



FORMATO EUROPEO PER IL CURRICULUM VITAE

INFORMAZIONI PERSONALI

Cognome e Nome

Indirizzo

Telefono

e-mail

Nazionalità

Luogo di nascita

Data di nascita

Codice Fiscale

ESPERIENZA LAVORATIVA

Date

Nome e indirizzo del datore di lavoro

Tipo di azienda

Tipo di impiego

Principali mansioni e responsabilità

ISTRUZIONE E FORMAZIONE

Nome e tipo di istituto di istruzione

DI MARZIO LUIGI

1986 Ispettore Sanitario, 1992 Vice Direttore Sanitario, 1995-2021 Direttore Sanitario Ospedaliero

Azienda Sanitaria Locale n.3, via Ugo Petrella n.1, 86100 Campobasso

Ministero della Salute, Azienda Sanitaria Regionale del Molise, Ospedale Regionale "A. Cardarelli" Campobasso

Dirigente sanitario

Direzione tecnico-organizzativa di Ospedale : dal 1995 al 2018 Direttore dell'Ospedale Regionale "A. Cardarelli" Campobasso e dal luglio 2010 al marzo 2012 contemporaneamente anche Direttore dell'Ospedale "G. Vietri" di Larino (CB); dal gennaio 2019 al maggio 2021 Direttore Medico di Presidio Ospedaliero Unico Regionale

Dal 23/03/2018 in aspettativa per mandato parlamentare - XVIII Legislatura - Senatore della Repubblica

Dal 11/05/2021 in quiescenza per limiti di età

Diploma di Maturità Classica

Liceo Classico Campobasso

Laurea in Medicina e Chirurgia ed Abilitazione Professionale

Università Bologna

Specializzazione in "Igiene e Medicina Preventiva"

Università Parma

1987-1988: Corso biennale "Sperimentazione di una metodologia di formazione per il management delle USL"

IFAP (IRI) ed Assessorato Sanità Regione Molise

1997: Corso semestrale "Management sanitario"

Università degli Studi del Molise ed Assessorato Sanità Regione Molise

2000: Corso trimestrale "Management sanitario"

Scuola di Direzione Aziendale - Università "Bocconi" Milano

2002- 2003: Corso semestrale "Corso interregionale per la formazione di facilitatori/valutatori per le verifiche di accreditamento"

Agenzia Sanitaria Regionale Emilia e Romagna ed Assessorato Sanità Regione Molise

2004- 2005: Master universitario "Master di II livello in Management sanitario professionale"

Università degli Studi del Molise

Principali materie / abilità professionali oggetto di studio

Igiene, Epidemiologia, Medicina preventiva, Programmazione e organizzazione dei servizi sanitari, Legislazione sanitaria, Tecnica ospedaliera.

Qualifica conseguita

Direttore sanitario ospedaliero

Livello nella classificazione nazionale

Dirigente medico di II livello

CAPACITÀ E COMPETENZE PERSONALI

PRIMA LINGUA

ITALIANO

ALTRE LINGUE

INGLESE

Capacità di lettura

buona

Capacità di scrittura

sufficiente

Capacità di espressione orale

elementare

FRANCESE

Capacità di lettura

elementare

Capacità di scrittura ed espressione orale

/

SPAGNOLO

Capacità di lettura

elementare

Capacità di scrittura ed espressione orale

/

CAPACITÀ E COMPETENZE PROFESSIONALI

Vice direttore della "Scuola per la formazione professionale del personale paramedico" della ASL di Campobasso dal 1992 al 1995.
Direttore della "Scuola per la formazione professionale del personale paramedico" della ASL di Campobasso dal 1995 al 1996.
Docente nella "Scuola per la formazione professionale del personale paramedico" della ASL di Campobasso dal 1987 al 1996.
Docente nei Corsi di Laurea della Facoltà di Medicina e Chirurgia della Università Cattolica di Campobasso dal 1998 al 2012.
Docente nei Corsi di Laurea della Facoltà di Economia della Università Statale del Molise dal 2004 al 2022.
Docente nei Corsi di Laurea della Facoltà di Scienze del Benessere della Università Statale del Molise dal 2005 al 2007.
Docente nei Corsi di Laurea della Facoltà di Medicina e Chirurgia della Università di Roma "La Sapienza" dal 2005 al 2008.
Docente nei Corsi di Laurea della Facoltà di Medicina e Chirurgia della Università Statale del Molise dal 2007 al 2021.

Direttore Sanitario della ASL di Campobasso nel maggio/ottobre 1997.

Direttore Sanitario Aziendale vicario della ASL di Campobasso dal febbraio 2005 al febbraio 2006.

Direttore Sanitario Aziendale vicario della ASReM dal febbraio 2006 al settembre 2009.

Già Componente del comitato etico di Ateneo dell'Università Statale del Molise.

Già Componente del Nucleo regionale di Valutazione.

Già Componente del Comitato Controllo Malattie della Regione Molise.

Già Componente Coordinamento delle Regioni per la gestione del Rischio Clinico e la Sicurezza del Paziente.

PATENTE

B

DICHIARAZIONI SOSTITUTIVE DI CERTIFICAZIONI

(Art.46 D.P.R. 28.12.2000, n. 445 recante il "T.U. delle disposizioni legislative e regolamentari in materia di documentazione amministrativa")

DICHIARAZIONI SOSTITUTIVE DELL'ATTO DI NOTORIETÀ

(Art. 47 D.P.R. 28.12.2000, n. 445 recante il "T.U. delle disposizioni legislative e regolamentari in materia di documentazione amministrativa")

Il sottoscritto

COGNOME DI MARZIO NOME LUIGI
CODICE FISCALE NATO A PROV IL RESIDENTE
A PROV INDIRIZZO C.A.P. TELEFONO

consapevole che le dichiarazioni mendaci sono punite ai sensi del Codice Penale e delle leggi speciali in materia (in virtù di quanto disposto dall'art. 76 del D.P.R. 445 del 28.12.2000):

DICHIARA

1	di essere stato Vice Direttore e Direttore della "Scuola per la formazione professionale del personale paramedico" della ASL di Campobasso, presso la quale è stato altresì docente in discipline dell'area igienico-organizzativa dal 1987 al 1996 ;
2	di essere stato docente nei Corsi di Laurea della Facoltà di Medicina e Chirurgia della Università Cattolica del Sacro Cuore di Campobasso in discipline dell'area igienico-organizzativa dal 1998 al 2012 ;
3	di essere stato docente nei Corsi di Laurea della Facoltà di Economia della Università Statale del Molise in discipline dell'area igienico-organizzativa dal 2004 al 2022;
4	di essere stato docente nei Corsi di Laurea della Facoltà di Medicina e Chirurgia della Università Statale del Molise in discipline dell'area igienico-organizzativa dal 2007 al 2021 ;
5	di essere stato docente nei Corsi di Laurea della Facoltà di Scienze del Benessere della Università Statale del Molise in discipline dell'area igienico-organizzativa dal 2005 al 2007;
6	di essere stato docente nei Corsi di Laurea della Facoltà di Medicina e Chirurgia della Università di Roma 'La Sapienza' e della Università Statale del Molise in discipline dell'area igienico-organizzativa dal 2005 al 2008;
7	di essere in possesso della Laurea in Medicina e Chirurgia conseguita presso l'Università degli Studi di Bologna ;
8	di essere in possesso della Specializzazione in Igiene e Medicina Preventiva conseguita presso l'Università degli Studi di Parma ;
9	di aver conseguito il Master Universitario di II livello in 'Management sanitario' presso l'Università degli Studi del Molise ;
10	di essere stato dipendente della ASReM con la qualifica di Direttore Sanitario ospedaliero in servizio presso l'Ospedale Regionale 'A.Cardarelli' di Campobasso fino all'epoca del collocamento in quiescenza per limiti di età in data 11/05/2021.

Il sottoscritto è informato che i dati personali forniti con la presente richiesta sono trattati nel rispetto del D. Lgs. 196/2003 "Codice in materia di protezione dei dati personali".

Campobasso, 10 maggio 2022

Il dichiarante*

* Nel caso di dichiarazione sostitutiva dell'atto di notorietà, qualora la dichiarazione non sia sottoscritta davanti al dipendente addetto a ricevere la documentazione, deve essere accompagnata da un valido documento di riconoscimento (Art. 38 D.P.R. n. 445 del 28.12.2000).

Il cancro della prostata

1 - EPIDEMIOLOGIA ed EZIOPATOGENESI

R. LATTANZIO - G. DI GIOVACCHINO - A. COMO* - G. DI LORETO
L. DI MARZIO

ULSS n. 12 - Pres. Osped. Popoli
Divisione di Chirurgia Generale (Primario: Prof. A. Pomidori)
ULSS n. 07 - Pres. Osp. Lanciano
* Divisione di Urologia (Primario: Dr. F. Piccinini)

ESTRATTO DALLA RIVISTA "PANTA REI" - SUPPL. AL VOL. IV - FASCICOLO 1 - 1985

Tip. GIANNINI Pescara

Il cancro della prostata

2 - FISIOPATOLOGIA

G. DI GIOVACCHINO - R. LATTANZIO - A. COMO* - L. DI MARZIO
G. DI LORETO

ULSS n. 12 - Pres. Osped. Popoli
Divisione di Chirurgia Generale (Primario: Prof. A. Pomidori)
ULSS n. 07 - Pres. Osp. Lanciano
* Divisione di Urologia (Primario: Dr. F. Piccinini)

ESTRATTO DALLA RIVISTA "PANTA REI" - SUPPL. AL VOL. IV - FASCICOLO 1 - 1985

Tip. GIANNINI Pescara

Il cancro della prostata

4 - TERAPIA

G. DI GIOVACCHINO - R. LATTANZIO - L. DI MARZIO - A. COMO*
L. LIBERATORE

ULSS n. 12 - Pres. Osped. Popoli
Divisione di Chirurgia Generale (Primario: Prof. A. Pomidori)
ULSS n. 07 - Pres. Osp. Lanciano
* Divisione di Urologia (Primario: Dr. F. Piccinini)

ESTRATTO DALLA RIVISTA "PANTA REI" - SUPPL. AL VOL. IV - FASCICOLO 1 - 1985

Tip. GIANNINI Pescara



the
European Iron Club
For Professionals in Biomedical Inorganic Iron



EUROPEAN IRON CLUB

7 - 10 MEETING IN
April INNSBRUCK
2016



CONCLUSION: The modified IAI is a fairly good predictor in non-PPI using homozygous C282Y HH patients, to differentiate who needs ≥ 3 maintenance phlebotomies per year. Therefore, this index helps to select patients that might benefit from an alternative less frequent therapy, e.g. erythrocytapheresis.

P08: LIPOSOMIAL IRON IS SAFE AND COST-EFFECTIVE IN HCV PATIENTS WITH TYPE II DIABETES AND ANEMIA DUE TO ESOPHAGEAL OR GASTRIC BLEEDING

GIULIO GIORDANO¹, ALBINO PARENTE², FABIO D'AMICO², GIUSEPPE BERARDI³, ANTONIETTA LICIANCI¹, ROSANNA GIGLI¹, MARILU' MAGRI¹, GIOVANNA NIRO¹, LUIGI DI MARZIO¹
¹REGIONAL HOSPITAL ANTONIO CARDARELLI, VIA MONTE SANTO N 16 - CAMPOBASSO, ITALY, ²MOLISE UNIVERSITY - MEDICINE, CAMPOBASSO, ITALY, ³GENERAL MEDICINE, CAMPOBASSO, ITALY

OBJECTIVE: Aim of this study is to verify if sucrosomial oral iron support vs ferric gluconate iv iron support vs transfusional support is safe and effective in patients with HCV treatment with iron deficiency anemia.

MATERIALS AND METHODS: 35 patients with HCV related anemia for esophageal varices and gastric bleeding with a median Hb level of 8g/dl (R 8-9.5 g/dl), were treated 15 with sucrosomial oral iron 30mg 1 tablet t.i.d for 3 months (group A), 10 with i.v. ferric gluconate 62.5mg/day for 15 days (group B) and 10 with 1 blood transfusion/day (group C) until Hb increase level of 1g/dl was reached. Median Hb and glucose level in group A were 8g/dl and 140 mg/dl respectively, in group B 9.5 g/dl and 130 mg/dl, in group C were 7 g/dl and 160 mg/dl. All patients received an abdomen echography to detect hepatocellular carcinoma (HCC) at 1, 3, 6 months.

Results: Patients in group A gained 1 g/dl Hb after 1 month (R 3-6 weeks), with a median blood glucose level of 130 mg/dl (R 120-230) and a median cost of 30€/month (R 20-80), patients in group B gained 1 g/dl in 7 days (R 6-13 days), with a median blood glucose level of 310 mg/dl (R 190-430) and a median cost of 1240€/month (R 830-2800), patients in group C gained 1 g/dl in 1 day (R 2-4 days), with a median blood glucose level of 210 mg/dl (R 160-330) and a median cost of 400€/month (R 350-950). Only 1 patient in group B and 1 patient in group C developed HCC at 6 months. Worsening of liver function blood test was observed only in group C.

Conclusion: Liposomal iron is safe and cost-effective in HCV patients with type II diabetes and anemia due to esophageal or gastric bleeding

P09: The Jak1/Jak2 Inhibitor Momelotinib Inhibits ACVR1/Alk2, Decreases Hepcidin Production and Ameliorates Anemia of Chronic Disease (ACD) in Rodents

Malte Asshoff¹, Matthew Warr², David Haschka¹, Piotr Tymoszek¹, Verena Petzer¹, Egon Demetz¹, Pat Maciejewski², Markus Seifert¹, Kristina Auer¹, Manfred Nairz¹, Wilfried Posch³, Peter Fowles², Guenter Weiss¹, Andy Whitney², Igor Theurl¹
¹Department of Internal Medicine IV, (Infectiology & Immunology/Tropical Medicine, Rheumatology and Pneumology), Medical University Innsbruck, Innsbruck, Austria, ²Gilead Sciences, Branford, United States, ³Division of Hygiene and Medical Microbiology, Medical University Innsbruck, Innsbruck, Austria

Objective: Results from a phase 2 study for the treatment of myelofibrosis (MF) with the Jak1/2 inhibitor momelotinib (MMB) demonstrated that MMB provided an anemia benefit,

Background: Chromatin regulation is an essential mechanism by which the heart controls gene expression in response to stimuli. Genome-wide studies of histone modifications indicate that methylation profiles are altered in diseased hearts. Histone methylation is dynamically regulated by histone methyltransferases and histone lysine demethylases. The demethylase KDM4A, previously implicated in cardiac hypertrophy in both humans and mice, is a 2-oxoglutarate-dependent dioxygenase, and *in vitro*, requires ferrous iron for catalytic activity. However, the question remains whether these observations also hold true *in vivo* and to what extent iron modulates KDM4A activity and downstream epigenetic regulation.

Objectives: To determine whether iron-deficiency affects KDM4A activity and histone methylation profile, and to identify the downstream gene targets and their role in cardiac function.

Methods: For a dietary model of iron-deficiency, wild-type C57BL6 mice were put on either iron-adjusted (200ppm) or iron-deficient (2-5ppm) diet immediately after weaning. The well-established model of iron-deficiency anemia – TMPR knock-out mice – were also used in this study.

Results: The mono-, di-, and tri-methylation states of KDM4A substrates H3K9 and H3K36 are altered in relation to haemoglobin levels, both in a dietary iron-deficiency and TMPR KO system. Mechanistically, the data suggests KDM4A regulation is altered at both transcriptional and translational levels. Finally, we observe a dose-dependent response on methylation patterns to desferrioxamine treatment in cardiac HL-1 cells in both endogenous and KDM4A over-expression assays.

Conclusion: Based on these observations, it would be of interest to determine the changes in gene expression downstream of these histone marks by ChIP-seq and RNA-seq.

P27: ORAL HIGH DOSE LIPOSOMIAL IRON VS INTRAVENOUS IRON IN SIDEROPENIC ANEMIA PATIENTS INTOLERANT/REFRACTORY TO IRON SULPHATE. MULTICENTRIC RANDOMIZED STUDY

GIULIO GIORDANO¹, ALBINO PARENTE², LUCA LUCIANO², FABIO D'AMICO², ROBERTO FRATANGELO², GIUSEPPE BERARDI³, ANTONIO COMMATTEO³, DONATA BERARDI⁴, BRUNO CARABELLESE¹, ANTONIETTA LICIANCI¹, LUIGI DI MARZIO¹

¹REGIONAL HOSPITAL ANTONIO CARDARELLI, VIA MONTE SANTO N 16 - CAMPOBASSO, ITALY, ²MOLISE UNIVERSITY - MEDICINE, CAMPOBASSO, ITALY, ³GENERAL MEDICINE, CAMPOBASSO, ITALY, ⁴LA SAPIENZA UNIVERSITY - MEDICINE, ROME, ITALY

OBJECTIVE: To verify if high doses of oral liposomal iron are safe, cost-effective and well tolerated as standard doses of intravenous ferrugluconate in patients with iron deficiency anemia intolerant/refractory to iron sulphate.

MATERIALS AND METHODS: We considered two group of patients (RANDOMIZED 1:1) with iron deficiency anemia without other relevant comorbidities. In group A M/F was 2/3, 15 patients had haemorrhagic gastritis, 8 haemorrhagic enteric bleeding, angiodysplasia, 22 hypermenorrhoea, median level of hemoglobin (Hb) was 8.5 g/dl (R 6.5-10), median ferritin level was 5 ng/ml (R 3-21), with a normal level of CRP or ESR, and received liposomal iron 30 mg 4 tablet/day. In group B M/F was 2/3, 18 patients had haemorrhagic gastritis, 6 haemorrhagic enteric bleeding, angiodysplasia, 21 hypermenorrhoea, median level of Hb was 8.2 g/dl (R 7.5-9.5), median ferritin level was 7 ng/ml (R 2-19), with a normal level of CRP or ESR, and received iv sodium ferrugluconate 62.5 mg iv in NS 100 ml in 3h/day. The median treatment costs in each group were calculated considering the monthly global treatment cost for each patients in the treatment period. This provided an estimate of the costs, independent of the precise cost of the drug, but tied to the final outcome (efficacy) of the therapeutic strategy used during the observation period.

Results: In group A, 1 g Hb increase was observed after a median of 9 days (R 7-15), a target Hb level of 12 g/dl was achieved in a median time of 4 weeks (R 2-5) with a median cost

of €120/months (R 95-180), 12 (26%) patients showed adverse events (7 epigastralgia, 5 diarrhoea). In group B, 1g Hb increase was observed after a median of 7 days (R 6-11), a target Hb level of 12 g/dl was achieved in a median time of 3 weeks (R 1.5-4) with a median cost of €300/months (R 250-380), 10 (22%) patients showed adverse events (2 hypotension, 2 urticaria and headache).

Conclusion: Oral high dose liposomal iron support is safe, fast, well tolerated and cost-effective as intravenous iron in sideropenic anemia.

P28: Reduced insulin need in patients with type 2 diabetes mellitus (T2DM) with iron deficiency anemia treated with sucrosomial iron vs intravenous sodium ferrigluconate. Multicentric prospective study

GIULIO GIORDANO¹, ALBINO PARENTE², LUCA LUCIANO², ROBERTO FRATANGELO², FABIO D'AMICO², ANTONIO COMMATTEO³, BRUNO CARABELLESE¹, GIUSEPPE BERARDI³, DONATA BERARDI⁴, ANTONIETTA LICIANCI¹, LUIGI DI MARZIO¹, MAURIZIO GASPERI²
¹REGIONAL HOSPITAL ANTONIO CARDARELLI, C.DA TAPPINO 86100 CAMPOBASSO, ITALY, ²FACULTY OF MEDICINE - MOLISE UNIVERSITY, CAMPOBASSO, ITALY, ³GENERAL MEDICINE, CAMPOBASSO, ITALY, ⁴LA SAPIENZA UNIVERSITY - FACULTY OF MEDICINE, ROME, ITALY

OBJECTIVE

Aim of this study is to assess whether the use of sucrosomial iron involves less use of insulin in patients with T2DM with iron deficiency anemia

MATERIALS AND METHODS

This study is a multicentric randomized study. We considered 40 T2DM patients with iron deficiency anemia, with TIBC saturation <10% and hemoglobin <10g/dl, without documented infections, tumors or autoimmune diseases. All patients received diabetic diet. They received lispro insulin TID + glargine insulin once daily. In group A 20 patients, M:F=12/8, median age 75 years (R 65-82), median blood glucose 230mg/dl (R 170-350), median CRP at onset 10mm/lh (R 2-22), were treated with sodium ferrigluconate 62.5mg in 250 cc NS iv in 4 hours/day for 12 days. In group A, 10 patients had anemia by gastrointestinal hemorrhage, 5 by atrophic gastritis, 5 by insufficient intake. In group B, 20 patients, M:F=11/9, median age 78 years (R 67-83), median blood glucose 220mg/dl (R 180-380), median CRP at onset 12mm/lh (R 2-20), were treated with sucrosomial iron 1CP 30mg orally x2/day for 30 days. In group B, 12 patients had anemia by gastrointestinal hemorrhage, 4 by atrophic gastritis, 4 by insufficient intake. Differences between the two groups were not statistically significant. Statistical analysis was done with Fisher exact test and with Chi Square test.

RESULTS

In group A at day 6 of iron support the median values of CRP were 38mm/lh (R 4-127), with 5 documented infections (urinary 3, lung 1, skin 1); only 8 patients achieved blood glucose values < or = 140 mg/dl with a median total lispro insulin dose of 42U (R 25-60) and glargine insulin dose of 22U (R 10-28). In group B at day 6 of iron support the median values of CRP were 12mm/lh (R 2-12), with 2 documented infections (urinary 2); 15 patients achieved blood glucose values < or = 140mg/dl with a median total lispro insulin dose of 20U (R 12-23) and glargine insulin dose of 20U (R 10-22).

CONCLUSION

In diabetic patients with iron deficiency anemia supported with sucrosomial iron the median lispro insulin need appears to be lower than that of the patients supported with i.v. sodium ferrigluconate. This study needs confirmation on a larger cohort of patients.

7. refinement of prototype; 8. user testing Phase 2; 9. development of final intervention.

Results

Multidisciplinary partnerships between stakeholders, academics, clinicians and patient representatives were key to effective intervention development. Review of the literature revealed some promising intervention components namely psychosocial support and CBT but a dearth of studies targeting self-efficacy. Important techniques associated with self-efficacy enhancement include modelling, goal setting, planning, provision of feedback and self-monitoring, all of which are integral to the intervention. An iterative process of user testing, including think aloud activities honed the final intervention. RESTORE consists of five sessions covering introduction to CRF, principles of goal setting, home and work life, personal relationships and emotional adjustment.

Conclusions

An evidence-based and theoretically driven web-based intervention can be successfully "co-created". This is a novel account of the development of such an intervention in a cancer population. An exploratory trial to test 'proof of concept' of the intervention has also been conducted.

06-12-P

CANCER RELATED FATIGUE AND SELF-CARE WHILE UNDERGOING CHEMOTHERAPY: PATIENT'S PERSPECTIVES

P. O'Regan¹, J. Hegarty¹, G. Mc Carthy¹

¹School of Nursing and Midwifery, University College Cork, Cork, Ireland

Introduction

Cancer related fatigue (CRF) is considered the most severe, debilitating and under-managed symptom of cancer. Patients receiving chemotherapy experience high levels of CRF which profoundly impacts their lives.

Objectives

- To explore and measure CRF and determine the most effective self-care strategies to combat CRF in patients with a diagnosis of cancer (breast cancer, colorectal cancer, Hodgkin's and Non-Hodgkin's lymphoma).
- To explore self-care agency and its relationship to CRF.

Methods

Mixed methodology which incorporated a descriptive, comparative, correlational design and qualitative descriptions of patients' ($n=362$) experiences gleaned through open ended questions and diary. The Revised Pipers Fatigue Scale, Appraisal of Self-Care Agency; and a researcher developed Fatigue Visual Analogue Scale, Fatigue Self-Care Survey, and Diary were utilised.

Results

The majority of participants (75 %) experienced moderate/severe fatigue. Having breast cancer, Hodgkin's and non-Hodgkin's lymphoma; being female, using the strategies of counseling, taking a 20–30 min nap, resting and sleeping, self-monitoring and complementary therapies were associated with increased odds of developing fatigue. Increased self-care agency; being divorced / separated, being widowed; increased length of time since commencement of chemotherapy; engagement in exercise, and socializing indicated a reduced risk of developing fatigue.

Four key qualitative categories emerged which demonstrated the distressing nature of fatigue.

Keeping a diary was considered very beneficial and cathartic.

Conclusions

Fatigue severely impacted the daily lives of patients undergoing chemotherapy. There are a range of self-care strategies that patients should use e.g. exercise, socializing. The enhancement of self-care agency and use of diaries should also be considered.

06-13-P

LIPOSOMIAL IRON IMPROVES FATIGUE IN PATIENTS WITH MYELODYSPLASTIC SYNDROMES AS REFRACTORY ANEMIA. MULTICENTRIC STUDY

G. Giordano¹, L. di marzio², A. Iliciani², D. berardi³, G. berardi⁴, R. gigli⁵, M. magri⁶, G. niro⁶, L. di iullo⁶

¹Oncology, Cardarelli Hospital, Campobasso, Italy

²Hospital Management, Cardarelli Hospital, Campobasso, Italy

³Medicine, University "La Sapienza", Rome, Italy

⁴Family Medicine, Asrem, Campobasso, Italy

⁵Laboratory Medicine, Cardarelli Hospital, Campobasso, Italy

⁶Oncology, Cardarelli Hospital, Campobasso, Italy

Introduction

Fatigue is the most invalidating symptom in neoplastic disease. Fatigue frequently is linked to an iron deficiency. In inflammatory diseases as myelodysplastic syndromes fatigue might be linked to a functional iron deficiency with elevated ferritin level and a saturation of total iron binding capacity < 20 %.

Objectives

Aim of this study is to verify if liposomal iron support in myelodysplastic syndromes as refractory anemia improves fatigue perception in patients with a saturation of total iron binding capacity < 20 %.

Methods

Between June 2011 and December 2014, 20 patients affected by refractory anemia were studied. Median follow-up was 12 months (R10-24). Patients were randomized 1:1 to receive in group A alpha erythropoietin 40000 IU/week+calcium levofolate 7.5 mg/day orally+Vitamin B12:400 mg/day orally. In group B patient received liposomal iron 14mg tablet orally/day+alpha erythropoietin 40000 IU/week+calcium levofolate 7.5 mg/day orally+Vitamin B12:400 mg/day orally. In group A median age was 60 years (R65-70), M/F:8/2. In group B median age was 66 years (R60-75), M/F:6/4. Cytotype was normal in group A and B patients. Median level of haemoglobin was 9 g/dl in group A (R8.5-11) and 8.8 g/dl (R8.5-11.5) in group B. Fatigue was measured with Modified Fatigue Impact Scale (FISC - Fisk 1994).

Results

Patients in group A reached a median hemoglobin level of 11.5 g/dl after 3 month of therapy and referred a median FISC score of 74 (R65-80). Patients in group B reached a median hemoglobin level of 12.5 g/dl after 3 month of therapy and referred a median FISC score of 54 (R42-68).

Conclusions

Liposomal iron support improves fatigue perception in patients with refractory anemia. This study needs confirmation on a larger cohort of patients.

06-14-P

FATIGUE SCORES IN PATIENTS RECEIVING PALLIATIVE RADIOTHERAPY FOR PAINFUL BONE METASTASES

N. Palenzas¹, P. Cheon¹, L. Zhang¹, E. Mauti¹, E. Wong¹, N. Thavarajah¹, M. Tsao¹, C. Danjoux², L. Holden¹, C. DeAngelis², N. Lao¹, E. Chow¹

¹Rapid Response Radiotherapy Program, Odette Cancer Centre, Toronto, Canada

²Department of Pharmacy, Odette Cancer Centre, Toronto, Canada

Introduction

Radiation therapy is used in patients with bone metastases to relieve pain and improve quality of life (QOL).

undergoing increasingly myelotoxic induction chemotherapy. The patients were compared with a chi-square and Mann–Whitney tests. Groups were compared with a log-rank test. A *p* value below 0.05 was considered as being statistically significant.

Results

We evaluated 48 patients in 282 episodes of hospitalization (table 1). The number of BSI was superior in patients with AML ($p<0.001$) although we registered a similar number of CRBSI between AML and ALL patients ($p<0.40$). The incidence of BSI caused by gram-negative bacteria was higher in AML patients ($p<0.01$), however ALL patients shows more BSI caused by Gram-positive bacteria ($p<0.05$) (table 2). Neutropenic fever was found in 214 episodes (136 AML and 78 ALL, $p<0.001$). The number of negative blood cultures were higher when ANC >500 cells/mm³ ($p<0.01$) and the number of positive blood cultures decreased in consecutive samples collected from patients with refractory fever. All the third blood cultures were negative ($p<0.001$).

	AML	ALL	Total	<i>p</i>
Number of patients (n)	31	17	48	< 0.01
Sex				
- Male	15 (48.4%)	11 (64.7%)	26 (54.2%)	.27
- Female	16 (51.6%)	6 (35.3%)	22 (45.8%)	
Age				.04
- Med.	53 years	41 years	47 years	
- [Min-Max]	[27-72] years	[16-68] years	[16-72]	
Admissions				—
- Total	147	135	282	
- Med.	5	8	6.5	
- [Min-Max]	[1-10]	[1-14]	[1-14]	
Internment Days				.25
- Total	2264 days	1535 days	3799 days	
- Med.	70 days	85 days	77.5 days	
- [Min-Max]	[11-188] days	[23-179] days	[11-188] days	
No. CV/Days	2137	1341	3478	.23
- Med	67	85	76	
- [Min-Max]	[11-188]	[10-153]	[10-188]	

Table 1

Microorganism recovered	AML (31 patients)	ALL (17 patients)	Total (48 patients)	<i>p</i>
<i>R. Ornitholytica</i>	1	0	1	.37
<i>K. Pneumoniae</i>	5	2	7	.61
<i>E. Coli</i>	7	2	9	.72
<i>P. Aeruginosa</i>	2	0	2	.30
<i>S. Aureus</i>	0	1	1	.47
<i>S. Mitis</i>	4	2	6	.16
<i>S. Epidermidis</i>	1	3	4	.22
<i>Candida Glabrata</i>	1	0	1	.47

Table 2

Conclusions

This study suggest that AML patients have more febrile syndrome compared to ALL patients and exists an impact of the ANC on the probability of obtained positive blood cultures.

13-21-P

LOW-RISK MYELODYSPLASTIC PATIENTS SUPPORTED WITH ERYTHROPOIETIN PLUS LIPOSOMIAL IRON SHOW A REDUCED NUMBER OF FEBRILE EPISODES THAN PATIENTS WITH INTRAVENOUS IRON SUPPORT

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Introduction

Intravenous iron support simultaneous to erythropoietin administration improve hemoglobin response in myelodysplastic patients. There are many evidences that iron, useful for bacterial growth, might increase risk of infection.

Objectives

Aim of this study is to verify incidence of number of febrile episodes in low-risk myelodysplastic patients supported with iron.

Methods

This study is a retrospective, multicentric study. Between July 2008 and December 2014, 107 patients affected by low-risk refractory anemia were studied. Median follow-up was 24 months (R12-60). Twenty patients had no support, 27 epo support, 30 epo + liposomal iron (14 mg 2 tablets orally/day for 3 months), 15 epo + iron sulfate (525 mg 2 tablets orally/day for 3 months), 15 epo + iv sodium ferrigluconate (62.5 mg iv in NS100 ml in 1 h/day for 5 day/month). Statistical analysis was performed by Chi Square test and Fisher exact test.

Results

In group with no support median packed red blood cells unit (PRBCU) transfused was 0.2/month (R0-0.5). Median number of febrile episodes/year was 1.5 (R0-2). In group supported with epo only median PRBCU transfused was 0.4/month (R0-0.7). Median number of febrile episodes/year was 2 (R0-2). In group supported with epo + iron sulfate median PRBCU transfused was 0.3/month (R0-0.6). Median number of febrile episodes/year was 3 (R0-3). In group supported with i.v. sodium ferrigluconate median PRBCU transfused was 1.5/month (R1-3). Median number of febrile episodes/year was 6 (R0-9). In group supported with liposomal iron median PRBCU transfused was 0.2/month (R0-1). Median number of febrile episodes/year was 1 (R0-2).

Conclusions

Number of febrile episodes seem not related to basal neutrophil count or hemoglobin level reached after 3 month treatment. Number of febrile

episodes is higher in group with higher transfusion need and in group treated with i.v.sodium ferriglucanate ($p=0.02$). Probably liposomal iron support provides a reduced amount of non-transferrin bound iron that might block bacterial growth. These data need confirmation on a larger cohort of patients.

13-22-P

CEFTAZIDIME MONOTHERAPY IN PATIENTS WITH COLORECTAL CANCER (CC) AND FEBRILE NEUTROPENIA (FN) AFTER CHEMOTHERAPY

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Introduction

Febrile neutropenia can develop in any form of neutropenia, but is most generally recognized as a complication of chemotherapy.

Objectives

The aim of this study was to confirm the safety and efficacy of ceftazidime monotherapy in patients with FN after chemotherapy.

Methods

We studied all cases with hospital treatment by FN and ceftazidime monotherapy between January 2009 and December 2013. Hospital treatment of febrile ($>38^{\circ}\text{C}$) neutropenia induced by chemotherapy, suspected bacterial infection and received empirical ceftazidime (2 g X 3/24 h) monotherapy and filgrastim (5mcg/kg per day). The failure criteria were fever or new signs and symptoms of infection 48 h after initiation ceftazidime, change antibiotic or death by infection.

Results

There were 42 patients with CC and 54 FN events. The median age was 44, 2, female 24, male 18. Neutropenia grade: 1–2 (27 %) and 3–4 (73 %). Performance status (ECOG): 1–2 (75 %), 3–4 (25 %). The infection sites were: non-clinical infection evidence 39 %, gastrointestinal 15 %, pneumonia 28 %, genitourinary 14 %, other 4 %. Median duration of hospitalization was 5.6 days and the median duration of neutropenia was 3.2 days. The median duration with fever was 1.5 days, 92 % of cases responded in the first 48 h of treatment.

Conclusions

Ceftazidime is a safety and efficacy empirical treatment in patients with colorectal cancer and febrile neutropenia induced by chemotherapy.

13-23-P

SIGNIFICANT RISK FACTORS OF NEUTROPENIA IN PATIENTS WITH SOLID TUMORS AFTER CHEMOTHERAPY

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Introduction

The risk of serious infection increases as the absolute neutrophil count (ANC) falls to the severely neutropenic range. Patients with neutropenia are more susceptible to bacterial infections and the condition may become life-threatening.

Objectives

The aim of this study was to evaluate the risk factors of chemotherapy-induced neutropenia in patients with solid tumors.

Methods

Sixty-five cases of patients with solid tumors and neutropenia after chemotherapy were retrospectively analyzed. The selection of significant risk factors of neutropenia has been done with logistic regression analysis.

Results

Among 65 patients with solid tumors, 99 episodes of 44 patients experienced neutropenic events, grade 3 and 4 neutropenia was 21 and 11.4 % respectively. Patients who experienced one neutropenic event had a higher risk of a second event, $p=0.04$. Advanced age, poor staging and anorexia were associated with greater risk of neutropenia, $p=0.01$. Multiple logistic regression analysis indicated that anorexia and poor staging were the most significant risk factors of grade 3 and 4 neutropenia, and anorexia was the most significant risk factor of grade 1 and 2 neutropenia.

Conclusions

Anorexia, poor staging and advanced age were the significant risk factors of neutropenia in patients with solid tumors.

13-24-P

A RARE CASE OF ACHROMOBACTER SPECIES SUBDURAL EMPYEMA IN A PATIENT WITH HAEMATOLOGIC MALIGNANCY

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Introduction

Achromobacter species are gram-negative coccobacillary rods found chiefly in water supplies. They are opportunistic pathogens that affect immunosuppressed patients and are usually involved in sepsis, pneumonia, and urinary tract infections. Infections from Achromobacter species cause significant morbidity and mortality in debilitated individuals.

Objectives

Report a rare case of a subdural empyema from achromobacter species in a patient with hematologic malignancy.

Methods

A 39-year old female with multiple myeloma was admitted with fever, headache, vomiting, gait disturbance, and seizures since 4 days. Neurological examination revealed left hemiparesis, nuchal rigidity, and positive Babinski and Kernig's sign. CT and MRI brain scan were suggestive of right frontal subdural empyema and abscess formation with perifocal edema and contrast enhancement.

Results

The patient underwent right frontal craniotomy and complete removal of subdural empyema and abscess. *Achromobacter* species was identified from blood samples collected in triplicate and pus cultured on MacConkey agar. The patient received a combination of Piperacillin-tazobactam and TMP/SMX intravenously and gradually recovered. Brain inflammation disappeared during the course of antibiotic therapy within 2 weeks, and the patient was maintained on oral TMP/SMX for a total of 3 months.

Conclusions

Achromobacter species is rarely recognized as a human pathogen. However, it can cause serious infections in patients with certain underlying illnesses. Eradication of these infections requires prolonged therapy with antimicrobial agents and treatment of any pathogenic source. Isolation of Achromobacter from subdural space was a completely unusual finding. Microbiology laboratories must be vigilant and meticulous about the laboratory diagnosis of Achromobacter family.

13-25-P

SUCCESSFUL OUTCOME OF MUCORMYCOSIS WITH ANTIFUNGAL TREATMENT AND SURGERY IN A CHILD WITH ACUTE LEUKEMIA

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Background: Sickle Cell Disease (SCD) is the most frequent severe genetic disease worldwide. It's the most prevalent genetic disorder in France and the UK; its frequency is steadily rising in several European countries, including Italy and Ireland. Sickle SC disease (HbSC) is the second commonest form of SCD after sickle cell anaemia (HbSS/HbSB*) and accounts for 25–30% of cases. Neurological events are among the most frequent and disabling complications in children with SCD with an important impact on quality of life, health and educational system costs. Overt stroke, silent infarcts and psycho-cognitive impairment are reported to occur also in HbSC disease, although at a lower frequency than in HbSS. Studies suggest that the life-time risk of stroke in HbSC is 2–3%. At present, a screening program is available for stroke prevention using Transcranial Doppler (TCD) according to the Stroke Prevention Trial criteria, but only for HbSS/HbSB* patients. There is no specific evidence to guide stroke prevention in HbSC. TCD ranges of velocities in the Middle Cerebral Artery (MCA) and in the distal Internal Carotid Artery (dICA) used to stratify patients with HbSS/HbSB* in risk categories might be inappropriate for HbSC patients. The Sickle Cell Anaemia transcranial Doppler Educational Study (SCATES) is a Multicenter European Educational Study to facilitate a screening program with the purpose to achieve systematic evaluation of stroke risk in children. It has the objectives to standardize TCD application in different European Settings and make TCD a common practice in routine health care of children with SCD across United Kingdom, Ireland and Italy.

Aims: To determine mean reference values of velocities in MCA and dICA in a European prospective cohort of children with HbSC. To evaluate possible clinical and hematological risk factors of high velocities in HbSC disease.

Methods: TCD was performed at least once a year in children with HbSC disease aged 2–18 years. TCD, clinical and hematological data were prospectively collected in clinical charts and transferred in a web based database for statistical analysis. Descriptive statistics and regression analysis were performed.

Results: 227 HbSS and 61 HbSC were enrolled in SCATES. In HbSC patients mean MCA velocity was 95.70 cm/sec (range 54.3–132, SD 19.07) and dICA was 79.81 cm/sec (range 29–138, SD 19.29), while in SS patients velocities were much higher: MCA was 122.47 cm/sec (range 57–190, SD 24) and dICA was 107 cm/sec (range 61–176, SD 22.21). Bootstrap analysis allowed to define a mean velocity in the MCA of 98.68 cm/sec (95%CI 93.75–103.60 (N), 94.00–103.77 (P), 94.06–103.92 (BC)). There was no significant correlation between high velocities in the MCA or dICA in HbSC patients and any clinical or hematological parameters except for Diastolic Blood Pressure (p 0.030, 95%CI 0.0939–1.593). Evaluation of Magnetic Resonance Imaging (MRI) available for 15 patients did not show any correlation between stenosis and TCD velocities of the corresponding vessels.

Summary and Conclusions: This is the largest cohort of pediatric patients with HbSC disease evaluated for stroke risk using a standardized protocol, reproducible across Europe. Mean velocities are lower than the reported ones for HbSS/SB* patients and could aid in defining stroke risk categories for this group. Diastolic Blood Pressure is an important risk factor and prompts to a regular Blood Pressure monitoring and control in children with HbSC.

P381

INTRAVENOUS IRON CARBOXYMALTOSE VERSUS STANDARD CARE IN THE MANAGEMENT OF POSTOPERATIVE ANAEMIA: A PROSPECTIVE RANDOMIZED CONTROLLED TRIAL

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Background: Data from literature suggest that by having postoperative normal Haemoglobin (Hb), patients will recover significantly better after major surgery. There is growing evidence that improving the recovery period after surgery will impact on overall outcome of the surgical procedures. Despite the significant efforts in management of the preoperative, it has been found that there is a significant, although unknown, number of patients who have postoperative iron deficiency anaemia. Furthermore, there is no data regarding prevalence and management of postoperative iron deficiency anaemia and the requirement of blood transfusion in patients who undergo different surgeries.

Aims: This study is aiming to show that repleted iron stores and hence improved haemoglobin post-operatively, will improve outcomes of major surgery. Furthermore, this approach is aiming to minimise requirement for blood transfusion and the patient's stay in hospital and to lower the overall cost of procedures and to relieve the extra burden on health systems.

Methods: A prospective randomized controlled study was offered after an informed consent to adult patients who are 18 years old and above with docu-

mented Hb level at day 1 postoperatively between 70 and 120 g/L and reduced iron stores with ferritin <100 or iron saturation <20%. Patients were randomized between standard care versus active intervention with a single intravenous iron carboxymaltose infusion. Assessment during hospital stay and at 4 weeks was conducted to measure patients' outcomes. During the period between December 2014 and March 1st 2015, we have recruited 106 patients postoperatively after major surgery at the Launceston General hospital, a tertiary referral hospital for Northern Tasmania, Australia. Male to female ratio was 52:54 with median age of 65 years (range, 22:90). Vast majority of patients underwent major orthopaedic surgery (68%), then come abdominal (18) and genitourinary surgery (12), and others (8).

Results: Mean day 1 postoperative Hb was 103 g/L with a median of 105 g/L. At four weeks assessment of Hb, there was a significant increase of mean Hb in the intervention group to 131 g/L with reduction in transfused blood units versus Hb of 116 g/L in the standard care group (p <0.01). Intravenous single iron carboxymaltose was commenced in average of 1000 mg as short infusion over 15 minutes and was well tolerated by the patients postoperatively.

Summary and Conclusions: Our data show the feasibility and safety of applying iron carboxymaltose in the postoperative anaemia setting. Delays in the identification of patients with preoperative anaemia may delay both, proper anaemia management and the operative procedure. We employed a pragmatic alternative or complementary approach to preoperative assessment for anaemia at day 1 postoperatively. A significant number of surgical patients who lost blood during surgery with an underlying iron deficiency could benefit from postoperative management with iron infusion. The new therapy with iron carboxymaltose was well tolerated. Further trials to assess our novel approach in treatment of the post-operative anaemia are warranted.

Trial registration: The study was approved by the Tasmanian Human Research Ethics Committee, Australia and registered in the Australian New Zealand Clinical Trials Registry (<http://www.ANZCTR.org.au/ACTRN12614001261606>).

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ORAL HIGH DOSE LIPOSOMIAL IRON SUPPORT IS SAFE, FAST, WELL TOLERATED AND COST-EFFECTIVE AS INTRAVENOUS IRON IN SIDEROPEMIC ANEMIA. MULTICENTRIC RANDOMIZED STUDY

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Background: In iron deficiency anemia support with intravenous iron allows a faster anaemia correction and a faster ferritin increase than iron sulfate. Frequently iron sulfate and intravenous iron generate adverse events as hypotension, urticarial reactions, shock, epigastralgia, constipation or diarrhea. High doses of oral iron frequently are poorly tolerated because of adverse events.

Aims: Aim of this study is to verify if high doses of oral liposomal iron are safe, cost-effective and well tolerated as standard doses of intravenous ferrugluconate in patients with iron deficiency anemia.

Methods: We considered two group of patients (RANDOMIZED 1:1) with iron deficiency anemia without other relevant comorbidities. In group A M/F was 2/3, 7 patients had haemorrhagic gastritis, 3 haemorrhagic enteric bleeding angiodysplasia, 10 hypermenorrhoea, median level of hemoglobin (Hb) was 8 g/dl (R 7-10), median ferritin level was 10 ng/ml (R 3-20), with a normal level of CRP or ESR, and received liposomal iron 30 mg 4 tablet/day. In group B M/F was 1/3, 9 patients had haemorrhagic gastritis, 1 haemorrhagic enteric bleeding angiodysplasia, 10 hypermenorrhoea, median level of Hb was 8.5 g/dl (R 8-9.5), median ferritin level was 8 ng/ml (R 2-18), with a normal level of CRP or ESR, and received iv sodium ferrugluconate 62.5 mg iv in NS 100 ml in 3 h/day. The median treatment costs in each group were calculated considering the monthly global treatment cost for each patient in the treatment period. This provided an estimate of the costs, independent of the precise cost of the drug, but tied to the final outcome (efficacy) of the therapeutic strategy used during the observation period.

Results: In group A, 1 g Hb increase was observed after a median of 8 days (R 7-12), a target Hb level of 12 g/dl was achieved in a median time of 4 weeks (R 2-4) with a median cost of € 110/months (R 82-162). 6 (30%) patients showed adverse events (3 epigastralgia, 3 diarrhoea). In group B, 1 g Hb increase was observed after a median of 7 days (R 6-10), a target Hb level of 12 g/dl was achieved in a median time of 3.5 weeks (R 1.5-4) with a median cost of € 326/months (R 250-360). 4 (20%) patients showed adverse events (2 hypotension, 2 urticaria and headache).

Summary and Conclusions: Oral high dose liposomal iron support is safe, fast, well tolerated and cost-effective as intravenous iron in sideropenic anemia. This study needs confirmation on a larger cohort of patients.

Methods: From March 2008 to October 2013, 50 patients, aged 40 years and older (median age: 69, 40-84 years) with diagnosis of MDS (WHO2008 categories: 22.4% RA/RMCD, 32.6% RAEB-1, 28.5% RAEB-2, 12.2% CMML, 4% AML), were treated with 5-azacitidine (75 mg/m²/day for 7 days every 4 weeks), both in on-label and off-label drug use setting. Forty-four percent of patients had intermediate-2 or high International Prognostic Scoring System, 68% were neutropenic and 12% had high MDS-Comorbidity Index. Prophylactic antibiotics were administered to 12 patients (24%), prophylactic antifungal to 17 patients (34%) and granulocyte colony-stimulating factor was administered to 24 patients (48%).

Results: Median number of cycles received by a single patient was 5 (range 1-21); 48% received more than 6 cycles of therapy. 30.4% of the entire cohort was considered responsive to treatment (14.4% hematologic improvement, 8% partial response, 8% complete response, according to IWG2006 criteria); 24% of patients achieved a stable disease. Out of 50 patients, 25 (50%) developed 25 infectious events (1 for each patient), during 325 treatment cycles (7.7%); 14/25 (56%) events required hospitalization. Only one patient died from an infectious complication. Twenty-two of 25 infectious events (88%) were bacterial, mostly pneumonia; 3 (12%) were fungal (invasive aspergillosis) and 1 (4%) was viral (H1N1). Infectious events did not significantly affect overall survival (27 vs 18 months, $p=0.606$), progression free survival (6.0 vs 6.1 months, $p=0.48$) or overall response to therapy (13 vs 17.4%, $p=0.693$). However, no complete responses were documented in the cohort of patients who suffered from infectious episodes. In a univariate analysis, age, sex, low neutrophil count, high comorbidity index, antibiotic prophylaxis and use of G-CSF were not found to be associated with infections. Only high IPSS and the presence of pancytopenia, seemed to be correlated with an increased risk for infections.

Summary and Conclusions: Infectious events, specifically bacterial infections, are one of the most frequent complications during therapy with azacitidine in patients with MDS. These data suggest that there are not predisposing risk factors for infection in patients except those connected with disease severity (high IPSS and pancytopenia). Routine antibiotics, antifungal prophylaxis and/or use of G-CSF appear not to reduce the incidence of infectious events. Moreover, bearing in mind the risk of bacterial and fungal resistance associated with extended use of anti-infective drugs, they should be used with caution in selected subsets of MDS patients.

E1182

EVALUATION OF SERUM GALACTOMANNAN ASSAY FOR THE DIAGNOSIS OF INVASIVE ASPERGILLOSIS IN CHILDREN WITH HEMATOLOGICAL MALIGNANCIES

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Background: Fungal infection is a major concern during treatment of hematological malignancies. Establishing diagnosis is a challenge and often frustrating for the treating physicians. Rapid and diagnostic test is valuable for timely intervention. Galactomannan assay is a non-invasive test, however its efficacy needs to be validated in our population. Only few studies in Indian population, hence to establish a clinically relevant cut off value this prospective study is done.

Aims: Diagnostic efficacy of galactomannan assay (GA) for invasive aspergillosis (IA) is variable, the cut off value is debated.

Methods: Children ≤ 14 -years with hematological malignancies and fever were enrolled prospectively. Blood sample for GMA was drawn on day of admission; levels were measured with Platelia Aspergillus enzyme immunoassay. Diagnostic criteria were adapted from EORTC-MSG. GMA was evaluated at various cut-offs, with proven, probable and possible episodes being considered as disease group.

Results: 100 febrile episodes in 78 patients were included. Mean-age was 6.1 years. Majority (75%) episodes were in patients with ALL, followed by AML (17%). CT-scan-lung was performed in 23 episodes. BAL, transbronchial-lung-biopsy and functional-endoscopic-sinus-surgery were performed in 2-episodes, each. Post-mortem investigations included autopsy (1) and organ biopsies (6). Diagnosis of IA was proven and probable in one case each. A possible diagnosis was made in 23 episodes; remaining 75 were categorized as "No IA". Other fungal infections diagnosed included mucormycosis (3), candidiasis (1) and fusariosis (1). Best results were obtained with a cut-off value of 1.0, with sensitivity, specificity, positive and negative predictive value of 60%, 93%, 75 and 87, respectively. With GMA >1.0 as cut-off, the probability of a positive test to be true or false positive was 0.71 (95% CI: 0.48-0.88) and 0.28 (95% CI: 0.12-0.52), respectively. For a negative test, the probability of true negative was 0.87 (95% CI: 0.78-0.93) and false negative was 0.13 (95% CI: 0.16-0.22). The sensitivity dropped to 40%, at cut-off value of 1.5 and specificity was 38%, at a cut-off of 0.5. Significant correlation of a higher GMA was observed with pulmonary nodules ($p=0.037$), duration of Amphotericin >10-days ($p=0.043$) and mortality ($p=0.001$).

Summary and Conclusions: Confirming the diagnosis of aspergillosis is a challenge; this renders assessment of efficacy of GMA difficult. At a cut-off value of 1.0, the sensitivity and specificity were 60% and 93%, respectively.

E1183

ANIDULAFUNGIN THERAPY FOR HIGH RISK OF INVASIVE FUNGAL INFECTION HEMATOLOGIC PATIENTS: ITS ROLE IN REAL-LIFE SINGLE CENTER EXPERIENCE.

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Background: Anidulafungin is an echinocandin licensed for the treatment of invasive candidiasis in adult non-neutropenic patients. This drug is neither metabolized by the liver, nor has renal elimination. Liver dysfunction is common after allogeneic stem cell transplantation and intensive chemotherapy. In our hospital patients who fulfill criteria of high risk for invasive fungal infection (IFI) routinely receive antifungal prophylaxis with voriconazole. It has become routine clinical practice to substitute voriconazole for anidulafungin in cases with hepatic involvement of GVHD and/or liver toxicity manifested as elevated liver function tests (LFTs).

Aims: The aim of this study is to analyze the safety, toxicity and feasibility of off label anidulafungin as prophylaxis and treatment of high risk of IFI hematologic patients in a real life scenario.

Methods: We have retrospectively studied all episodes of adult high risk of IFI hematological patients treated with anidulafungin in our hospital from March 2010 to October 2014. IFI was defined according to EORTC guidelines.

Results: Fifty patients were included, 38 were treated once, 9 twice and 3 thrice, thus 65 different therapy episodes were finally analyzed. Median age was 50 years (IQR 39.2-61.2), with 63.1% ($n=41$) cases being male. Most (81.6%) had undergone allogeneic stem cell transplantation (Allo-SCT). The most common baseline diagnoses were acute leukemia in 31 (47.7%) and non Hodgkin's lymphoma in 12 (8.3%). Fifty-five cases (85%) had no prior history of IFI. The remaining ten cases previously had proven ($n=3$), probable ($n=5$) or possible ($n=2$) IFI and therefore received secondary anti-fungal prophylaxis. Anidulafungin was administered as prophylaxis in 48 episodes (73.9%). In 3 episodes for proven candidiasis (4.6%) and in 14 (21.5%) as empirical treatment of IFI. Elevated LFTs was the most common cause to commence on anidulafungin ($n=46$, 71.8%), in 19 of them (29.7%) voriconazole had to be discontinued. Other reasons to start anidulafungin were chronic graft versus host disease ($n=6$), voriconazole intolerance ($n=4$), hallucinations due to voriconazole ($n=3$), candidiasis ($n=3$), and others ($n=3$). Median number of days on therapy was 11 (IQR 5-19.5). Treatment with anidulafungin was well tolerated in most of our patients (93.8%). The drug was withdrawn in three cases: one due to acute kidney failure, one due to drug intolerance during infusion and one due to progressive liver failure. Among the 48 cases receiving anidulafungin as prophylaxis there were 36 with abnormal LFTs and 6 with liver GVHD. In this very high risk of IFI cohort there were 3 proven (2 cases of mucormycosis and one *C. guilliermondii* candidemia), 2 probable and one possible IFI, during the duration of prophylaxis or in the week following the discontinuation of anidulafungin. In addition, 4 more proven IFIs were diagnosed in the following 100 days: one disseminated histoplasmosis (day 11), one *C. krusei* candidemia (day 18), one pulmonary invasive aspergillosis (day 10) and one esophageal candidiasis (day 36). All patients but the last one, had received other anti-fungal agent after anidulafungin was discontinued. Nearly half of the patients receiving anidulafungin as prophylaxis (45.8%) died during the 100 days follow up period, 2 of them (9.6%) due to IFI.

Summary and Conclusions: Anidulafungin is a safe and feasible alternative to azole therapy, especially in patients with elevated LFTs or liver involvement by GVHD. Further studies are needed to establish the role of anidulafungin in this patient population.

E1184

LOW-RISK MYELODYSPLASTIC PATIENTS SUPPORTED WITH ERYTHROPOIETIN PLUS LIPOSOMAL IRON SHOWS A REDUCED NUMBER OF FEBRILE EPISODES THAN PATIENTS WITH INTRAVENOUS IRON SUPPORT.

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Background: Intravenous iron support simultaneous to erythropoietin administration improve response to erythropoietin in myelodysplastic patients. Oral liposomal iron, bypassing normal intestinal mechanism of absorption, shows similar effects, better than oral iron sulfate, usually poorly absorbed. There are many evidences that iron, useful for bacterial growth, might increase risk of infection.

Aims: Aim of this study is to verify incidence of number of febrile episodes in low-risk myelodysplastic patients without support or supported with erythropoietin (epo) only or with epo plus oral liposomal iron, oral iron sulfate or iv sodium ferrugluconate.

Methods: This study is a retrospective, multicentric study. Between July 2006 and december 2014, 107 patients affected by low-risk refractory anemia were

studied. Median follow-up was 24 months (R12-60). 20 patients had no support, 27 epo support, 30 epo+liposomal iron (14 mg 2 tablets orally/day for 3 months), 15 epo+iron sulfate (525 mg 2 tablets orally/day for 3 months), 15 epo+iv sodium ferrugluconate (62.5 mg iv in NS 100 ml in 1 h/day for 5 days/month). All patients supported with epo received calcium levofolinate 7.5 mg/day orally + Vitamin B12: 400 mg/day orally. Epo support was performed with originator or biosimilar epo alpha or epo zed 40000 IU sc/week or with epo beta 30000 IU sc/week. Statistical analysis was performed by Chi Square test and Fisher exact test.

Results: In group with no support median hemoglobin level was 9.5 g/dl (R8-11). Median neutrophils count was 1000/mcl (R300-2500). Median packed red blood cells unit (PRBCU) transfused was 0.2/month (R0-0.5). Median number of febrile episodes/year was 1.5 (R0-2). In group supported with epo only median hemoglobin level after 3 month treatment was 11 g/dl (R7.5-12). Median neutrophils count was 800/mcl (R400-1200). Median packed red blood cells unit (PRBCU) transfused was 0.4/month (R0-0.7). Median number of febrile episodes/year was 2 (R0-2). In group supported with epo+iron sulfate median hemoglobin level after 3 month treatment was 10.5 g/dl (R8-12). Median neutrophils count was 750/mcl (R300-1100). Median packed red blood cells unit (PRBCU) transfused was 0.3/month (R0-0.6). Median number of febrile episodes/year was 3 (R0-3). In group supported with i.v. sodium ferrugluconate median hemoglobin level after 3 month treatment was 12 g/dl (R9-13). Median neutrophils count was 700/mcl (R250-1000). Median packed red blood cells unit (PRBCU) transfused was 1.5/month (R1-3). Median number of febrile episodes/year was 6 (R0-9). In group supported with liposomal iron median hemoglobin level after 3 month treatment was 12.8 g/dl (R10-13). Median neutrophils count was 280/mcl (R150-1300). Median packed red blood cells unit (PRBCU) transfused was 0.2/month (R0-1). Median number of febrile episodes/year was 1 (R0-2).

Summary and Conclusions: Number of febrile episodes is low in each treatment group. Febrile episodes seem not related to basal neutrophil count or hemoglobin level reached after 3 month treatment. Number of febrile episodes is higher in group with higher transfusion need and in group treated with i.v. sodium ferrugluconate ($p=0.02$). Probably liposomal iron support provides a reduced amount of non-transferrin bound iron that might block bacterial growth. These data need confirmation on a larger cohort of patients.

E1185

RISK FACTORS FOR FEBRILE NEUTROPENIA AND BLOODSTREAM INFECTIONS IN RECIPIENTS OF HEMATOPOIETIC STEM CELL TRANSPLANTS

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Background: Number and indications for Hematopoietic Stem Cell Transplantation (HSCTs) in adults continue to grow worldwide. Febrile neutropenia (FN) remains one of the most common complications in the HSCT patients. Bloodstream bacterial infections (BSI) stay common causes of FN among neutropenic patients. Choice of initial strategy of antibacterial treatment in FN patients is based mainly on clinical and epidemiological risk factors, because of the low frequency of culture isolation and reduced clinical manifestations of infection.

Aims: The aim of the study was to determine the risk factors for febrile neutropenia or microbiologically proven bloodstream infection in adult patients receiving HSCT.

Methods: 242 patients undergoing allogeneic or autologous HSCT at the Belarus National Centre for Hematology and Bone Marrow Transplantation from January 2013 to January 2015 were monitored and their clinical data was reviewed. Age of the patients included in this study was 18-65 years, 42% of them were male, 58% - female. The primary outcome was the episode of FN (fulfilled criteria of Freifeld et al., 2011), the secondary outcome was microbiologically proven bacterial bloodstream infection (BSI). Isolation of pathogens was performed by standard means with BacT/ALERT Standard Aerobic/Anaerobic bottles and BacT/ALERT 3D automated microbial detection system, identification and antibiotic resistance was studied with VITEK 2 system and disc-diffusion methods.

Categorical variables were analyzed with χ^2 test and Fisher's exact test, and continuous variables were analyzed with the Mann-Whitney U test and Odds Ratio. A multivariate analysis with logistic regression was conducted for the categorical variables with P -value ≤ 0.2 in previously performed univariate analysis. Significant P -value considered to be <0.05 .

Results: There were 87 patients with episodes of FN, the incidence of FN in HSCT recipients was 36%. Among them 39 patients had microbiologically proven BSI, i.e. 16% of all HSCT recipients or 45% of those who had FN. Most of the cases of BSI were caused by *E. coli*, *K. pneumoniae*, *P. aeruginosa*, *A. baumannii*, *Streptococcus* spp. Among independent statistically significant risk factors for both FN and BSI were: profound neutropenia (OR 2.34, 95% CI 1.19-13.24, $p=0.012$ for FN; OR 2.44, 95% CI 1.98-9.54, $p=0.005$ for BSI); neutropenia duration >14 days (OR 1.37, 95% CI 1.08-12.95, $p=0.049$ for FN; OR 1.68, 95% CI 1.14-8.73, $p=0.045$ for BSI) and active main disease on start of HSCT procedure (OR 3.41; CI 2.32-8.63, $p=0.01$ for FN; OR 1.28, CI 1.04-3.81, $p=0.049$ for BSI). Prior to HSCT patients colonization with ESBL-positive *Enterobacteriaceae* spp. and prior ICU hospitalization had a trend towards the statis-

tical significance as a risk factors of BSI, what may be proved by using larger number of patients in the future studies (OR 1.64, 95% CI 0.89-4.36, $p=0.64$ for colonization; OR 2.31, 95% CI 1.27-6.41, $p=0.72$ for ICU hospitalization).

Summary and Conclusions: The above named risk factors and most common pathogens should be taken into account when choosing a clinical approach to empiric antibacterial treatment and prophylaxis in adult HSCT patients.

E1186

ANALYSIS OF 75 CASES OF ACUTE LEUKEMIA WITH INVASIVE FUNGAL DISEASE

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Background: Acute leukemia patients are susceptible to invasive fungal disease, proper diagnosis and treatment is important for reducing morbidity and mortality.

Aims: To analyze the clinical characteristics of invasive fungal infections in patients with acute leukemia (AL), explore the early diagnosis and prevention strategy.

Methods: Acute leukemia patients with invasive fungal disease (IFD) treated in cancer center of the First Hospital of Jilin University from 2014 January -12 months were analyzed retrospectively according to the "criteria for the diagnosis and treatment principles of hematological malignant patients with invasive fungal disease (The Fourth Edition of China)", the outcome of the disease and the curative effect were analyzed simultaneously.

Results: In 211 cases of AL patients, 75 cases (35.5%) include 49 AMLs and 26 ALLs occurred IFD, the male to female ratio was 49:26, the median age was 48 years old (8-83 years old). 73 cases were lungs IFD, 1 case was liver and spleen IFD, 1 case was intestinal IFD. Among of the 75 cases, there were 1 case with proven IFD (blood culture positive for *Candida*), 8 cases with probable IFD, 23 cases with possible IFD and 43 cases with uncertain IFD. Host factors included neutropenia (70 cases, 93.3%), the application of hormone for more than 3 weeks (10 cases, 13.3%), a history of previous fungal infection (4 cases, 5.3%), allogeneic transplantation (1 case, 1.3%), prior application of broad-spectrum antibiotics was confirmed in 69 patients (92%). 31 cases (41.3%) showed specific CT signs, wherein the air crescent sign in 1 case, pulmonary cavity in 1 case, liver and spleen buphthalmos sign in 1 case, and the rest cases showed compact, clear boundary lesions, including 5 cases with halo sign. 30 cases (40%) of patients showed non-specific CT signs, such as small nodules, multiple patchy shadow, ground glass shadow, emphysema or bronchiectasis. Positive G test was found in 12 patients and positive GM test was in 10 cases, of which both test positive was in 9 cases. All 23 patients with possible IFD were identified as fungal infections according to the subsequent treatment response and disease evolution, 23 cases (53.5%) were eventually identified as fungal infection in 43 uncertain IFD patients, so in total 75 patients, 55 patients were eventually identified as fungal infection, accounting for 26.6% of all patients with 211 leukemia patients. All 75 patients received antifungal treatment, including 9 cases of target therapies, 46 cases of diagnosis driven therapies, 20 cases of empiric therapies. 7 cases (77.8%) were effective in target therapies, 36 cases (78.3%) was eventually identified as fungal infection in 46 diagnosis driven therapies patients, in which 31 case (86.1%) were effective. 10 cases (50%) was confirmed with fungal infection in 20 empiric treatment patients, and were all effective. The overall effective rate was 89.1% (48/55).

Summary and Conclusions: IFD is one of the main causes of infection in acute leukemia patients. High resolution CT and G test, GM test were important in the diagnosis of IFD. Early diagnosis and treatment is the key to improve the efficacy of IFD. The application of "criteria for the diagnosis and treatment principles of hematological malignant patients with invasive fungal disease (The Fourth Edition of China)" can be a very good guide for the clinical diagnosis and treatment.

E1187

ACINETOBACTER BAUMANNII SURVEILLANCE MEASURES IN HAEMATOLOGICAL MALIGNANCIES PATIENTS

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Background: *Acinetobacter baumannii* is a gram-negative, strictly aerobic, non-fermentative coccobacillus that causes infections in immunocompromised and chronically ill patients. Recently, it has emerged as a major cause of health care-associated infections (HCAIs) in addition to its capacity to cause community-acquired infections. It is associated with multidrug resistance and it is considered to be among the most difficult anti-microbial-resistant bacilli to control and treat. Given to its antimicrobial resistance, treatment options are severely limited, and to the best of our knowledge there aren't any controlled trials to guide therapeutic choices. In severely ill patients multidrug-resistant *Acinetobacter* infections are associated with an extremely high morbidity and mortality rate. It is therefore necessary the development of measures that can prevent or early identify *Acinetobacter* infection.

PB1982

PREVALENCE AND TREATMENT OF MANTLE CELL LYMPHOMA (MCL) IN GERMANY: AN ANALYSIS OF SICKNESS FUNDS

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¹Janssen-Cilag GmbH, Neuss, Germany**Background:** No central registries for patients with mantle cell lymphoma (MCL) exist in Germany.**Aims:** The objective of this analysis was to determine the number of patients with MCL diagnosed (with or without other diagnoses of cancer) and to characterize the types of treatment being utilized and care settings using sickness funds claim data.**Methods:** This analysis evaluates data from 1,771,225 beneficiaries in 2012 from different statutory sick funds (SHI). MCL patients were identified by ICD-10 C83.1, oncological co-diagnoses by ICD-10 C00-79; D37-49 and chemotherapy by Anatomical Therapeutic Chemical (ATC) Code L01*, pharmacy number (PZN) 999092 and/or operating and procedure code (OPS) 854*.**Results:** 78 patients with a diagnosis of MCL (C83.1) could be identified (4/100,000). Overall gender ratio was 76.9% male and 23.1% female. Additional oncological diagnoses were found in 43.6% of patients. 20.7% had malignant neoplasms of ill-defined, other secondary and unspecified sites (C76-80), 17.2% had malignant neoplasms of digestive organs (C15-26), 13.8% had melanoma (C43-44), 10.3% had neoplasms of uncertain behavior, polycythemia vera and myelodysplastic syndromes (D37-48), 8.6% had malignant neoplasms of urinary tract (C64-68) and malignant neoplasms of lip, oral cavity and pharynx (C00-14) (multiple diagnoses possible). The outpatient diagnosis rate was 64.1%, inpatient rate 15.4% and in- and outpatient 20.5%. From a total of 78 patients 44 (56.4%) patients received chemotherapy (40 men [90.9%] and 4 women [9.1%]) in 2012. 25.0% of patients received both out- and in-patient treatment, 65.9% received out-patient treatment and 9.1% in-patient treatment. Identification of the administered substances was possible when ATC codes were reported. The most commonly used treatments were rituximab (34.7%), bendamustine (14.9%), cyclophosphamide (11.9%), vincristine (8.9%), doxorubicin (21.8%) and other treatments (21.8%) (multiple treatments possible).**Summary and Conclusions:** Prevalence and gender ratio 3:1 was consistent with previously reported^{1,2}. Most patients were diagnosed and treated as outpatients. Other oncological disorders are higher than in chronic lymphocytic leukemia³. About half of the patients were treated with chemotherapy within a year.

PB1983

THE SOUTHERN TRANSYLVANIA HEMATOLOGICAL PATIENTS' OPINION ON THE QUALITY OF MEDICAL CARE

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PB1984

LIPOSOMIAL IRON IMPROVES FATIGUE IN PATIENTS WITH MYELODYSPLASTIC SYNDROMES AS REFRACTORY ANEMIA. MULTICENTRIC STUDY.

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Biosimilar epoetin- α is as effective as originator epoetin- α plus liposomal iron (Sideral[®]), vitamin B12 and folates in patients with refractory anemia: A retrospective real-life approach

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DOI: 10.3892/mco_XXXXXXX

Abstract. Several biosimilar versions of recombinant human erythropoietin are currently approved for use in Europe, including a biosimilar epoetin- α . The aim of this study was to verify that biosimilar epoetin- α is similar in terms of efficacy, safety and cost to originator epoetin- α for the treatment of refractory anemia in patients with myelodysplastic syndrome. A total of 92 patients with myelodysplasia and refractory anemia were investigated. The patients received either originator (group A) or biosimilar (group B) epoetin- α . In addition, they received liposomal iron (Sideral[®]), calcium levofolate and vitamin B12. Moreover, the median monthly overall costs were calculated for each group. The results demonstrated that hemoglobin (Hb) levels increased by 1 g/dl after a median time of 5 weeks in group A and 4 weeks in group B. In group A, a Hb level of >12 g/dl was achieved after 12 weeks, while in group B after 10.5 weeks. The median cost of therapy was 1,536 euros/month in group A and 1,354 euros/month in group B. A total of 5 patients required transfusion support in group A and 7 in group B. In conclusion, biosimilar epoetin- α appears to be comparable to originator epoetin- α in terms of efficacy and safety for the treatment of refractory anemia.

Introduction

Biosimilar drugs are similar, but not identical, versions of biological medicines that have already been approved. 'Biosimilar' is a regulatory term used to indicate a biopharmaceutical product that has been approved under a well-defined regulatory pathway, such as the one established by the European Medicines Agency (EMA). Several biosimilar versions of recombinant human erythropoietin are currently approved for use in Europe, including a biosimilar epoetin- α (HX575). HX575 is a biosimilar version of human recombinant erythropoietin (epoetin- α) that was approved for use in Europe in 2007 under the EMA biosimilar approval pathway. HX575 was approved by the EMA in Europe after it exhibited similarity/comparability to originator epoetin- α in terms of protein structure, equivalence with respect to pharmacokinetic and pharmacodynamic profiles and comparable clinical efficacy and safety profiles in studies (1-3). Although the use of erythropoiesis-stimulating agents (ESAs) for low-risk patients with myelodysplastic syndromes (MDS) is currently supported by all major MDS treatment guidelines regarding hematopoietic growth factors (4-8), data on the use of biosimilar ESAs in this population are lacking. The aim of this study was to determine whether HX575 is similar in terms of efficacy, safety and cost to originator epoetin- α for the treatment of refractory anemia in patients with MDS.

Materials and methods

Patients. Between July, 2008 and June, 2012, a total of 92 MDS patients with refractory anemia were included in the study. The patients included 45 men and 47 women, with a median age of

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Key words: myelodysplastic syndrome, liposomal iron, hemoglobin, anemia

75 years (range, 60–81 years). Patients with the 5q- syndrome were excluded from the study. A total of 29 patients exhibited chromosomal abnormalities, namely loss of the Y chromosome (n=3), 20q- karyotype (n=2), trisomy of chromosome 8 (n=2) and other chromosomal abnormalities (n=22), excluding loss of chromosome 7, 5q- and complex karyotype. The main comorbidities were type 2 diabetes in 32 patients, chronic obstructive pulmonary disease (COPD) in 22 patients, congestive heart failure (CHF) in 11 patients and other chronic diseases in 18 patients. All the patients had anemia following a complete blood count and had an International Prognostic Scoring System value low or intermediate-1.

All the procedures followed were in accordance with the ethical standards of the responsible Committee on Human Experimentation and with the principles of the Declaration of Helsinki. Written informed consent was obtained from all the participants.

Laboratory evaluation. This was a two-centre, non-randomized, retrospective study. All the patients underwent complete blood count, bone marrow aspiration, renal and liver function tests and bone marrow karyotyping at diagnosis. We also measured the endogenous erythropoietin level, vitamin B12 level, folate, ferritin, transferrin, transferrin saturation, blood iron content and erythrocyte sedimentation rate. The patients received epoetin- α if the hemoglobin (Hb) level was <10 g/dl, as suggested by Italian Society of Hematology guidelines (9).

Treatment. Patients with Hb levels <12 g/dl received supportive treatment with epoetin- α if symptomatic. All the patients received supportive treatment with vitamin B12 (400 mg/day orally) and calcium levofolate (7.5 mg/day orally), in order to support erythropoiesis and prevent vitamin B12 and folate deficiency subsequent to erythropoiesis stimulation. Patients with normal or high ferritin levels and transferrin saturation 10–20% received 2 capsules of oral liposomal iron daily (Sideral[®]; PharmaNutra, Pisa, Tuscany, Italy) during erythropoiesis support (each capsule containing 14 mg iron + ascorbic acid 60 mg + vitamin B12). Patients with low ferritin or transferrin saturation $<10\%$ were excluded from the study. The patients received either originator (group A, n=46) or biosimilar (group B, n=46) epoetin- α 40,000 IU weekly by subcutaneous administration. In addition, all the patients received liposomal iron (60 mg, 2 tablets/day orally), calcium levofolate (7.5 mg/day orally) and vitamin B12 (400 mg/day orally). When a Hb level of 12 g/dl was achieved, the patients received a maintenance dose of 40,000 IU epoetin every 2 weeks. If Hb level subsequently decreased, weekly administration was resumed; if Hb level increased, epoetin was administered at intervals of once every 3 weeks or more.

Follow-up. All the patients underwent monthly physical examination, complete blood count and blood renal and liver function tests; they also underwent monthly measurements of vitamin B12 level, folate, ferritin, transferrin, transferrin saturation and blood iron content. A patient was considered to be a non-responder if the Hb level did not increase ≥ 1.5 g/dl after 3 months of epoetin treatment (9). The data reported herein are from the cohort of patients who responded to epoetin in each group. The monthly treatment cost per patient was calculated

Table I. Patient characteristics at the initiation of the study (n=92).

Characteristics	Group A	Group B
Gender		
Male/female	18/28	25/21
Age, years		
Median (range)	70 (63–75)	66 (60–81)
Karyotype		
Low-risk	30	32
Intermediate	13	11
Not evaluable	3	3
Comorbidities		
NIDDM	18	14
COPD	14	8
CHF	5	6
Hb level, g/dl		
Median (range)	8.5 (8–11)	9.2 (8.5–11.5)
Basal epoetin level		
Availability	15/46 (32%)	21/46 (46%)
Inappropriate	5/15 (33%)	9/21 (43%)

NIDDM, non-insulin-dependent diabetes mellitus; COPD, chronic obstructive pulmonary disease; CHF, chronic heart failure; Hb, hemoglobin.

by dividing overall costs (including drug costs, transfusion costs, cost of disposable items and nursing/medical work cost) by the number of months of observation; the median monthly overall cost for each group was then determined.

Results

Patient characteristics. The characteristics of the patients in each group are listed in Table I. The median Hb at the initiation of treatment was ~ 8.5 g/dl in group A and 9.2 g/dl in group B. Data regarding basal erythropoietin levels were available for only 15 patients in group A (32%) and 21 patients in group B (46%). Inappropriate levels of basal erythropoietin were observed in 5 patients in group A and in 9 patients in group B.

Follow-up. The results are summarized in Table II. The median follow-up was 22 months (range, 3–34 months). A total of 2 patients in group A with COPD and a Hb level of 11 g/dl and 2 patients in group B with CHF and Hb levels of 11 and 11.5 g/dl, received transfusions for symptomatic anemia. In group A, 2 patients succumbed to disease progression and 1 patient to myocardial infarction. In group B, 2 patients succumbed to disease progression, 1 to sepsis in a background of non-insulin-dependent diabetes mellitus and 1 due to hemorrhage. In group A, 1 patient reported headache and 2 reported an increase in blood pressure. In group B, 2 patients reported headache and 2 an increase in blood pressure. In group A, 23 patients (50%) responded to originator epoetin and

in group B, 20 patients (43%) responded to biosimilar epoetin treatment. Transfusion support was required for 5 patients in group A and 7 in group B.

Treatment effectiveness. The Hb level increased by 1 g/dl after a median time of 5 weeks (range, 4-9 weeks) in group A and 4 weeks (range, 3-8 weeks) in group B. In group A, a Hb level of >12 g/dl, with a consequent epoetin dose reduction, was achieved after a median of 12 weeks (range, 4-18 weeks); in group B, a Hb level of >12 g/dl, with a consequent epoetin dose reduction, was achieved after a median of 10.5 weeks (range, 3-16 weeks). A maintenance dose was administered with a median of every 2 weeks (range, 2-4 weeks) in group A, while in group B a maintenance dose was administered with a median of every 3 weeks (range, 2-5 weeks). A total of 5 patients in group A and 7 patients in group B required transfusion support. Loss of response to epoetin was observed in 2 patients in group A and 3 patients in group B.

Discussion

It has been demonstrated that Hb levels may be increased with epoetin- α treatment in patients with MDS and other conditions characterized by bone marrow failure (10-14). However, data regarding the use of HX757 in MDS are currently lacking.

ESA monotherapy typically results in erythropoietic response rates of 20-30% in the general MDS population. Response rates are higher when patients are carefully selected based on pretreatment serum erythropoietin level or other factors. The median duration of ESA response is ~2 years and is, on average, longer among patients who achieve a larger treatment-associated Hb increment compared with those who experience only a minor Hb increase (15,16).

In 1995, Hellström-Lindberg (17) reviewed 205 patients with MDS treated with ESAs in 17 small studies and identified three major factors as predictive of a Hb response, namely pretreatment serum erythropoietin level <200 U/l, a form of MDS other than refractory anemia with ringed sideroblasts and absence of a red blood cell transfusion requirement. A total of 4 patients in groups A and B (2 per group) succumbed due to disease progression to leukemia. Based on currently available evidence, progression to leukemia is unlikely to be the result of epoetin treatment. A prospective clinical trial of ESAs in MDS (ECOG E1996 trial) evaluated the efficacy and long-term safety of epoetin, with or without granulocyte colony-stimulating factor plus supportive care (SC; n=53) vs. SC alone (n=57) for the treatment of anemic patients with lower-risk MDS (18). The presence of older patients with more comorbidities and the lack of data regarding basal serum epoetin level may explain the marginally worse time-to-response to epoetin and the most frequent administration of maintenance epoetin dose in group A. In fact, older age was identified as an adverse prognostic factor in a number of different MDS prognostic scoring systems (19-21). A subsequent study demonstrated that only a limited number of patients with pretreatment serum erythropoietin levels >500 U/l respond to ESA therapy (22).

The proportion of patients in our study responding to epoetin was similar between the originator and biosimilar epoetin- α groups. Overall, 43 of the 92 patients (47%) exhibited a response to epoetin; this proportion was higher compared

Table II. Summary of main results.

Results	Group A	Group B
Symptomatic patients transfused, no. (Hb, g/dl)		
COPD	2 (11)	-
CHF	-	2 (11 and 11.5)
Patients responding to EPO treatment, no. (%)	23 (50)	20 (43)
Patients deceased, no.		
PD	2	2
MI	1	-
Sepsis in NIDDM	-	1
Hemorrhage	-	1
Side effects, no.		
Headache	1	2
Increased blood pressure	2	2
Patients transfused, no.	5	7
Median time for increase of Hb level by 1 g/dl with EPO, weeks (range)	5 (4-9)	4 (3-8)
Time-to-reduction of EPO after achieving Hb 12 g/dl, weeks (range)	12 (4-18)	10.5 (3-16)
Interval of maintenance dose, weeks (range)	2 (2-4)	3 (2-5)
Median cost of EPO therapy, euros/month (range)	1,536 (1,240-1,850)	1,354 (954-1,550)
Patients exhibiting loss of response to EPO, no.	2	3

EPO, epoetin; NIDDM, non-insulin-dependent diabetes mellitus; COPD, chronic obstructive pulmonary disease; CHF, chronic heart failure; PD, progressive disease to overt acute myeloid leukemia; MI, myocardial infarction; Hb, hemoglobin.

with that reported in the literature (23), although the lack of data regarding endogenous erythropoietin level for some patients and the low number of patients included make it difficult to draw meaningful conclusions based on response rate.

With prolonged follow-up (median, 5.8 years), no differences were observed in the overall survival of patients in the epoetin vs. SC arms (median, 3.1 vs. 2.6 years, respectively) or in the incidence of transformation to acute myeloid leukemia (7.5 and 10.5% of the patients, respectively). Other adverse effects, such as headache and small increases in blood pressure, occurred with a similar incidence in the two treatment groups and are not considered clinically relevant.

The cost analysis in our study suggested lower overall costs in the group who received biosimilar epoetin- α compared with

that in the group that received originator epoetin- α , although these findings require confirmation using more robust measures of cost-effectiveness, such as quality-adjusted life years.

The rationale behind the use of liposomal iron is that patients with MDS frequently exhibit a functional deficit of iron, with elevated ferritin levels and low transferrin saturation (<20%). In these patients, an increase in the level of the protein hepcidin is observed, which inhibits intestinal iron absorption and iron release from tissue macrophages (24). In patients with functional iron deficiency, intravenous (i.v.) iron may be effective in supporting erythropoiesis, although several studies have demonstrated oral iron to be ineffective (25-28). However, the results of preliminary studies indicate that oral liposomal iron may be as effective as i.v. iron in myelodysplastic and neoplastic patients (29-31). For this reason, the patients in our study received oral liposomal instead of i.v. iron. Our study had several limitations, including its retrospective nature, the absence of data regarding basal serum endogenous erythropoietin for all the patients and the limited number of patients (responders) evaluated (43/92). However, despite these limitations, biosimilar epoetin- α appears to be as safe and effective and potentially more cost-effective compared with originator epoetin- α for the treatment of MDS patients with refractory anemia.

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DICHIARAZIONI SOSTITUTIVE DI CERTIFICAZIONI

(Art.46 D.P.R. 28.12.2000, n. 445 recante il "T.U. delle disposizioni legislative e regolamentari in materia di documentazione amministrativa")

DICHIARAZIONI SOSTITUTIVE DELL'ATTO DI NOTORIETÀ

(Art. 47 D.P.R. 28.12.2000, n. 445 recante il "T.U. delle disposizioni legislative e regolamentari in materia di documentazione amministrativa")

Il sottoscritto

COGNOME **DI MARZIO** **NOME** **LUIGI**
CODICE FISCALE **NATO A** **PROV** **IL** **RESIDENTE**
A **PROV INDIRIZZO** **,** **C.A.P.** **TELEFONO**

consapevole che le dichiarazioni mendaci sono punite ai sensi del Codice Penale e delle leggi speciali in materia (in virtù di quanto disposto dall'art. 76 del D.P.R. 445 del 28.12.2000):

DICHIARA

1	di essere stato Vice Direttore e Direttore della "Scuola per la formazione professionale del personale paramedico" della ASL di Campobasso, presso la quale è stato altresì docente in discipline dell'area igienico-organizzativa dal 1987 al 1996 ;
2	di essere stato docente nei Corsi di Laurea della Facoltà di Medicina e Chirurgia della Università Cattolica del Sacro Cuore di Campobasso in discipline dell'area igienico-organizzativa dal 1998 al 2012 ;
3	di essere stato docente nei Corsi di Laurea della Facoltà di Economia della Università Statale del Molise in discipline dell'area igienico-organizzativa dal 2004 al 2022;
4	di essere stato docente nei Corsi di Laurea della Facoltà di Medicina e Chirurgia della Università Statale del Molise in discipline dell'area igienico-organizzativa dal 2007 al 2021 ;
5	di essere stato docente nei Corsi di Laurea della Facoltà di Scienze del Benessere della Università Statale del Molise in discipline dell'area igienico-organizzativa dal 2005 al 2007;
6	di essere stato docente nei Corsi di Laurea della Facoltà di Medicina e Chirurgia della Università di Roma 'La Sapienza' e della Università Statale del Molise in discipline dell'area igienico-organizzativa dal 2005 al 2008;
7	di essere in possesso della Laurea in Medicina e Chirurgia conseguita presso l'Università degli Studi di Bologna ;
8	di essere in possesso della Specializzazione in Igiene e Medicina Preventiva conseguita presso l'Università degli Studi di Parma ;
9	di aver conseguito il Master Universitario di II livello in 'Management sanitario' presso l'Università degli Studi del Molise ;
10	di essere stato dipendente della ASReM con la qualifica di Direttore Sanitario ospedaliero in servizio presso l'Ospedale Regionale 'A.Cardarelli' di Campobasso fino all'epoca del collocamento in quiescenza per limiti di età in data 11/05/2021.

Il sottoscritto è informato che i dati personali forniti con la presente richiesta sono trattati nel rispetto del D. Lgs. 196/2003 "Codice in materia di protezione dei dati personali".

Campobasso, 10 maggio 2022

Il dichiarante*

* Nel caso di dichiarazione sostitutiva dell'atto di notorietà, qualora la dichiarazione non sia sottoscritta davanti al dipendente addetto a ricevere la documentazione, deve essere accompagnata da un valido documento di riconoscimento (Art. 38 D.P.R. n. 445 del 28.12.2000).

