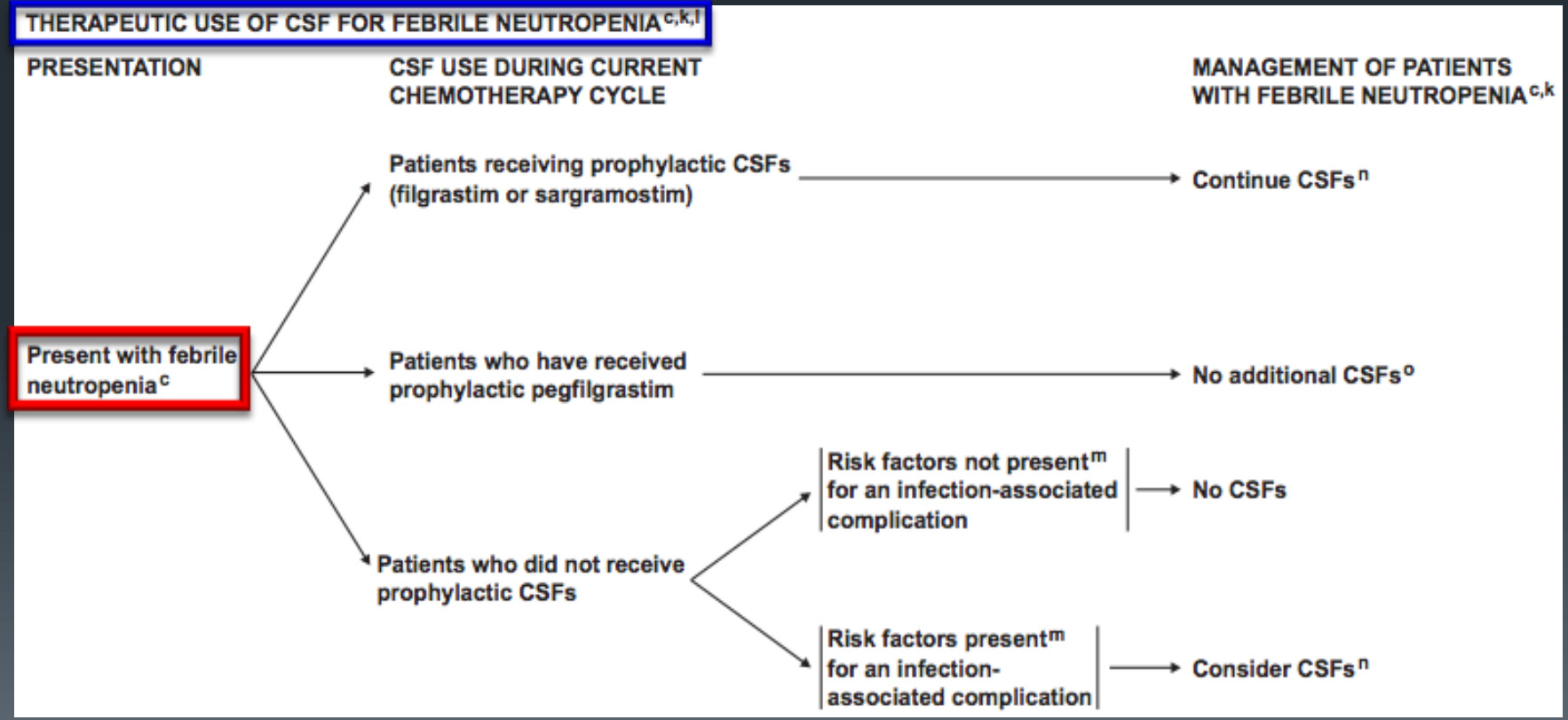


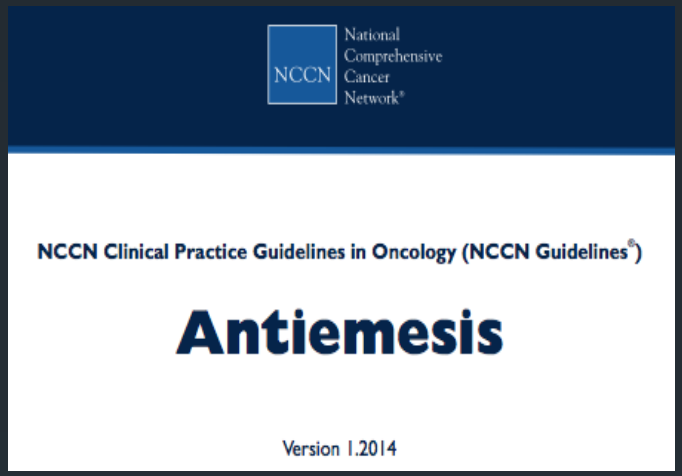
PATIENT RISK FACTORS FOR DEVELOPING FEBRILE NEUTROPENIA

In addition to the risk of the chemotherapy regimen and the specific malignancy being treated, these factors need to be considered when evaluating a patient's overall risk for febrile neutropenia.

- Older patient, notably patients age 65 and older (See NCCN Guidelines for Senior Adult Oncology)
- Previous chemotherapy or radiation therapy
- Preexisting neutropenia or bone marrow involvement with tumor
- Preexisting conditions
  - Neutropenia
  - Infection/open wounds
  - Recent surgery
- Poor performance status
- Poor renal function
- Liver dysfunction, most notably elevated bilirubin

THERAPEUTIC USE OF CSF FOR FEBRILE NEUTROPENIA[c,k,l]





HIGH EMETIC RISK INTRAVENOUS CHEMOTHERAPY - ACUTE AND DELAYED EMESIS PREVENTION[a,b,c]

Start before chemotherapy[c,d]

Neurokinin 1 antagonist containing regimen consisting of the following:

- **Serotonin (5-HT3) antagonist (Choose one):[e,f]**
  - **Dolasetron 100 mg PO [g]**
  - **Granisetron 2 mg PO daily or 1 mg PO BID or 0.01 mg/kg (max 1 mg) IV day 1[g] or transdermal patch as 3.1 mg/24 h patch (containing 34.3 mg granisetron total dose) applied approximately 24-48 h prior to first dose of chemotherapy; maximum duration of patch is 7 days**
  - **Ondansetron 16-24 mg PO or 8-16 mg IV day 1[g,h]**
  - **Palonosetron 0.25 mg IV day 1 (preferred)[i]**

  AND
- **Steroid (Choose one):[j]**
  - **Dexamethasone 12 mg PO or IV day 1, 8 mg PO daily days 2-4 (with aprepitant 125 mg)**
  - **Dexamethasone 12 mg PO or IV day 1, 8 mg PO day 2, then 8 mg PO BID days 3 and 4 (with fosaprepitant 150 mg IV day 1)**

  AND
- **Neurokinin 1 antagonist (Choose one):**
  - **Aprepitant 125 mg PO day 1, 80 mg PO daily days 2-3**
  - **Fosaprepitant 150 mg IV day 1 only**
- **± Lorazepam 0.5-2 mg PO or IV or sublingual either every 4 hours or every 6 hours days 1-4**
- **± H2 blocker or proton pump inhibitor**

OR

- **Olanzapine-containing regimen[k]**
  - **Olanzapine 10 mg PO days 1-4**
  - **Palonosetron 0.25 mg IV day 1**
  - **Dexamethasone 20 mg IV day 1**
- **± Lorazepam 0.5-2 mg PO or IV or sublingual either every 4 hours or every 6 hours days 1-4**
- **± H2 blocker or proton pump inhibitor**

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CRITICAL REVIEWS IN Oncology Hematology Incorporating Geriatric Oncology

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State of the art for cardiotoxicity due to chemotherapy and to targeted therapies: A literature review

Rossana Berardi *, Miriam Caramanti, Agnese Savini, Silvia Chiorrini, Chiara Pierantoni, Azzurra Onofri, Zelmira Ballatore, Mariagrazia De Lisa, Paola Mazzanti, Stefano Cascinu

Incidence of cardiotoxicity due to chemotherapy [29].

Chemotherapy agents	Incidence (%)		
	LV Dysfunction	Ischemia	Bradycardia
Anthracyclines			
Doxorubicin	3–26%	-	-
Epirubicin	0.9–3.3%		
Alkylating agents			
Cyclophosphamide	7–28%	-	-
Ifosfamide	17%		
Antimicrotubule agents			
Docetaxel	2.3–8%	1.70%	
Paclitaxel		1–5%	0.1–31%
Antimetabolites			
Capecitabine	-	3–9%	-
Fluorouracil		1–68%	

Incidence of cardiotoxicity due to targeted therapies [29].

Targeted therapy	Incidence (%)				
	LV Dysfunction	Ischemia	Hypertension	QT prolungation	Arterial tromboembolism
Monoclonal antibody-based tyrosine kinase					
Bevacizumab	1.7–3.0%	0.6–1.5%	4.0–35.0%	-	3.80%
Trastuzumab	2.0–28.0%	-	-	-	-
Small molecule tyrosine kinase inhibitors					
Sorafenib	-	2.7–3.0%	17.0–43.0%	-	-
Sunitinib	2.7–11.0%		5.0–47.0%	-	-
Lapatinib	1.5–2.2%			16%	-

PREVENTION

- Pts undergoing anticancer therapy should be encouraged to follow standard guidelines for reducing CV risk, such as BP control, lipid level reduction, smoking cessation and lifestyle modifications (ESMO guidelines)
- A medical treatment of pts, even asymptomatic, who show LVD at doppler echocardiogram after antracycline chemo is mandatory, especially if they could have long-term survival. All pts should receive a combination of an ACE inhibitor or an angiotensin II receptor blocker and a beta-blocker unless contraindicated (American College of Cardiology/American Heart Association/HF Society of America guidelines)

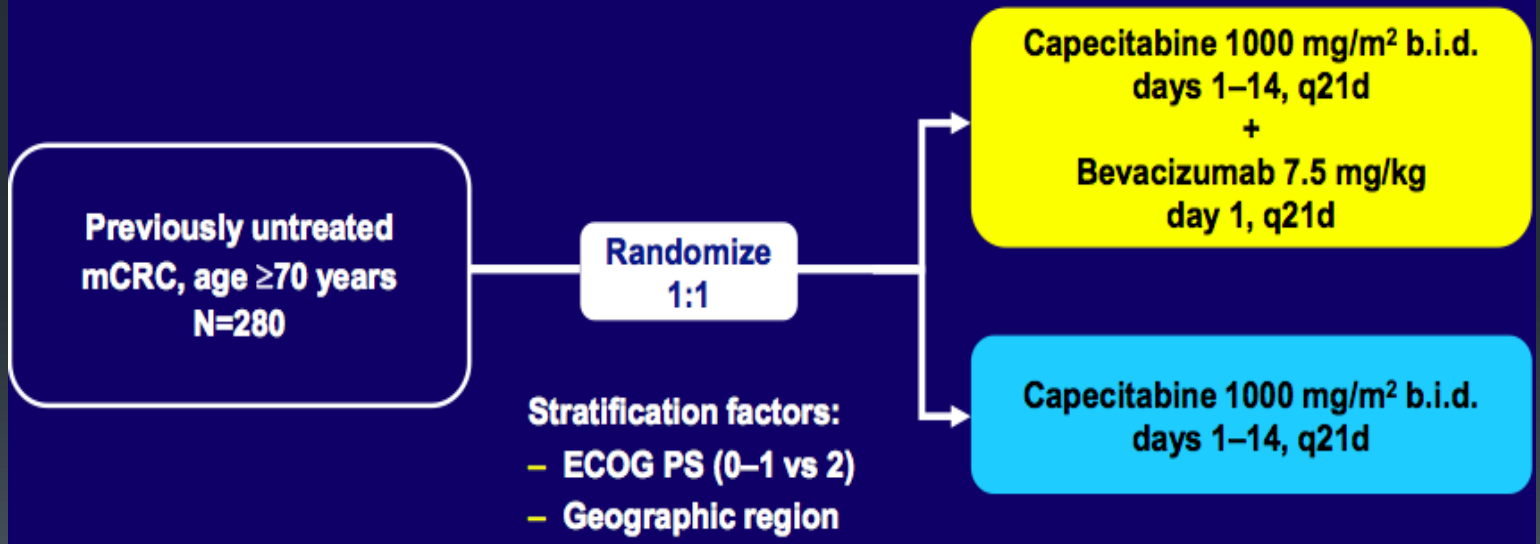
TREATMENT

Treatment of cardiotoxicity.

Cardiotoxicity	Therapy	Results
Heart failure	ACE inhibitors; angiotensin II receptor blockers; β-blockers	Reverse remodeling; recovery of cardiac function; improve survival [53,54]
Hypertension	ACE inhibitors; angiotensin II receptor blockers	Prevent proteinuria; restore adeguate blood pressure [29]
Cardiomyopathy	ACE inhibitors	Protect and slow the progression of chemotherapy-induced cardiomyopathy [94]
Ventricular dysfunction	ACE inhibitors (enalapril); β-blocker (carvedilol)	Preservation and complete or partial recovery of left ventricular systolic function [91]
Tromboembolism	Anticoagulant therapy with warfarin or low-molecular-weight heparin	Restore normal endothelial function [95]

Bevacizumab in combination with capecitabine for the first-line treatment of elderly patients with metastatic colorectal cancer (mCRC): Results of a randomized international phase III trial (AVEX)

David Cunningham,[1] Istvan Lang,[2] Eugenio Marcuello,[3] Vito Lorusso,[4] Janja Ocvirk,[5] Dong Bok Shin,[6] Derek Jonker,[7] Stuart Osborne,[8] Niko Andre,[9] Daniel Waterkamp,[8] Mark P. Saunders[10]

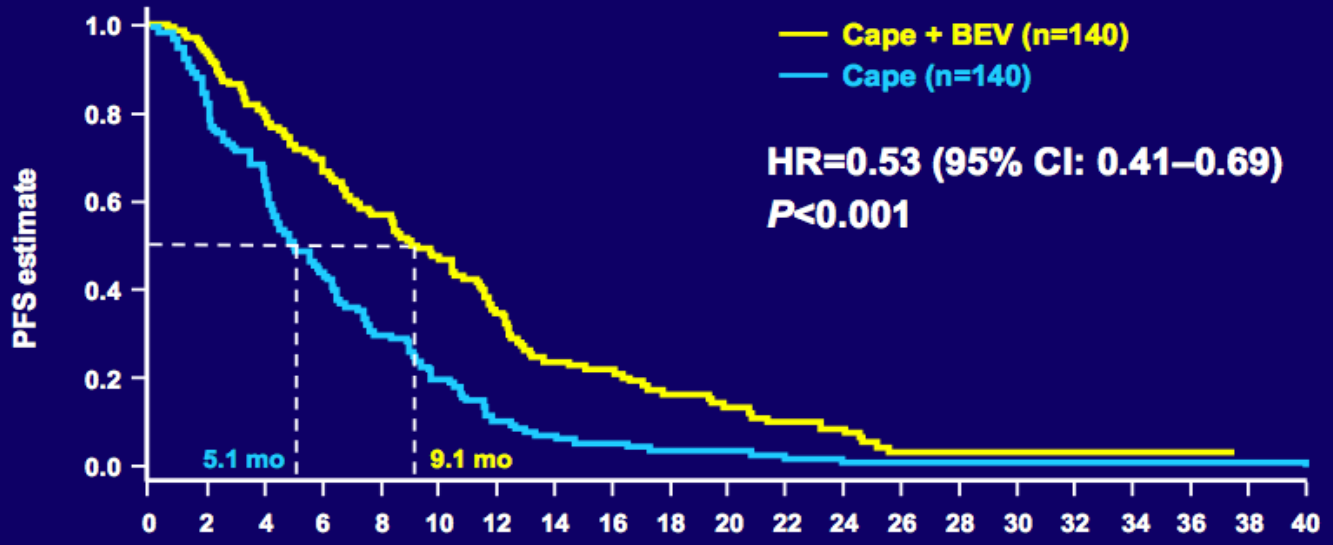


- **Key inclusion criteria**
  - ECOG PS 0–2
  - Prior adjuvant chemotherapy allowed if completed >6 month before inclusion
  - Not optimal candidates for a combination chemotherapy with irinotecan or oxaliplatin

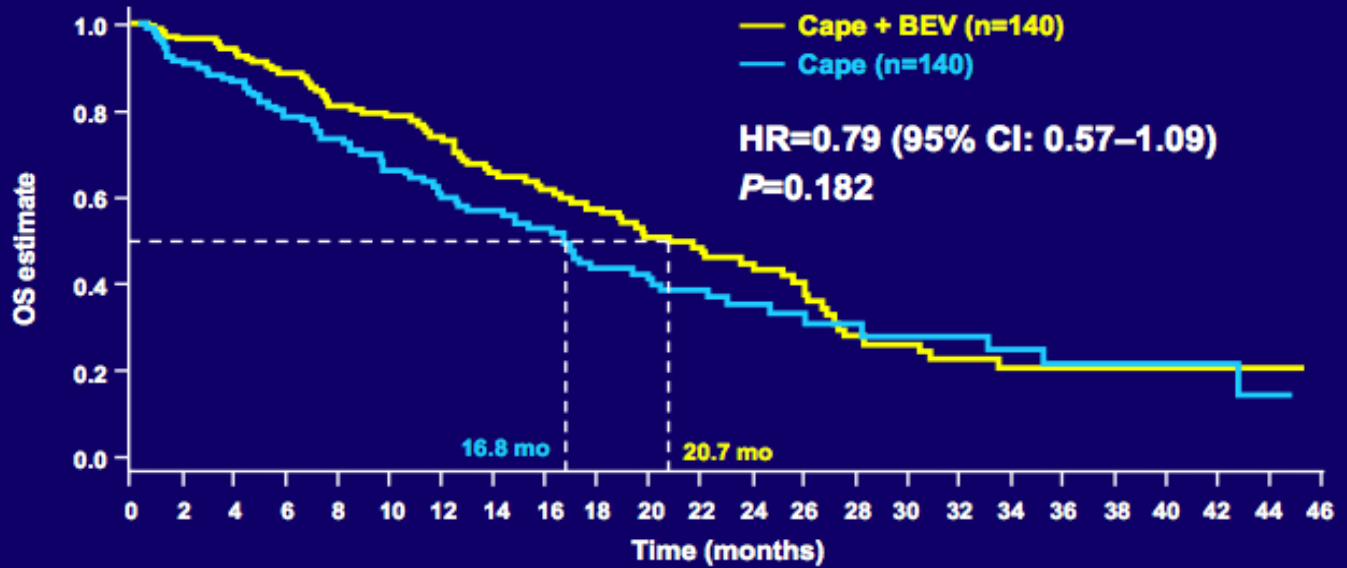
Select baseline patient characteristics

		Cape + BEV (n=140)	Cape (n=140)
Sex, %	Female	40.0	40.0
Median age, years (range)		76 (70–87)	77 (70–87)
	<75 years, %	39.3	32.9
	≥75 years, %	60.7	67.1
ECOG performance status, %	0	50.0	42.9
	1	41.4	47.9
	2	7.1	7.9
Prior adjuvant therapy, %	Yes	32.1	18.6
Site of metastatic disease, %	Liver	62.9	67.9
	Lung	35.7	40.7
	Other	35.0	22.9
	Liver only	37.1	38.6
Surgical resection, %	Yes	73.6	63.6
Location of primary disease, %	Colon only	57.9	54.3
	Rectum	31.4	25.0
	Colon and rectum	10.7	19.3

Progression-free survival



Overall survival



Contraindicated Use of Bevacizumab and Toxicity in Elderly Patients With Cancer

Dawn L. Hershman, Jason D. Wright, Emerson Lim, Donna L. Buono, Wei Yann Tsai, and Alfred I. Neugut

A B S T R A C T

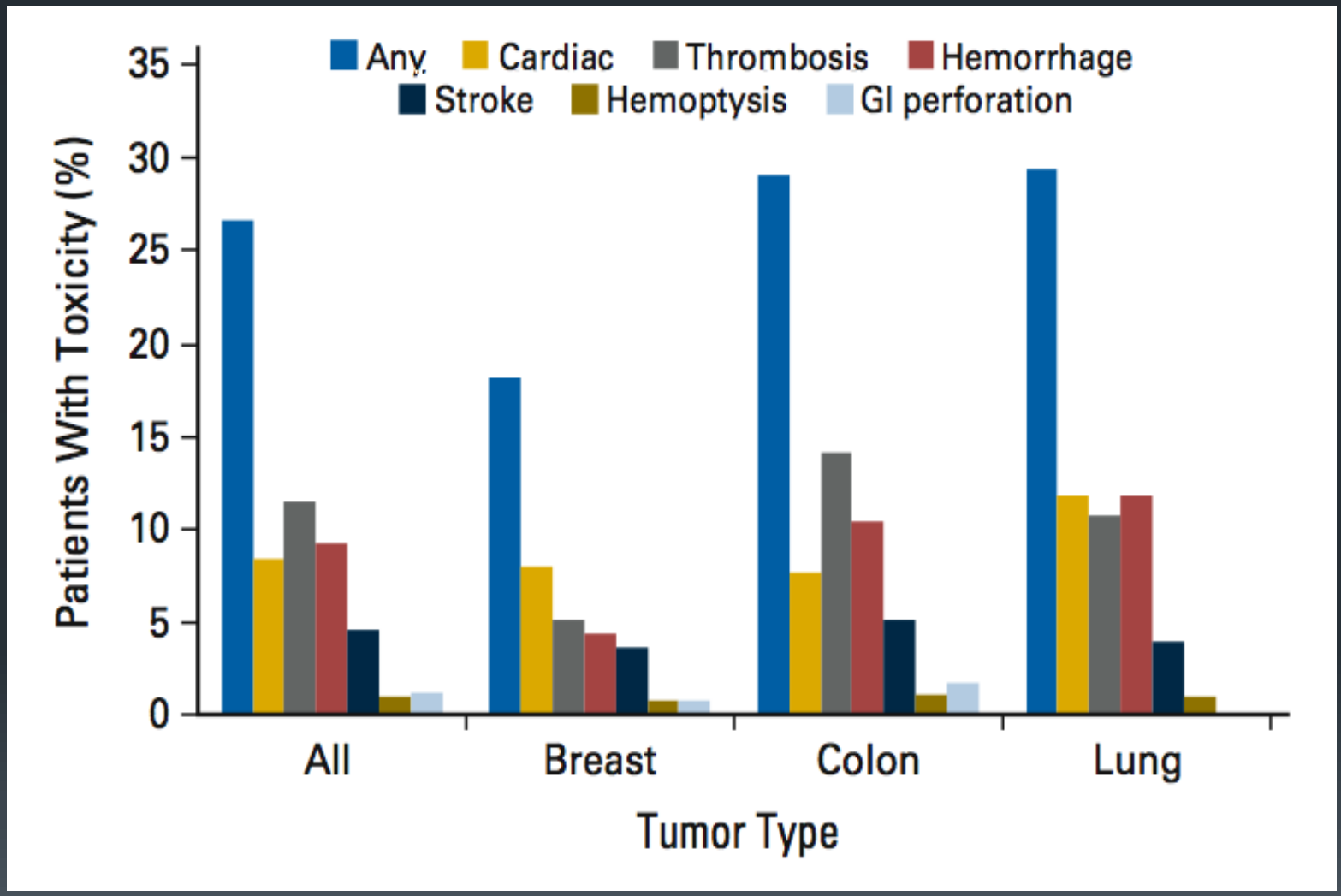
Purpose
Drugs are approved on the basis of randomized trials conducted in selected populations. However, once approved, these treatments are usually expanded to patients ineligible for the trial.

Patients and Methods
We used the SEER-Medicare database to identify subjects older than 65 years with metastatic breast, lung, and colon cancer, diagnosed between 2004 and 2007 and undergoing follow-up to 2009, who received bevacizumab. We defined a contraindication as having at least two billing claims before bevacizumab for thrombosis, cardiac disease, stroke, hemorrhage, hemoptysis, or GI perforation. We defined toxicity as first development of one of these conditions after therapy.

Results
Among 16,085 metastatic patients identified, 3,039 (18.9%) received bevacizumab. Receipt of bevacizumab was associated with white race, later year of diagnosis, tumor type, and decreased comorbid conditions. Of patients who received bevacizumab, 1,082 (35.5%) had a contraindication. In multivariate analysis, receipt of bevacizumab with a contraindication was associated with black race (odds ratio [OR] = 2.6; 95% CI, 1.4 to 4.9), increased age, comorbidity, later year of diagnosis, and lower socioeconomic status. Patients with lung (OR = 1.7; 95% CI, 1.1 to 2.4) and colon cancer (OR = 1.4; 95% CI, 1.1 to 1.9) were more likely to have a contraindication. In the group with no contraindication, 30% had a complication after bevacizumab; black patients were more likely to have a complication than were white patients (OR = 1.9; 95% CI, 1.21 to 2.93).

Conclusion
Our study demonstrates widespread use of bevacizumab among patients who had contraindications. Black patients were less likely to receive the drug, but those who did were more likely to have a contraindication. Efforts to understand toxicity and efficacy in populations excluded from clinical trials are needed.

J Clin Oncol 31:3592-3599.


Any
Cardiac
Thrombosis
Hemorrhage
Stroke
Hemoptysis
GI perforation
Patients With Toxicity (%)
35
30
25
20
15
10
5
0
All
Breast
Colon
Lung
Tumor Type

DEFINITION OF PALLIATIVE CARE (PC)

PC is a special kind of pt- and family-centered health care that focuses on effective management of pain and other distressing symptoms, while incorporating psychosocial and spiritual care according to pt/family needs, values, beliefs, and cultures. The goal of PC is to anticipate, prevent, and reduce suffering and to support the best possible QoL for pts and their families, regardless of the stage of the disease or the need for other therapies. PC begins at diagnosis and should be delivered concurrently with disease-directed, life-prolonging therapies and should facilitate pt autonomy, access to information, and choice. PC becomes the main focus of care when disease-directed, life-prolonging therapies are no longer effective, appropriate, or desidered. PC should be initiated by the primary oncology team and then augmented by collaboration with an interdisciplinary team of palliative care experts

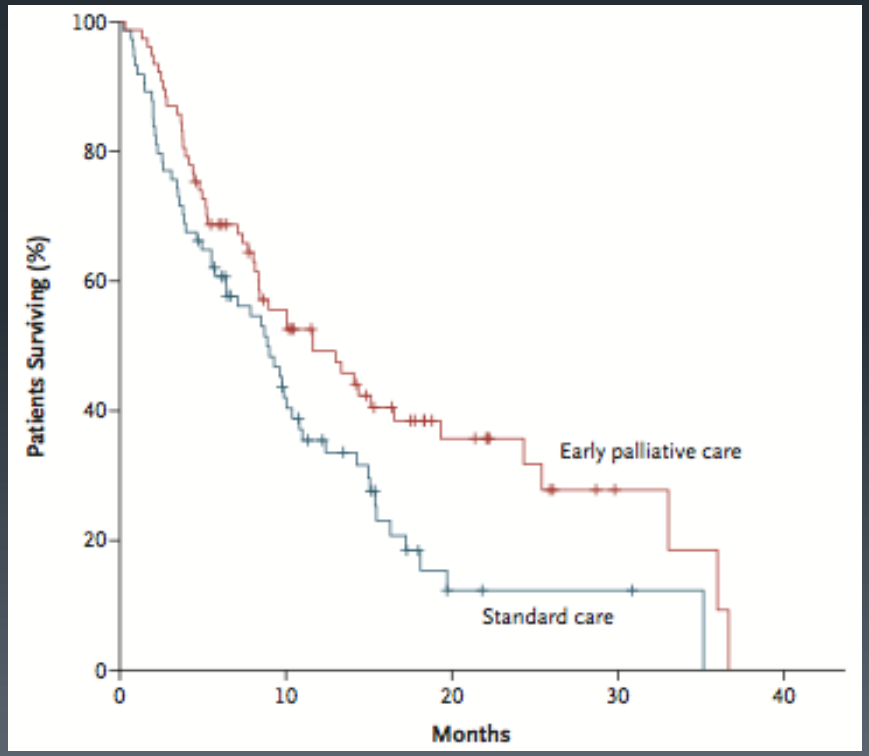
Hui D et al. J Pain Symptom Manage 2012;43:582

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Early Palliative Care for Patients with Metastatic Non–Small-Cell Lung Cancer

Jennifer S. Temel, M.D., Joseph A. Greer, Ph.D., Alona Muzikansky, M.A., Emily R. Gallagher, R.N., Sonal Admane, M.B., B.S., M.P.H., Vicki A. Jackson, M.D., M.P.H., Constance M. Dahlin, A.P.N., Craig D. Blinderman, M.D., Juliet Jacobsen, M.D., William F. Pirl, M.D., M.P.H., J. Andrew Billings, M.D., and Thomas J. Lynch, M.D.



N Engl J Med 2010;363:733-42.

SHORTAGE OF HEALTH-CARE PROFESSIONALS

- There is a clear discrepancy between supply and demand (currently, in USA, there is one geriatrician for every 2620 pts over the age of 75, but by the year 2030, the number of pts per geriatrician is expected to increase to 3798)
- This is going to have clear implications during our time as oncologists in terms of our workforce, and it is going to lead to evolving models of care. We are going to be partnering with our allied health professionals, physician assistants, and nurses. We'll be involving rehab, pharmacists, and social workers to help us with this care. And probably most importantly, we are going to be partnering at home, with families, family caregivers, and home care aides
- If we are all going to be caring for this population, there is a clear need for education and training

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The latest version is at http://jco.ascopubs.org/cgi/doi/10.1200/JCO.2013.49.6489

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Marital Status and Survival in Patients With Cancer

Ayal A. Aizer, Ming-Hui Chen, Ellen P. McCarthy, Mallika L. Mendu, Sophia Koo, Tyler J. Wilhite, Powell L. Graham, Toni K. Choueiri, Karen E. Hoffman, Neil E. Martin, Jim C. Hu, and Paul L. Nguyen

Results

Married patients were less likely to present with metastatic disease (adjusted odds ratio [OR], 0.83; 95% CI, 0.82 to 0.84; $P < .001$), more likely to receive definitive therapy (adjusted OR, 1.53; 95% CI, 1.51 to 1.56; $P < .001$), and less likely to die as a result of their cancer after adjusting for demographics, stage, and treatment (adjusted hazard ratio, 0.80; 95% CI, 0.79 to 0.81; $P < .001$) than unmarried patients. These associations remained significant when each individual cancer was analyzed ($P < .05$ for all end points for each malignancy). The benefit associated with marriage was greater in males than females for all outcome measures analyzed ($P < .001$ in all cases). For prostate, breast, colorectal, esophageal, and head/neck cancers, the survival benefit associated with marriage was larger than the published survival benefit of chemotherapy.

TAKE HOME MESSAGES

- By 2030, our largest shift in growth is going to be in the 80-plus population, a group where we really have had very limited data in best practices
- The primary challenge for clinical oncologists should be performing dedicated clinical trials rather than discussing indirect evidence
- If elderly population with cancer is selected by CGA/CRASH score to the treatment plan, toxicities are often manageable
- Pt must have decision-making capacity
- Effective strategies to prevent and treat toxicities of chemotherapy and biologic agents
- Polypharmacy
- Early palliative "simultaneous" care
- Shortage of health-care professionals (→ key-role of caregivers)