POSTER DISCUSSION
ESMO 2012

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COI

Dr Aapro is a consultant for

Amgen, BMS, Celgene, GSK, Helsinn, Novartis, Merck, Merck Serono, Pfizer, Pierre Fabre, Roche, Sandoz, Vifor

and has received honoraria for lectures at symposia of

Amgen, Bayer Schering, Cephalon, GSK, Helsinn, Hospira, Ipsen, JnJ OrthoBiotech, Merck, Merck Serono, Novartis, Pfizer, Pierre Fabre, Roche, Sandoz, Sanofi Aventis, Vifor

2 different areas

NEUTROPENIA

1547PD

G-CSF as secondary prophylaxis of chemotherapy-induced neutropenia in patients with solid tumors: Results of a prospective, observational study

Gilles Freyer, FR

1548PD

Absolute neutrophil counts in a study of lipegfilgrastim compared with pegfilgrastim in patients with breast cancer who are receiving chemotherapy

Oleg Gladkov, RU

PSYCHOSOCIAL

1462PD

Integration of psychosocial care into routine cancer care: final results of a large collaborative, hospital-based, quality improvement study (HUCARE project)

Rodolfo Passalacqua, IT

Integration of psychosocial care into routine cancer care: final results of a large collaborative, hospital-based, quality improvement study (HUCARE project)

R. *Passalacqua, C.Caminiti, M. Annunziata, C. Borreani, F. Diodati, D. Fagnani, S.Filiberti, L.Isa, M.G. Ollari, J. Saleri.*

From the Oncology Division Istituti Ospitalieri, Cremona
and other participating Institutions
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GICO progetto HuCare

Background

- **Despite scientific evidence supporting the use of interventions aiming to improve the psychosocial status of patients, these aspects of care are often neglected [Surbone et al. Support Care Cancer 2010].**

- **One of the main reasons for this is that the mere dissemination of guidelines is not enough to translate evidence into practical behaviors [Dijkstra et al. BMC 2006; Baker, Cochrane Database Syst Rev 2010] .**

- **Context factors (social, organizational and economic elements) are important determinants to achieve the desired improvement or change [Van Bokhoven et al. Qual Saf Health Care 2003].**

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Interventions

1. Give to patients a **Question Prompt List (QPL)** to facilitate communication with the doctor and nurses, since the first visit
2. Ensure participation of all doctors and nurses to **communication training courses**
3. Create in every department the **Point of Information and Support (PIS)** with experienced nursing staff
4. Assign to each patient a **referring nurse**
5. Screen all patients for **anxiety, depression and social needs**

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End Points

- **Improvement of communication skill in at least 75% of professionals (pre-post course measurements)**
- **Use of the question prompt list in at least 75% of patients** (evidence in clinical documentation)
- **Access of patients to the PIS Point of Information and Support in at least 75% of cases** (evidence in clinical documentation)
- **Referring nurse assigned to at least 75% of patients** (evidence in clinical documentation)
- **Screen for psychological distress and social needs, at least 75% of patients** (evidence of the results in clinical documentation)

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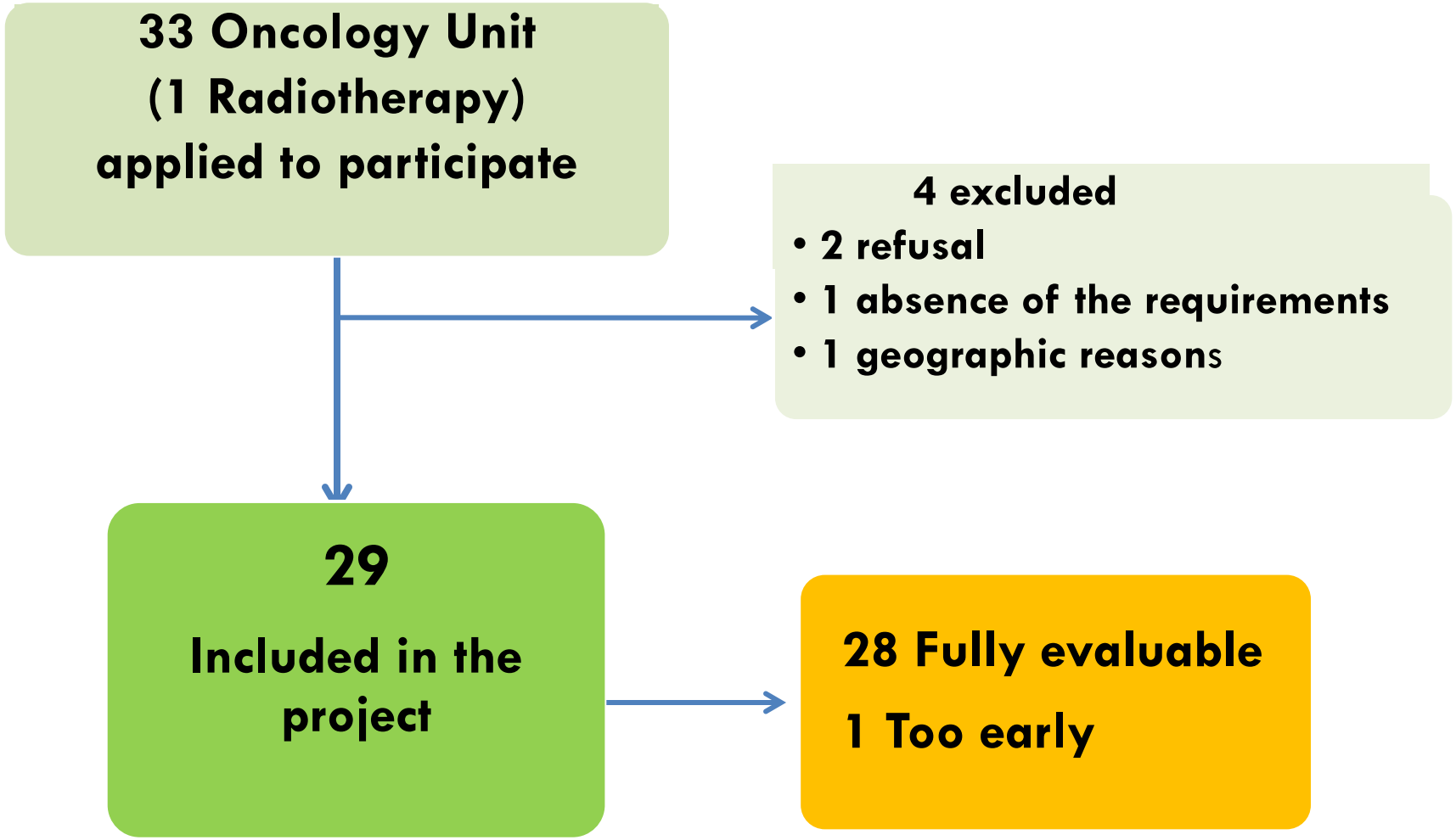
Participating Centers



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Changes in oncology centers

INTERVENTIONS	Pre- implementation	Post- implementation
EBM TRAINING COURSES (No of attendee, oncologists plus nurses)	0/598 (0%)	557/598 (93%)
REFERRING NURSE (RN) (No and % of pts with a RN)	0/305 (0%)	265/305 (86%)
PIS Point of Information and Support (No and % of Units with a PIS)	4/29 (17%)	24/29 (83%)
USE OF THE QPL Question Prompt List (QPL) (No and % of pts who receive the QPL)	0/305 (0%)	223/305 (73%)
PSYCHO-SOCIAL EVALUATION (No and % of screened patients)	0/305 (0%)	253/305 (83%)

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AUTHOR's CONCLUSION

USING THIS METHODOLOGY, A SUCCESSFUL IMPLEMENTATION OF EBM MEASURES IS POSSIBLE IN THE VAST MAJORITY OF ONCOLOGICAL CENTERS AND YIELDS SIGNIFICANT IMPROVEMENT IN THE DELIVERY OF PSYCHOSOCIAL CARE

Definition of Supportive Care

- **Supportive Care is the prevention and management of the adverse effects of cancer and its treatment.**
- **This includes physical and psychosocial symptoms and side effects across the entire continuum of the cancer experience including the enhancement of rehabilitation and survivorship.**

Importance of Supportive Care

- Allows patients to tolerate and benefit from active therapy more easily
- Alleviates symptoms and complications of cancer
- Reduces or prevents toxicities of treatment
- Supports communication with patients about their disease and prognosis
- Eases emotional burden of patients and care givers
- Helps cancer survivors with psychological and social problems

COMMENT
To which extent does support modify cancer outcomes?

Annals of Oncology 23: 1932–1934, 2012
doi:10.1093/annonc/mds239

Supportive care and palliative care: a time for unity in diversity

emotional burden of patients and caregivers, helps cancer survivors with psychological and social problems [1].


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2 different areas

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1547PD: G-CSF as secondary prophylaxis of chemotherapy-induced neutropenia in patients with solid tumors: Results of a prospective, observational study

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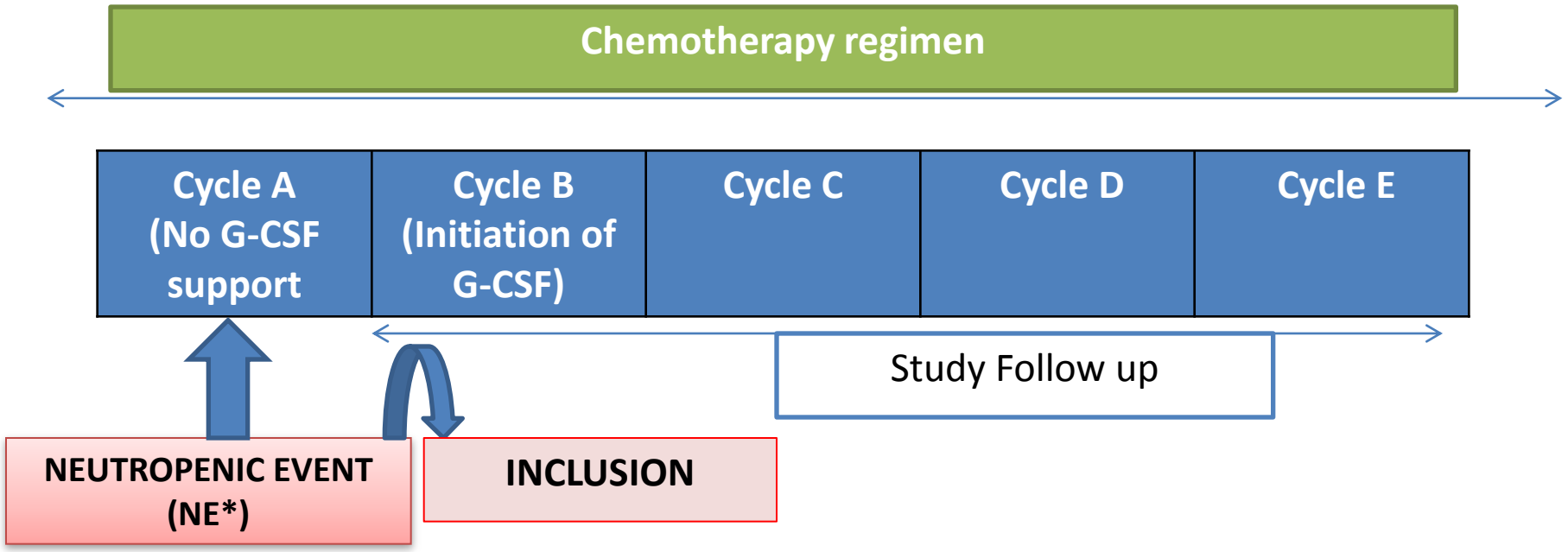
G-CSF has significant efficacy as secondary prophylaxis of chemotherapy-induced neutropenia in patients with solid tumors: Results of a prospective study.

Poster # 1547PD

Freyer G[1, 2], Jovenin N[3], Yazbek G[4], Villanueva C[5], Hussein A[6], Berthune A[7], Rotarski M[7], Simon H[8], Boulanger V[9], Hummelsberger M[10]

1. Université de Lyon, 2. Centre Hospitalier Lyon Sud, Hospices Civils de Lyon, Lyon, France; 3. Institut Jean Godinot, Reims, France ; 4. Centre Hospitalier Universitaire de Besançon, Besançon, France ; 5. Centre Hospitalier de Quimper, Quimper, France ; 6. Centre René Huguenin, Saint Cloud, France ; 7. Centre Oncologie du Pays Basque, Bayonne, France ; 8. Centre Hospitalier Morvan, Brest, France ; 9. Centre Hospitalier de Carcassonne, Carcassonne, France ; 10. Centre de Radiothérapie et d'Oncologie Médicale, Béziers, France

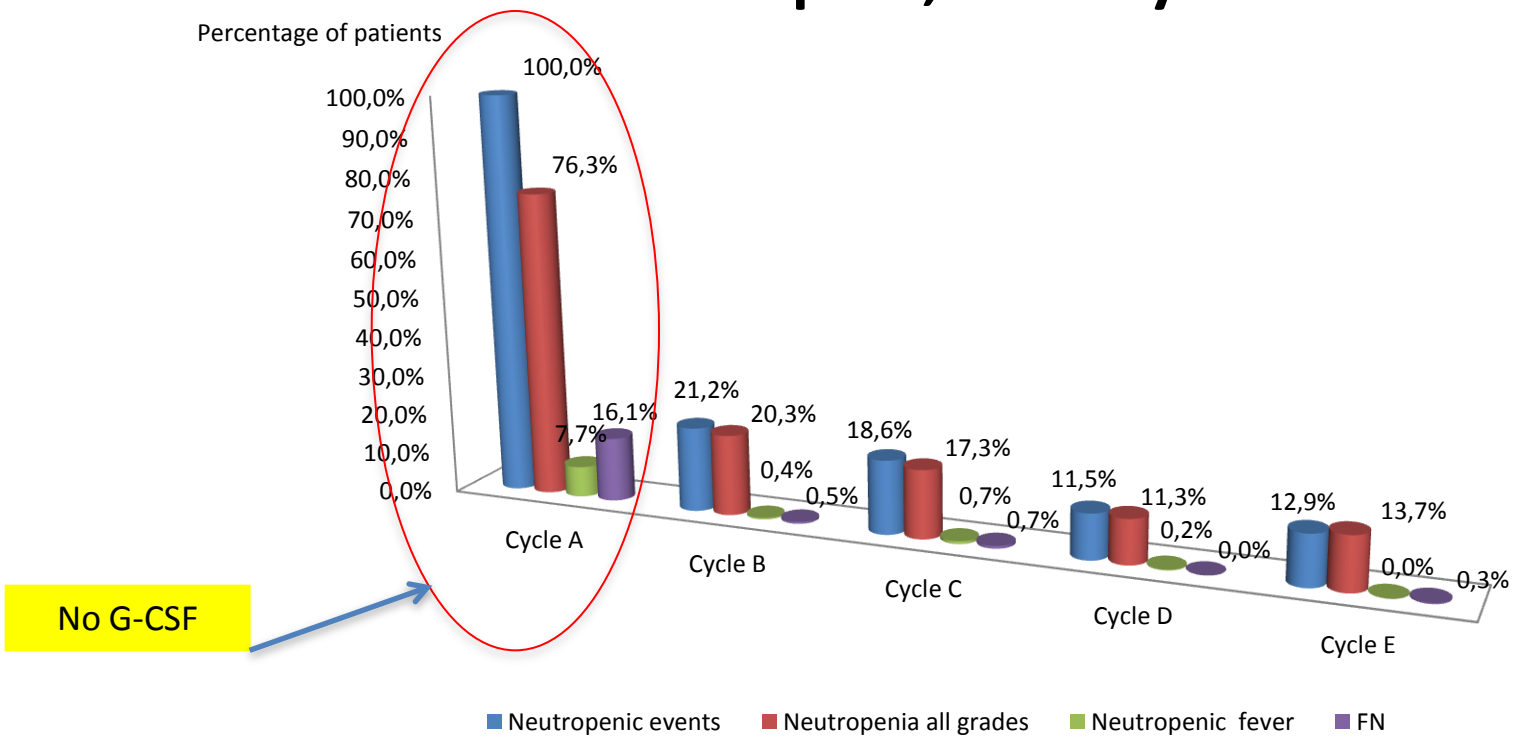
Study Design



*NE definition (1): FN or Neutropenia that impacted on subsequent cycle (i.e., cycle delay and/or dose reduction and/or G-CSF use).

(1) National Comprehensive Guidelines Network. Myeloid Growth Factors. Available from: http//nccn.org

Incidence of NE
N=548 pts, all cycles



NE: FN, or neutropenia with a significant impact on the next cycle of chemotherapy: cycle delay and/or dose and/or prescription of G-CSF; FN: single temperature ≥ 38.3°C orally or ≥ 38.0°C over one hour and neutrophils < 500/mm^3 or < 1000//mm^3 or decline of neutrophils to ≤ 500/mm^3 over the next 48h; Neutropenic fever: grade 1-3 neutropenia with fever.

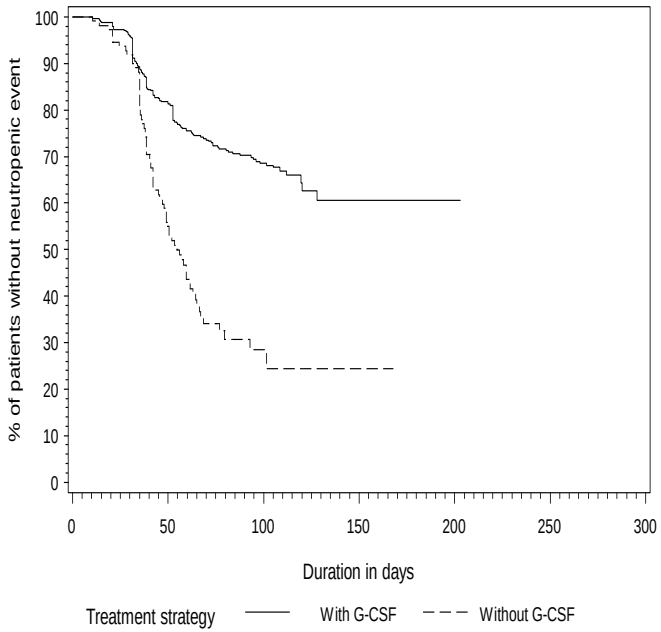
Prophylactic strategies developed during the study (N=548, All Cycles)

Prophylactic strategies	Cycle B N= 548	Cycle C N=548	Cycle D N=442	Cycle E N=344
Cycle delay (n; %)	244 (44.5)	44 (8.0)	23 (5.2)	18 (5.2)
Dose reduction (n%)	122 (22.3)	27 (4.9)	17 (3.8)	12 (3.5)
Use of prophylactic G-CSF (n ; %)	466 (85.0)	413 (75.4)	332 (75.1)	247 (71.8)
Type of G-CSF				
➢Pegfilgrastim	278 (59.7)	253 (61.3)	211 (63.6)	152 (61.5)
➢Filgrastim	48 (10.3)	39 (9.4)	30 (9.0)	22 (8.9
➢Lenograstim	127 (27.3)	11 (26.9)	84 (25.3)	67 (27.1)
➢Biosimilar	10 (2.1)	9 (2.2)	6 (1.8)	6 (2.4)

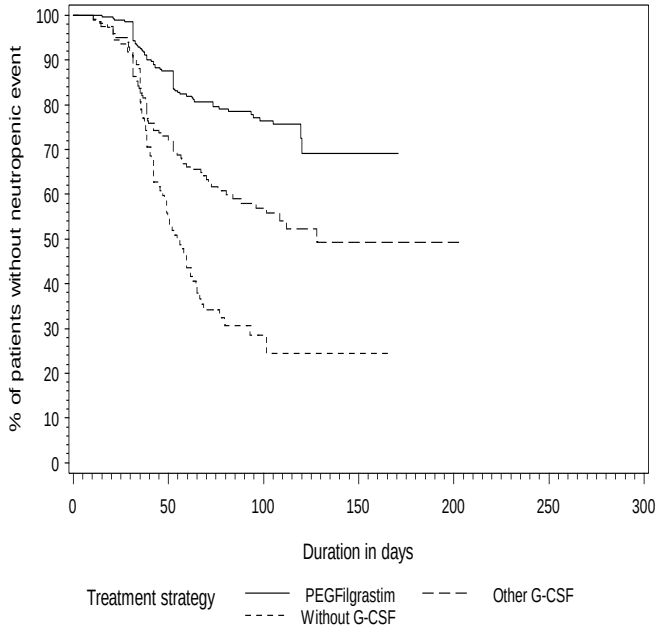
Prophylactic strategies included cycle delay and/or dose reduction and/or prophylactic G-CSF.
Cycle delay or dose reduction in cycle B to E were relative to the previous cycle, while G-CSF use was the proportion of the subjects in the given cycle.

Predictive Factors of NE Recurrence (Multivariate Analysis)

Incidence of NE following the first event in the subsequent cycles, according to **the prophylactic strategy with or without G-CSF** (Left Panel) and **the type of G-CSF: Pegylated Vs others** (Right Panel)-Kaplan Meier curve for the time to recurrence of NE; N=548; all cycles).



Prophylaxis (Vs no use o G-CSF)	HR (95% CI)	P value
	0.32 (0.24; 0.43)	< 0.001



	HR (95% CI)	P value
Pegfilgrastim prophylaxis (Vs others)	0.23 (0.16; 0.32)	< 0.001

THE LATEST META-ANALYSIS

Pegfilgrastim

is superior to filgrastim

Table 2 Summary of febrile neutropenia incidence based on meta-analyses of trials of G-CSFs

Treatment 1	Treatment 2	No of studies	No of patients	Relative risk of FN (95% CI)	p-value	I^2 (heterogeneity)
Pegfilgrastim	No primary G-CSF	5	2060	0.30 (0.14 to 0.65)	p = 0.002	76%
Filgrastim	No primary G-CSF	10	2183	0.57 (0.48 to 0.69)	p < 0.00001	50%
Lenograstim	No primary G-CSF	5	467	0.62 (0.44 to 0.88)	p = 0.007	64%
Any G-CSF	No primary G-CSF	20	4710	0.51 (0.41 to 0.62)	p < 0.00001	74%
Pegfilgrastim	Filgrastim	5	606	0.66 (0.44 to 0.98)	p = 0.04	0%

KL Cooper, et al BMC Cancer 2011

Updated Guidelines: 2010 published 2011

EUROPEAN JOURNAL OF CANCER 47 (2011) 8–32

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available at www.sciencedirect.com

ScienceDirect

journal homepage: www.ejconline.com

Position Paper

2010 update of EORTC guidelines for the use of granulocyte-colony stimulating factor to reduce the incidence of chemotherapy-induced febrile neutropenia in adult patients with lymphoproliferative disorders and solid tumours

M.S. Aapro [a,*,m], J. Bohlius [b,n], D.A. Cameron [c,o], Lissandra Dal Lago [d,p], J. Peter Donnelly [e,q], N. Kearney [f,r], G.H. Lyman [g,s], R. Pettengell [h,t], V.C. Tjan-Heijnen [i,u], J. Walewski [j,v], Damien C. Weber [k,w], C. Zielinski [l,x]

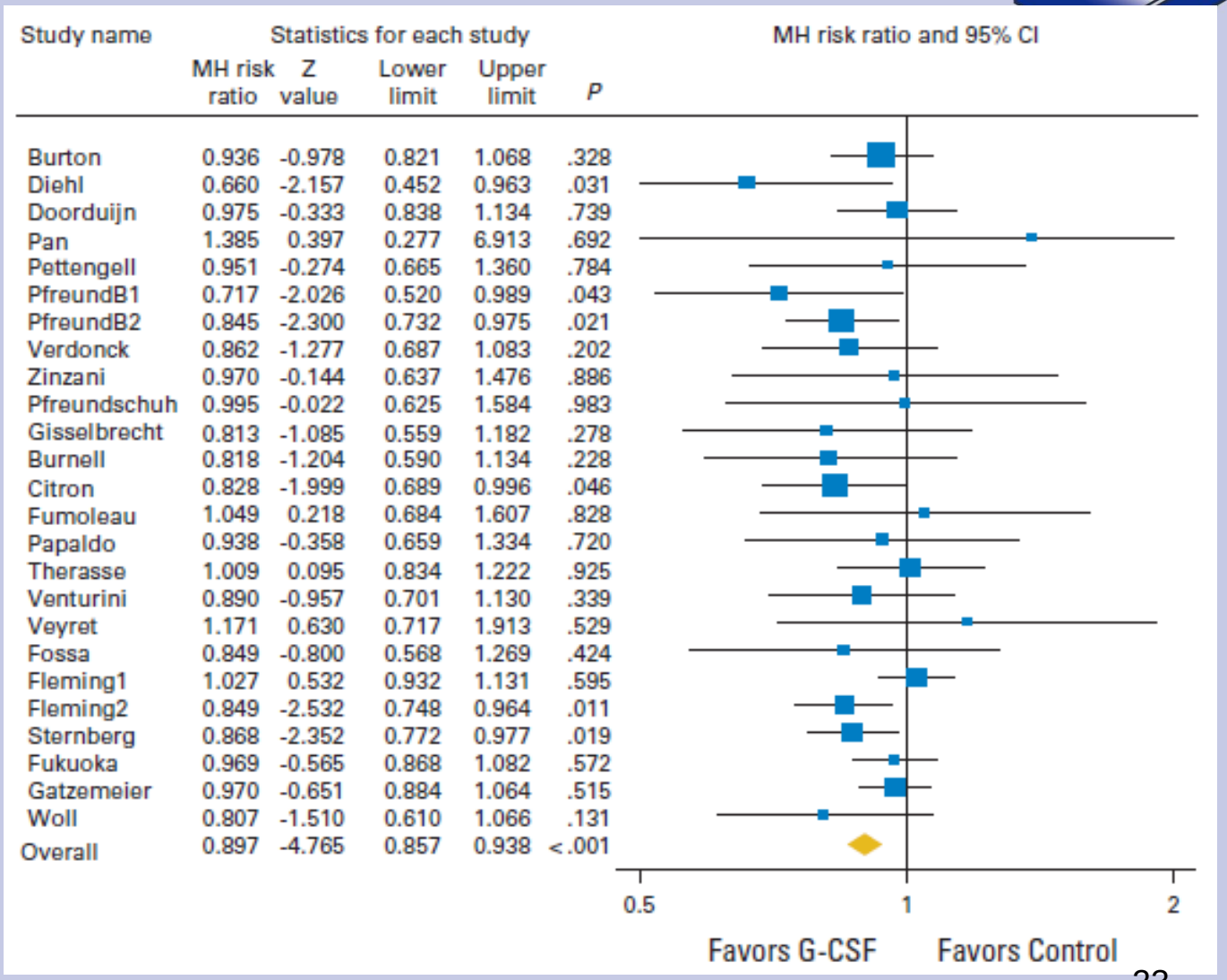
G-CSF supportive therapy reduces mortality: HR: 0.897 (95% CI, 0.857 to 0.938; p<0.001)

Greater mortality reduction in:

- larger trials
- greater RDI
- dose-dense chemo

More secondary AML and MDS

- RR: 1.92
- AR: 0.41%



Lyman GH et al. *J Clin Oncol* 2010;28:2914–2924

Suboptimal use of G-CSF is associated with worse patients outcomes

- US healthcare claims database study focusing on all patient cycles in which filgrastim administered on or before cycle day 5 (prophylaxis)
- Examined the relationship between duration of filgrastim and risk of hospitalisation for neutropenia or infection

	Patients	Chemo cycles	Duration of filgrastim, Mean ± SD	Reduced risk of hospitalisation for neutropenia or infection with each additional day of filgrastim, odds ratio (95% CIs)
NHL	133	332	6.5 ± 3.1	0.81 (0.70-0.93), p=0.003
Breast cancer	205	482	6.1 ± 2.9	0.77 (0.66-0.90), p=0.001
Lung cancer	260	522	4.3 ± 3.1	0.91 (0.81-1.01), p=0.084

Weycker et al. *Ann Pharmacother* 2006;40:402-7

The six EORTC recommendations
Recommendation 6 (2010)

6. WHICH choice of formulation

Filgrastim, lenograstim and pegfilgrastim have clinical efficacy and we recommend the use of any of these agents,according to current administration guidelines, to prevent FN and FN-related complications, where indicated.

Filgrastim biosimilars are now also a treatment option in Europe.

No biosimilars in 2006

Recommendation grade: A.

Paraphrased from Aapro MS et al. Eur J Cancer 42: 2433-53, 2006

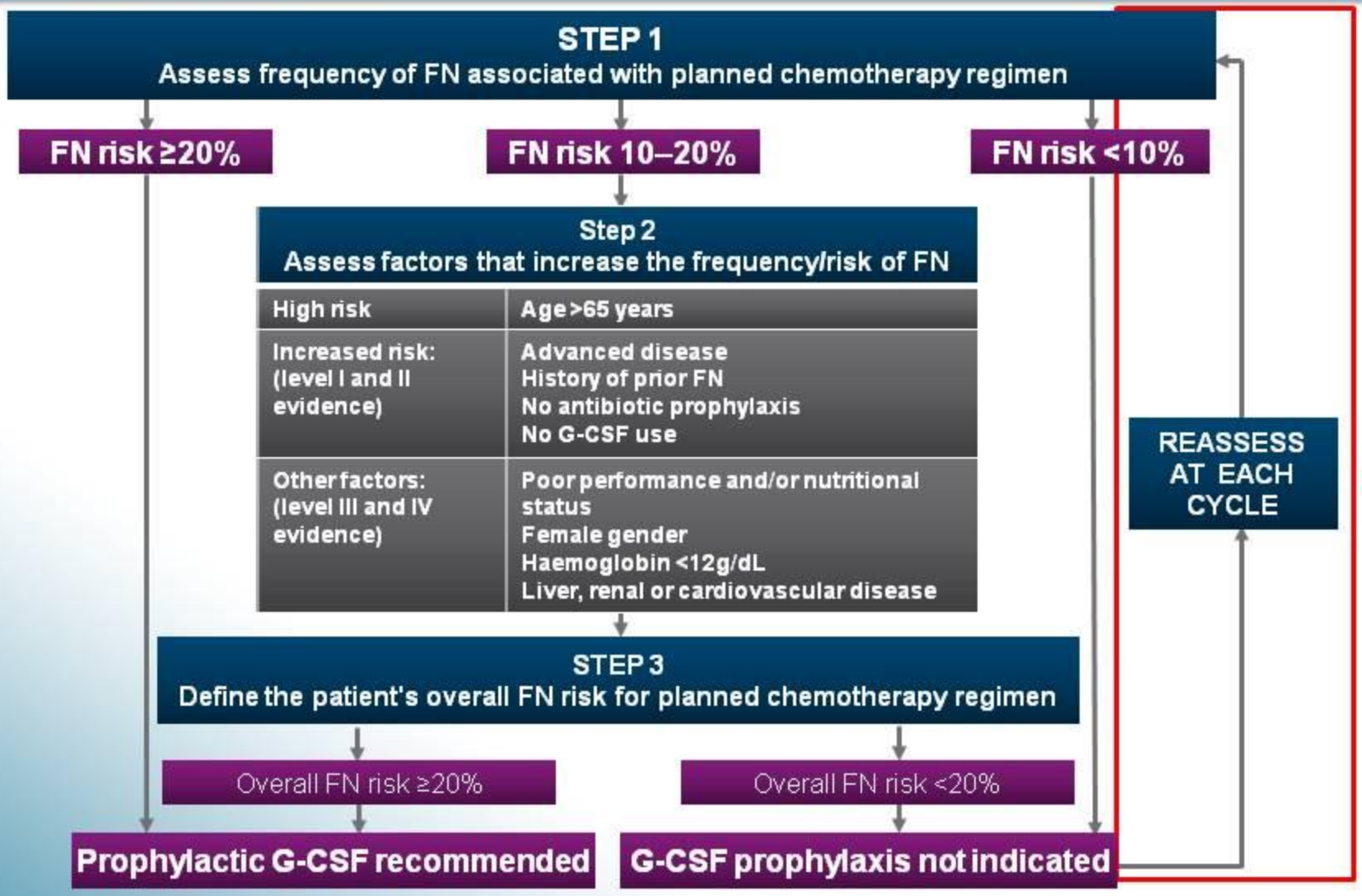
Aapro MS et al. Eur J Cancer 47: 8-32, 2011

Commentary on Recommendation 6

- Daily dosing with filgrastim should continue until the expected neutrophil nadir is passed and the neutrophil count has recovered to the normal range. Following established chemotherapy for solid tumours, lymphomas, and lymphoid leukaemias, it is expected that the duration of treatment required to fulfil these criteria will be up to 14 days.
- In patients receiving cytotoxic chemotherapy, a transient increase in neutrophil counts is typically seen 1 to 2 days after initiation of filgrastim therapy. However, for a sustained therapeutic response, filgrastim therapy should not be discontinued before the expected nadir has passed and the neutrophil count has recovered to the normal range. Premature discontinuation of filgrastim therapy, prior to the time of the expected neutrophil nadir, is not recommended.

http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/001142/WC500093661.pdf.
Last accessed: 18 October 2010

EORTC guidelines recommend a prophylactic approach and risk assessment at the start of each cycle



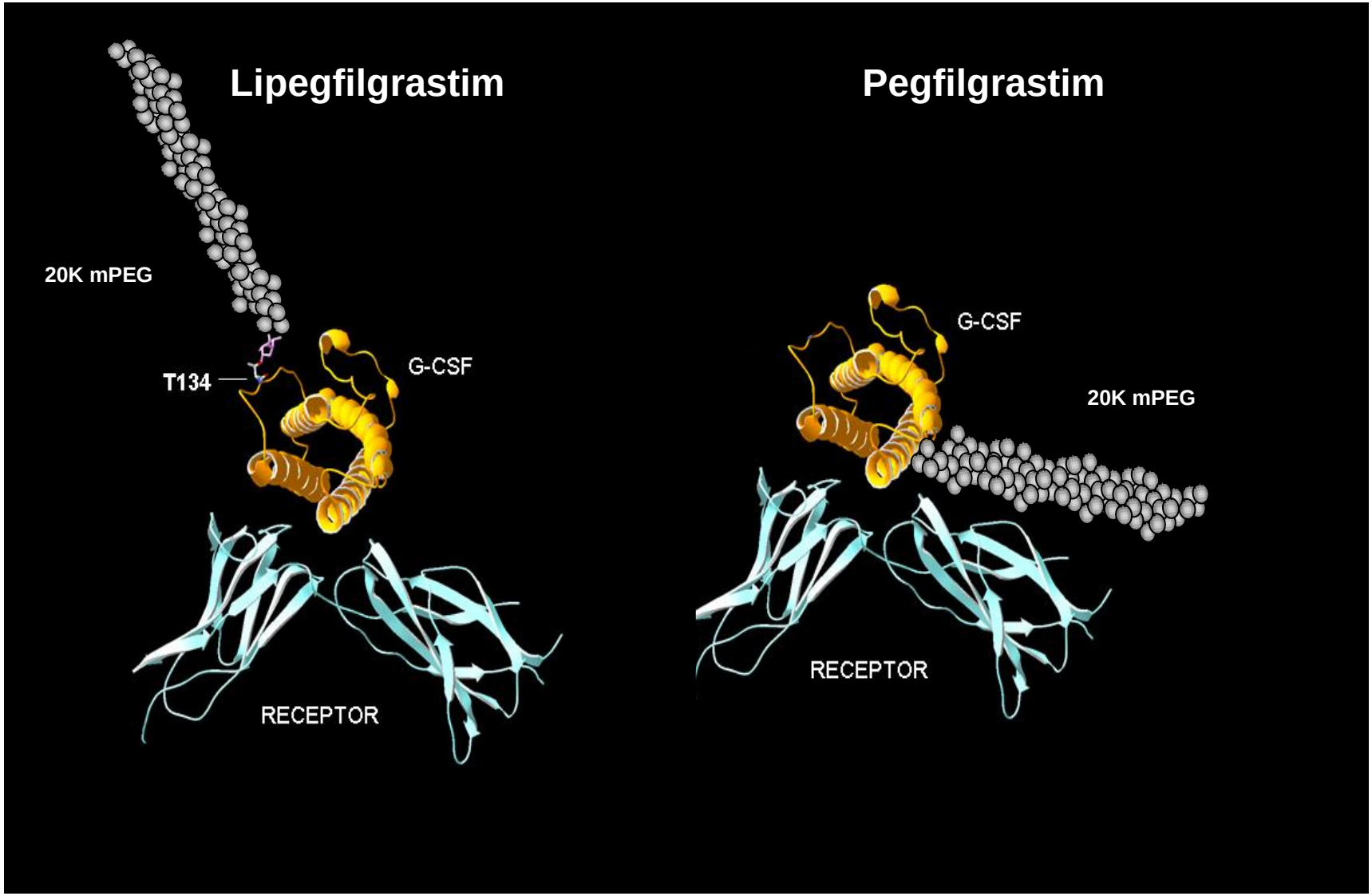
Aapro et al. Eur J Cancer 2011;47:8–32.

AN ORIGINAL AGENT, NOT A BIOSIMILAR

LIPEGFILGRASTIM

- Pegylation attached in an ORIGINAL way
- In vitro activity demonstrated
- Phase III studies presented
- Submitted to EMA

Structure of pegfilgrastim and lipegfilgrastim



Clinical Development of Lipegfilgrastim

Phase I		
XM22-01-CH	PK/PD single dose, bodyweight adjusted dosing	N=53 25/50/100 µg/kg lipegfilgrastim
XM22-05-CH	PK/PD single dose, fixed dose	N=36 6 mg lipegfilgrastim
XM22-06	PK at three different injection sites (upper arm, abdomen, thigh)	N=20 6 mg lipegfilgrastim
Phase II/III		
XM22-02	Dose finding with three different doses of lipegfilgrastim (with expanded cohort) compared to 6 mg pegfilgrastim in breast cancer patients	N=208 3/4.5/6 mg lipegfilgrastim
Phase III		
XM22-03	Efficacy and safety of 6 mg lipegfilgrastim compared to 6 mg pegfilgrastim in breast cancer patients	N=202 6 mg lipegfilgrastim
XM22-04	Efficacy and safety of 6 mg lipegfilgrastim compared to placebo in non-small cell lung cancer patients	N=373 6 mg lipegfilgrastim

Absolute neutrophil counts in a study of lipegfilgrastim compared with pegfilgrastim in patients with breast cancer who are receiving chemotherapy (A 60 Doce 75)

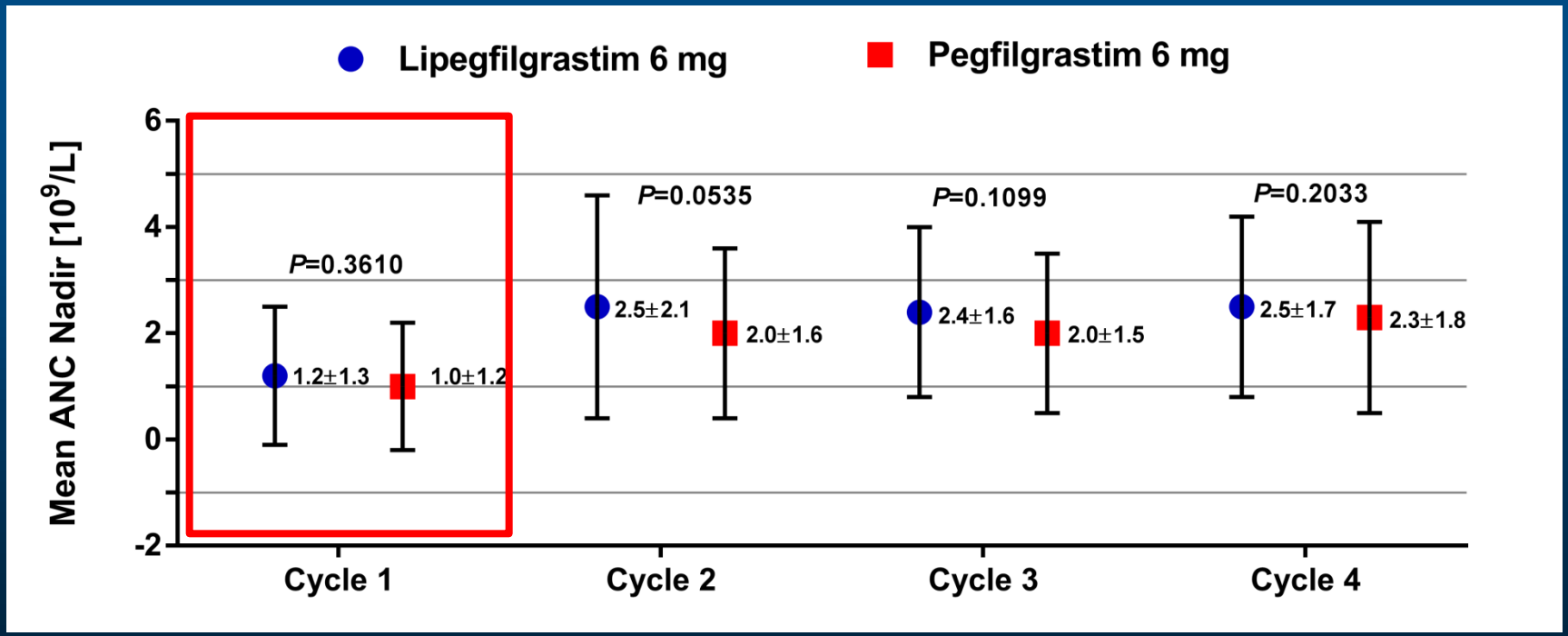
Oleg A. Gladkov, MD;
Igor M. Bondarenko, MD, PhD;
Reiner Elsaesser, MSc; Anton Buchner, MD;
Peter Bias, MD

Poster # 1548

European Society for Medical Oncology (ESMO) September 28 – October 2, 2012; Vienna, Austria.

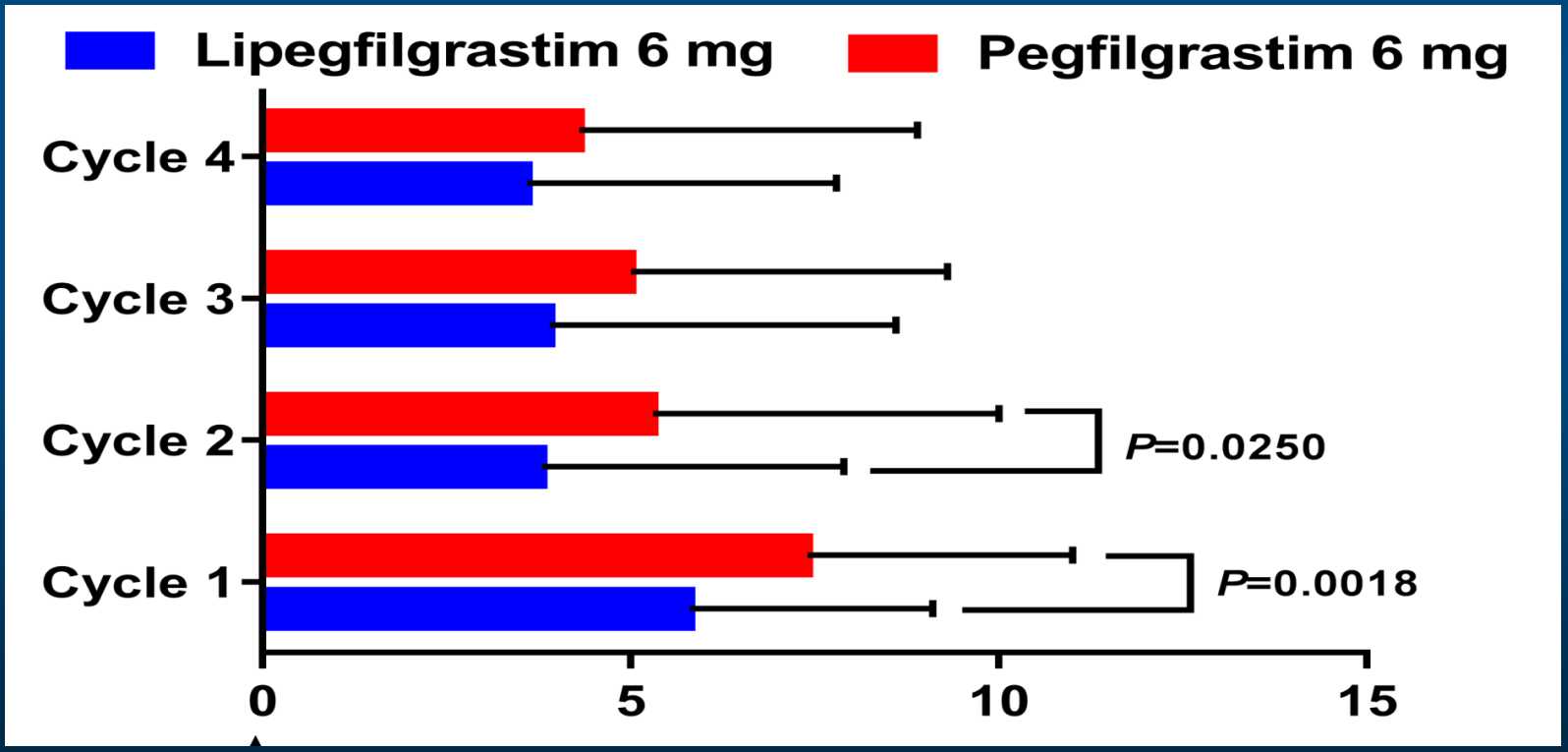
RESULTS: ANC Nadir in Cycles 1–4

- The time to ANC nadir was comparable between groups in each cycle (median 6 days throughout)
- The depth of ANC nadir in cycle 1 was comparable between treatment groups (*P*=0.3610)



RESULTS: Time to ANC Recovery in Cycles 1–4

- Time to ANC recovery: longest in cycle 1 (both groups)
- Time to ANC recovery: significantly shorter for lipegfilgrastim patients in cycles 1 and 2*



*Differences in cycles 3 and 4 were not significant

Author's Summary and Conclusions

- Lipegfilgrastim and pegfilgrastim were comparable with respect to time to and depth of ANC nadir:
  - All numerical differences in efficacy parameters were consistently in favour of lipegfilgrastim treatment
- Rates of adverse events were comparable between arms:
  - Most adverse events were attributable to complications of chemotherapy or progression of the primary disease

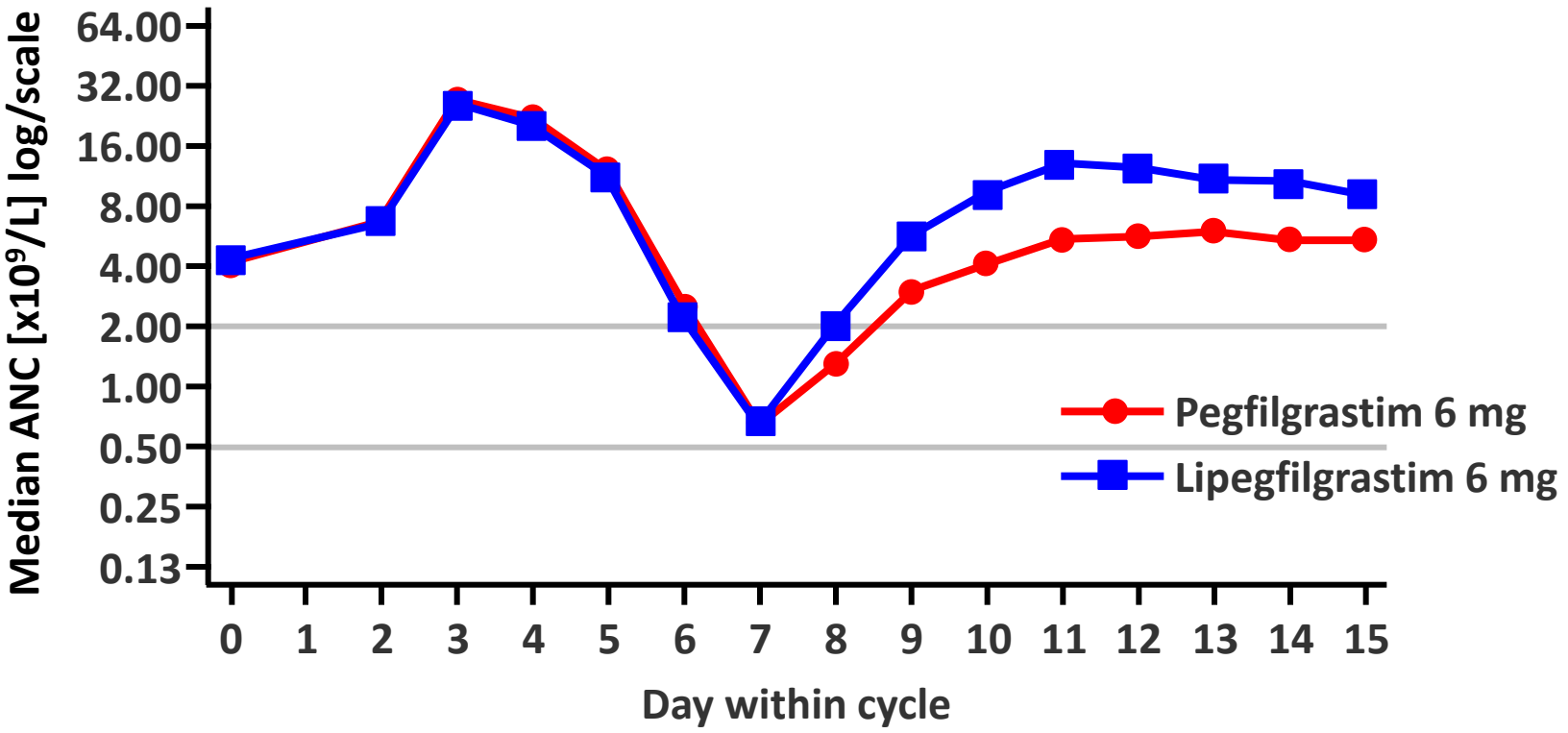
DISCUSSANT's CONCLUSION

- These data support an equivalence of both agents
- The slightly more rapid recovery from a clinically non-significant nadir is probably of limited importance
- Time does not allow review of all data

Lipegfilgrastim
Phase III breast cancer study

Presented at MASCC 2012

Lipegfilgrastim – Phase III breast cancer study: course of ANC in first cycle of chemotherapy



Lipegfilgrastim – Phase III breast cancer study: **safety** (ITT population)

Most frequent side effects occurring in ≥3 patients in a treatment group				
Side effects	**Pegfilgrastim 6 mg (n=101)**		**Lipegfilgrastim 6 mg (n=101)**	
	[n]	**[%]**	[n]	**[%]**
Bone pain	10	**9.9**	13	**12.9**
Myalgia	5	**5.0**	7	**6.9**
Erythema	3	**3.0**	6	**5.9**
Arthralgia	0	**-**	3	**3.0**
Nausea	3	**3.0**	2	**2.0**

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