PBM: organizzazione, clinica e scenari futuri

Cesena, 28 – 29 Marzo 2019

ANEMIA CLINIC IN ONCOLOGIA

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disclosure

Il sottoscritto, in qualità di Relatore
dichiara che

nell'esercizio della Sua funzione e per l'evento in oggetto, NON È in alcun modo portatore di interessi commerciali propri o di terzi; e che gli eventuali rapporti avuti negli ultimi due anni con soggetti portatori di interessi commerciali non sono tali da permettere a tali soggetti di influenzare le mie funzioni al fine di trarne vantaggio.

Dott.ssa Erminia Di Bartolomeo

BACKGROUND

- L'anemia è comune in molti pazienti con cancro
- È un fattore indipendente di outcome
- La sua correzione impatta positivamente su trattamento cancro-relato

H. Ludwig et al. The European Cancer Anaemia Survey (ECAS): A large, multinational, prospective survey defining the prevalence, incidence, and treatment of anaemia in cancer patientsEuropean Journal of Cancer 40 (2004) 2293–2306

DIMENSIONI DEL PROBLEMA

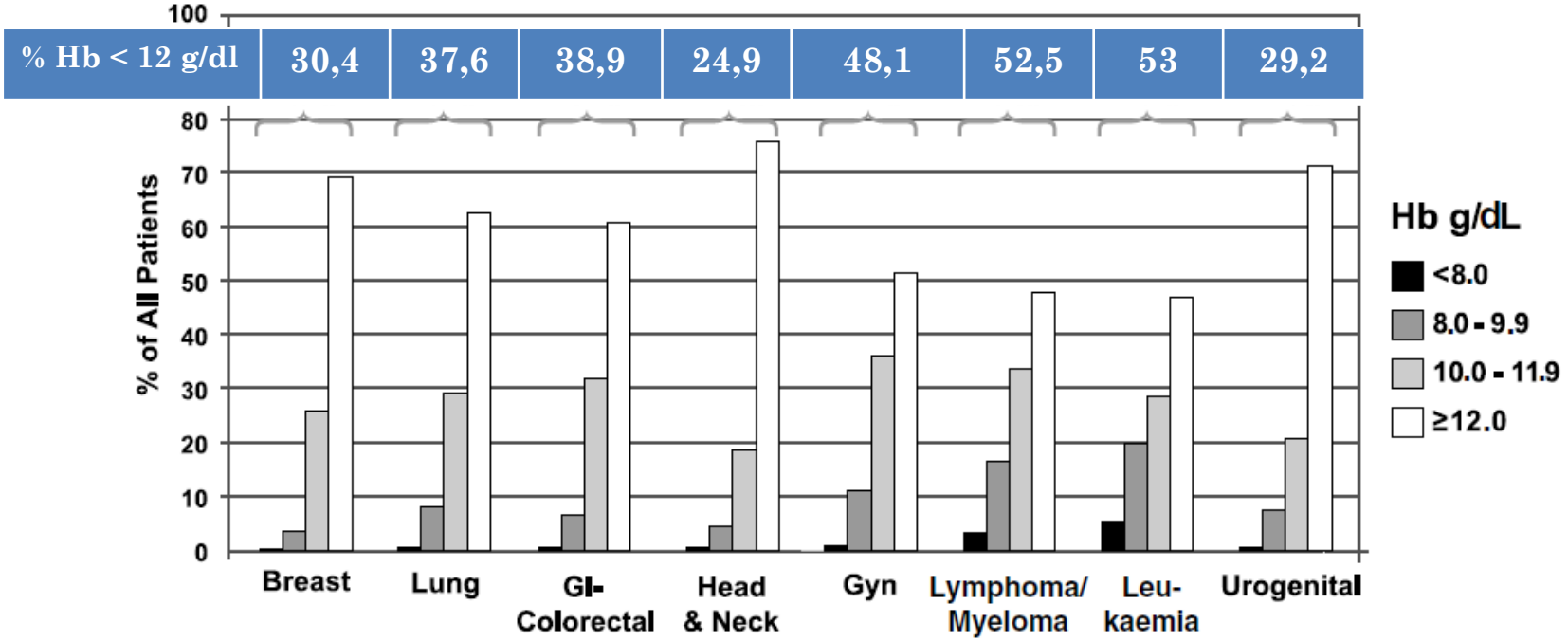
THE EUROPEAN CANCER ANAEMIA SURVEY (ECAS): A LARGE, MULTINATIONAL, PROSPECTIVE SURVEY DEFINING THE PREVALENCE, INCIDENCE, AND TREATMENT OF ANAEMIA IN CANCER PATIENTS

748 cancer centres in 24 European countries

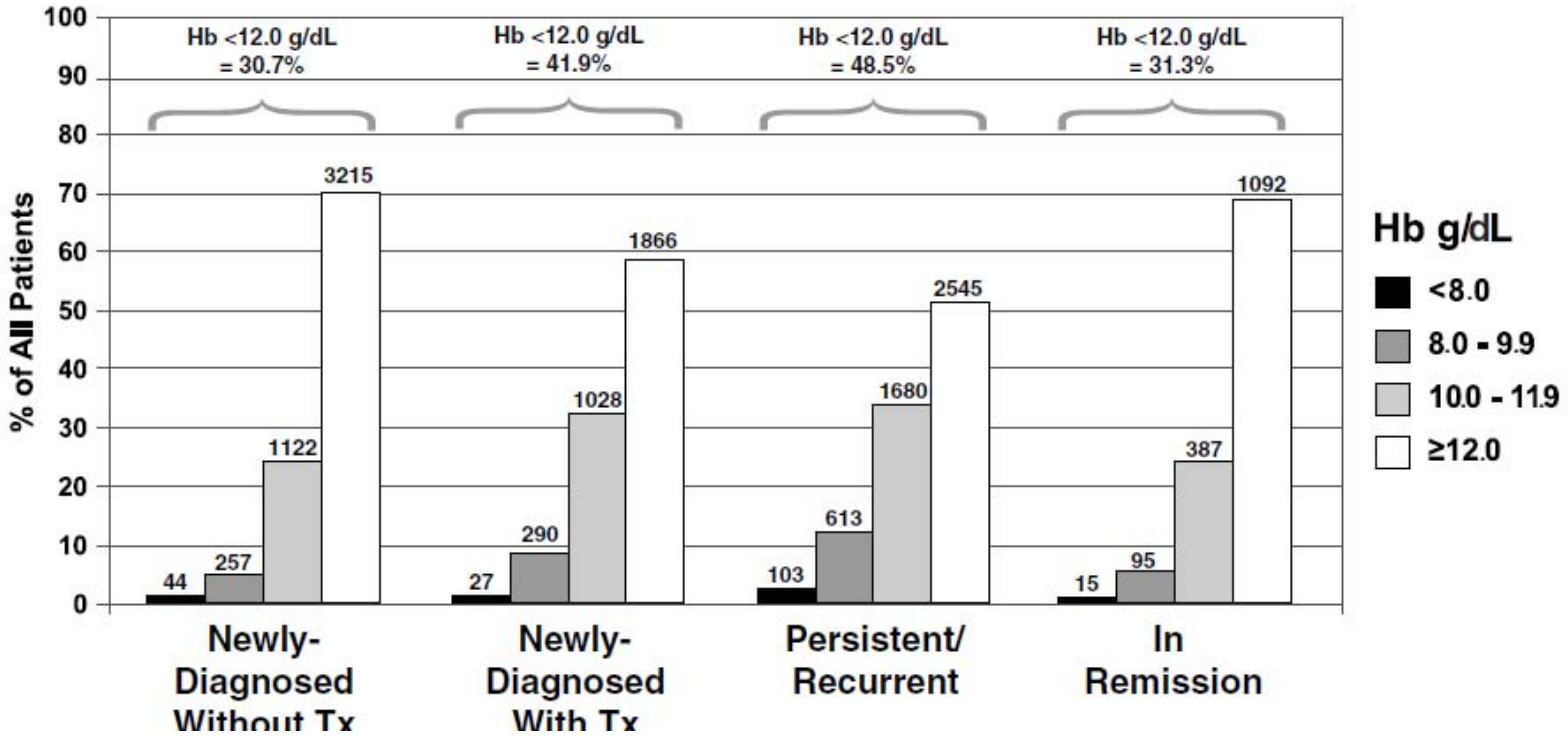
Analysis Population **N 14.520**

Anno 2004

Prevalenza 39.3%

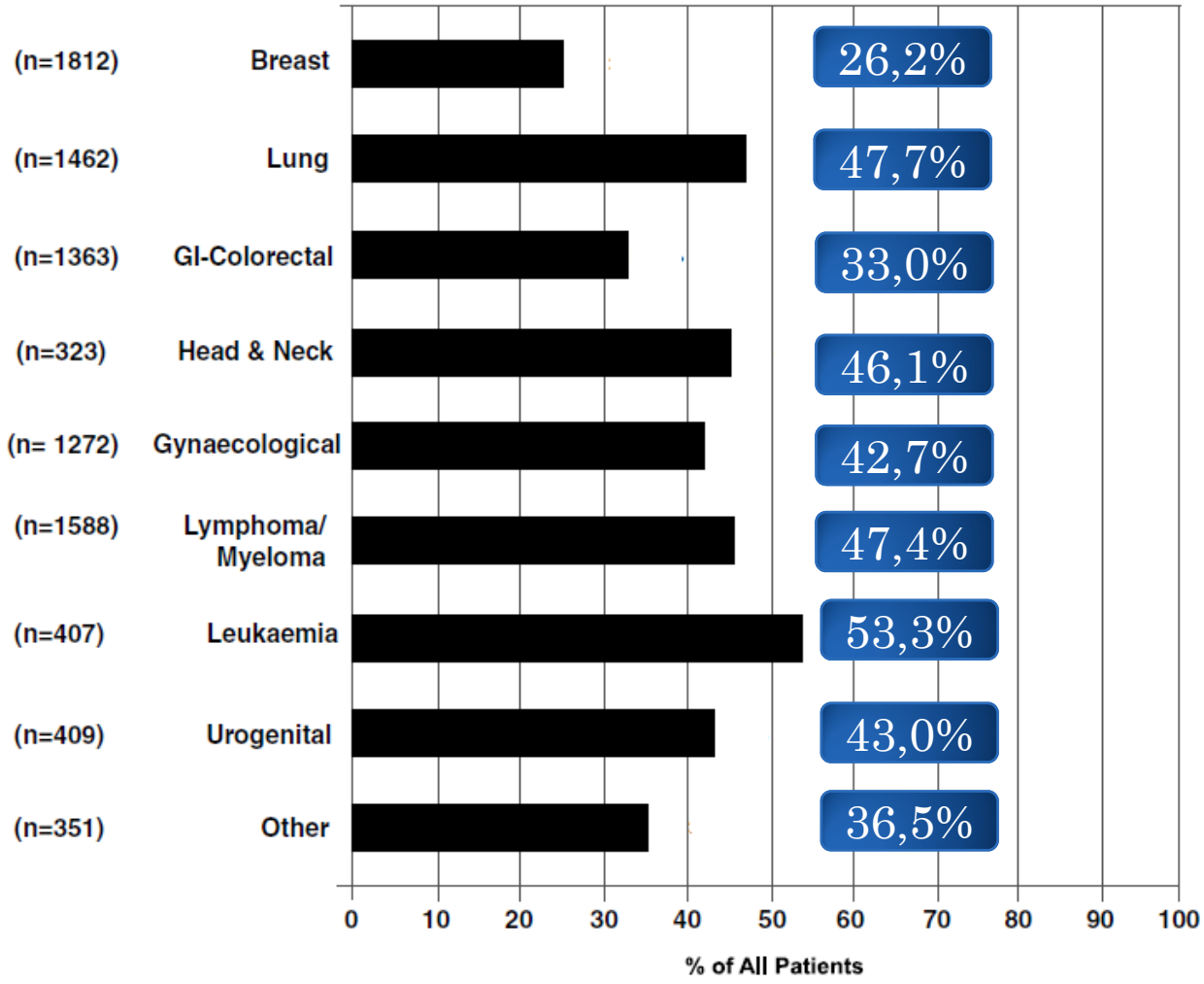


L'INCIDENZA RISENTE DEL TRATTAMENTO E DELLO STATO DI MALATTIA

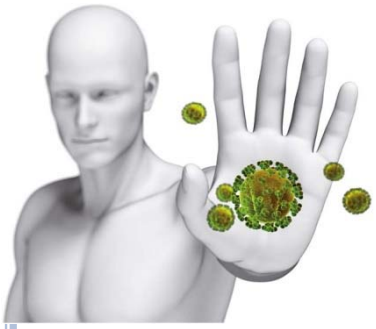


H. Ludwig et al. The European Cancer Anaemia Survey (ECAS): A large, multinational, prospective survey defining the

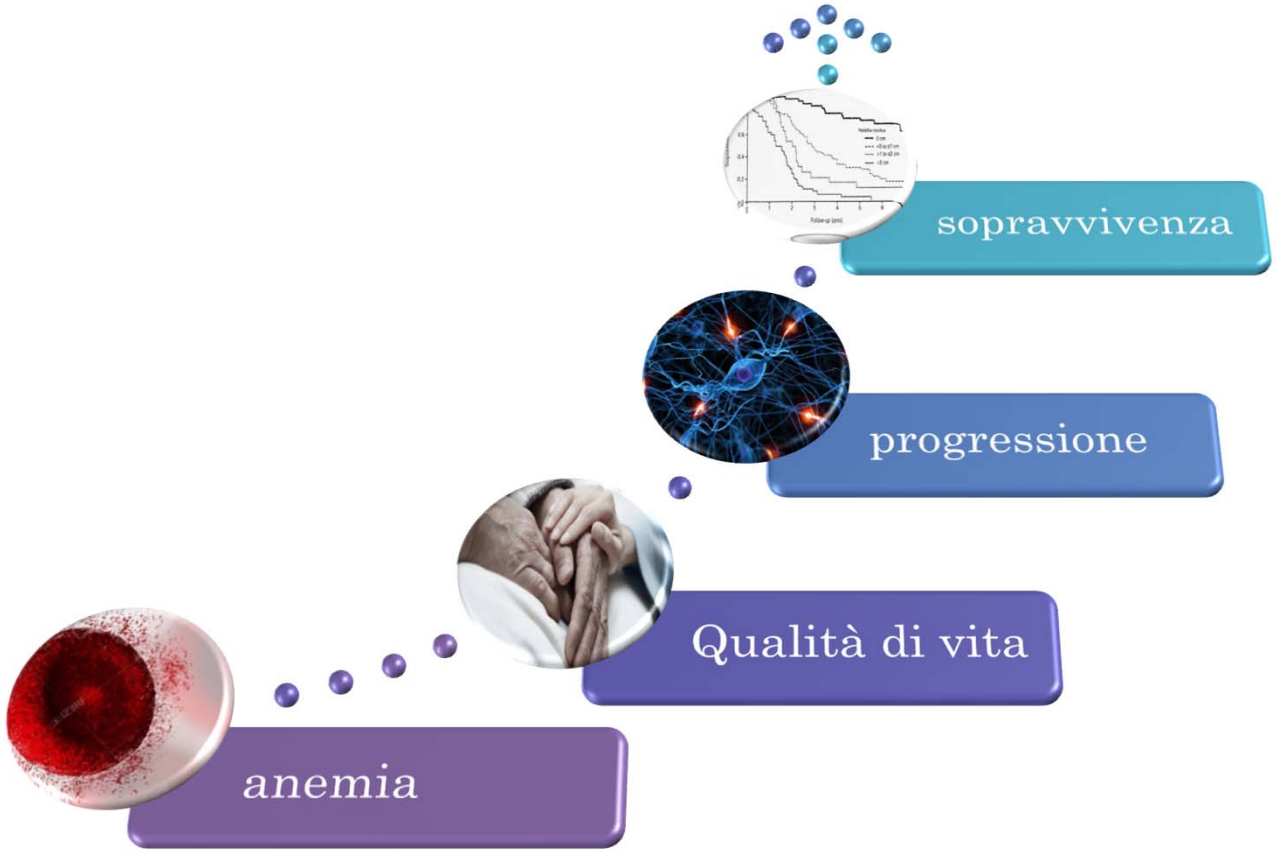
Percentage of patients who received anaemia treatment



H. Ludwig et al. The European Cancer Anaemia Survey (ECAS): A large, multinational, prospective survey defining the



PERCHÉ È IMPORTANTE GESTIRE L'ANEMIA NEL PAZIENTE ONCOLOGICO



ANEMIA È UN FATTORE INDIPENDENTE DI OUTCOME

521 pazienti con carcinoma squamoso della testa e del collo stadio III o IV

Variable	Risk ratio	95% CI	*p* value
Hemoglobin level	1.494	(1.144, 1.950)	0.0032
ETA	1.057	(0.832, 1.343)	0.6493
Age	1.014	(0.794, 1.295)	0.9113
Sex	1.069	(0.809, 1.411)	0.6391
T-stage	1.516	(1.183, 1.944)	0.0010
N-stage	1.356	(1.052, 1.747)	0.0186
KPS	0.621	(0.486, 0.795)	0.0002
RT to primary	0.812	(0.632, 1.042)	0.1017
Overall treatment time	0.999	(0.986, 1.012)	0.8793

Analisi multivariata

P= 0,0016

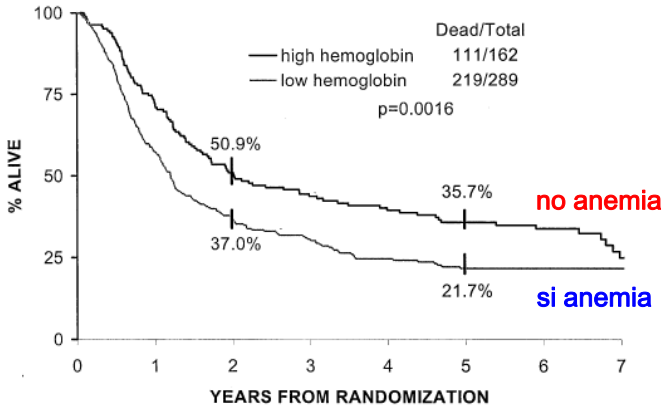


Fig. 1. Overall survival for all patients according to hemoglobin level.

P= 0,00028

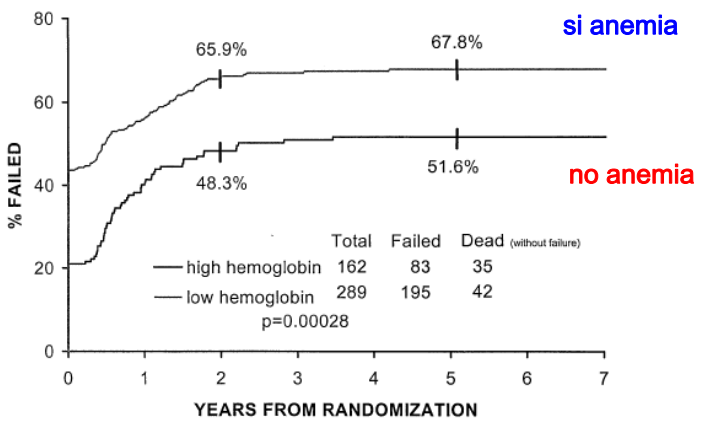
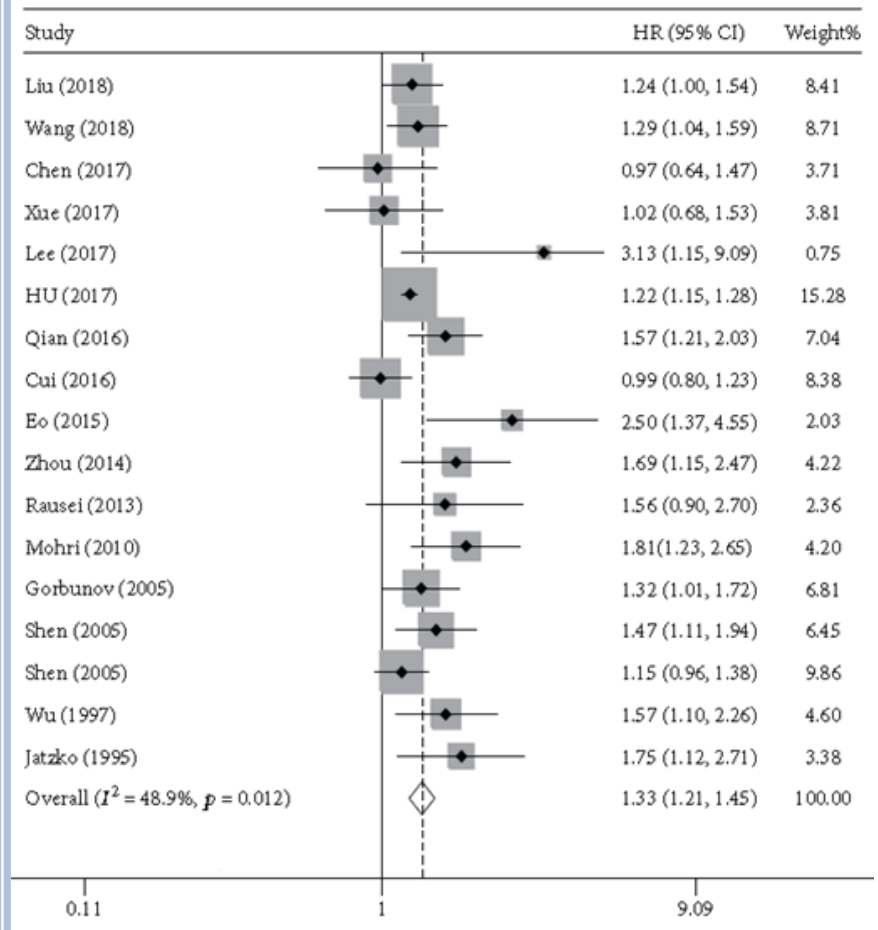


Fig. 2. Locoregional failure for all patients according to hemoglobin level.

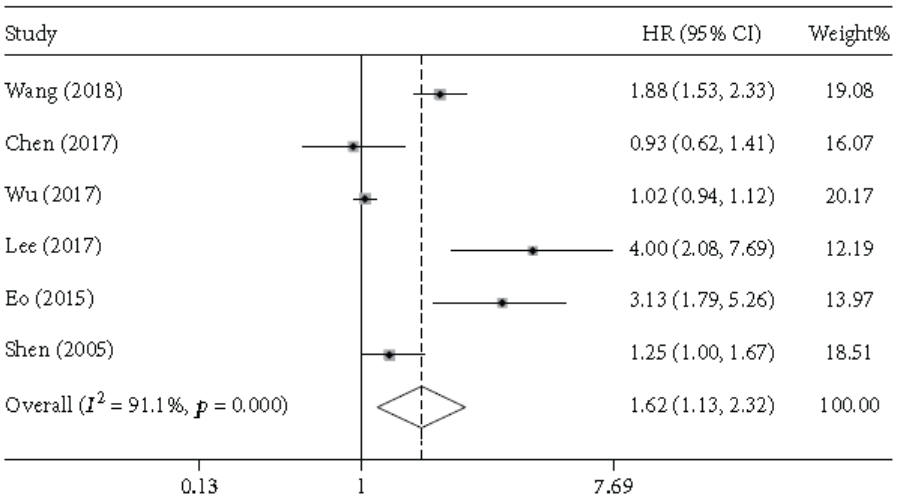
W. ROBERT LEE et al. Int. J. Radiation Oncology Biol. Phys., Vol. 42, No. 5, pp. 1069–1075, 1998

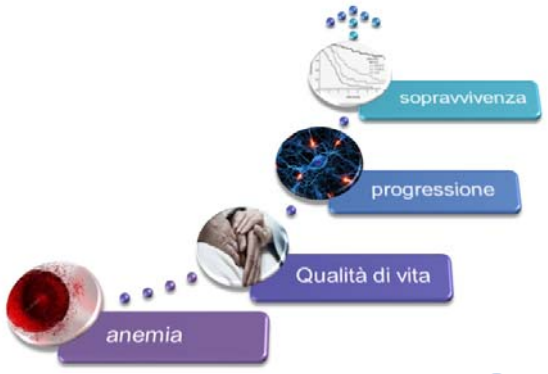
ANEMIA È UN FATTORE INDIPENDENTE DI OUTCOME

overall survival



disease-free survival

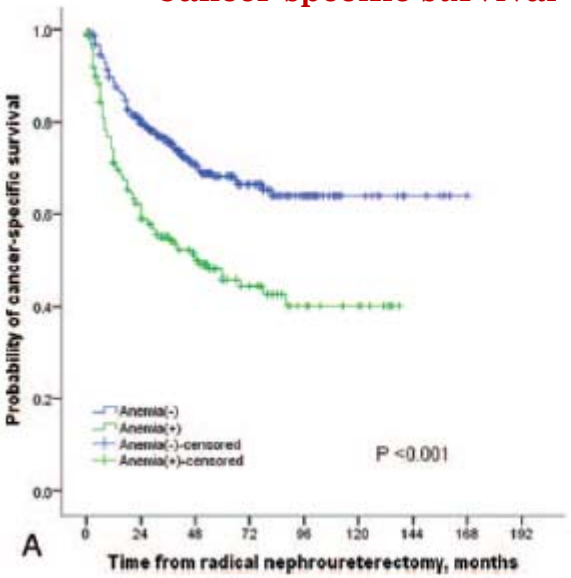




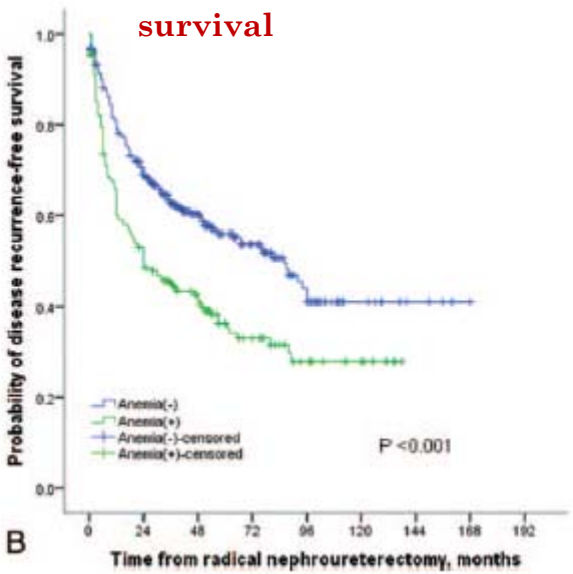
Prognostic impact of preoperative anemia on upper tract urothelial carcinoma

Pazienti totali 620 con carcinoma uroteliale del tratto superiore (UTUC) sottoposti a uterectomia
Pazienti anemici 246

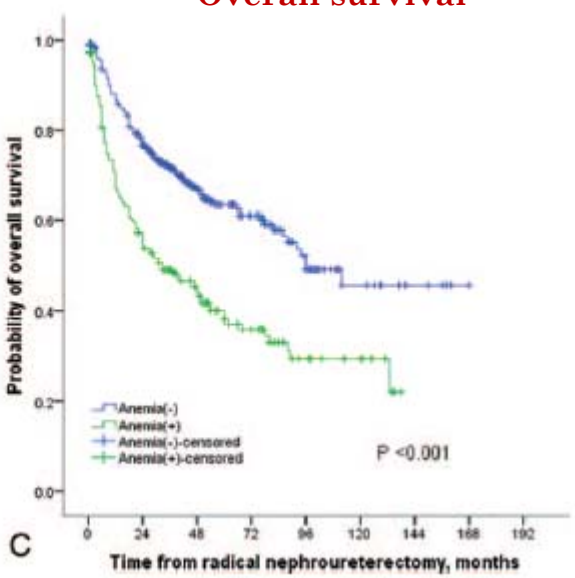
Cancer-specific survival



Recurrence-free survival



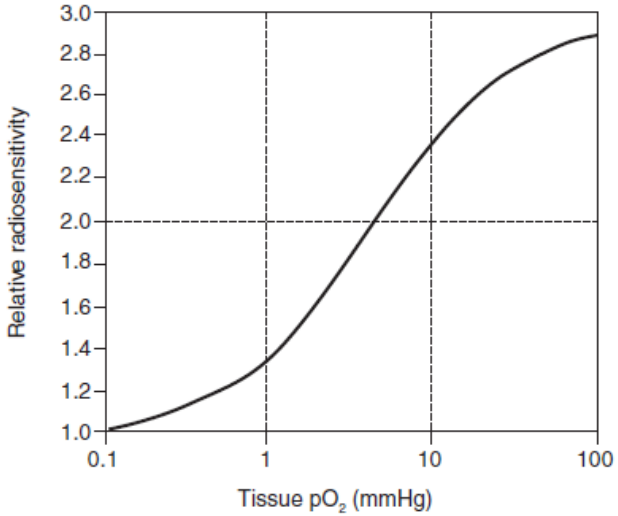
Overall survival

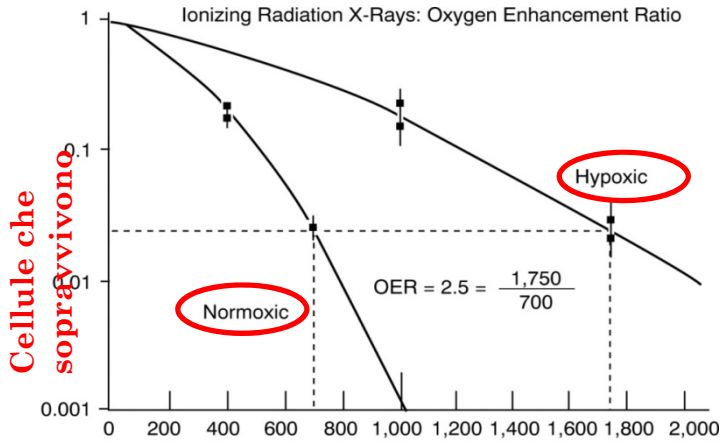


Tan et al. Medicine (2018) 97:37

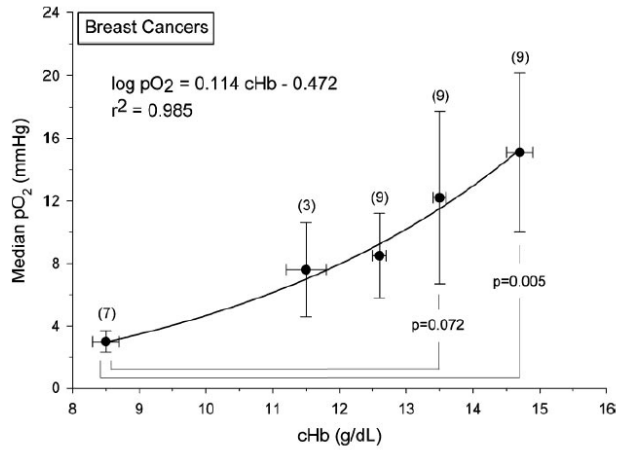
Anemia come fattore di ipossia nel cancro

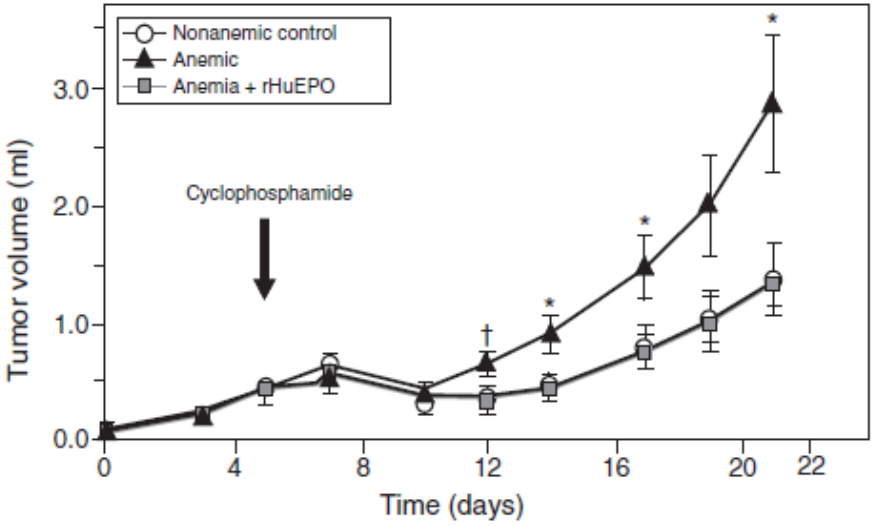
Harrison, Blackwell et al Hypoxia and Cancer Treatment ResponseThe Oncologist 2004;9 (suppl 5):31-40
Kumar P The Oncologist 2000; 5:13-18
Peter Vaupel et al. CANCER RESEARCH 63, 7634–7637, November 15, 2003]



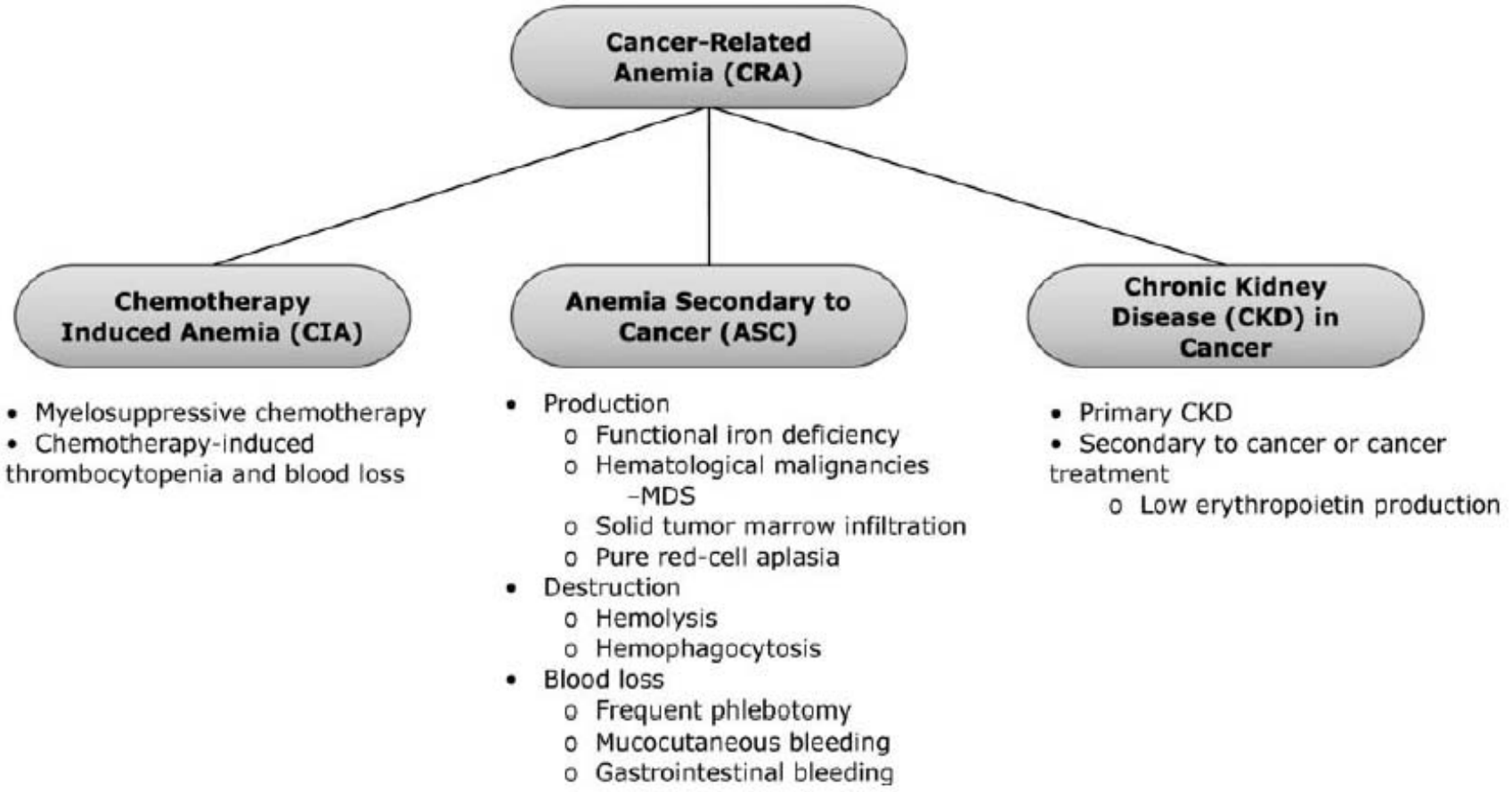


Dose di radiazione (cGy)



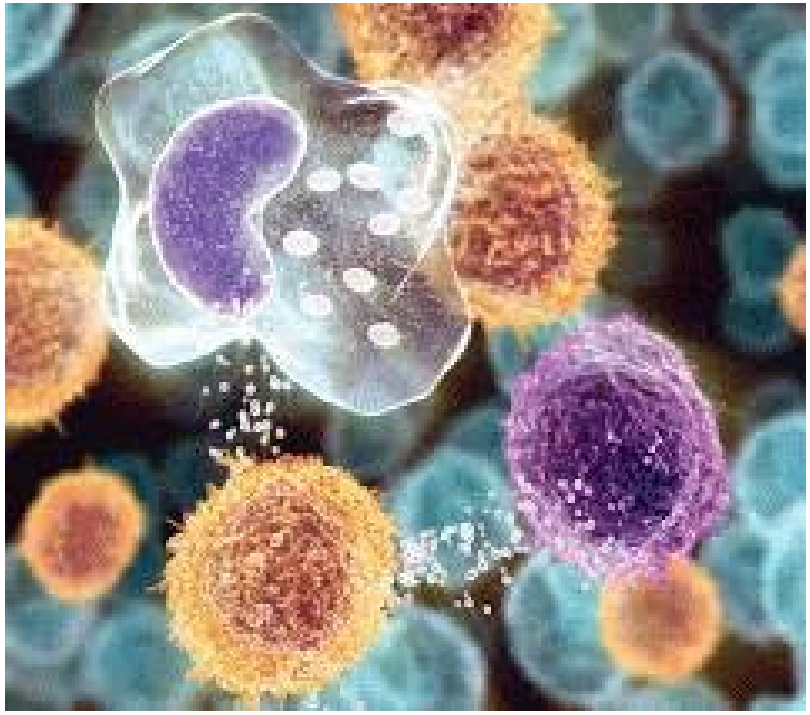


PATOGENESI DELL'ANEMIA NEL PAZIENTE NEOPLASTICO



Gilreath et al. Diagnosis and treatment of cancer-related anemiaAmerican Journal of Hematology, Vol. 89, No. 2, February 2014

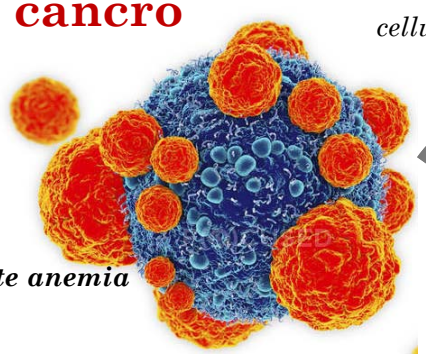
STROMA NEOPLASTICO



Con la progressione del tumore, si crea uno " **stroma reattivo**", che rilascia una serie di segnali i quali inducono cambiamenti nel fenotipo delle cellule tumorali, costituito principalmente da fibroblasti associati al cancro (CAF), cellule endoteliali e periciti che formano vasi sanguigni e linfatici, e cellule infiammatorie (macrofagi associati al tumore, TAM), attratti da chemochine tumorali (Mueller M. et al., 2004).

Complesso sistema di interazioni tra le cellule tumorali e il sistema immune

Eziologia dell'anemia da cancro



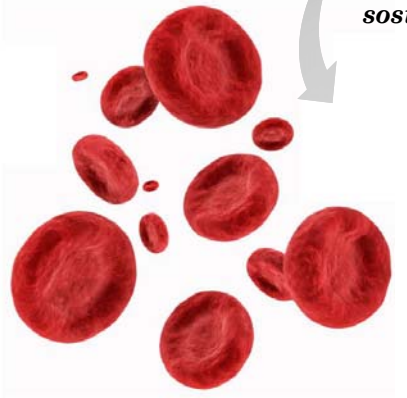
cellula tumorale

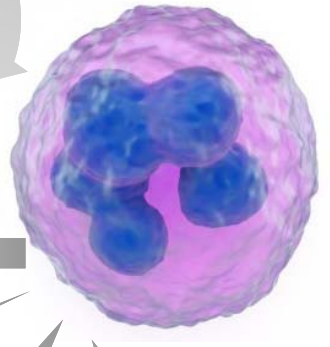
Attivazione immunitaria

eritrociti

macrofagi

AIS
sostanza inducente anemia





ERITROFAGOCITOSI

TNF

DISERITROPOIESI

Ridotta sopravvivenza

IL-1 α β
TNF

IFN-g
IL-1
TNF
a_1-antitripsina

IFN- γ
IL-1
TNF

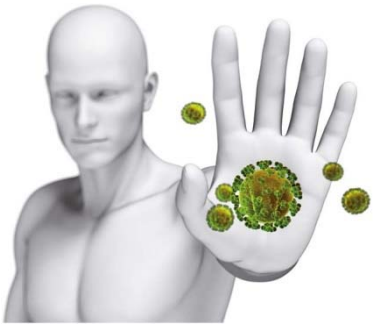
ANEMIA

Ridotta produzione di EPO

Soppressione delle BFU-e CFU-e

Alterata utilizzazione del ferro

Birgegård et al. Cancer-Related Anemia: Pathogenesis, Prevalence and Treatment Oncology 2005;68(suppl 1):3–11



Management of anemia in cancer patients often requires a multidisciplinary approach

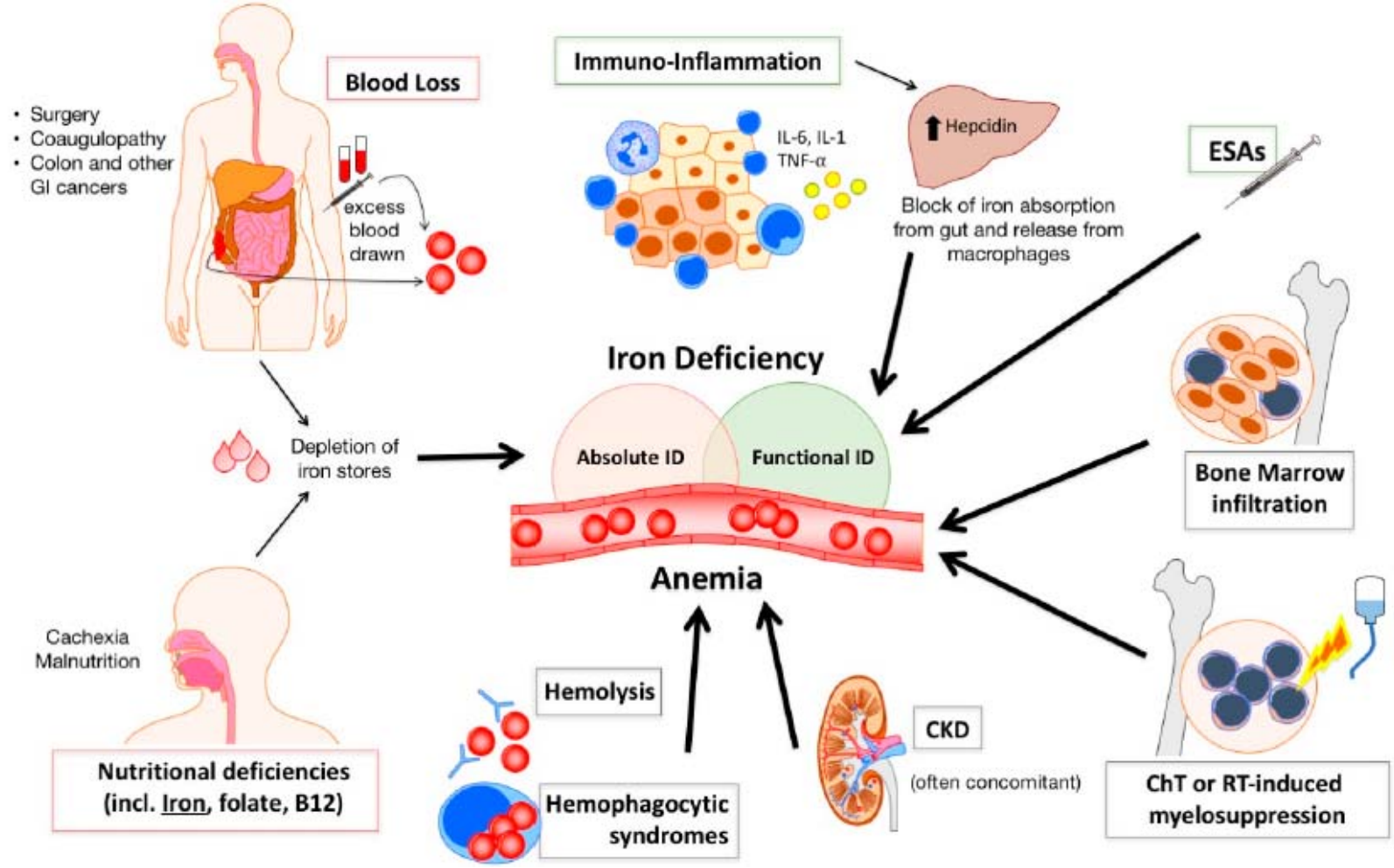
MIRATO ALLA CORREZIONE DEI DIVERSI MECCANISMI CHE CONTRIBUISCONO ALLA GENESI DELL'ANEMIA

1) Ridotta utilizzazione del Fe
2) Ridotta sopravvivenza eritrocitaria
3) Soppressione dei progenitori eritroidi
4) Inappropriata produzione di EPO

Ridotta utilizzazione del Fe

Terapia Marziale

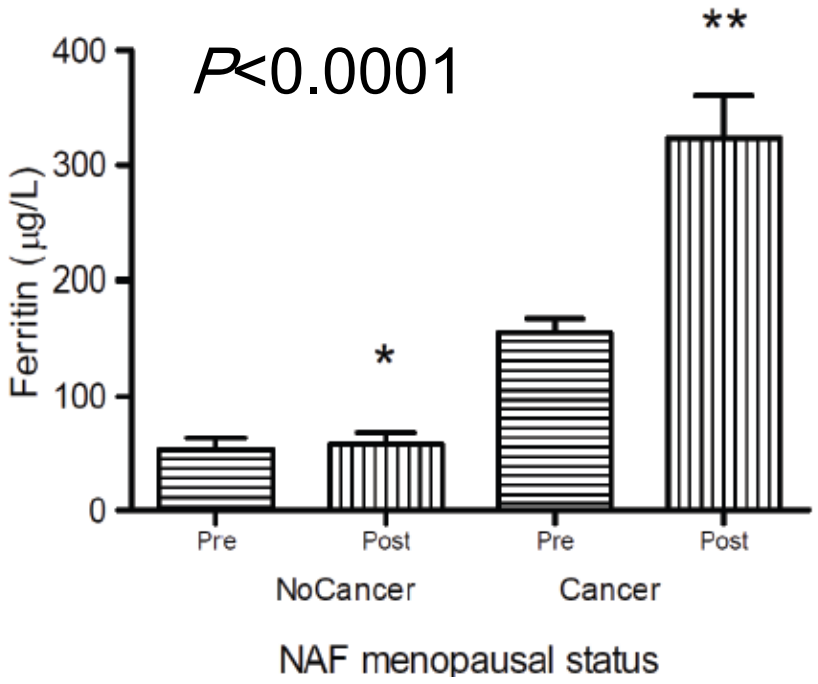
ANEMIA AND IRON DEFICIENCY IN CANCER

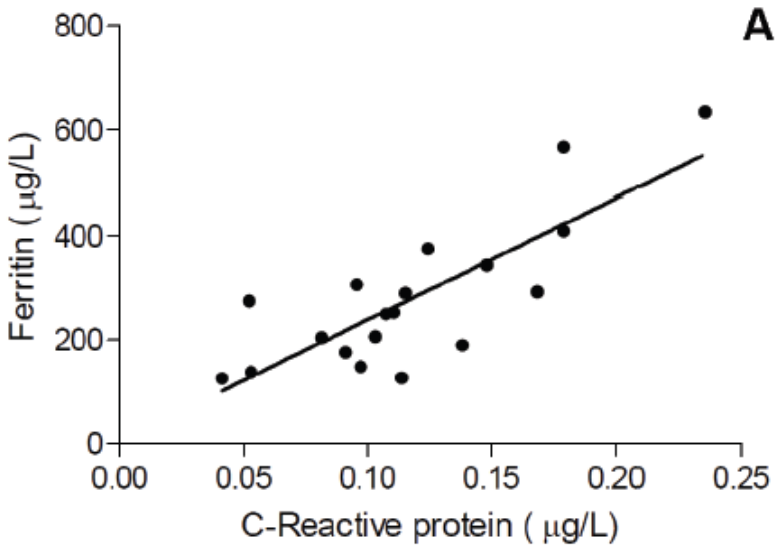


Iron-binding proteins and C-reactive protein in Nipple Aspirate Fluids: role of Iron-driven inflammation in breast cancer microenvironment?

Ferdinando Mannello

Am J Transl Res 2011;3(1):100-113

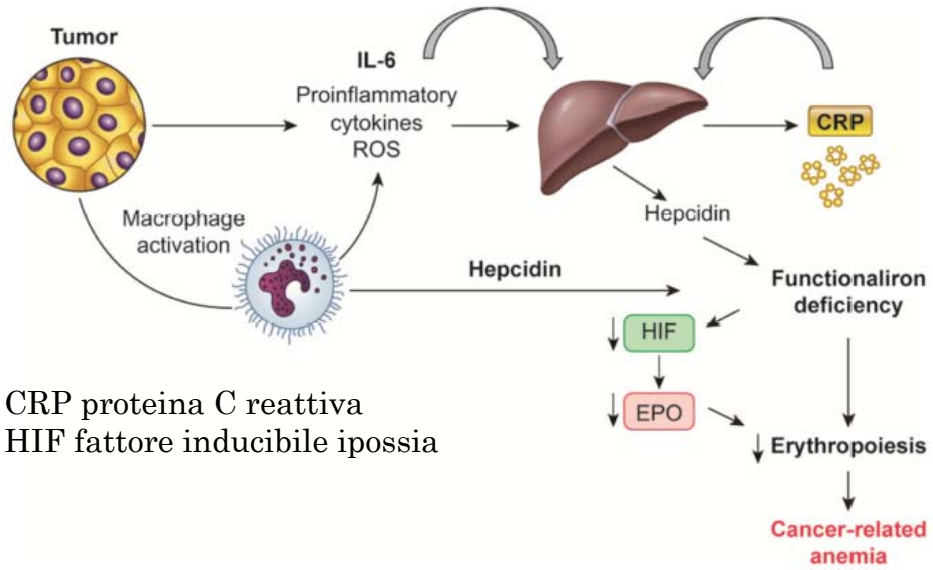




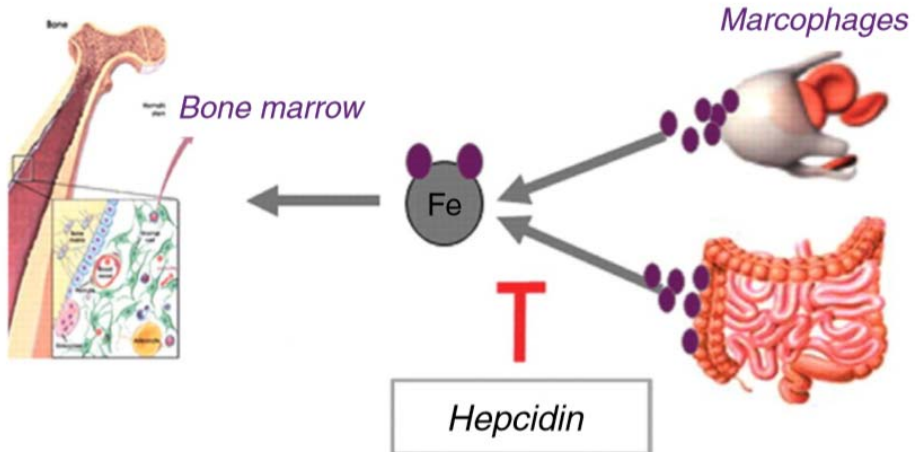
EPCIDINA

Regolatore negativo dell'assorbimento del ferro degli alimenti e del rilascio del ferro dai macrofagi

La funzione principale dell'epcidina e quella di down regolare la ferroportina (FNP), legandosi ad essa e determinandone l'endocitosi e conseguente degradazione



CRP proteina C reattiva
HIF fattore inducibile ipossia



C Madaddu et al. Frontiers in Physiology September 2018 Vol 9

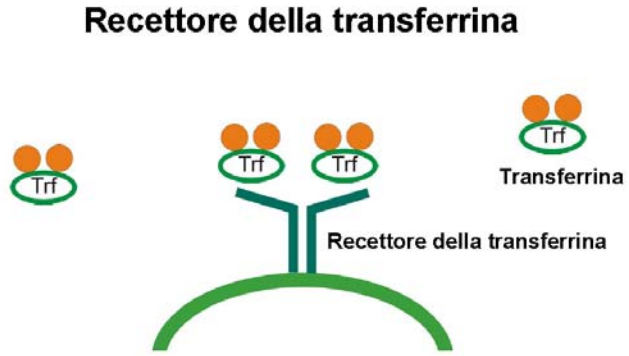
TRANSFERRINA

- È la proteina che trasporta il ferro all'interno dell'organismo, dai distretti in cui il ferro viene assorbito (intestino) a quelli che lo utilizzano (in particolare il midollo osseo, dove vengono prodotti i globuli rossi) o agli organi di deposito (in particolare il fegato).

- In caso di necessità, il ferro dagli organi di deposito viene ceduto alla transferrina che provvede al suo trasporto ai diversi tessuti.

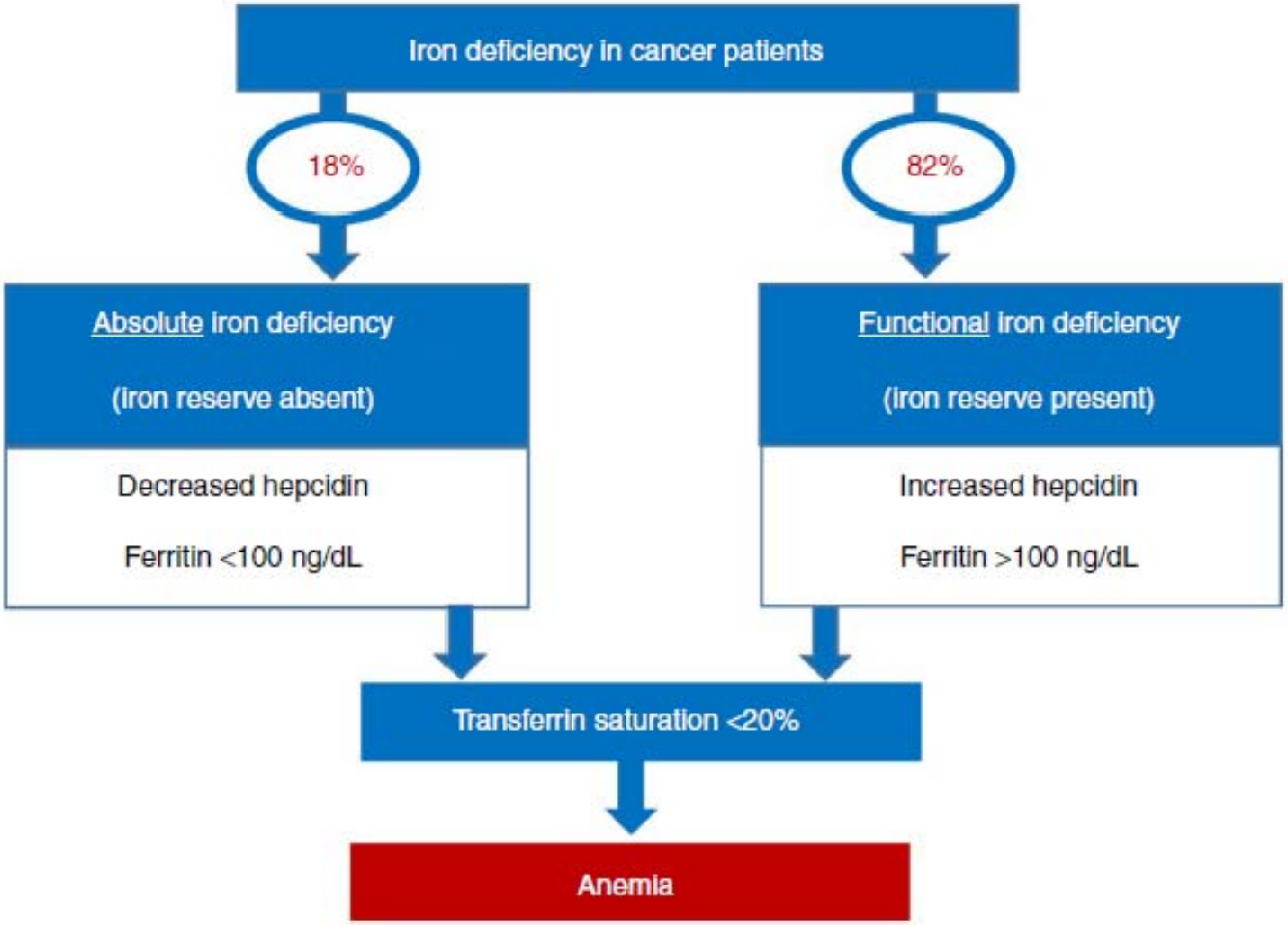
- Ogni molecola di transferrina può legare al massimo due atomi di ferro.

La misurazione della *saturazione della transferrina* è un esame molto importante per stabilire lo stato del ferro di un individuo. Infatti se inferiore al 18% è indice di uno stato ferro-carenziale e se superiore al 50% è indice di un sovraccarico di ferro



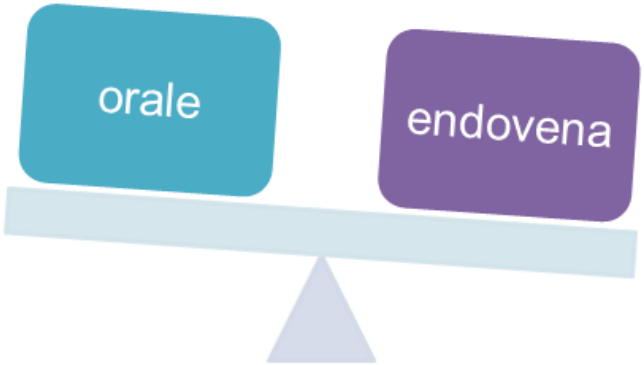
Le cellule che necessitano di ferro esprimono in superficie un numero elevato di **recettori**

L'IMPORTANZA DI UNA DIAGNOSI CORRETTA



FA Naoum. Iron deficiency in cancer patients Rev Bras Hematol Hemoter. 2016; 38 (4):325–330

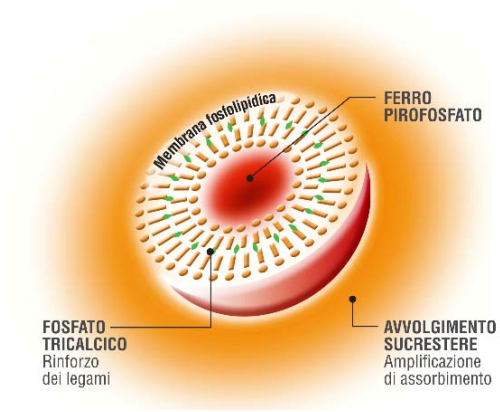
LA TERAPIA MARZIALE

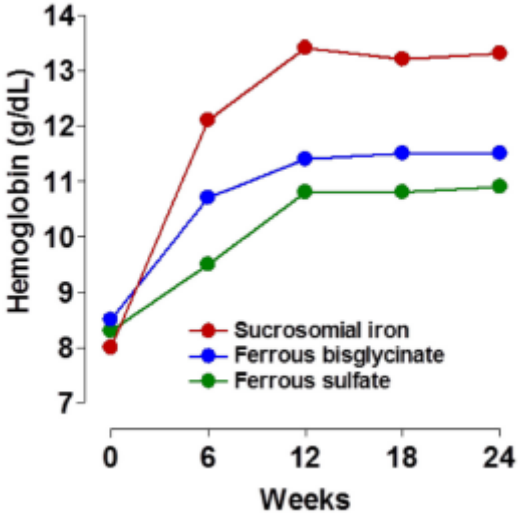


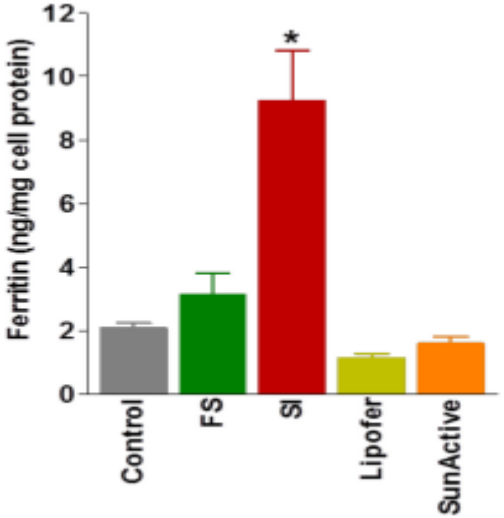
Scelta della modalità di intervento

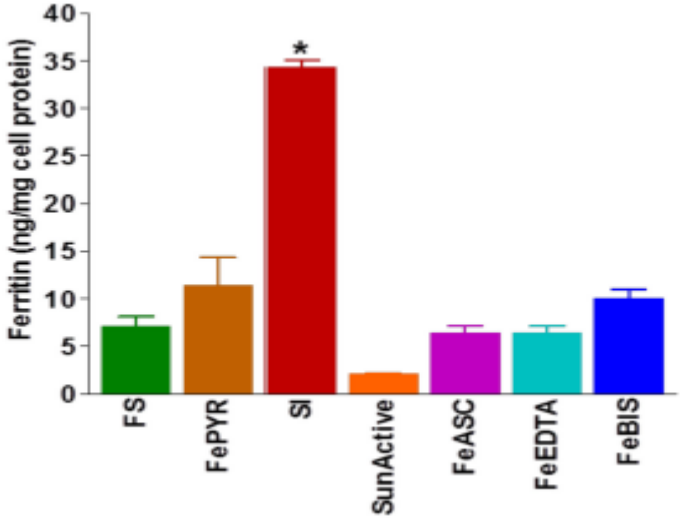
- gravità dell'anemia
- età
- presenza di comorbidità
- quadro clinico, indice di fatigue
- entità carenza
- **tempo necessario per il ripristino di valori "accettabili" di Hb**

COMPOSTI MICROCAPSULATI









Bioavailability experiments

S. Gomez- Ramírez et al Sucrosomial® Iron: A New Generation Iron for Improving Oral Supplementation Pharmaceuticals 2018, 11, 97

Effects of micronised microencapsulated ferric pyrophosphate supplementation in patients with advanced cancer and iron deficiency: a single-centre cohort pilot study

A Pappalardo et al. Blood Transfus 2019

Studio osservazionale prospettico
Follow-up 10 mesi
42 pz con cancro (T0)

33% dei pazienti raggiunge Hb >12 g/dl

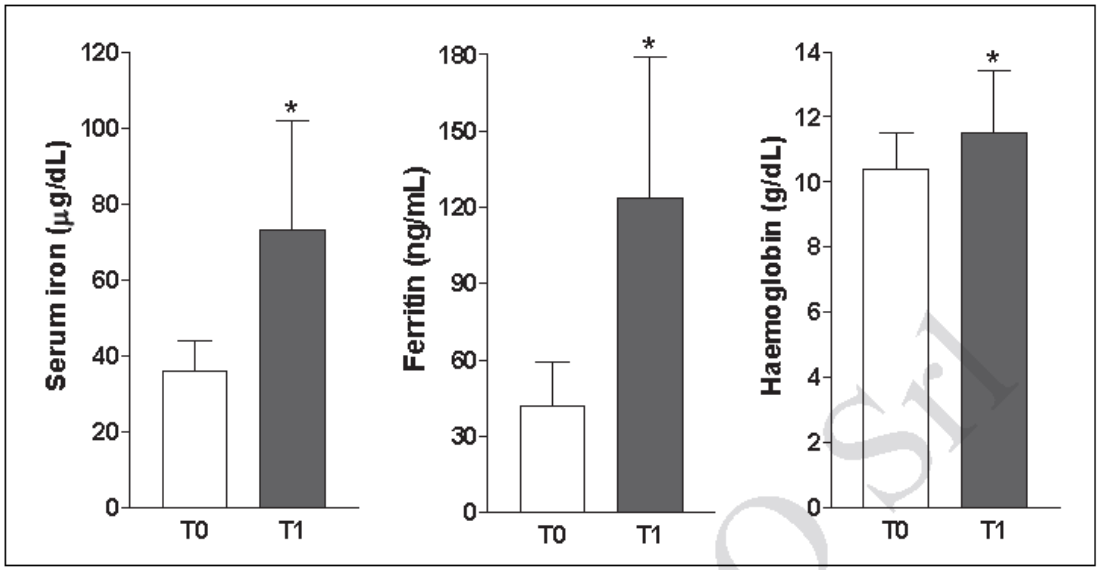
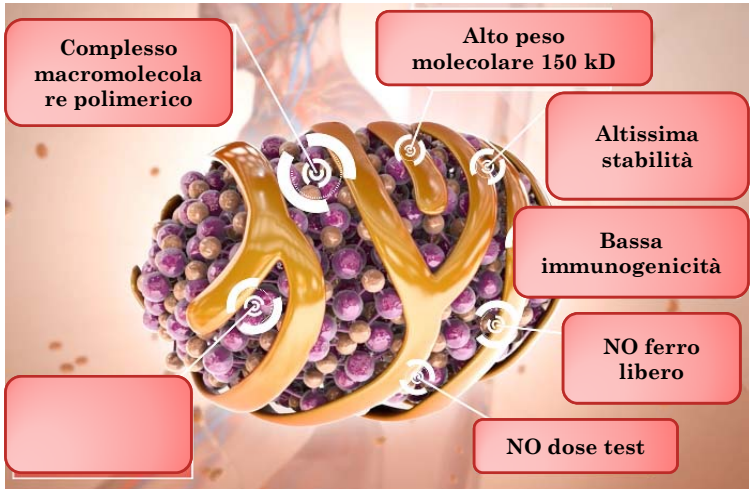


Figure 1 - Haematologic parameters (sideraemia, ferritinaemia and haemoglobin) at baseline (T0) and at 30 days after micronised microencapsulated ferric pyrophosphate supplementation (T1). $p<0.001$.

Trattamento 30 mg MMFP e 80 mg acido ascorbico per **30 giorni (T1)**

L'impiego di formulazioni microcapsulate incrementa i livelli di emoglobina e migliora idepositi di ferro nei pazienti con cancro in assenza di eventi avversi significativi, in virtù della migliore biodisponibilità

FERRO CARBOSSIMALTOSIO



Laboratory parameters	Before FCM	3 months post-FCM	p
Haemoglobin, g/dL	12.78 ± 1.90	13.68 ± 1.56	<0.001
Haematocrit, %	38.61 ± 6.37	41.65 ± 4.91	<0.001
Serum iron, µg/dL	62.53 ± 25.65	97.08 ± 35.81	<0.001
Serum ferritin, µg/L	74.71 ± 85.97	375.54 ± 247.85	<0.001
TSAT, %	16.00 ± 11.69	31.69 ± 11.69	<0.001

A Robles-Mezcua et al International Journal of Cardiology (2016) 118–120

National Comprehensive Cancer Network guidelines suggest that IV iron could be considered for ferritin levels up to 800 ng/mL

CENTRO NAZIONALE SANGUE

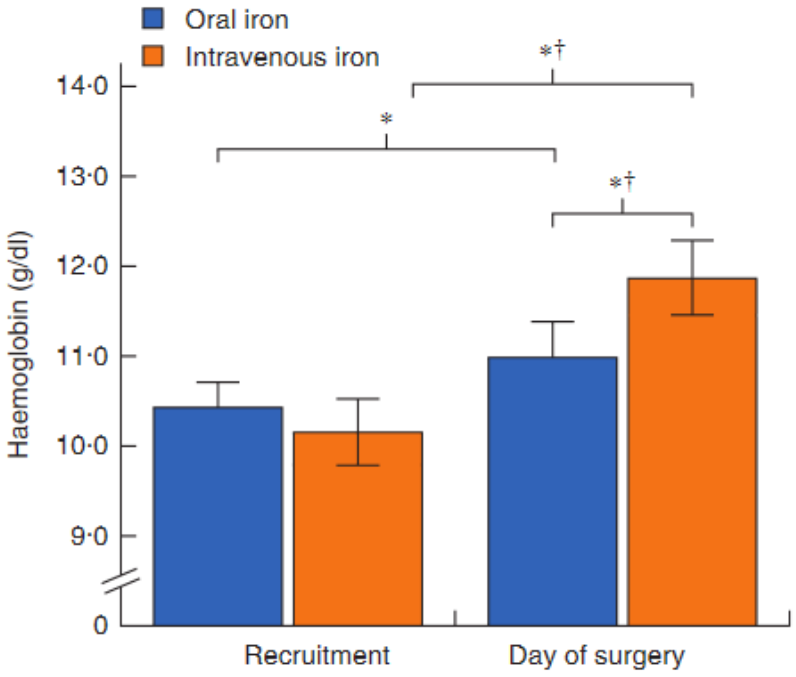
Raccomandazioni per l'implementazione del programma di *Patient Blood Management*
Applicazione in chirurgia ortopedica maggiore elettiva dell'adulto

1ª Edizione

Si suggerisce di evitare la somministrazione di ferro per via endovenosa nei pazienti con valori di ferritina > 300-500 ng/mL e con saturazione della transferrina > 50% **[2C]**

Randomized clinical trial of preoperative oral versus intravenous iron in anaemic patients with colorectal cancer

	Oral iron ($n = 61$)	Intravenous iron ($n = 55$)
Age (years)*	74·7 (67·9–80·8)	73·8 (67·4–78·6)
Sex ratio (M : F)	37 : 24	35 : 20
Height (m)†	1·67 (1·64, 1·70)	1·68 (1·66, 1·71)
Weight (kg)†	72·8 (68·7, 76·9)	79·0 (74·9, 83·2)
Receiving oral iron at recruitment	30	25
Duration of iron before treatment (days)*	20 (6–34)	26·5 (13–37)
Preoperative risk assessment		
ASA fitness grade		
I–II	43	30
III–IV	18	25
CR-POSSUM mortality score at recruitment (%)*	3·58 (2·58–9·29)	3·48 (2·58–6·62)
Tumour details		
T category‡		
T1–2	5	8
T3–4	52	45
Tumour size (mm)*	45 (35–60)	41 (34–55)



Conclusion: Intravenous iron did not reduce the blood transfusion requirement but was more effective than oral iron at treating preoperative anaemia and iron deficiency in patients undergoing colorectal cancer surgery.

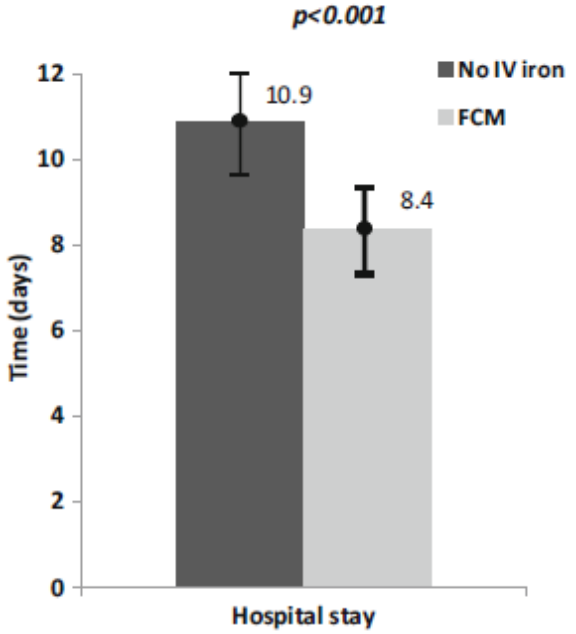
B.D. Keeler Br J Surg. 2017 Feb;104(3):214-221

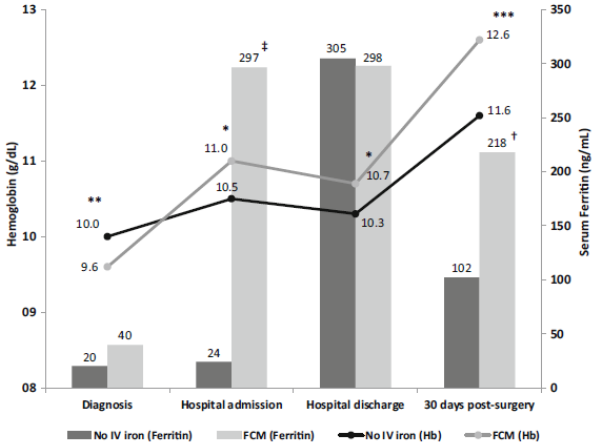
José Luis Calleja et al. Int J Colorectal Dis (2016) 31:543–551

Scopo	Valutare efficacia terapia ferro ev vs ferro os in pz con cancro del colon –chirurgici-
Metodo	266 pazienti 111 FCM (dose media 1000 mg) 155 terapia orale

	No-IV iron	FCM	*p*
Need for RBC transfusion (overall), %	38.7	9.9	<0.001
Need for RBC transfusions (peri-surgery period), %	31.8	8.3	<0.001
Need for RBC transfusion (post-surgery until day 30), %	16.7	5.0	0.005
Need for RBC transfusion (by surgery), %			
Open surgery, %	37.7	17.1	<0.05
Laparoscopic, %	25.4	0.0	<0.0001
Mean units of RBC transfused (overall)	0.8	0.2	<0.0001
Mean units of RBC transfused (peri-surgery)	0.5	0.1	<0.0001
Mean units of RBC transfused (post-surgery until day 30)	0.3	0.1	<0.05
Mean units of RBC transfused (by surgery)			
Open surgery	1.0	0.4	<0.01
Laparoscopic	0.6	0.0	<0.0001

FCM ferric carboxymaltose, *RBC* red blood cell



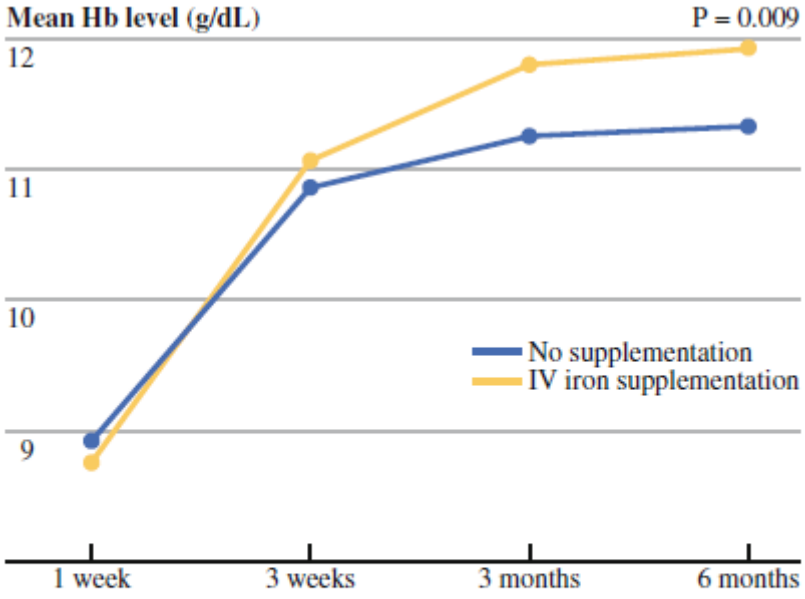


CONCLUSIONI

Trattamento preoperatorio con FCM riduce significativamente il fabbisogno trasfusionale e il numero di giorni di degenza ospedaliera, raggiungendo miglior tasso di risposta in termini di normalizzazione dei livelli di emoglobina sia al ricovero ospedaliero che 30 giorni dopo l'intervento

Effect of Intravenous Iron Supplementation for Acute Postoperative Anemia in Patients Undergoing Gastrectomy for Gastric Carcinoma: A Pilot Study

Oh Jeong et al Ann Surg Oncol (2014) 21:547–552



Mean Hb level (g/dL)				
No supplementation	8.8	11.1	11.8	11.9
IV iron supplementation	8.9	10.9	11.2	11.3
P	0.603	0.984	0.109	0.046

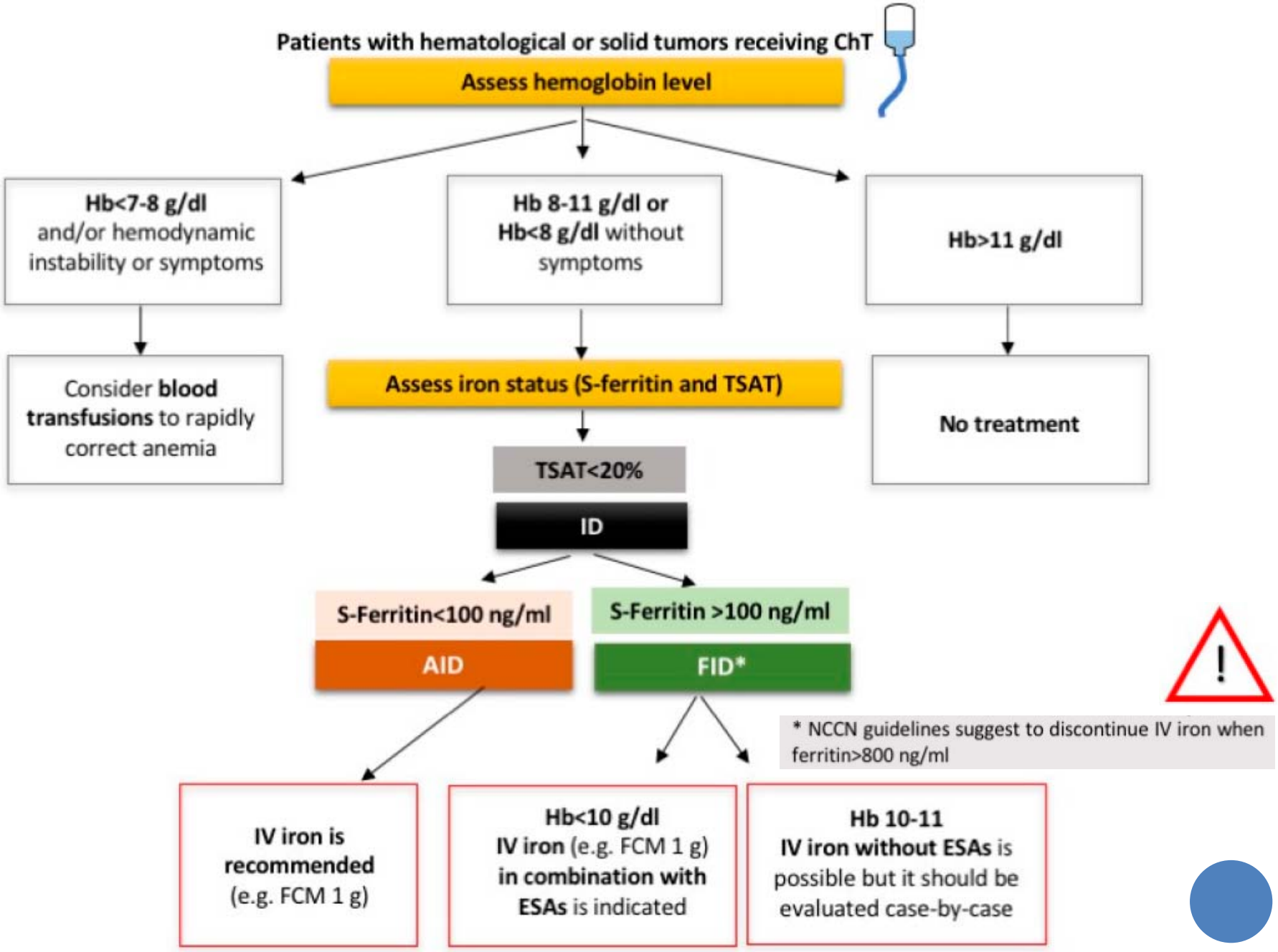
Serial changes of Hb value between the two groups at different time points after surgery

Multivariate analysis of factors affecting the recovery of Hb at postoperative 6 months

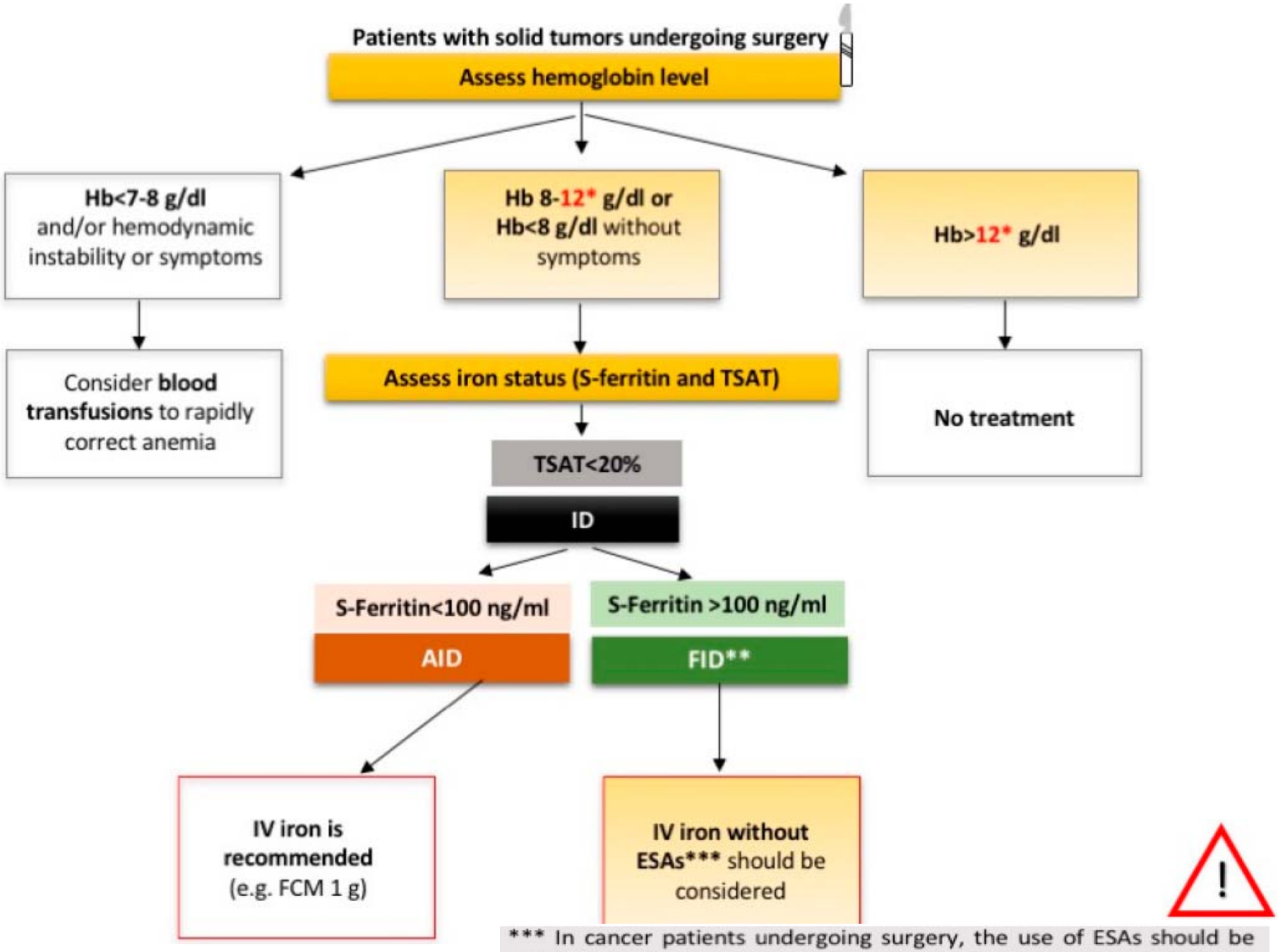
	Standardized β coefficient	p value[a]
Age (years)	0.028	.727
Sex (male)	0.202	.017
IV iron supplementation	0.228	.007
Resection type (total)	−0.143	.092
Operative approach (laparoscopy)	0.142	.129
Adjuvant chemotherapy	−0.017	.870
TNM stage	−0.017	.299

[a] Multiple regression analysis

142 pazienti



Fabiana Busti et al. Pharmaceuticals 2018, 11, 94;



Fabiana Busti et al. Pharmaceuticals 2018, 11, 94;

Inappropriata produzione di EPO

Eritropoietina

ERYTHROPOIETIN OR DARBEPOETIN FOR PATIENTS WITH CANCER (REVIEW)

2077 studies screened

↓

318 full-text articles assessed for elegibility

↓

91 included in quantitative synthesis

20.102 patients

51 solid tumours
14 haematological disease
18 both solid and haematological

Primary Outcomes
Haematological response (increase in Hb level of 2 g/dL)
Patients receiving RBC transfusions
Number of RBC units transfused
Overall survival
On-study mortality

Secondary Outcomes
Tumour response (complete response)
Changes in quality of life
Adverse events

Tonia, T., Mettler, A., Robert, N., Schwarzer, G., Seidenfeld, J., Weingart, O., et al. (2012). Erythropoietin or darbepoetin for patients with cancer. Cochrane Database Syst. Rev. 1

RISULTATI

Haematological response (increase in Hb level of 2 g/dL)	Haematological response was observed more often in participants receiving ESAs (RR 3.93;
Patients receiving RBC transfusions	reduced the relative risk of red blood cell transfusions (risk ratio (RR) 0.65
Number of RBC units transfused per patient	received one unit of blood less than the control group (mean difference (MD) -0.98
Overall survival	ESAs decrease overall survival (HR 1.05;
On-study mortality	There was strong evidence that ESAs increase mortality during active study period (hazard ratio (HR) 1.17; 95% CI 1.06 to 1.29
Tumour response (complete response)	There was insufficient evidence to support an effect of ESA on tumour response (fixed-effect RR 1.02;
Changes in quality of life	Favours Treatment
Adverse events	Favours NO Treatment

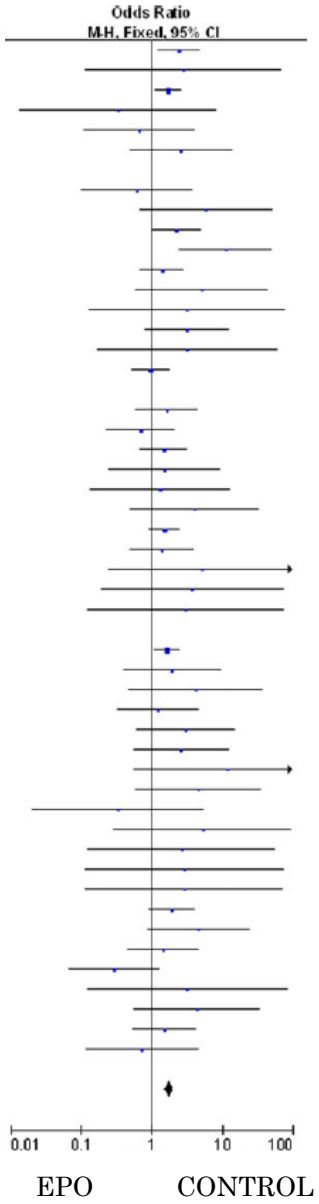
Tonia, T., Mettler, A., Robert, N., Schwarzer, G., Seidenfeld, J., Weingart, O., et al. (2012). Erythropoietin or darbepoetin for patients with cancer. Cochrane Database Syst. Rev. 1

ADVERSE EVENTS

- The risk ratio for thromboembolic complications was increased in patients receiving ESAs compared to controls (RR 1.52, 95% CI 1.34 to 1.74; 57 trials, N = 15,498).
- ESAs may also increase the risk for hypertension (fixed-effect model: RR 1.30; 95% CI 1.08 to 1.56; random-effects model: RR 1.12; 95% CI 0.94 to 1.33, 31 trials, N = 7,228)
- ESAs may also increase the risk for thrombocytopenia/haemorrhage (RR 1.21; 95% CI 1.04 to 1.42; 21 trials, N = 4,507).

Tonia, T., Mettler, A., Robert, N., Schwarzer, G., Seidenfeld, J., Weingart, O., et al. (2012). Erythropoietin or darbepoetin for patients with cancer. Cochrane Database Syst. Rev. 1

VENOUS THROMBOEMBOLISM RISK AND ERYTHROPOIESIS-STIMULATING AGENTS FOR THE TREATMENT OF CANCER-ASSOCIATED ANEMIA



increased RR for VTE in patients receiving ESAs

379 potentially relevant clinical studies on ESAs and treatment of cancer in the literature between January 2000 and January 2013

- Among patients receiving ESAs, the summary incidence of all-grade VTE was 7.78 %.
- Patients with cancer who received ESAs had increased VTE risks (RR=1.75 [95%CI, 1.50–2.05]).

Sheng Gao et al Tumor Biol. (2014) 35:603–613

Risk Factors for Cancer-Associated Thrombosis

Cancer-Associated Risk Factors

- Site of cancer
- Stage of cancer
- Histology of cancer
- Time after Diagnosis

Cancer-Treatment-Associated Risk Factors

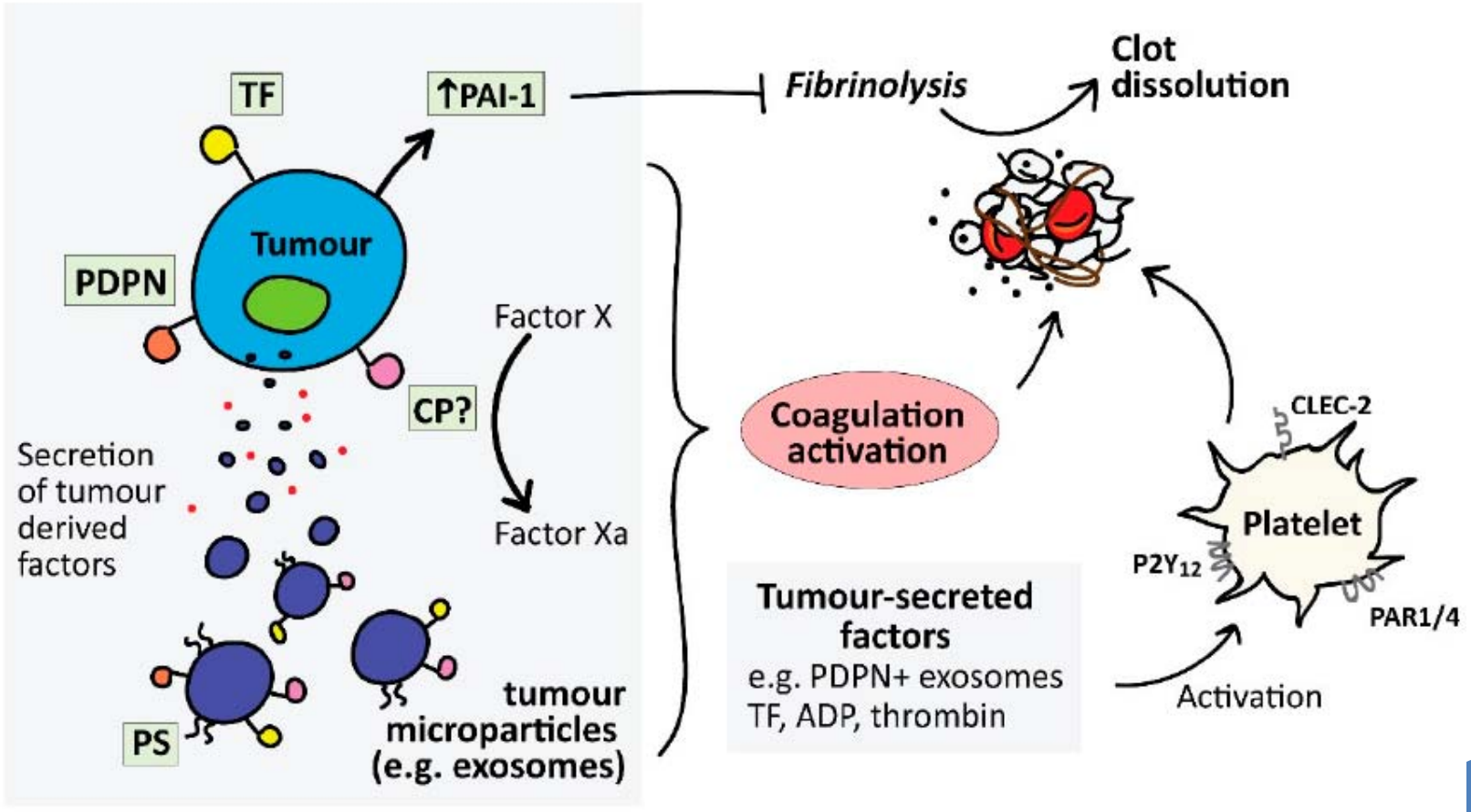
- Surgery and hospitalisation
- Chemoterapy
- Angiogenesis Inibithors
- Central Venous Catheters

L'immediato periodo che segue la diagnosi è quello in cui esiste un rischio maggiore di sviluppare trombosi

N Binti and A Razak et al. Cancer assocciated thrombosis: an overview of mechanism, risk factors, and treatment. Cancer 2018 10 380

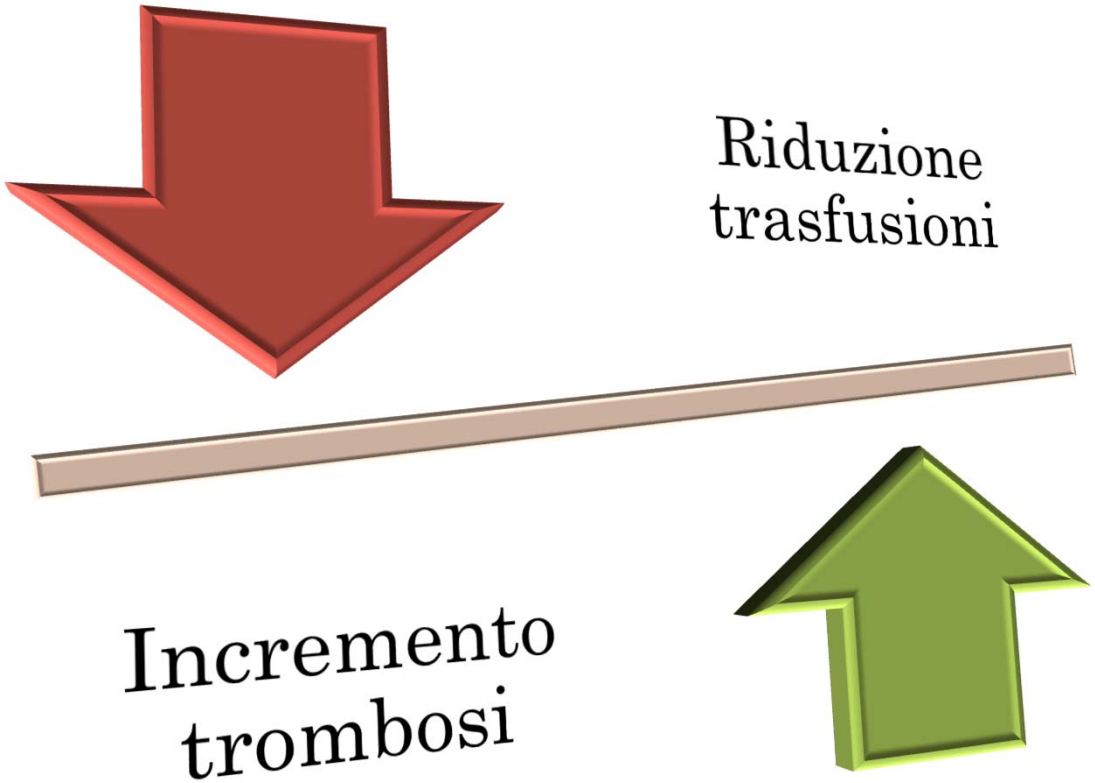
CANCER-ASSOCIATED THROMBOSIS

PDPN: podoplanin attivatore pistrinico
CP: cancer procoagulant
PS phosphaditil serine attivatore coagulazione



N Binti and A Razak et al. Cancer assocciated thrombosis: an overview of mechanism, risk factors, and treatment. Cancer 2018 10 380

EPO VALUTAZIONE RISCHIO BENEFICIO



AN INTERNATIONAL CONSENSUS STATEMENT ON THE MANAGEMENT OF POSTOPERATIVE ANAEMIA AFTER MAJOR SURGICAL PROCEDURES

Is there a role for erythropoiesis stimulating agents?

Is there a role for erythropoiesis-stimulating agents?

In patients without a previous indication, postoperative administration of rHuEPO is an off-label use of this medicinal product. The effects of postoperative rHuEPO have been evaluated in case series, mostly in Jehova's Witnesses and in two RCTs, yielding inconclusive results due to selection bias [58] or premature interruption [59].

In women with moderate-to-severe postpartum anaemia, five RCTs evaluated the effects of iron sucrose (300–1600 mg) or iron sucrose plus rHuEPO (20,000–40,000 IU) on haemoglobin recovery and transfusion needs [15]. A trend to faster haemoglobin increment was observed with rHuEPO plus i.v. iron compared with i.v. iron alone, but no significant differences in transfusion rates which were very low, were observed. The benefits seemed to be greatest in the rHuEPO-treated sub-group with elevated C-reactive protein levels after Caesarean section [15].

Although it does not strictly refer to surgical patients, a recent meta-analysis also found a reduction in mortality rates (risk ratio (RR) 0.63, 95%CI 0.49–0.79, $p < 0.0001$) in critically ill trauma patients who received rHuEPO (nine studies, 2607 patients), without increasing the risk of thromboembolic complications [90]. In cardiac surgery patients, rHuEPO seems to exert neurological and renal protective effect [91, 92]. The mechanisms underlying these non-erythropoietic effects of rHuEPO need to be elucidated before recommending its use in patients without an approved indication.

Short-term pre-operative (1–4 days before operation) administration of rHuEPO to anaemic patients, with or without i.v. iron, has been shown to reduce postoperative transfusion in elective orthopaedic and cardiac surgery [93, 94]. In hip fracture repair surgery, there are conflicting data. One RCT failed to show a reduction in red cell transfusion in patients receiving rHuEPO plus i.v. iron [95]. However, they included patients with haemoglobin < 100 $g.l^{-1}$ but did not study women with haemoglobin ≥ 120 $g.l^{-1}$, and transfused fixed amounts of red cells according to pre-defined transfusion thresholds (e.g. patients with haemoglobin ≤ 70 $g.l^{-1}$ received three units of red cells, and those with haemoglobin 71–89 $g.l^{-1}$ and severe symptoms received two units). In contrast, in an observational study of 196 anaemic hip fracture patients managed with peri-operative i.v. iron and a restrictive transfusion protocol, administration of rHuEPO on admission was associated with reduced transfusion requirements and higher haemoglobin levels on discharge and at postoperative day 30 [96]. An analysis including 544 women with haemoglobin < 130 $g.l^{-1}$ undergoing hip fracture repair showed that the blood-sparing effect of this strategy was restricted to those presenting with haemoglobin concentrations between 120 and 130 $g.l^{-1}$ (n = 305) [97].

Thus, in non-cancer patients with severe postoperative anaemia and blunted erythropoiesis due to infection and/or inflammation, as well as in those who refuse blood transfusion, we suggest considering treatment with rHuEPO. However, as stated above, some guidelines do not support the off-label use of this medicinal product [12].

Red blood cell transfusion: transfusion thresholds for whom and when?

Allogeneic red cell transfusion is associated with a significant increase in peri-operative morbidity and mortality [2, 98–100]. In addition, there is a worldwide shortage of blood, with substantial associated costs to the manufacturer and health systems [101]. Moreover, red cell transfusion risks infectious, immunological, haemolytic, non-haemolytic adverse reactions, cardiac and pulmonary complications [2, 98]. Despite successful implementation of PBM programmes, red cell transfusion is still widely used as a default treatment for the majority of patients with acute postoperative anaemia [102].

Historically, the standard for red cell transfusion was a liberal transfusion threshold, namely haemoglobin level < 100 $g.l^{-1}$ (or haematocrit < 30%). This arbitrary transfusion threshold has been gradually lowered towards haemoglobin 70–80 $g.l^{-1}$, according to data derived from a number of RCTs evaluating the effect on patient outcomes of restrictive vs. more liberal red cell transfusion strategies in a variety of clinical settings. When subjected to pooled analysis in several systematic reviews and meta-analyses (Supporting Information online, Appendix S2) [103–108], data from these RCTs show that, in terms of morbidity and mortality, a restrictive red cell transfusion strategy is equivalent to or more beneficial than a liberal strategy [101, 109].

In addition, evidence-based guidelines have translated the results of RCTs and meta-analyses into clinical practice [7, 10–12, 47–49]. One of the most recently published guidelines on red cell transfusion thresholds recommends a restrictive red cell transfusion threshold (haemoglobin < 70 $g.l^{-1}$) for hospitalised adult patients who are haemodynamically stable, including critically ill patients [49]. However, a transfusion threshold of at least 80 $g.l^{-1}$ is suggested for patients undergoing

In patients without a previous indication, postoperative administration of rHuEPO is an off-label use of this medicinal product

Thus, in non-cancer patients with severe postoperative anaemia and blunted erythropoiesis due to infection and/or inflammation, as well as in those who refuse blood transfusion, we suggest considering treatment with rHuEPO

……guidelines do not support the off-label use of this medicinal product

M. Munoz et al. Anaesthesia **2018**, 73, 1418–1431

- Nonostante sia chiaramente dimostrato che l'EPO può ridurre il fabbisogno trasfusionale nei pazienti critici, rimane da dimostrare che ciò abbia un impatto favorevole in termini di beneficio clinico, in particolare riduzione della mortalità, della morbilità, della durata del ricovero, e in termini di riduzione dei costi.

- Di conseguenza l'EPO può essere utilizzata nei soggetti che rifiutano la trasfusione o in pazienti selezionati, come quelli con complessi problemi immunoematologici, con insufficienza renale o anemia cronica, eventualmente abbinata a terapia marziale per via orale o parenterale (*Grado di raccomandazione:* 2C+)

CONCLUSIONI

- complesso programma PBM incentrato sulla normalizzazione dei livelli di emoglobina prima dell'intervento migliora outcome dopo chirurgia onologica
- La valutazione dello stato del ferro ha un'importanza cruciale per una corretta strategia terapeutica
- Sebbene si è dimostrata in grado di ridurre incidenza di trasfusioni la somministrazione di EPO è associata ad un aumentato rischio di TEV e quindi va attentamente valutato il rapporto rischio beneficio


Grazie

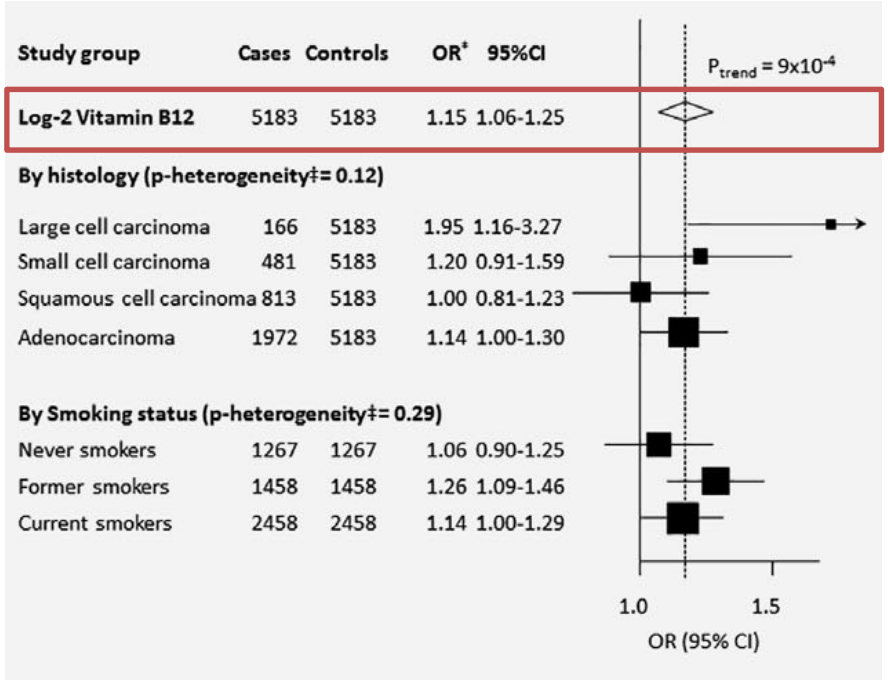
Ridotta soppressione eritroidi

Ruolo della supplementazione vitaminica

IS HIGH VITAMIN B12 STATUS A CAUSE OF LUNG CANCER?

International Agency for Research on Cancer (IARC/WHO) Int. J. Cancer: (2019)

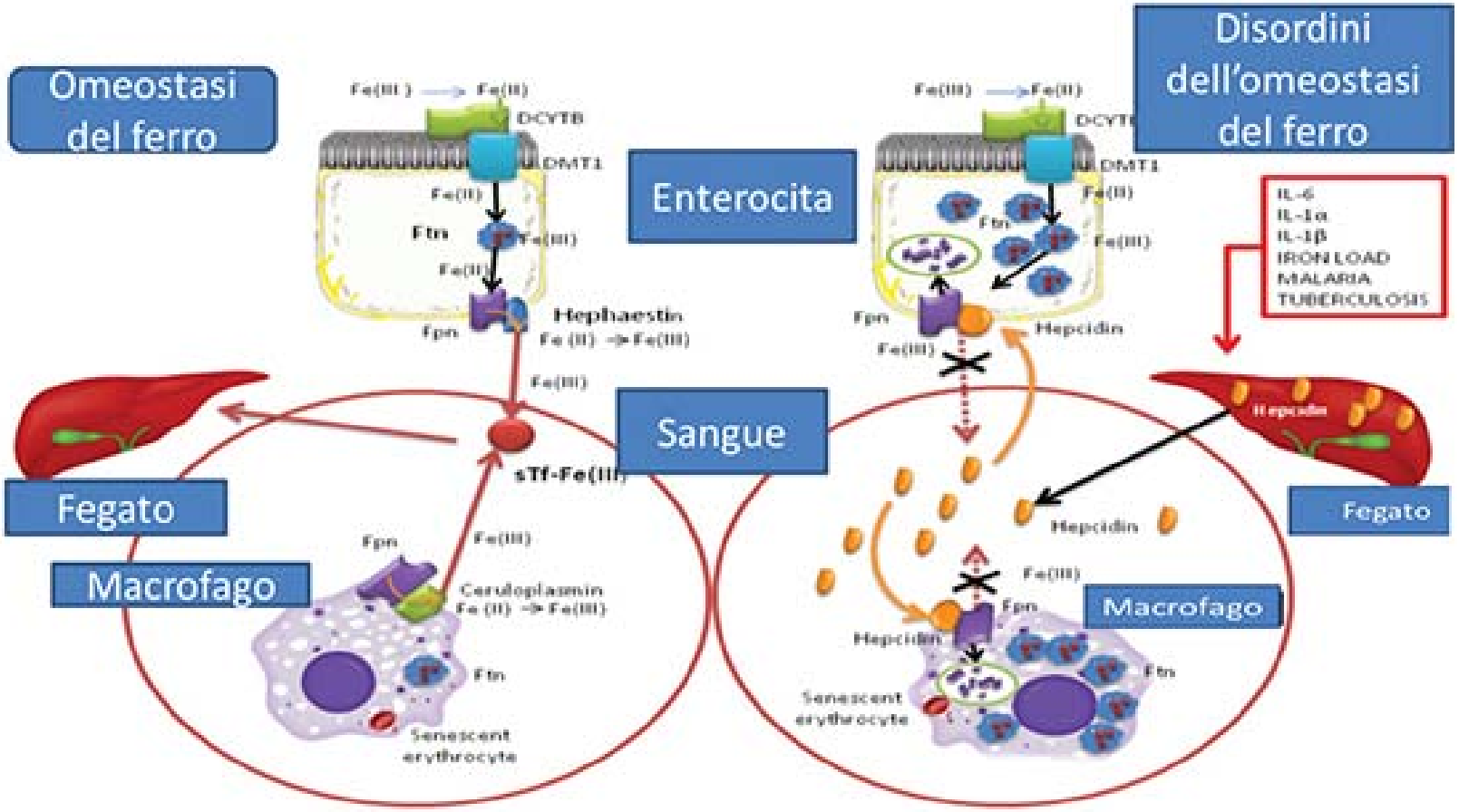
Mirato a chiarire il ruolo della vitamina B12 nell'eziologia del cancro del polmone attraverso misurazioni dirette di concentrazioni di vitamina B12 circolanti pre-diagnostiche in uno studio caso-controllo nidificato, integrato con un approccio di randomizzazione mendeliana (MR) in un campione indipendente di controllo del caso. Abbiamo utilizzato dati di biomarker pre-diagnostici da 5183 coppie caso-controllo annidate in 20 coorti prospettiche e dati genetici da 29.266 casi e 5650 controlli.



La vitamina B12 circolante è positivamente associata al rischio complessivo di cancro del polmone in modo dose-risposta (odds ratio per un raddoppio in B12 [ORlog2B12] = 1,15, intervallo di confidenza al 95% (IC 95% = 1,06-1,25).

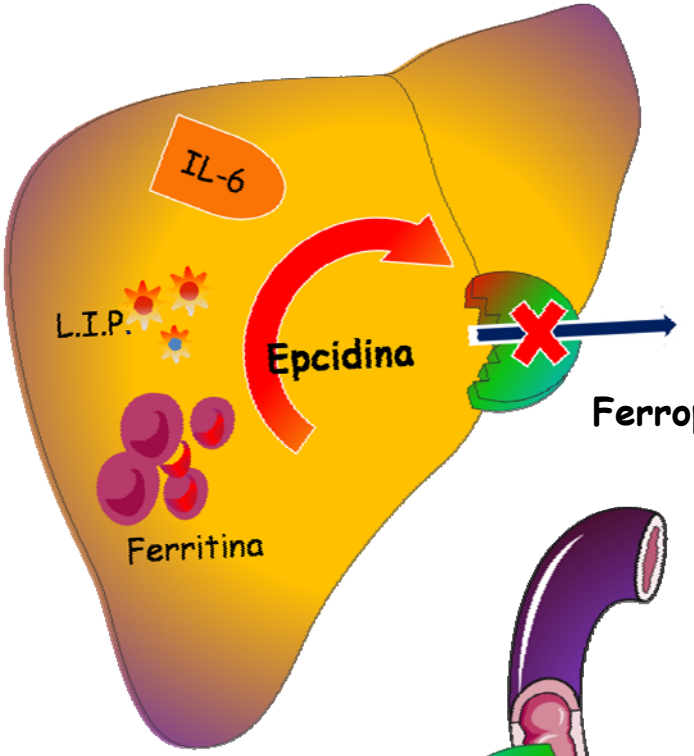
Le due analisi indipendenti e complementari supportano l'ipotesi che l'elevato livello di vitamina B12 aumenti il rischio di cancro ai polmoni.

OMEOSTASI DEL FERRO



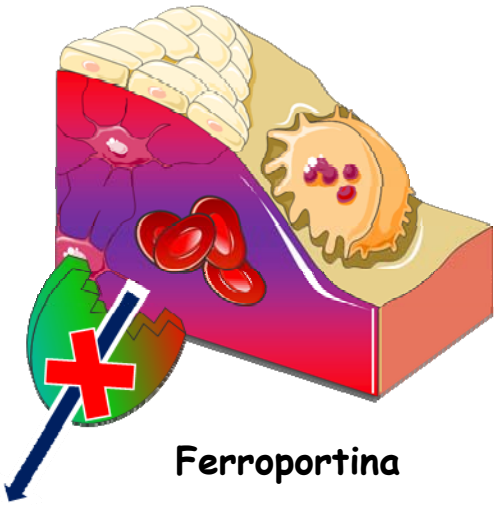
Ruolo dell'Epcidina

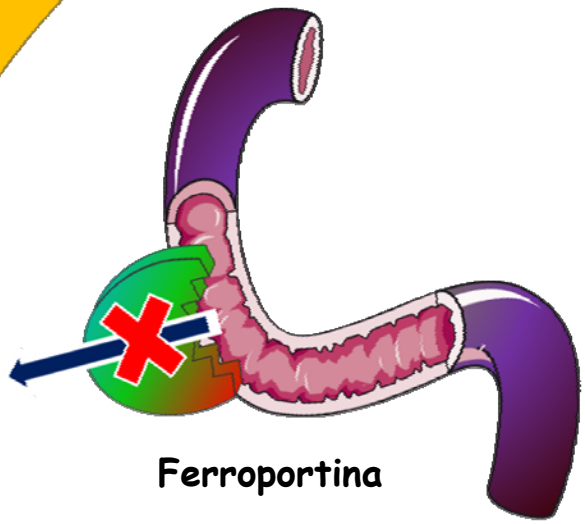
Regolatore negativo dell'assorbimento del ferro degli alimenti e del rilascio del ferro dai macrofagi



Viene prodotta in quantità definite in funzione:

- dei livelli di ferro ematico
- dei depositi di Fe
- dell'attività eritropoietica





Svolge la sua azione modulatoria legandosi alla Ferroportina inibendo così la liberazione del ferro dalle cellule intestinali e di deposito R.E. al sangue.
L'epcidina determina, pertanto, una riduzione dei livelli di ferro extracellulare

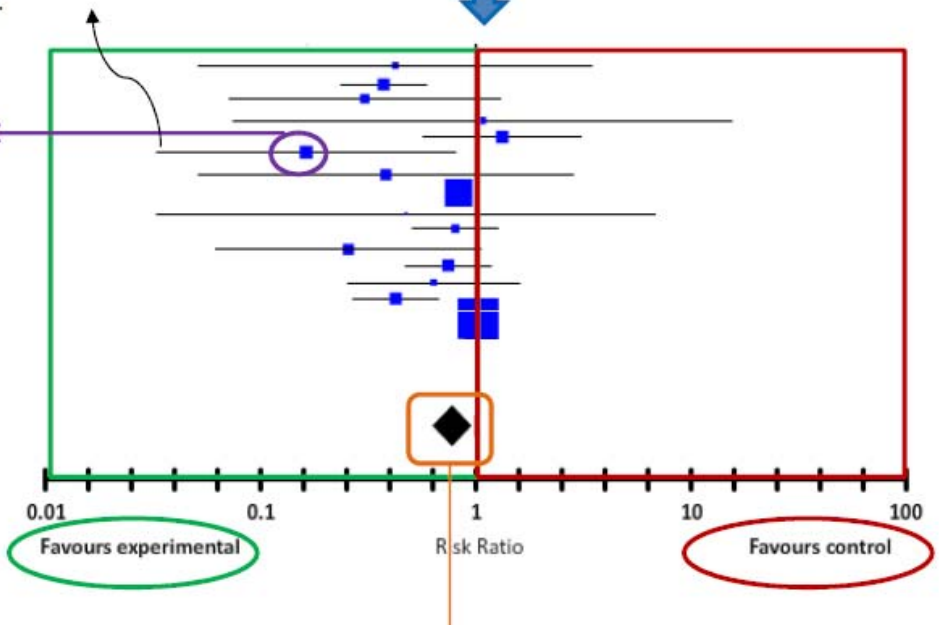
L'epcidina è inoltre una piccola proteina della fase acuta e si correla positivamente con i livelli di IL-6, sembra svolgere pertanto un ruolo chiave nella determinazione e nel mantenimento dell'anemia da infiammazione cronica

Come leggere il Forest Plot

IC che esprime il grado di incertezza dello studio. Tanto più è lunga tanto più i risultati sono incerti. Se l'IC attraversa la linea del "non-effetto" vuol dire che i risultati dello studio non sono statisticamente significativi.

Linea del "non-effetto": 1 per indicatore di rischio e 0 per indicatori continui

Stima puntuale di effetto del singolo studio, la cui grandezza è proporzionale al peso attribuito allo studio che a sua volta dipende dalla numerosità e dal numero di eventi.



Scala orizzontale

Il rombo rappresenta il risultato finale (stima complessiva). Il centro del rombo indica la stima puntuale, mentre l'ampiezza dei lati rappresenta l'intervallo di confidenza.