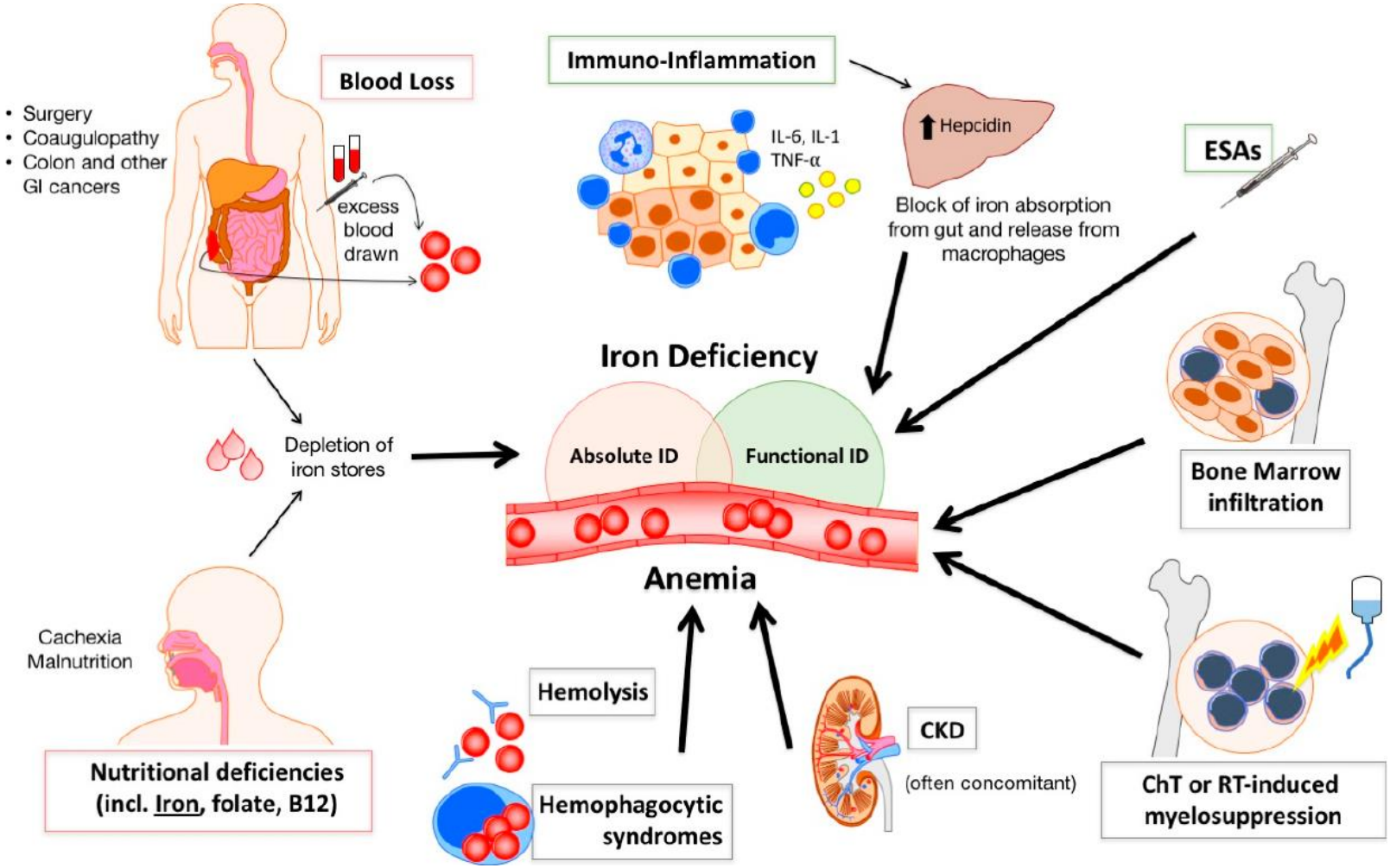
Ferro endovena nel paziente oncologico

Dott.ssa Rossella Calori,
S.C. Oncologia Medica
ASST di Vimercate

CAUSE ANEMIA NEL PZ ONCOLOGICO



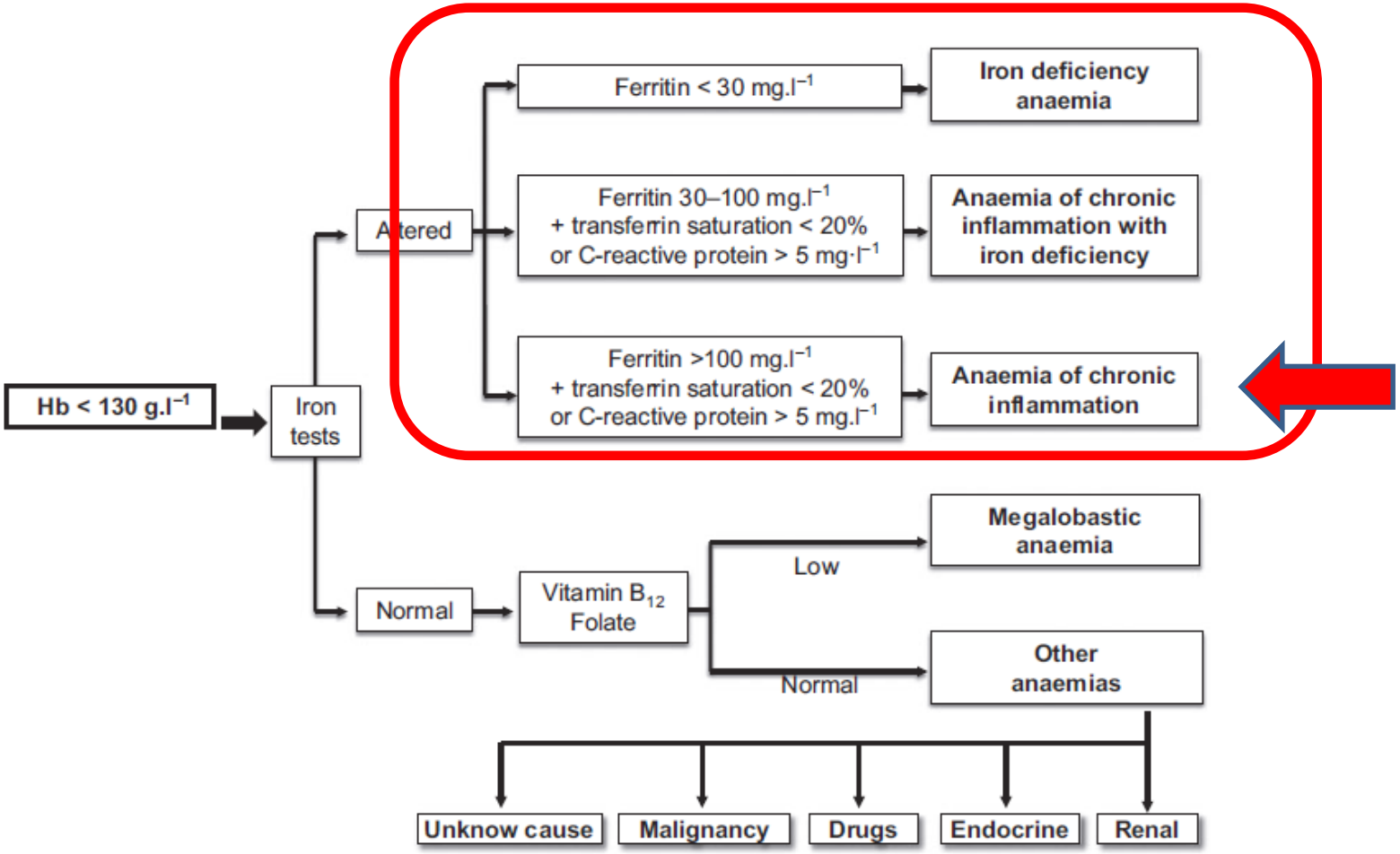
Busti et al., Pharmaceuticals 2018

CONSEGUENZE ANEMIA NEL PZ ONCOLOGICO

- ✓ Fatigue
- ✓ Confusione, depressione
- ✓ Nausea, perdita di appetito, dispnea, sincope soprattutto nei pz con comorbilità (es. disfunzione renale o cardio-polmonare)
- ✓ Ridotta capacità funzionale
- ✓ Ridotta Qol
- ✓ Ridotta OS

Anemia: predittore indipendente di prognosi sfavorevole

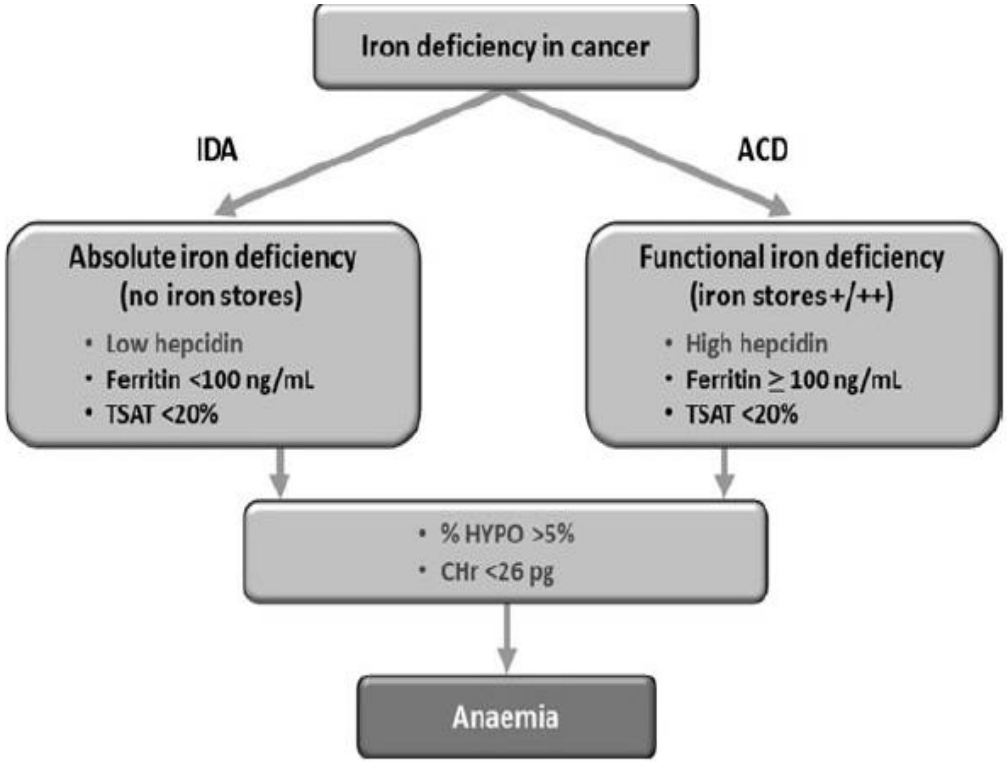
-> Importanza di corretta **diagnosi e gestione**



M. Munoz, Anaesthesia 2017, 72, 233–247

Carenza marziale (ID)

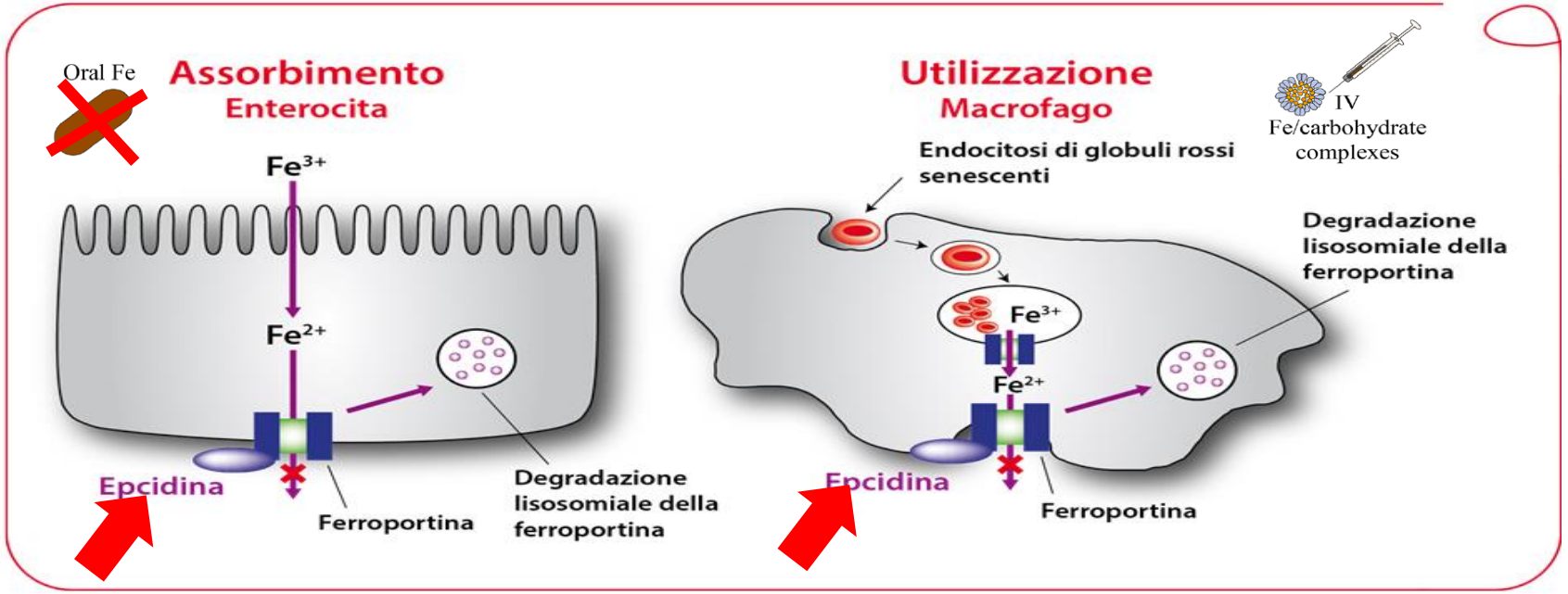
-> un problema comune, da definire correttamente



Aapro et al, Ann. Oncol 2012

L'OMEOSTASI DEL FERRO È REGOLATA DA EPCIDINA

Epcidina inibisce il rilascio di ferro alla transferrina circolante in quanto si lega alla proteina transmembrana ferroportina, determinandone l'internalizzazione e la degradazione lisosomiale



Nemeth E, et al. Science. 2004;306:2090-3

European Journal of Cancer 40 (2004)

The European Cancer Anaemia Survey (ECAS): A large, multinational, prospective survey defining the prevalence, incidence, and treatment of anaemia in cancer patients

- Survey epidemiologica prospettica in 34 paesi Europei
- 15000 soggetti con tumori solidi o ematologici tra 2001 e il 2002
- Hb <12 g/dL

Prevalenza Anemia

39% all'arruolamento
67% dopo 6 mesi di FU

- Anemia più frequente nei pz con recidive di malattia o malattia in stadio avanzato (es. early-stage K colon 40% vs 80% negli stadi avanzati) o in pz con CT in corso
- Prevalenza variabile a seconda del tipo di tumore (tra i tumori solidi incidenza > nel K mammella e K polmone).
- Prevalenza più alta nei tumori ematologici

PREVALENZA CARENZA DI FERRO?????????

- Più alta nel K colon-retto

Anemia trattata in < 40% dei casi e principalmente con ESA e trasfusioni

OPZIONI TERAPEUTICHE DISPONIBILI

1) Trasfusioni di globuli rossi
2) Agenti stimolanti l'eritropoiesi (ESA)
3) Ferro
4) Combinazione di ESA + ferro

PROFILO RISCHIO-BENEFICIO

Table 3. Benefit-risk profiles of treatments for anaemia and ID in cancer patients

	Benefits	Risks or limitations
ESAs	• Reduction of RBC transfusions • Improvement in anaemia-related symptoms	• Increase in thrombotic events • PRCA in rare cases[a] • Increased mortality in patients receiving no cancer therapy or only RT • Only effective in 60% of patients • Induction of functional ID and decreasing response over time
i.v. iron[b]	• Correction of ID anaemia • Reduction of RBC transfusions • Increase response to ESAs	• Long-term safety in oncology not yet fully established
RBC transfusions	• Immediate increase of Hb and haematocrit levels in 100% • Rapid improvement in anaemia-related symptoms	• Increase in thrombotic events • Transfusion reactions and circulatory overload • Transmission of known/unknown pathogens • Possibly decreased survival in certain types of cancer treated by surgery • Increased risk of infections due to immunosuppression

[a]Documented only in non-cancer chronic kidney disease patients.

[b]Oral iron to be considered only for patients with both absolute ID (ferritin < 100 ng/mL) and non-inflammatory conditions (CRP < 5 mg/L).

CRP, C-reactive protein; ESA, erythropoiesis-stimulating agent; Hb, haemoglobin; ID, iron deficiency; i.v., intravenous; PRCA, pure red cell aplasia; RBC, red blood cell; RT, radiotherapy.

Aapro M, et al Annals of Oncology 0:1-15, 2018

The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

Dan L. Longo, M.D., *Editor*

Indications for and Adverse Effects of Red-Cell Transfusion

Jeffrey L. Carson, M.D., Darrell J. Triulzi, M.D., and Paul M. Ness, M.D.

- tendenza verso regimi trasfusionali restrittivi
- programmi di patient blood management

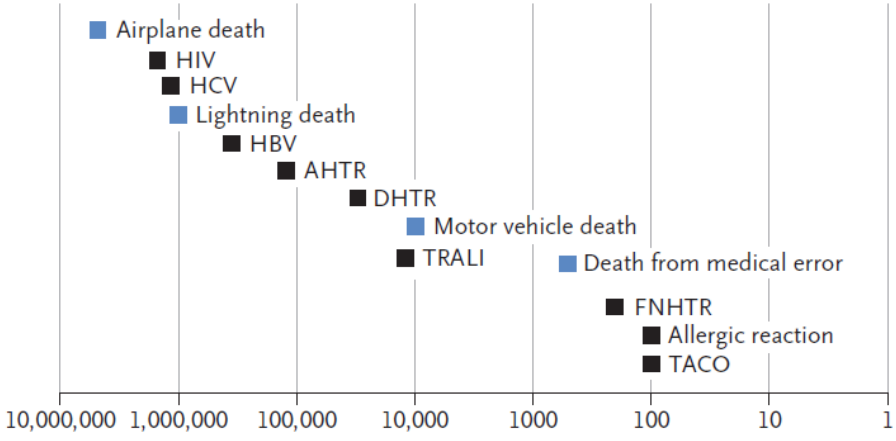


Figure 4. Infectious and Noninfectious Adverse Effects of Red-Cell Transfusions as Compared with Other, Unrelated Risks.

Adverse effects of transfusions (black boxes) are shown per transfused unit of red cells, except for transfusion-associated circulatory overload (TACO), which is per transfusion episode. For unrelated risks (blue boxes), the risk of an airplane death is per flight,[34] the risk of death from lightning is per year,[35] the risk of death from a motor vehicle accident is per 10,000 persons,[36] and the risk of death from medical error is per hospital admission.[37] AHTR denotes acute hemolytic transfusion reaction, DHTR delayed hemolytic transfusion reaction, FNHTR febrile nonhemolytic transfusion reaction, HBV hepatitis B virus, HCV hepatitis C virus, and TRALI transfusion-related acute lung injury.

Published in final edited form as:
Cancer Treat Rev. 2016 May ; 46: 1–8. doi:10.1016/j.ctrv.2016.03.010.

How Low Should We Go: A Systematic Review and Meta-Analysis of the Impact of Restrictive Red Blood Cell Transfusion Strategies in Oncology

Lauren S. Prescott, MD, MPH[1], **Jolyn S. Taylor, MD**[1], **Maria A. Lopez-Olivo, MD, PhD**[2], **Mark F. Munsell, MS**[3], **Helena M. VonVille, MLS, MPH**[4], **David R. Lairson, PhD**[4], and **Diane C. Bodurka, MD, MPH**[5]

[1]Department of Gynecologic Oncology and Reproductive Medicine, The University of Texas MD Anderson Cancer Center Houston, TX 77030 USA

Conclusion—Restrictive strategy appears to decrease blood utilization without increasing morbidity or mortality in oncology. This review is limited by a paucity of high quality studies on this topic. Better designed studies are warranted.

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

Annals of Oncology 0: 1–15, 2018
doi:10.1093/annonc/mdx758

CLINICAL PRACTICE GUIDELINES

Which patients should be considered for RBC transfusions?

In patients with Hb < 7–8 g/dL and/or severe anaemia-related symptoms (even at higher Hb levels) and the need for immediate Hb and symptom improvement, the administration of RBC transfusions without delay is justified [II, B].

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

Annals of Oncology 0: 1–15, 2018
doi:10.1093/annonc/mdx758

CLINICAL PRACTICE GUIDELINES

Table 1. Managing anaemia and ID in patients with solid tumours or haematological malignancies

When should ESA treatment be considered?

Treatment of anaemia with an ESA should be considered in patients under ChT after correction of ID and other underlying causes other than the cancer or its treatment [I, A].

Which patients should receive ESA therapy?

ESA therapy is recommended in patients with symptomatic anaemia who receive ChT [I, A] or combined RT-ChT [II, B] and present with an Hb level < 10 g/dL, as well as patients with asymptomatic anaemia who receive ChT and present with an Hb level < 8 g/dL.

Should patients who do not receive ChT treatment be treated with an ESA?

ESA treatment is not recommended in patients who are not on ChT [I, A].

What is the Hb target range for treatment with an ESA?

The Hb target is a stable level of ~ 12 g/dL without RBC transfusions [I, A].

At what doses should ESAs be given?

Dosing should follow the approved labels of the individual products; the currently recommended dosage is approximately 450 IU/week/kg body weight for epoetins alpha, beta and zeta; 6.75 μg/kg body weight every 3 weeks or 2.25 μg/kg body weight weekly for darbepoetin alpha; and 20 000 IU once weekly for epoetin theta [I, A].

Should ESA doses be increased or ESA preparations changed in patients not responding within 4–8 weeks?

Except for patients receiving epoetin theta (given at an intentionally low starting dose), ESA dose escalations and changes from one ESA to another in patients not responding within 4–8 weeks are not recommended. Patients who do not show evidence of at least an initial Hb response at this time should stop ESA therapy. The epoetin theta dose may be doubled after 4 weeks if Hb has not increased by at least 1 g/dL, unless functional ID is detected (see next recommendation) [I, A].

- Solo pazienti in chemio o chemioradio
- Previa correzione altre cause di anemia non correlate al tumore o al suo trattamento
- Hb<8; Hb< 10 se sintomi
- Max 8 settimane poi stop se non risposta

JAMA. 2008 Feb 27;299(8):914-24. doi: 10.1001/jama.299.8.914.

Venous thromboembolism and mortality associated with recombinant erythropoietin and darbepoetin administration for the treatment of cancer-associated anemia.

Bennett CL[1], Silver SM, Djulbegovic B, Samaras AT, Blau CA, Gleason KJ, Barnato SE, Elverman KM, Courtney DM, McKoy JM, Edwards BJ, Tigue CC, Raisch DW, Yarnold PR, Dorr DA, Kuzel TM, Tallman MS, Trifilio SM, West DP, Lai SY, Henke M.

Am J Hematol Oncol. 2008 Aug 1;7(8):327-332.

Risks of Venous Thromboembolism and Mortality Associated With Erythropoiesis-Stimulating Agents for the Treatment of Cancer-Associated Anemia.

Samaras AT[1], Bennett CL.

TERAPIA MARZIALE

- 7 RCTs dal 2004 al 2011 hanno dimostrato che *ferro ev aumenta efficacia degli ESA nei pz con carenza assolute o funzionali in corso di CT*
- Dal 2006 LG EORTC raccomandano di *correggere tutte le possibili cause di anemia, inclusa ID prima di iniziare il trattamento con ESA*
- *Ferro orale non/poco efficace e poco tollerato*
- **Controindicazione terapia marziale: infezioni attive**

Busti et al., Pharmaceuticals 2018

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

Annals of Oncology 0: 1–15, 2018
doi:10.1093/annonc/mdx758

CLINICAL PRACTICE GUIDELINES

Management of anaemia and iron deficiency in patients with cancer: ESMO Clinical Practice Guidelines†

M. Aapro[1], Y. Beguin[2,3], C. Bokemeyer[4], M. Dicato[5], P. Gascón[6], J. Glaspy[7], A. Hofmann[8], H. Link[9], T. Littlewood[10], H. Ludwig[11], A. Österborg[12], P. Pronzato[13], V. Santini[14], D. Schrijvers[15], R. Stauder[16], K. Jordan[17] & J. Herrstedt[18,19], on behalf of the ESMO Guidelines Committee*

- **Ferro ev** indicato in pz con anemia (Hb ≤11g/dl o riduzione Hb >2g/dl da un livello basale ≤ 12g/dl) e carenza marziale assoluta o funzionale (ferritina >100 TSAT <20%) **prima o durante ESA** (IA). No consensus su cut- off superiore di ferrina (800?)

- Ad oggi **indicazione specifica** per pz **in corso di CT o nel preoperatorio**

- Ferro ev senza altri trattamenti aggiuntivi da considerare in pz con carenze funzionali (IIIC)

- Mancano dati a lungo termine su safety e OS nei pz oncologici

I.V. iron compounds available in Italy

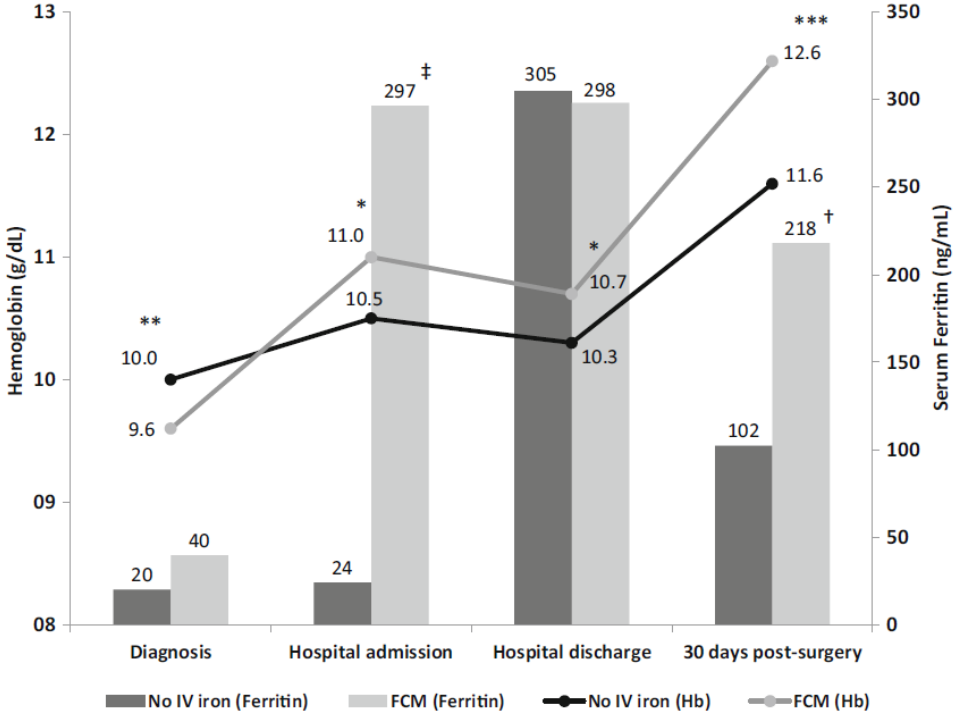
	Iron gluconate (Ferlixit®)	Iron saccarate (Venofer®)	Iron carboxymaltose (Ferinject®)
Maximum single dose	62.5-125 mg (max 2-3 for week)	200 mg (max 3 for week)	1,000 mg
Max. infusion rate	62.5 mg in 20 min	200 mg in 30 min	200 mg in bolus or 1000 mg in 15 min
Time required to administer 1 g of iron	320 min	150 min	15 min
No. of visits required to administer 1 g	8-16	5	1
Stability of elemental iron	Low	Medium	High
Toxicity (free iron)	High	Medium-low	Low
Percentage of **labile iron**	**3,5**	**3**	**0,5**

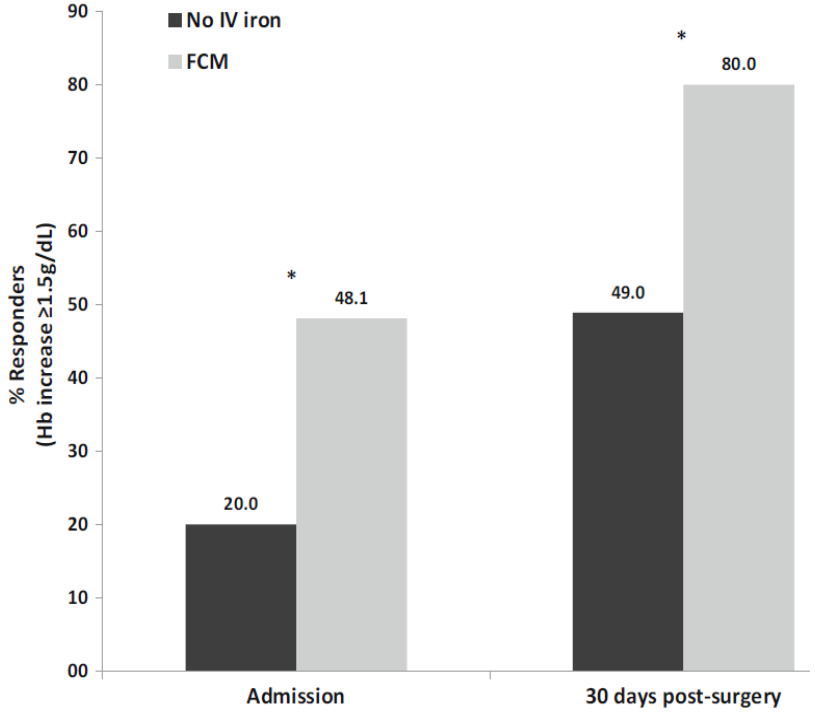
Int J Colorectal Dis (2016) 31:543–551
DOI 10.1007/s00384-015-2461-x

ORIGINAL ARTICLE

Ferric carboxymaltose reduces transfusions and hospital stay in patients with colon cancer and anemia

José Luis Calleja[1] · Salvadora Delgado[2] · Adolfo del Val[3] · Antonio Hervás[4] · José Luis Larraona[5] · Álvaro Terán[6] · Mercedes Cucala[7] · Fermín Mearin[8] · on behalf of the Colon Cancer Study Group





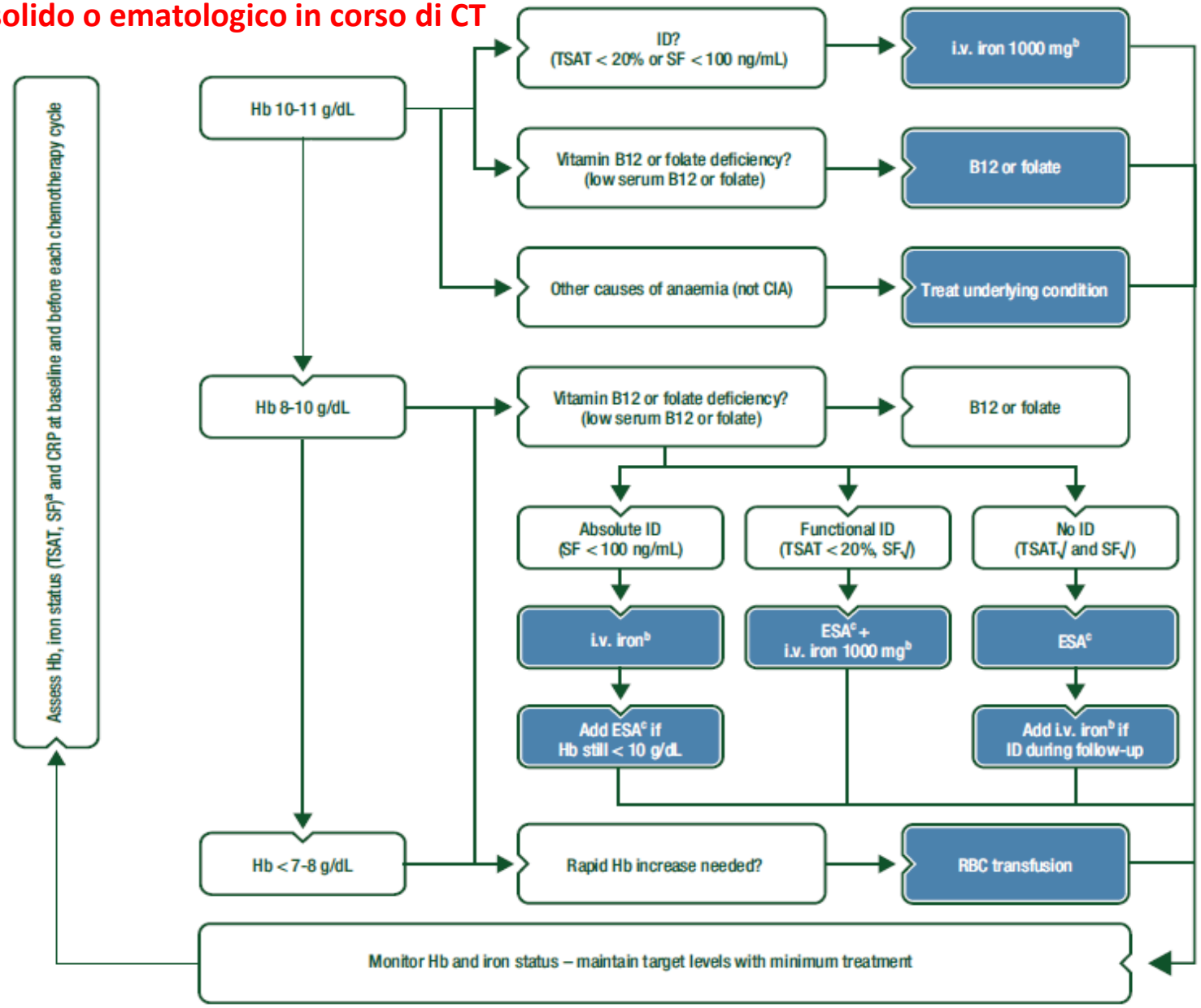
Studio multicentrico osservazionale, pre/post chirurgia

Il trattamento con FCM (dose mediana 1000 mg) riduce in maniera significativa il bisogno di trasfusioni e la durata della degenza ospedaliera

ALGORITMI DIAGNOSTICO-TERAPEUTICI

Annals of Oncology

Pz con tumore solido o ematologico in corso di CT



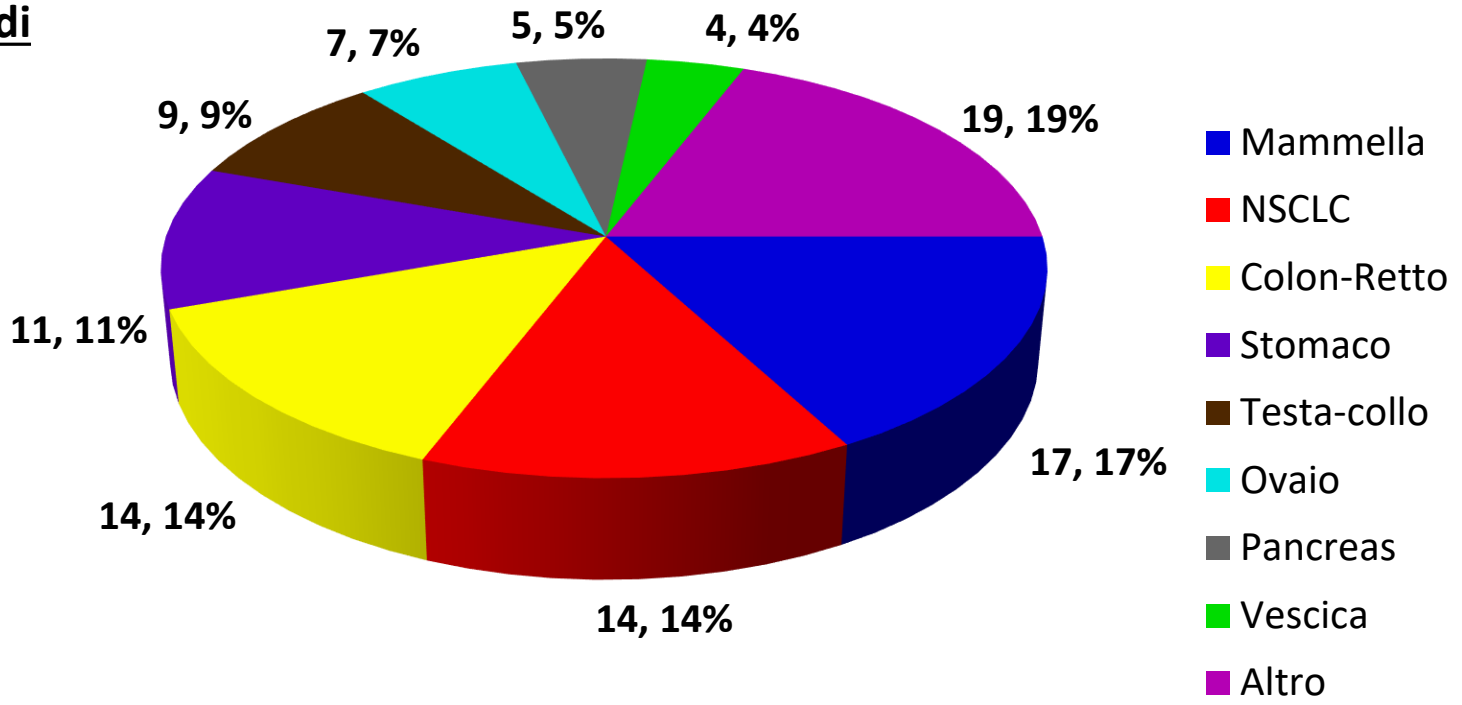
DALLE RACCOMANDAZIONI ALLA PRATICA CLINICA

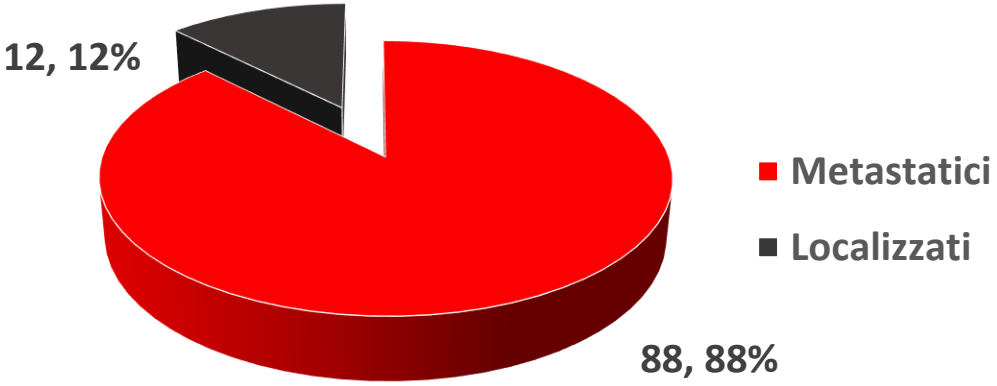
Dati di uso FCM **da gennaio 2018** presso UOC Oncologia ASST Vimercate:

- **PO di Vimercate**: **146 pz** con tumori solidi + **13 pz** con tumori ematologici
- **PO Carate: 95 pz**

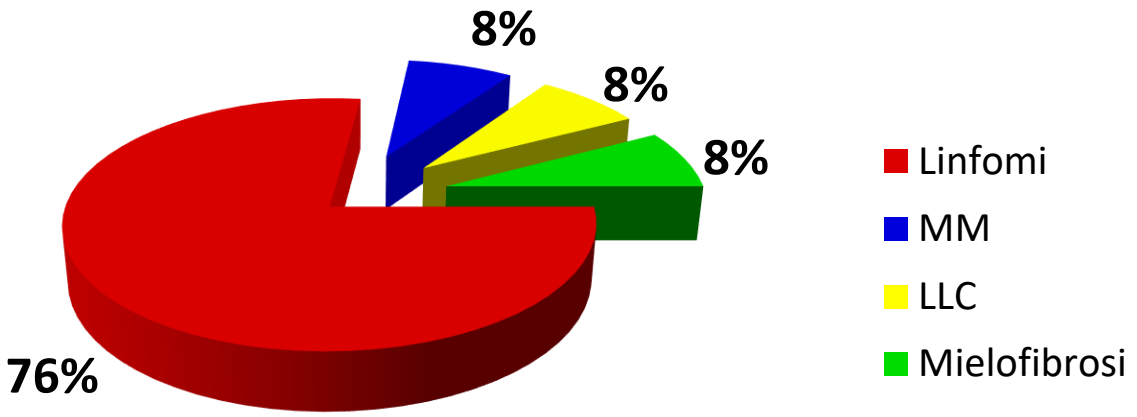
(15% dei pazienti sottoposti a chemioterapia nel periodo di osservazione)

Tumori solidi

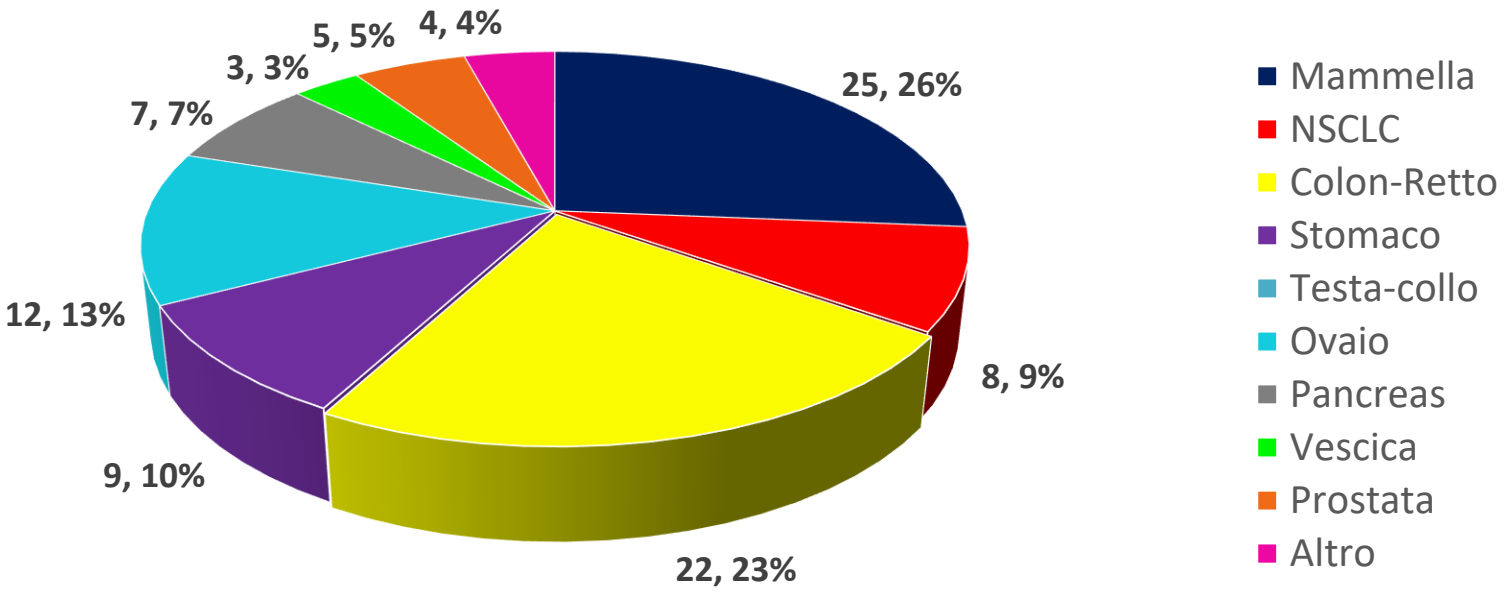




Tumori ematologici



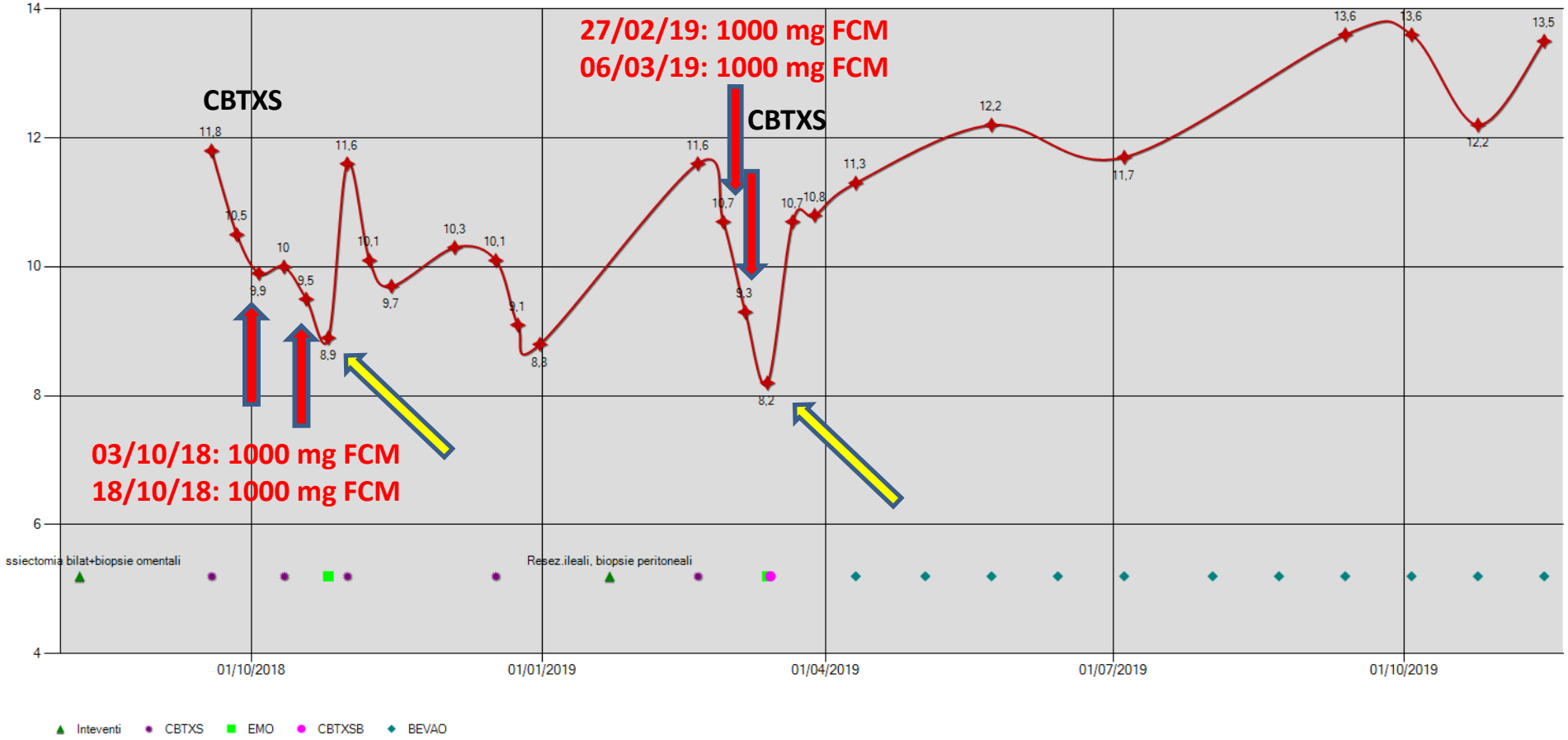
- **PO di Carate**



Caso clinico 1

77aa, K ovaio, peso 71 Kg
CT in corso

Hb

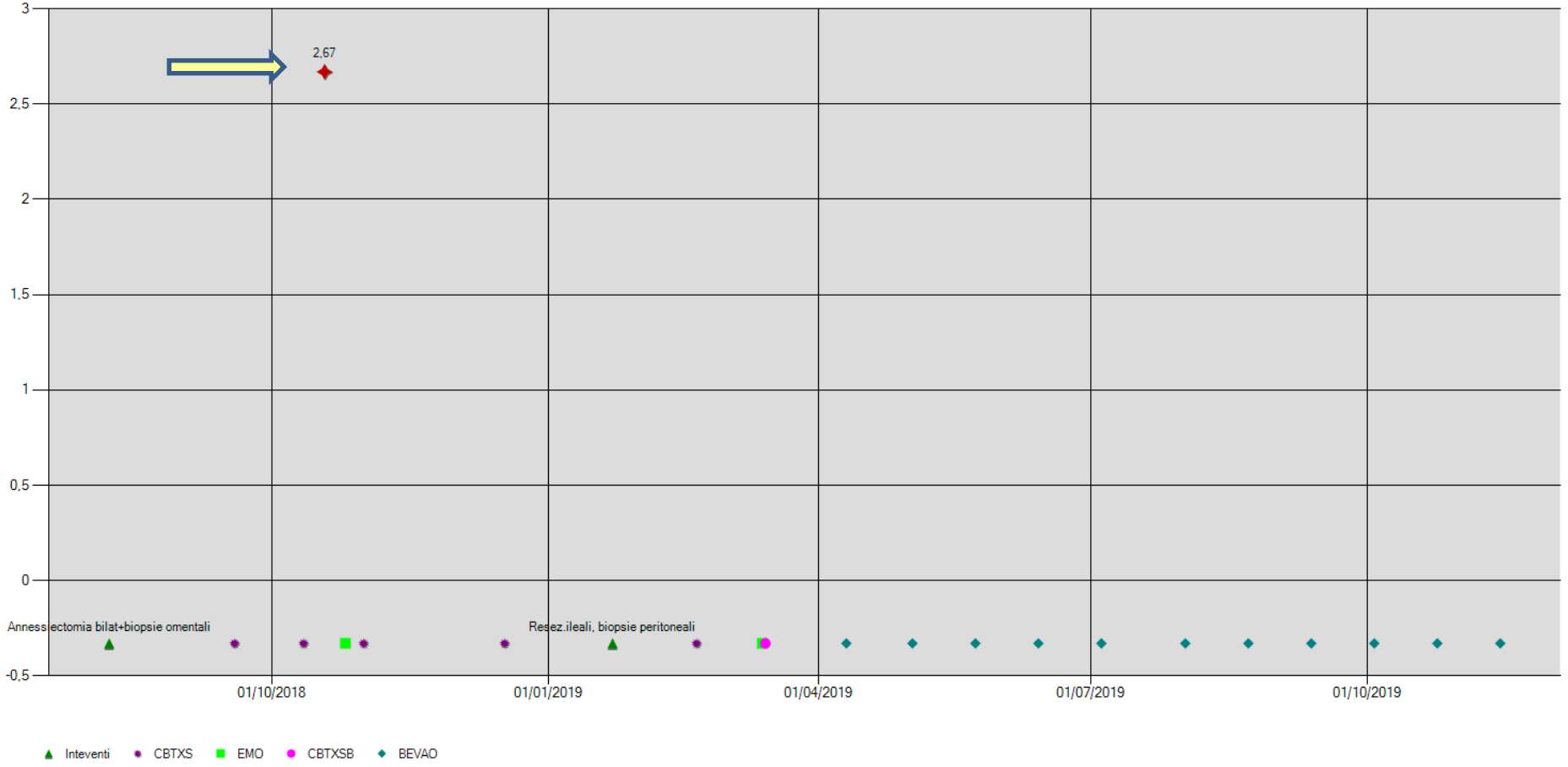


03/10/18: Hb 9,9; MCV 100,3; Fe 56 µg/dl, Ferritina 877 ng/mL, TSAT 18%

18/10/18: Hb 9,5, MCV 102,9

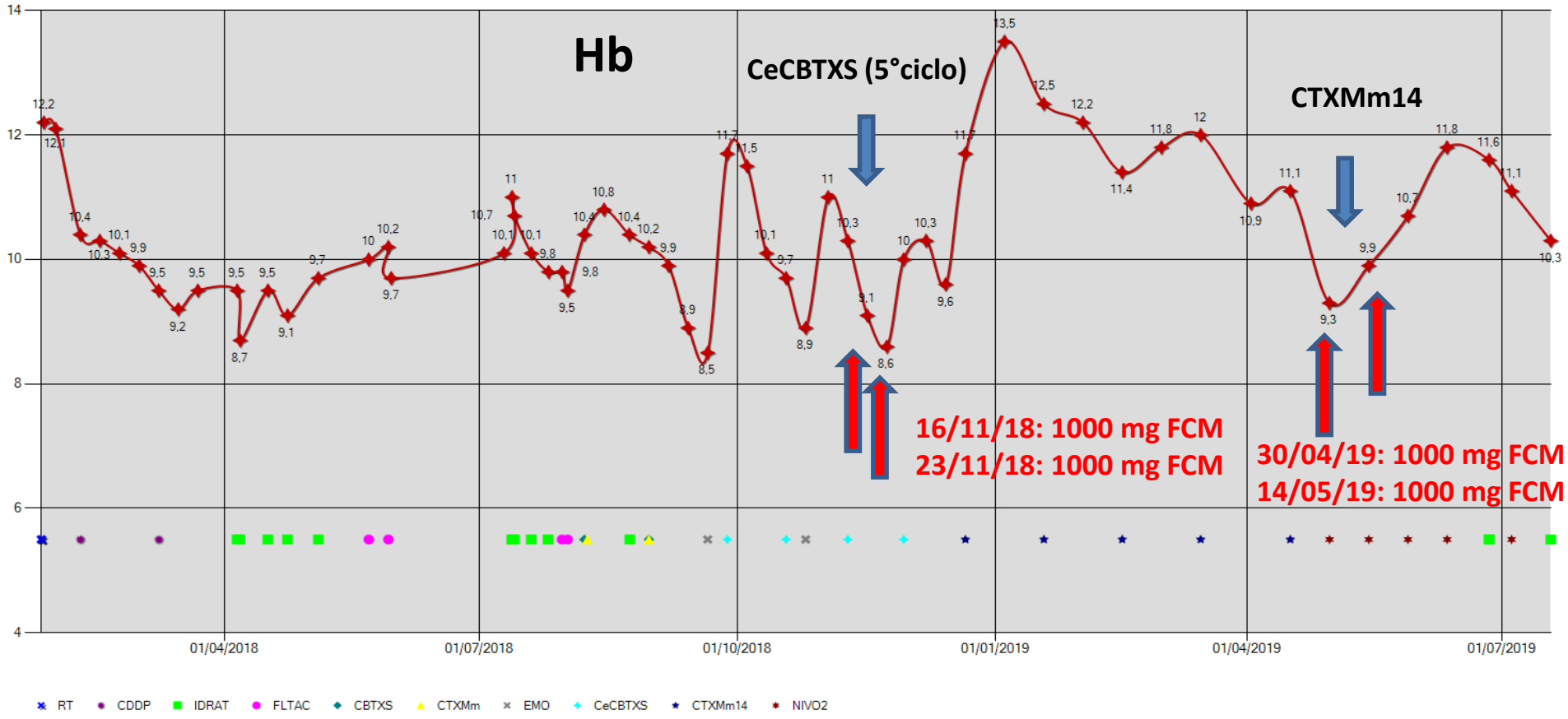
77aa

FOLATI


3
2,5
2
1,5
1
0,5
0
-0,5
2,67
Annessiectomia bilat+biopsie omentali
Resez.ileali, biopsie peritoneali
01/10/2018
01/01/2019
01/04/2019
01/07/2019
01/10/2019
Inteventi
CBTXS
EMO
CBTXSB
BEVAO

Caso clinico 2

55 aa, K testa-collo (orofaringe) metastatico, peso 72 Kg
CT in atto: CeCBTXS (5°ciclo)



<u>17 infusioni di FG</u> (tot 34 fiale) negli ultimi 9 mesi pre FCM + **<u>emotrasfusioni</u>** (4 sacche)
vs <u>4 infusioni di FCM</u> negli ultimi 12 mesi

EFFETTI AVVERSI

SU 254 PZ trattati con FCM:

- *3 rash cutanei (1.18%)*
- *1 artralgie transitorie (0.39%)*
- *1 addominoalgie (0.39%)*
- *1 dispnea grave con broncospasmo trattata con steroide (0.39%)*

Conclusioni - 1

- ✓ L'anemia nel pz oncologico è ***multifattoriale*** -> ***indagare*** ***<u>sempre</u>*** ***status del ferro, folati, B12***
- ✓ L'anemia impatta sulla ***qualità e*** *sulla* ***aspettativa di vita***
- ✓ **ferro ev > ferro per os**

Conclusioni - 2

L'uso appropriato di ***ferro e.v***. nella correzione della anemia nel paz oncologico

- ***Riduce la necessità di emotrasfusioni***
- ***Promuove una maggiore efficacia ESA***

L'uso di ***carbossimaltosio ferrico*** consente inoltre:

- ***Minor numero di infusioni con***
  - ***mantenimento patrimonio vascolare***
  - ***Riduzione del rischio di reazioni avverse***
  - ***Minor numero di accessi ospedalieri***
- ***Maggior durata della risposta***
- ***Riduzione dei costi per le complicanze post- chirurgiche***
- ***Possibile minor necessità di trattamento con ESA***

GRAZIE!!!!!!!

- Dott Daniele Fagnani, Direttore UOC Oncologia Vimercate
- Equipe medica e infermieristica dell'Oncologia
- Dott.ssa Federica Cazzaniga, data manager del Centro

Grazie a
tutti voi per
la pazienza
e
l'attenzione
!