Laboratorio SEIFEM

Le problematiche infettive nel paziente ematologico

Roma, 12 novembre 2024
Best Western Plus Hotel Universo

Presidente
Livio Pagano

Con il Patrocinio di
SIE - Società Italiana di Ematologia

SEIFEM

Prospective observational study on invasive fungal infection (IFI) incidence in Ph-negative acute lymphoblastic leukemia (ALL) patients

SEIFEM ALL-IFI 2022 Study - *ClinicalTrials.gov* Identifier*:* NCT06392581

SEIFEM Writing Committee
Chiara Cattaneo (UO di Ematologia, Spedali Civili di Brescia – CENTRO COORDINATORE)
Francesco Marchesi (UO Ematologia, Istituto Nazionale Tumori Regina Elena, Roma)
Irene Terrenato (UOSD Clinical Trial Center e Biostatistica e Bioinformatica, Istituto Nazionale Tumori Regina Elena, Roma)
Alessandro Busca (Chairman of the SEIFEM group)
Livio Pagano (President of the SEIFEM group)

Study objectives

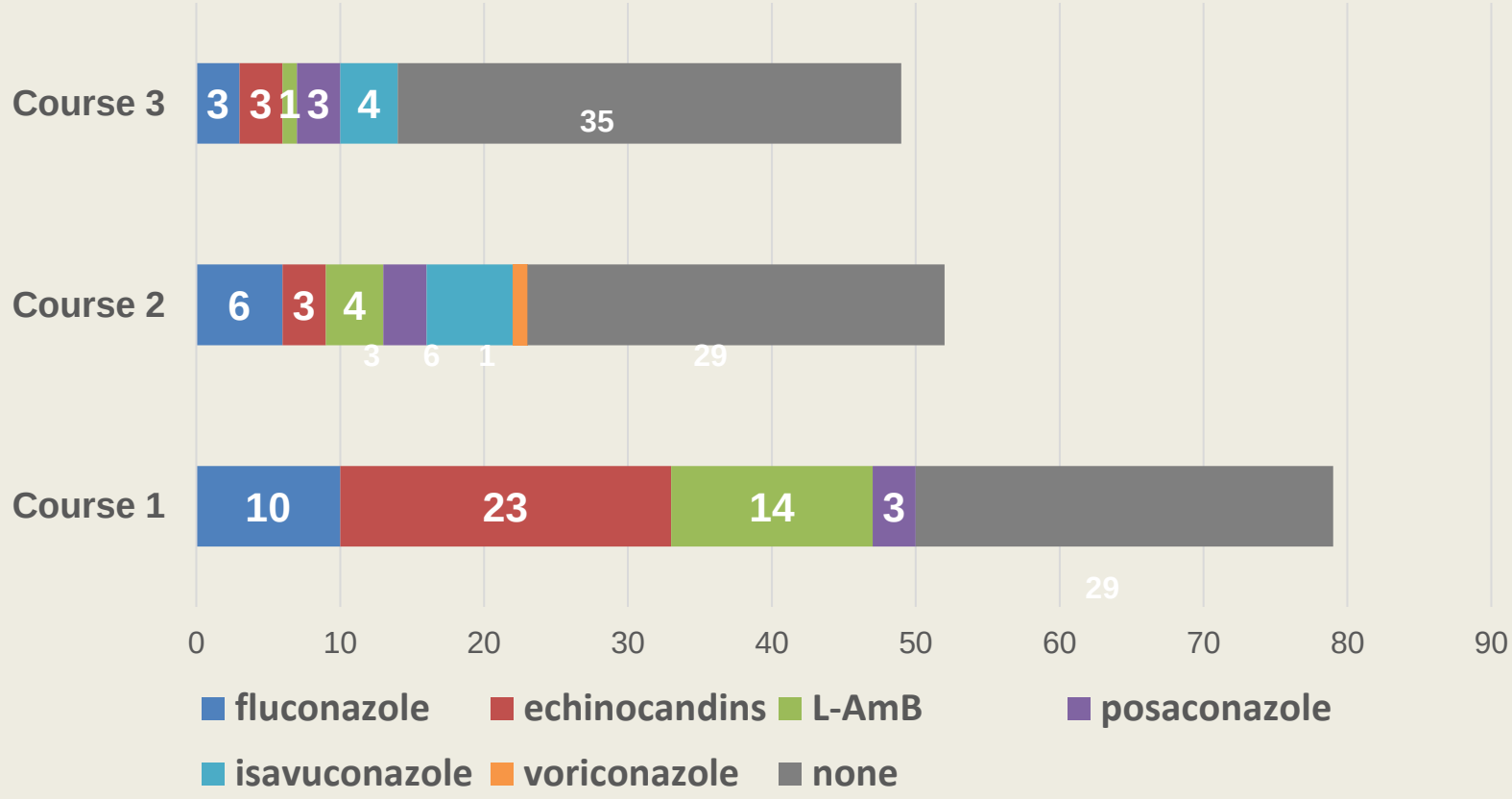
- **Primary objective**

- To evaluate the incidence of invasive fungal infections (IFI) during the first 3 courses

- **Secondary objectives**

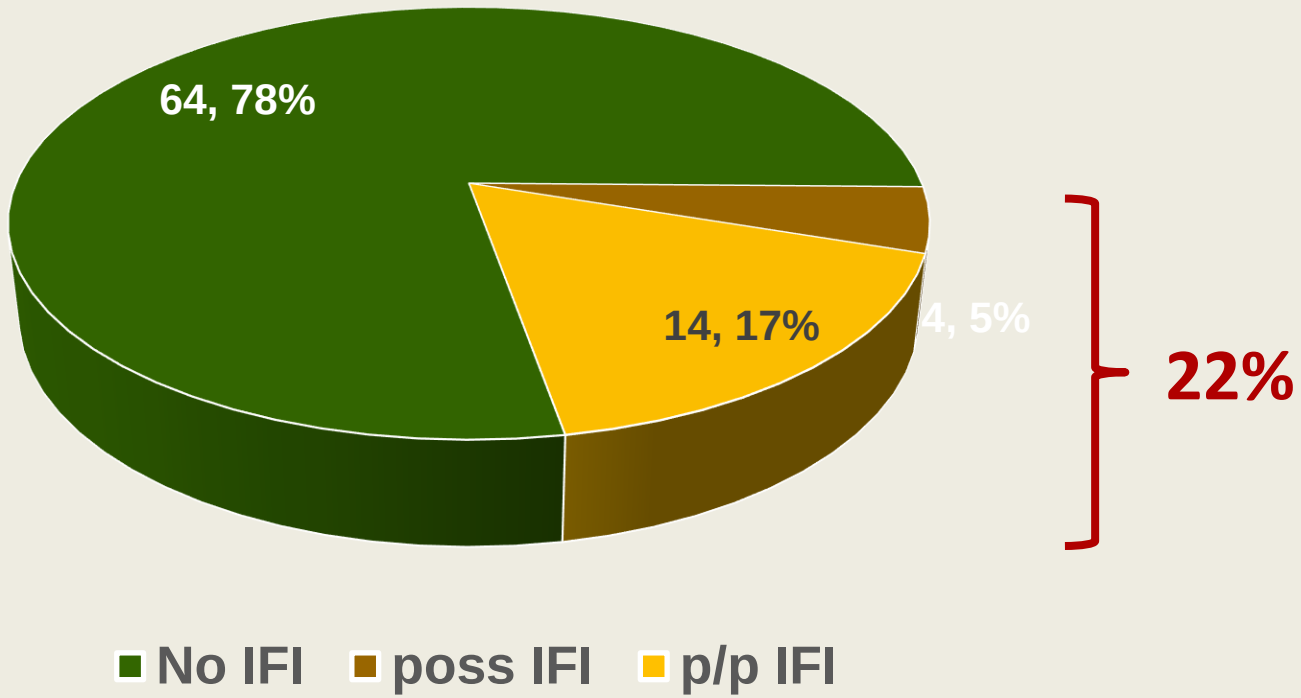
- To evalute IFI incidence in relation to:
  - Age
  - Antifungal prophylaxis
  - Duration of neutropenia
  - Type of steroid treatment
- To evaluate treatment delay in ALL patients with IFI
- To evaluate the outcome of ALL patients with IFI

Type of AF prophylaxis



IFI incidence

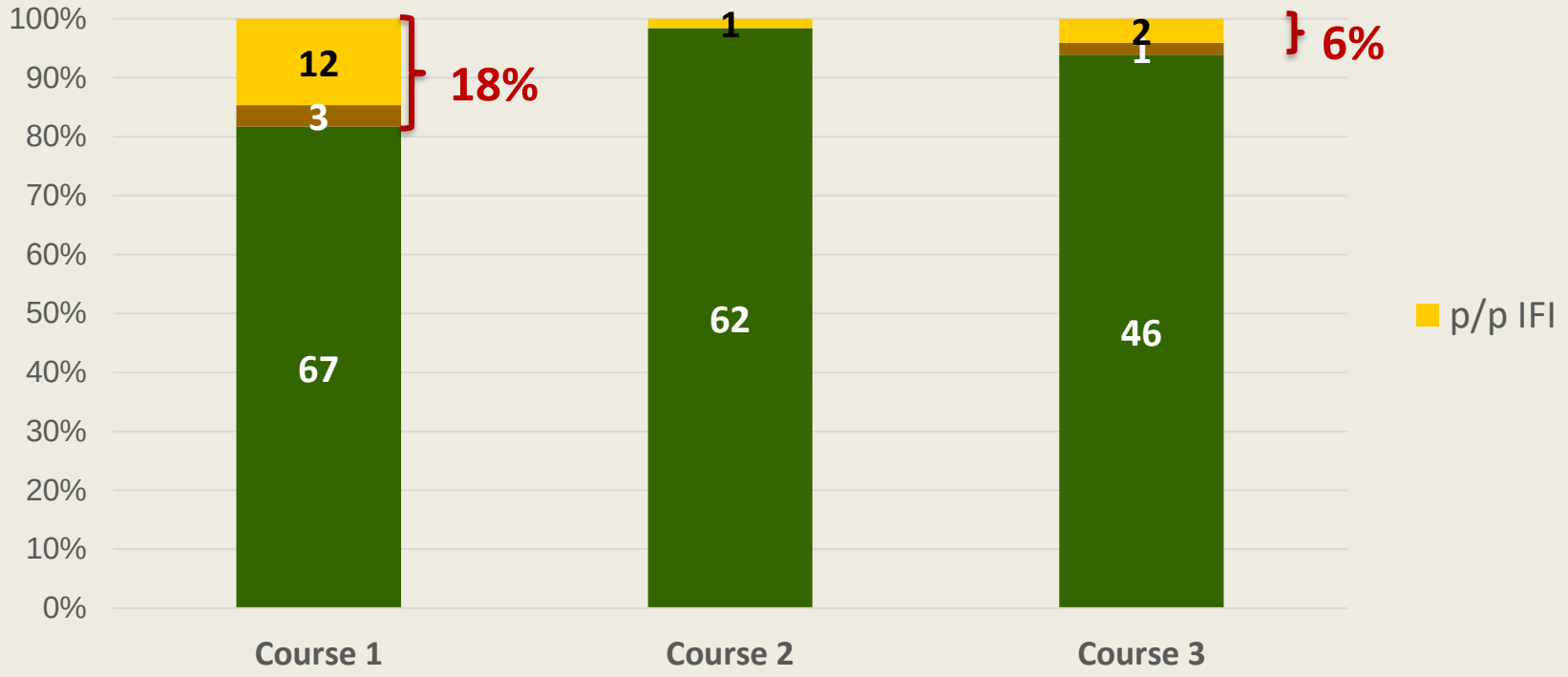
19 IFI* in 18 patients
(1 patient developed 2 IFI)



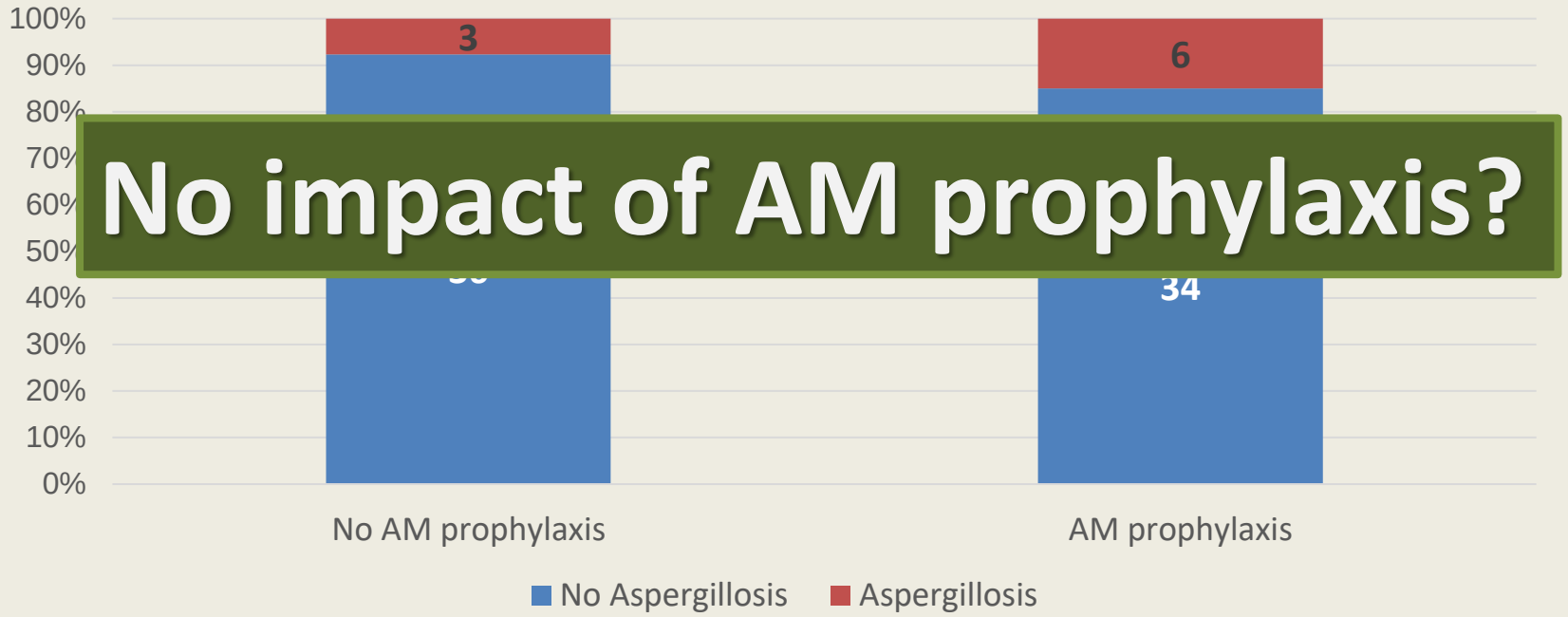
22%

***including 2 *P.jirovecii* pneumonia**

IFI incidence according to phase of treatment

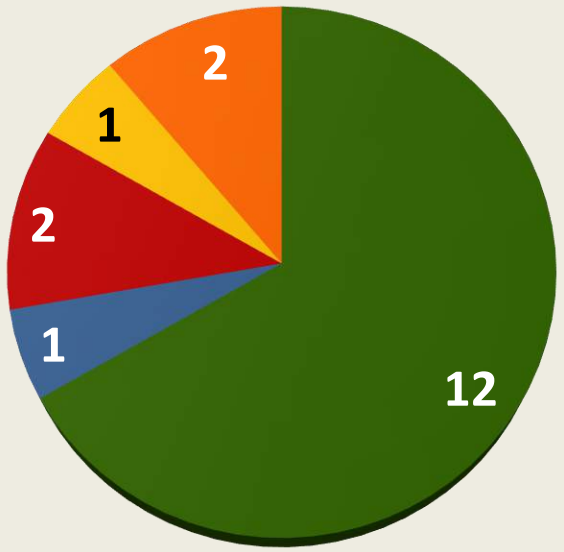


Invasive aspergillosis incidence according to antimold prophylaxis during induction



No impact of AM prophylaxis?

prov/prob IFI - epidemiology



- pulmonary aspergillosis
- pulmonary+sinus aspergillosis
- Candidemia
- Hepatosplenic candidiasis
- P.jirovecii pneumonia

Mortality

- Overall mortality 10/82 (12.2%)
  - 6 progressive disease
  - 3 infections (1 *C. parapsilosis* fungemia, 1 *P. aeruginosa* BSI, 1 neutropenic enterocolitis)

- Attributable IFI mortality 1/18 (5.6%) (*C. parapsilosis* fungemia)

Microbiota exploitation by CPX-351 in animal models

Luigina Romani, M.D., Ph.D.

Università degli Studi di Perugia

Seifem, 7 Novembre 2023

Comparative evaluation of the liposomal daunorubicin + cytarabine combination (CPX-351) versus the "7+3" combination on mucosal barrier function and intestinal microbiota

Project IST 11389

PI: Luigina Romani

Co-PI: Livio Pagano

Comparison of respiratory metagenomics/metabolomics/immunomics profiles in:

- Preclinical models
- Newly-diagnosed leukemic patients eligible for treatment with either CPX-351 or 7+3

The primary objective of this study is to comparatively evaluate the activity of CPX-351 and "7+3" within their respective groups of AML patients by means of variation of:

i) inflammatory markers (IL-1β, IL-6, TNFα)
ii) microbial (bacterial and fungal) composition
iii) metabolites

in nasal and oropharyngeal swabs.

Secondary Objectives:

- Correlate the variations of microbial and metabolic profiles with inflammatory markers and oral mucositis within each group of patient-treatment

- Correlate the variations of microbial and metabolic profiles with respiratory infections within each group of patient-treatment

A prospective, observational, multicenter study:
SURVEY OF UPPER AIRWAY MICROBIAL INTERACTION WITH FUNGI

SNIF

OBJECTIVES:

1. Characterization of the upper airway microbiome

2. Identification of a microbial signature of the upper airway microbiome predictive of the risk of fungal infections.

HR microbial signature:

- **Firmicutes** (i.e., the Staphylococcus and Enterococcus genera and Lactobacillaceae)
- **Gram-negative Proteobacteria** (i.e., Acinetobacter and Stenotrophomonas genera).

LR microbial signature:

- **Bacteroidota** (i.e., the Prevotella genus)
- **Actinobacteria**
- **oral taxa** (Veillonella, Neisseria, Leptotrichia, Gemella and Clostridia with the Lachnospiranaceae family).

To make the story shorts:

HR samples: abundance of genes involved in the

- Biosynthesis of L-tryptophan (trp)
- Glycolysis
- Homolactic fermentation
- Shikimate pathway, a metabolic pathway not found in animal cells that leads to the biosynthesis of aromatic amino acids, likely indicating an attempt to compensate for reduced levels of these molecules.

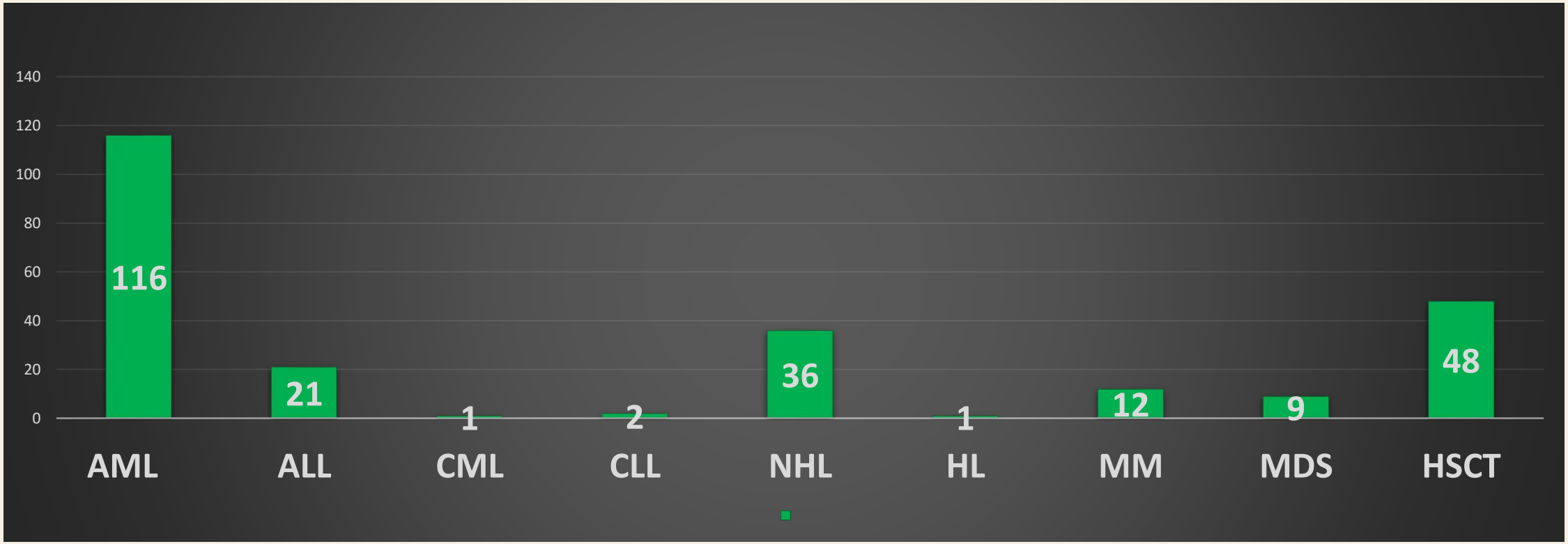
LR samples: abundance of genes involved in the fatty acid elongation and the starch degradation pathways (abundantly present in oral bacteria).

Original Project

STUDIO OSSERVAZIONALE SULL'UTILIZZO DELLE NUOVE COMBINAZIONI DI CEFALOSPORINE/INIBITORI DELLE BETA-LATTAMASI (CEFTOLOZANE/TAZOBACTAM E CEFTAZIDIME/AVIBACTAM): IMPATTO CLINICO NEL TRATTAMENTO DELLE INFEZIONI DA GRAM-NEGATIVI MULTIRESISTENTI NEL PAZIENTE ONCO-EMATOLOGICO.

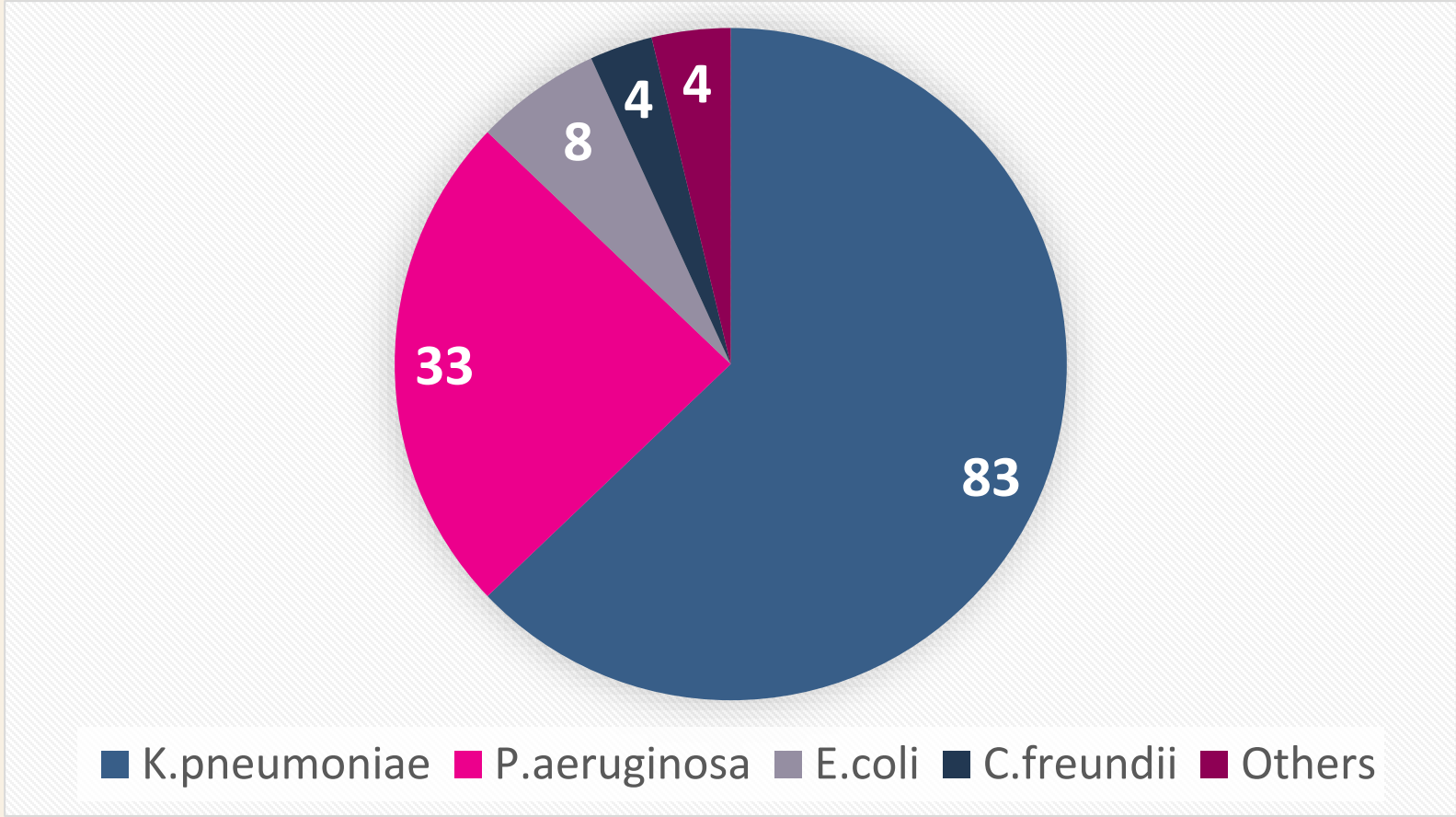
Prof. Mario Tumbarello
UOC Malattie Infettive e Tropicali, AOUS Senese
Dip. Biotecnologie Mediche, Università degli studi di Siena

HEMATOLOGICAL DISEASES



ETIOLOGY

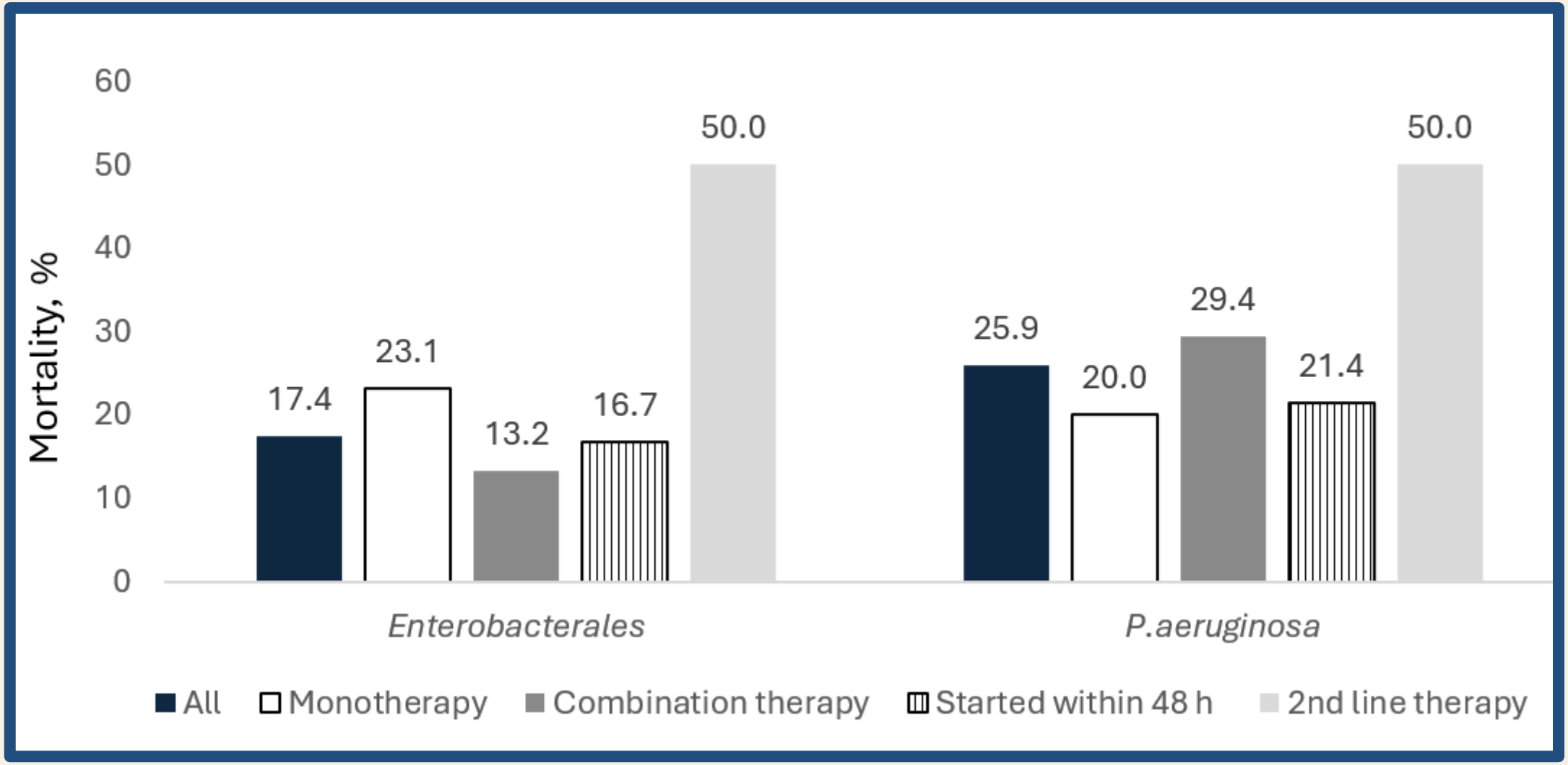
Enterobacterales	**98 (74.2)**
Klebsiella pneumoniae	83 (62.9)
Escherichia coli	8 (61.7)
Citrobacter freundii	4 (3.0)
Enterobacter cloacae	2 (1.5)
Proteus mirabilis	1 (0.8)
Non-fermenting Gram-negative bacilli	**33 (25.0)**
Pseudomonas aeruginosa	33 (25,0)
Others	**1 (0.8)**
Aeromonas hydrophila	1 (0.8)



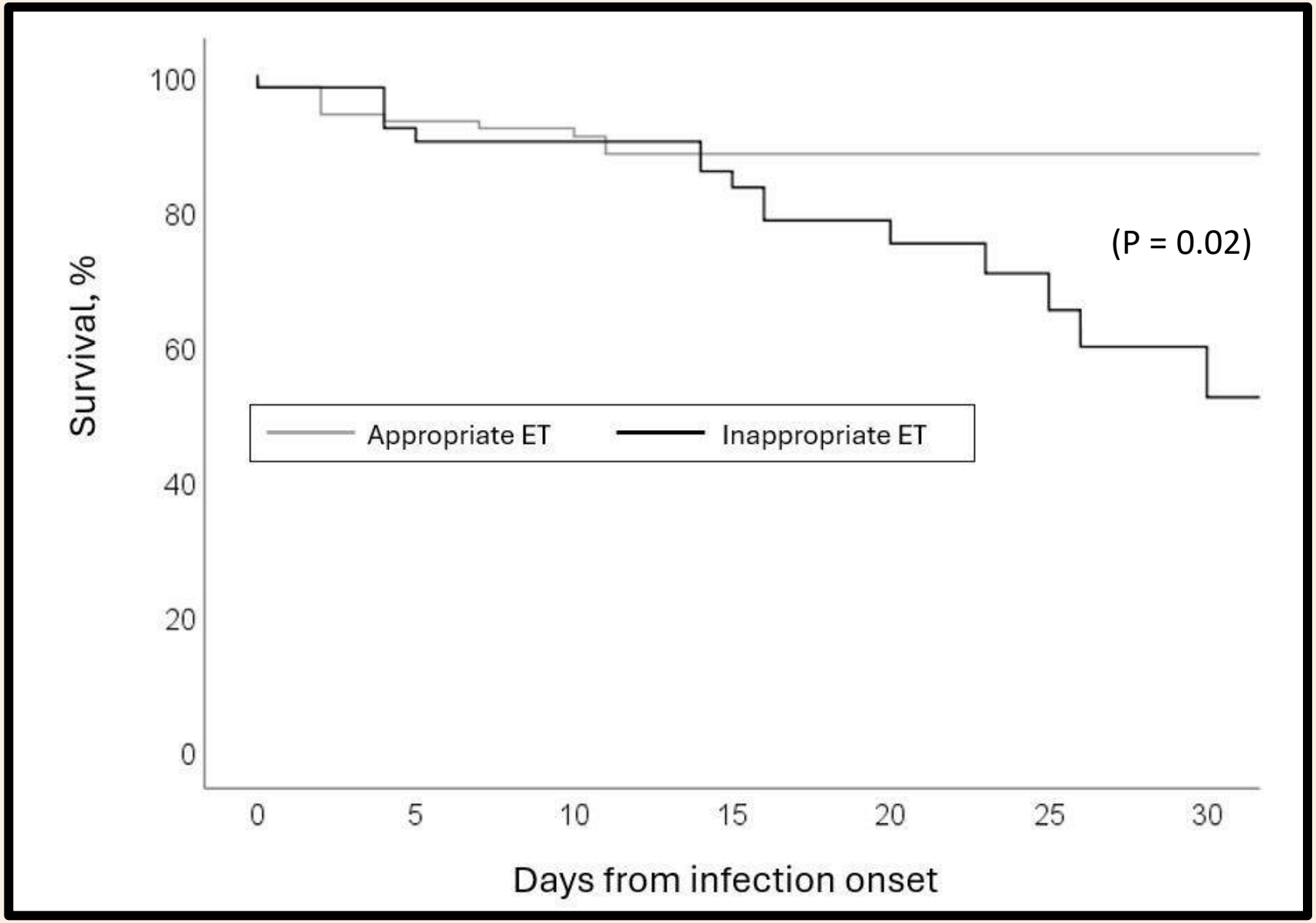
CAZ/AVI THERAPY CHARACTERISTICS AND OUTCOMES

Variable	All infection (n=198)	FUO (n=66)	MPI (n=132)	P value (FUO vs MPI)	Microbiologically proven infection types (n=132)			
					BSI (n=120)	LRTI (n=5)	cUTI (n=5)	Others (n= 2)
CAZ-AVI treatment variables								
Days of treatment - *median (IQR)*	12 [8-15]	12 [8-15]	12.5 [7-15]	0.96	13 [7-16]	11 [7-20]	11 [8-12]	10 [8-12]
Started empirically	91 (46.0)	66 (100)	25 (18.9)	<0.001	25 (20.8)	0	0	0
Started within 48 h of infection onset	72 (36.4)	-	72 (54.5)	-	67 (55.8)	1 (20.0)	4 (80.0)	0
Salvage therapy	31 (15.7)	31 (47.0)	-	-	-	-	-	-
Salvage therapy started within 72 h of infection onset	8 (4.0)	8 (12.1)	-	-	-	-	-	-
Monotherapy regimens	77 (38.9)	23 (34.8)	54 (40.9)	0.41	50 (41.7)	2 (40.0)	1 (20.0)	1 (50.0)
Combination regimens with:	121 (61.1)	43 (65.2)	78 (59.1)	0.41	70 (58.3)	3 (60.0)	4 (80.0)	1 (50.0)
Outcomes [a]								
30-day all-cause mortality	35 (17.7)	9 (13.6)	26 (19.7)	0.30	24 (20.0)	2 (40.0)	0	0
Infection relapse [b]	4 (2.0)	0	4 (3.0)	0.15	4 (3.3)	0	0	0
Development of *in vitro* CAZ-AVI resistance during treatment	1 (0.5)	0	1 (0.8)	1.0	1 (0.8)	0	0	0
Adverse reactions	2 (1.0)	2 (3.0)	0	0.11	0	0	0	0

MORTALITY OF BSI



IMPACT OF APPROPRIATENESS OF EMPIRIC ANTIBIOTIC THERAPY ON 30-DAY SURVIVAL FOR 132 HMS PATIENTS WITH MPI



(VERSIONE 1.0 DEL 09/11/2024)

TITOLO:

Utilizzo della profilassi antibiotica con fluorochinoloni nei pazienti con Leucemia Mieloide Acuta in Italia: studio multicentrico prospettico osservazionale HeMABIS-PRO-F (Haematologic Malignancies Associated Bloodstream Infections Surveillance registry - PROphylaxis with Fluoroquinolones)

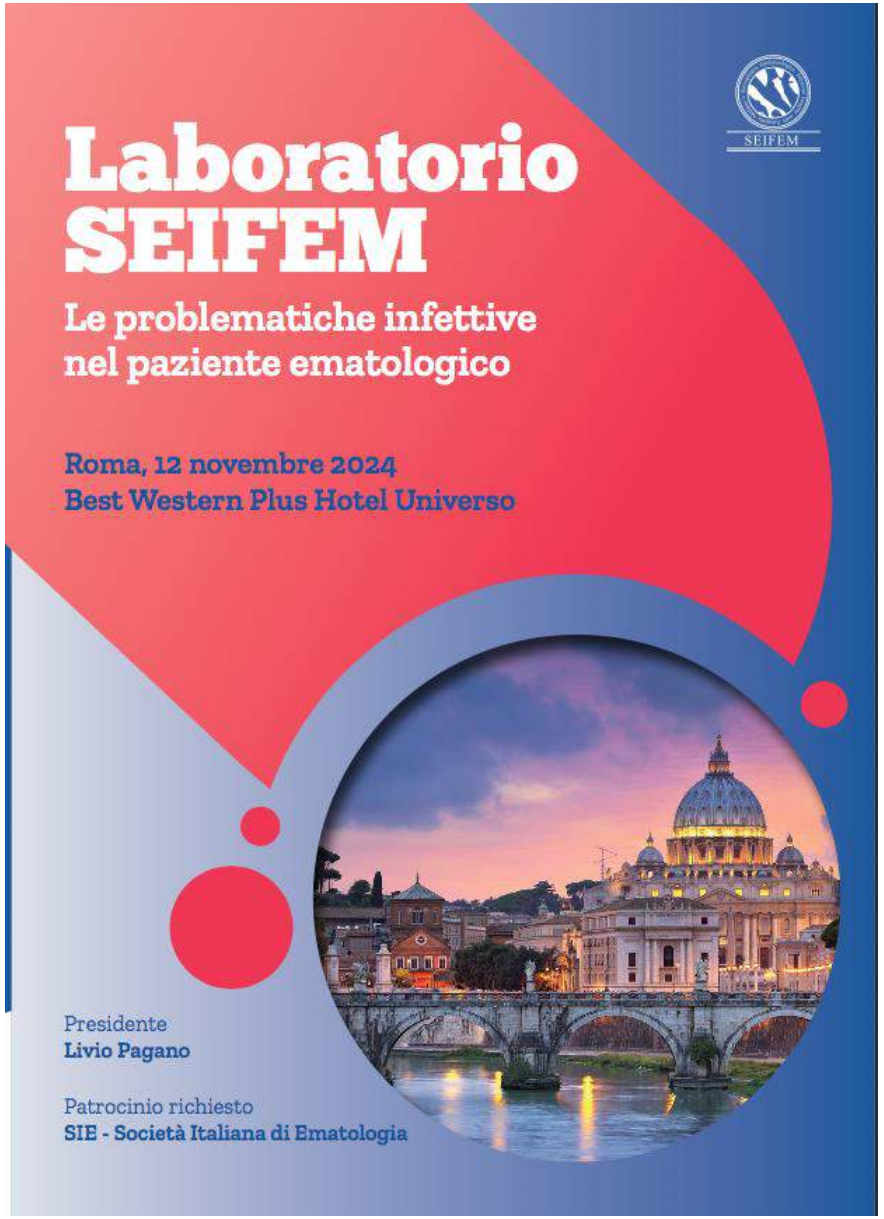
- Enrico Maria Trecarichi (Catanzaro)
- Chiara Cattaneo (Brescia)
- Francesco Marchesi (Roma)
- Irene Terrenato (Roma)
- Chiara Davoli (Catanzaro)

Durata dello studio	Il progetto di ricerca avrà una durata prevista di circa 8 mesi (e comunque subordinato alla conclusione dell'iter approvativo da parte dei Comitati Etici di ciascun centro partecipante e al raggiungimento della numerosità campionaria prevista).
Obiettivi principali	L'obiettivo primario dello studio è quello di descrivere e confrontare l'incidenza di episodi di neutropenia febbrile in pazienti ospedalizzati affetti da Leucemia Mieloide Acuta sottoposti a chemioterapie intensive che effettuano o no profilassi antibiotica con fluorochinoloni.
Obiettivi secondari	Gli obiettivi secondari sono quelli di descrivere e confrontare tra i pazienti sottoposti o no a profilassi con fluorochinoloni: • l'incidenza di episodi di batteriemie microbiologicamente documentate • i tassi di resistenza alle principali classi di antibiotici degli isolati batterici responsabili di batteriemie • l'incidenza di infezioni (diverse da batteriemie) clinicamente o microbiologicamente documentate • i trattamenti antibiotici empirici e/o eziologici effettuati • i fattori di rischio per neutropenia febbrile • fattori di rischio per episodi di batteriemie microbiologicamente documentate • l'*outcome* prognostico espresso come mortalità a 21 giorni e mortalità intra-ospedaliera e fattori di rischio correlati

TIPO E METODOLOGIA DELLO STUDIO		
Disegno dello studio		Spontaneo, multicentrico, prospettico, osservazionale.
Popolazione dello studio	**Numero**	Si prevede di arruolare circa 170 pazienti.
	Criteri di inclusione	- Pazienti adulti (età ≥18 anni) affetti da Leucemia Mieloide Acuta ospedalizzati e sottoposti a cicli di polichemioterapia intensiva di induzione - Sottoscrizione del consenso informato
	Criteri di esclusione	- Pazienti che non rientrano nei criteri di inclusione - Pazienti già precedentemente arruolati nel presente studio (ogni paziente verrà incluso solo una volta)

Struttura dello studio

Studio spontaneo, prospettico, osservazionale che prevede l'arruolamento di almeno 170 pazienti (vedi paragrafo "**Calcolo del *sample-size***") ricoverati presso i Centri coinvolti nello studio. La data di inizio dello studio è programmata per il 1° marzo 2025 e la data di fine per il 30 giugno 2025 (tuttavia le date di inizio e fine saranno subordinate alla conclusione dell'iter approvativo da parte dei Comitati Etici di ciascun centro partecipante e al raggiungimento della numerosità campionaria prevista). Verranno considerati tutti i pazienti ricoverati nel periodo di studio che rispondano ai criteri di inclusione.



INFECTIOUS COMPLICATIONS IN PATIENTS UNDERGOING ALLOGENEIC STEM CELL TRANSPLANTATION (HSCT) FOR ACUTE MYELOID LEUKEMIA AFTER CPX-351 TREATMENT: A "REAL-LIFE" MULTICENTER RETROSPECTIVE EXPERIENCE BY THE SEIFEM GROUP

Luana Fianchi

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Università Cattolica, Fondazione Policlinico A. Gemelli IRCCS, Roma

Multicenter Observational Retrospective Study on Febrile Events in Patients with Acute Myeloid Leukemia Treated with Cpx-351 in "Real-Life": The SEIFEM Experience

336 COURSES:
- 200 INDUCTION
- 118 CONSOLIDATION
- 18 SECOND INDUCTION

249

Febrile events

Onset of infection after CPX-351: 7 days (range 0-30)

193/218 (77.5%): 1° or 2° induction

56/118 (22.5%) 1° or 2° consolidation

40 (16%) clinically documented

92 (37%) febrile neutropenia of unknown origin (FUO)

117 (47%) Microbiologically documented

Overall 30-day mortality rate was 14% (28/200)
Induction attributable mortality-infection rate was 6%

88 patients (44%) underwent allogeneic stem cell transplantation (HSCT)

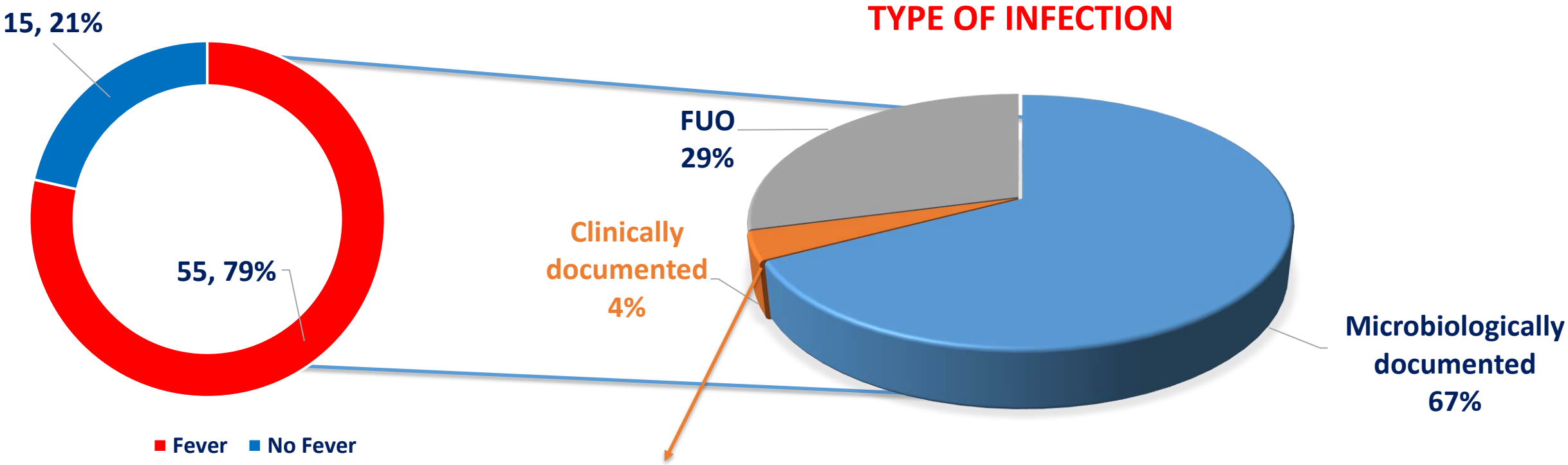
Fianchi L et al, Cancers 2023

Aims

The present study focused on the subgroup of transplanted patients by SEIFEM cohort in order to:

- Assess the rate of infections in patients previously treated with CPX-351 and undergoing HSCT
- Evaluate the outcome of these patients in terms of GVHD complications and survival

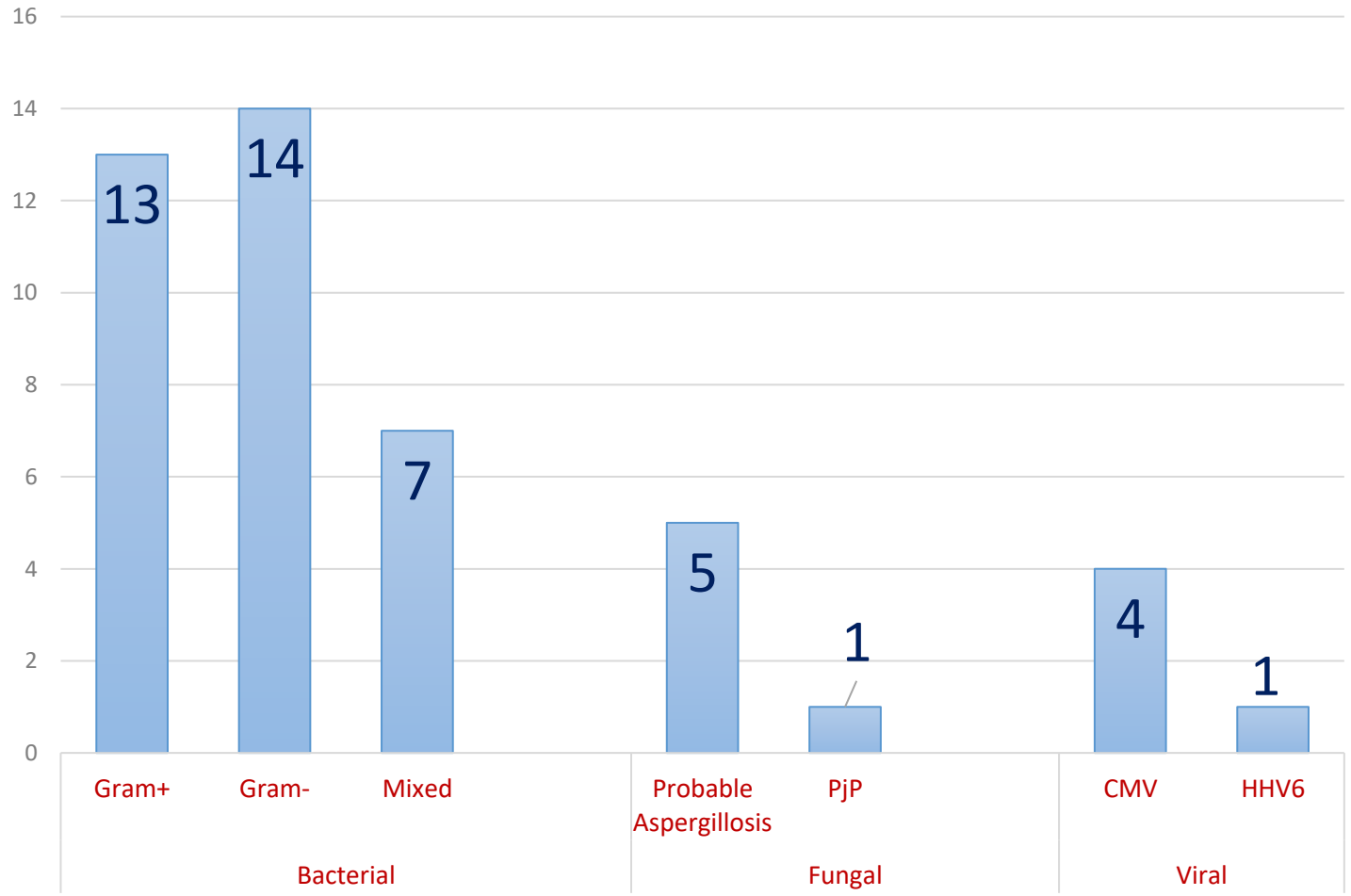
INFECTIOUS COMPLICATIONS



Pneumonia: 2

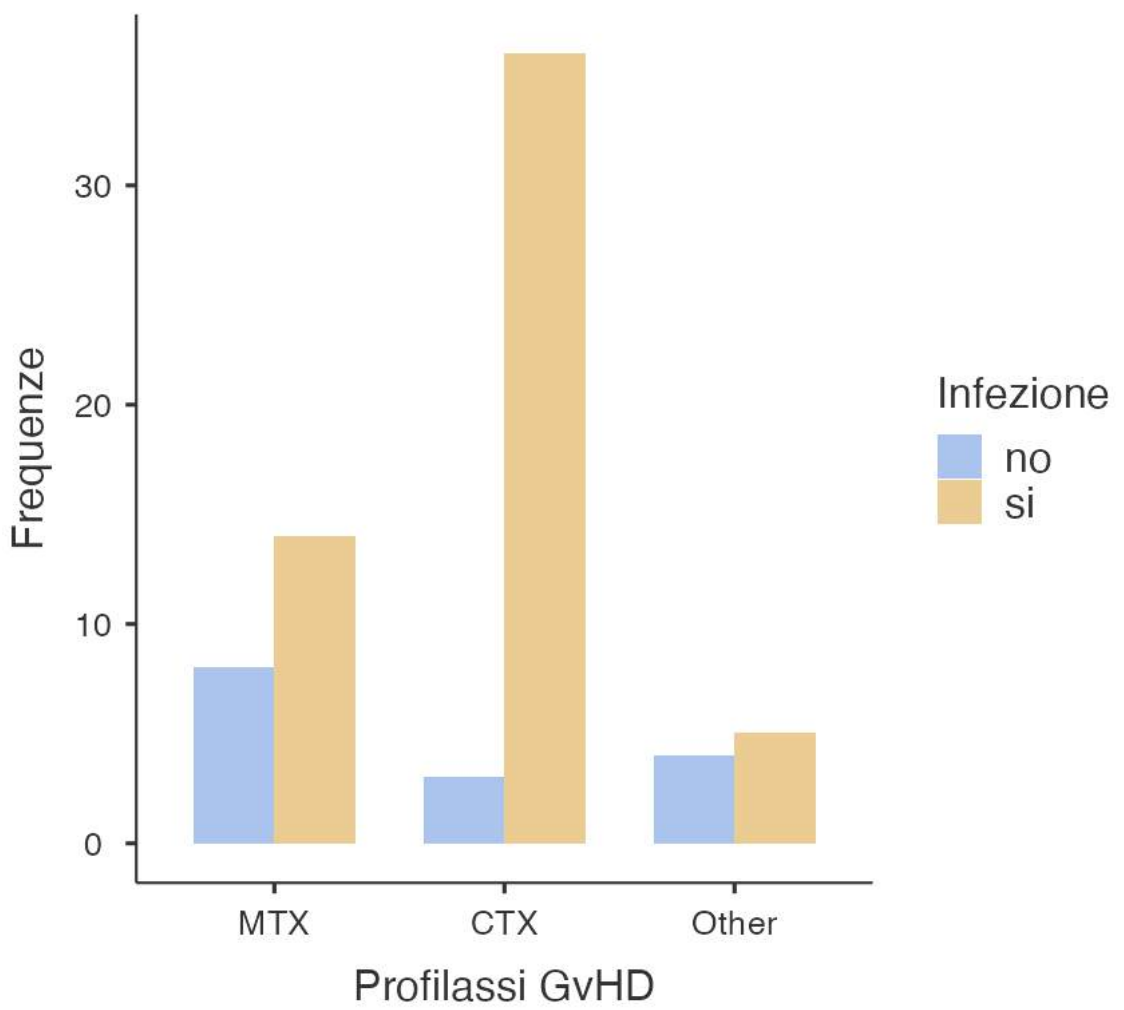
Microbiologically documented infection: 37

Type	n°
Bacterial	26 (70%)
Bacterial + Fungal	4 (11%)
Bacterial + Viral	4 (11%)
Fungal	2 (5%)
Viral	1 (3%)

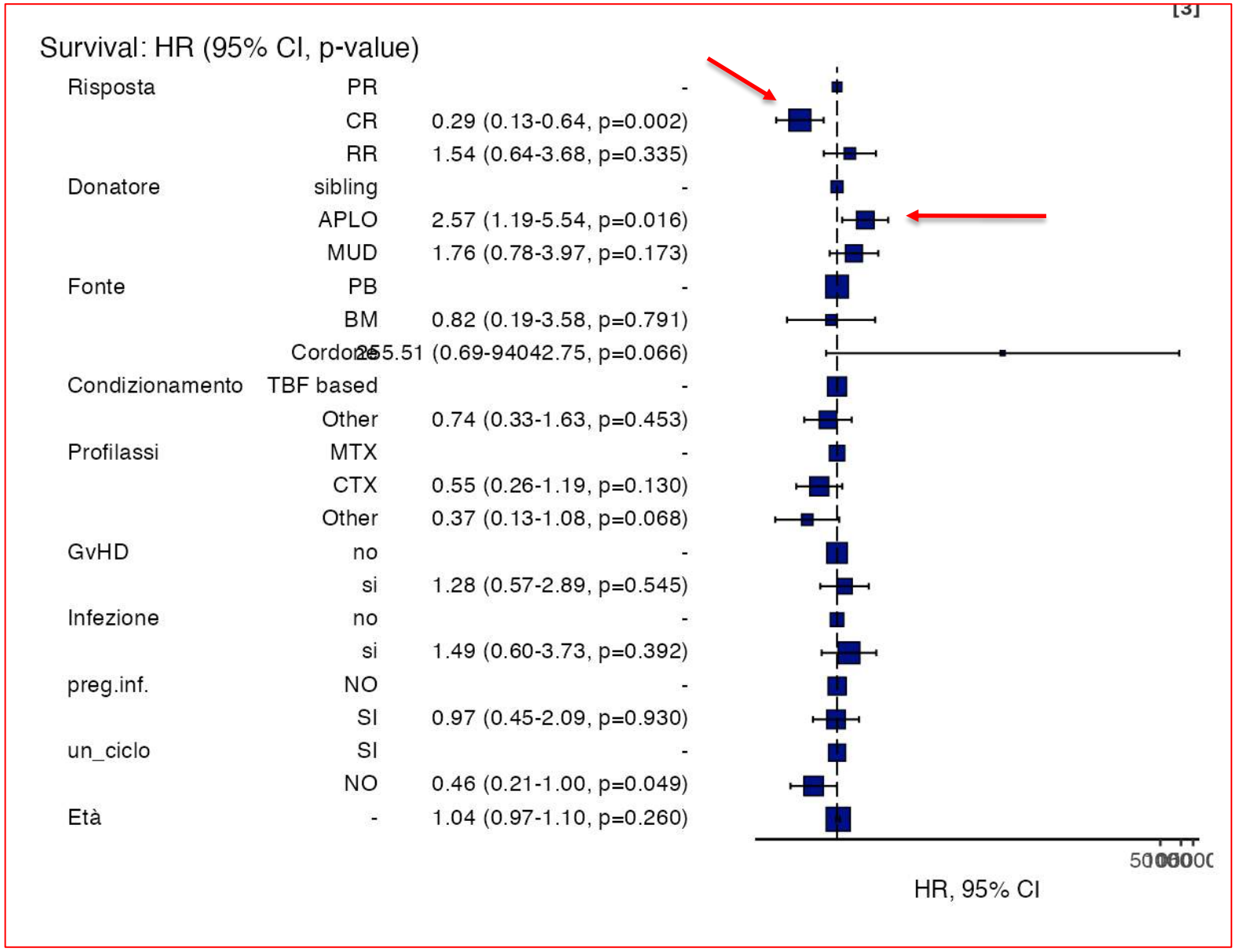


Risk factors for infection

	P-value
AML subtype AML –MRC vs t-AML	1.0
CPX-351 cycles - 1 vs 2/3 cycles	0.642
AML-status at HSCT CR vs PR vs R/R	0.647
Infection during CPX-351 treatment Yes vs No	0,970
HSCT Donor Sibiling vs MUD vs Haplo	0.366
Source PB vs BM vs CBU	0.782
Conditioning regimen TBF based vs other	0.153
GVHD prophylaxis CTX vs MTX vs other	**0.006**



Multivariate analysis for survival



SEIFEM

eha

Epidemiology of infection in AML: A European Haematology Association Survey (EPIAMLINF)

BACKGROUND

Infections following acute myeloid leukemia (AML) treatment still represent the most important cause of morbidity and mortality

Infections occur mainly due to profound and prolonged neutropenia associated with both the disease and treatments

Historically bacterial and fungal infections were the most relevant infectious complications in this setting of patients

There is broad incertainty nowdays about the proper antimicrobial prophylaxis in AML patients

Antifungal prophylaxis

Posaconazole use is well established

How to use it in older patients treated with less intensive regimens?

Antibacterial prophylaxis

Current guidelines still recommending to use quinolones

Increasing number of studies suggest limited uselfuness of this approach in view of the high rate of resistant strains isolated from AML patients

Antiviral prophylaxis

Some scientific societies gave recommendations

The current knowledge about this topic is definitely poor

Collecting information about the **incidence** of bacterial, fungal and viral **infections in AML** patients appears to be of vital importance in **improving** their **clinical management** and **decreasing morbidity** and **mortality** rate

Ambidirectional multicenter **non-interventional observational cohort study**.

Researchers from **different European countries** will be invited to participate in the study.

In the prospective phase of the study, the participating centres will review all infectious episodes occurring in all consecutive cases of AML identified at their institutions since **March 01, 2025 to February 28, 2026.**

AIMS

Primary objective

- **To evaluate the incidence** of bacterial/fungal/viral infections in AML patients undergoing induction, consolidation or salvage chemotherapy.

Secondary objectives

- To **stratify the incidence** of infections on the basis:
- - Type of AML chemotherapy
- - Phase of AML
- - Type and duration of antibiotic and antifungal prophylaxis (and of a possible anviral prophylaxis)
- **To evaluate the rate of infection-related mortality**

STUDY POPULATION

Inclusion criteria

- Age ≥18 years
- New diagnosis of AML (only cases diagnosed after 01/01/2025), APL are included
- Patients not elegible to any kind of chemotherapy but only best supportive care (BSC)
- AML patients treated with induction treatment, consolidation treatment, or relapsed/refractory (for these latter patients the first diagnosis must not be prior to March 01, 2025)
- All kind of infectious diseases, including parasites.
- Clinically or microbiologically diagnosed infections, including FUO

CLINICAL STUDY PROTOCOL

Study Title: Prospective, interventional, non-randomised, multicenter pharmacokinetic study to evaluate the plasma levels of gilteritinib in patients with relapsed/refractory FLT3+ acute myeloid leukemia in the presence or absence of triazoles.

Running Title: Pharmacokinetics of gilteritinib in R/R FLT3+ AML patients in the presence or absence of triazoles

Study Code: GTNIb_PK2023

FONDAZIONE
POLICLINICO UNIVERSITARIO
CAMPUS BIO-MEDICO

COMITATO ETICO

Prot. PAR 82.22

Dott. Pierantonio Menna
Fondazione Policlinico Universitario
Campus Bio-Medico
U.O.S. Farmacologia Clinica
Via Álvaro del Portillo, 200
00128 Roma

Roma, 18 Gennaio 2023

Oggetto: Parere del Comitato etico espresso nella seduta del 21 Dicembre 2022

N. REGISTRO STUDI CLINICI	2022.213
CODICE/ACRONIMO PROTOCOLLO	**GTNIb_PK2023**
TITOLO DELLO STUDIO	**Prospective, interventional, non-randomised, multicenter pharmacokinetic study to evaluate the plasma levels of gilteritinib in patients with relapsed/refractory FLT3+ acute myeloid leukemia in the presence or absence of triazoles** **Studio prospettico, interventistico, non randomizzato, farmacocinetico, multicentrico per valutare i livelli plasmatici di gilteritinib in pazienti con leucemia mieloide acuta FLT3+ recidivante/refrattaria in presenza o in assenza di triazoli**
VERSIONE E DATA PROTOCOLLO	Versione 1.0 del 05.12.2022
PROMOTORE	Fondazione Policlinico Universitario Campus Bio-Medico

FONDAZIONE
POLICLINICO UNIVERSITARIO
CAMPUS BIO-MEDICO

al termine della discussione, il Comitato etico ha espresso all'unanimità:

PARERE FAVOREVOLE CONDIZIONATO

Il Comitato Etico ha esaminato il preventivo della polizza assicurativa studio-specifica emesso in data 16 dicembre 2022 da HDI Global SE. Si richiede di fornire al Comitato Etico copia del contratto di polizza e certificato assicurativo finalizzati prima di avviare lo studio.

Respiratory viruses in patients with haematological malignancy in boreal Autumn/Winter 2023-2024: EPICOVIDEHA-EPIFLUEHA report

Dr. Jon Salmanton-García
Faculty of Medicine and University Hospital Cologne, Institute of Translational Research, Cologne Excellence Cluster on Cellular Stress Responses in Aging-Associated Diseases (CECAD), University of Cologne, Cologne, Germany
jon.salmanton-garcia@uk-koeln.de | @salmantongarcia

Background

- Community-acquired respiratory viral infections (CARV) are a major concern for patients…
  - Haematological malignancies (HM)
  - Post-hematopoietic stem cell transplantation (HSCT)
- CARV can undermine, posing significant complications…
  - Anti-cancer treatment effectiveness
- Recent advancements in understanding and managing CARV are reflected in increasing scientific literature and guidelines
- There is a scarcity of large-scale data from cooperative registries on CARV in HM, crucial for evidence-based strategies

Martino R, Ramila E, Rabella N, et al. *Clin Infect Dis* 2003; **36**(1): 1-8.
Gabutti G, De Motoli F, Sandri F, Toffoletto MV, Stefanati A. *Infect Dis Ther* 2020; **9**(3): 495-510.
Fontana L, Strasfeld L. *Infect Dis Clin North Am* 2019; **33**(2): 523-44.
Popescu CM, Ursache AL, Feketea G, et al. *Microorganisms* 2019; **7**(11).
von Lilienfeld-Toal M, Berger A, Christopeit M, et al. *Eur J Cancer* 2016; **67**: 200-12.
Hirsch HH, Martino R, Ward KN, Boeckh M, Einsele H, Ljungman P. *Clin Infect Dis* 2013; **56**(2): 258-66.
Engelhard D, Mohty B, de la Camara R, Cordonnier C, Ljungman P. *Transpl Infect Dis* 2013; **15**(3): 219-32.

More info: jon.salmanton-garcia@uk-koeln.de | @salmantongarcia

Background

- The EPICOVIDEHA registry, established in 2021, has collected extensive data on SARS-CoV-2 infections in HM patients, aiding clinicians during the COVID-19 pandemic
- Insights from the registry have informed scientific publications and preventive strategies for HM patients
- In 2023, was renamed EPICOVIDEHA-EPIFLUEHA to improve understanding of CARV epidemiology, risk factors, and outcomes in HM patients…

  - SARS-CoV-2
  - Influenza
  - RSV
  - Rhinovirus
  - Parainfluenza
  - Metapneumovirus
  - Enterovirus
  - Adenovirus
  - …

Salmanton-Garcia J, Busca A, Cornely OA, et al. Hemasphere 2021; 5(7): e612.
Salmanton-Garcia J, Marchesi F, Itri F, et al. Hemasphere 2023; 7(11): e970.

More info: jon.salmanton-garcia@uk-koeln.de | @salmantongarcia

UNIKLINIK KÖLN

Global Guideline Program – Candida Diseases

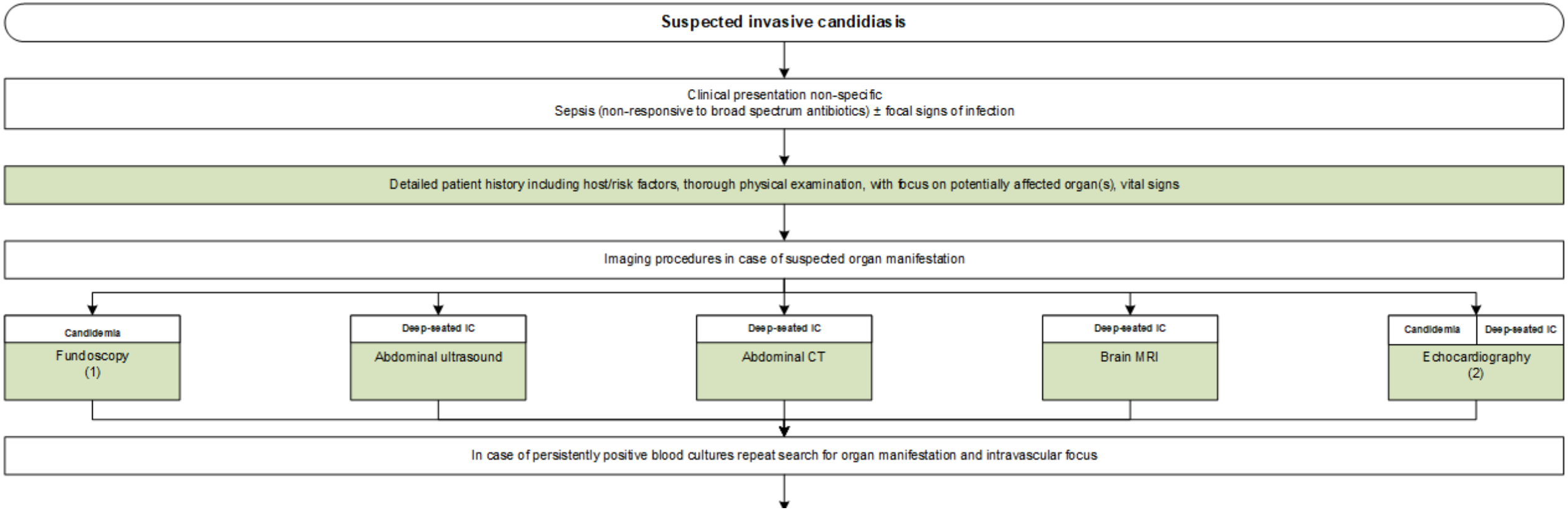
Professor Oliver A. Cornely MD, FECMM, FIDSA, FAAM, FACP

Director and Chair
Institute for Translational Research & Clinical Trials Center
University of Cologne

Consultant, Infectious Diseases
Director, European Mycology Excellence Center
University Hospital of Cologne

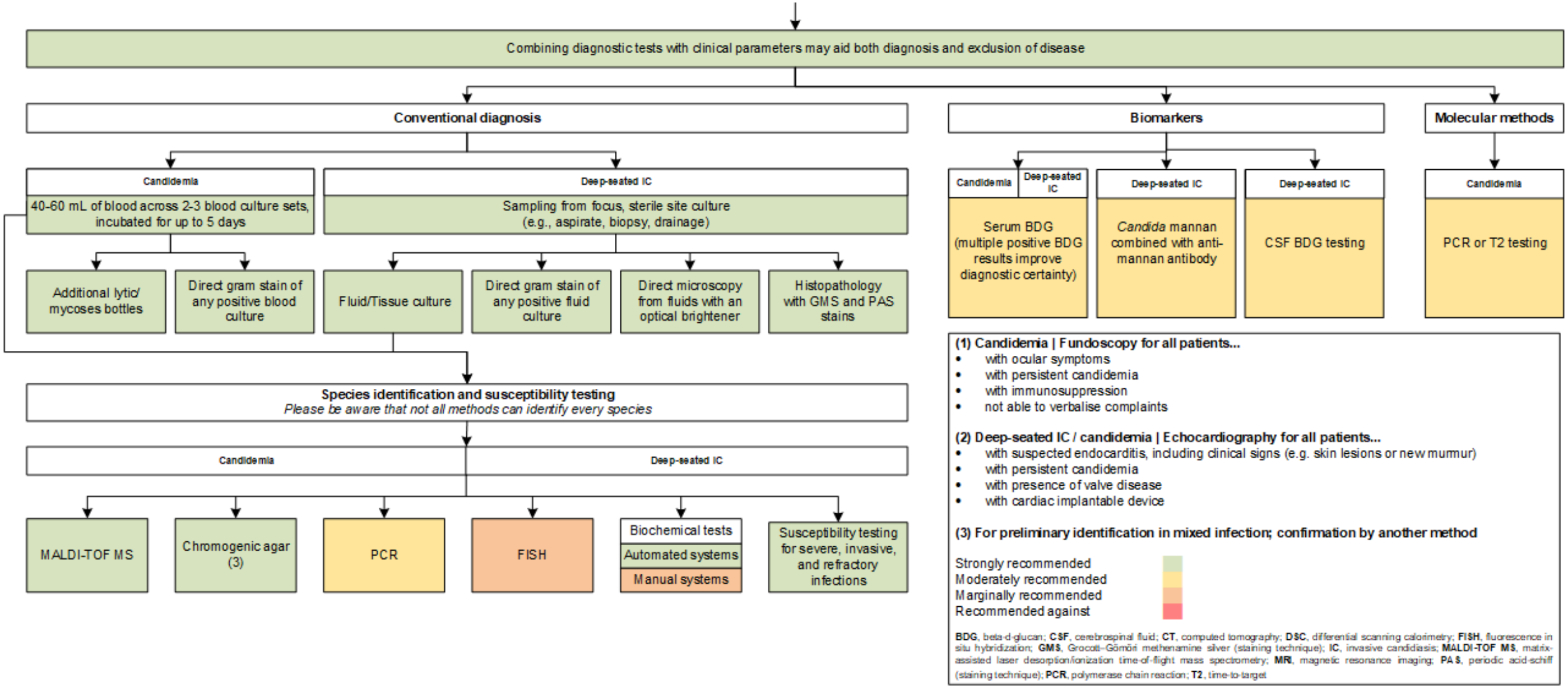
Guideline Convener ECMM

Suspected Invasive Candidiasis 1/2



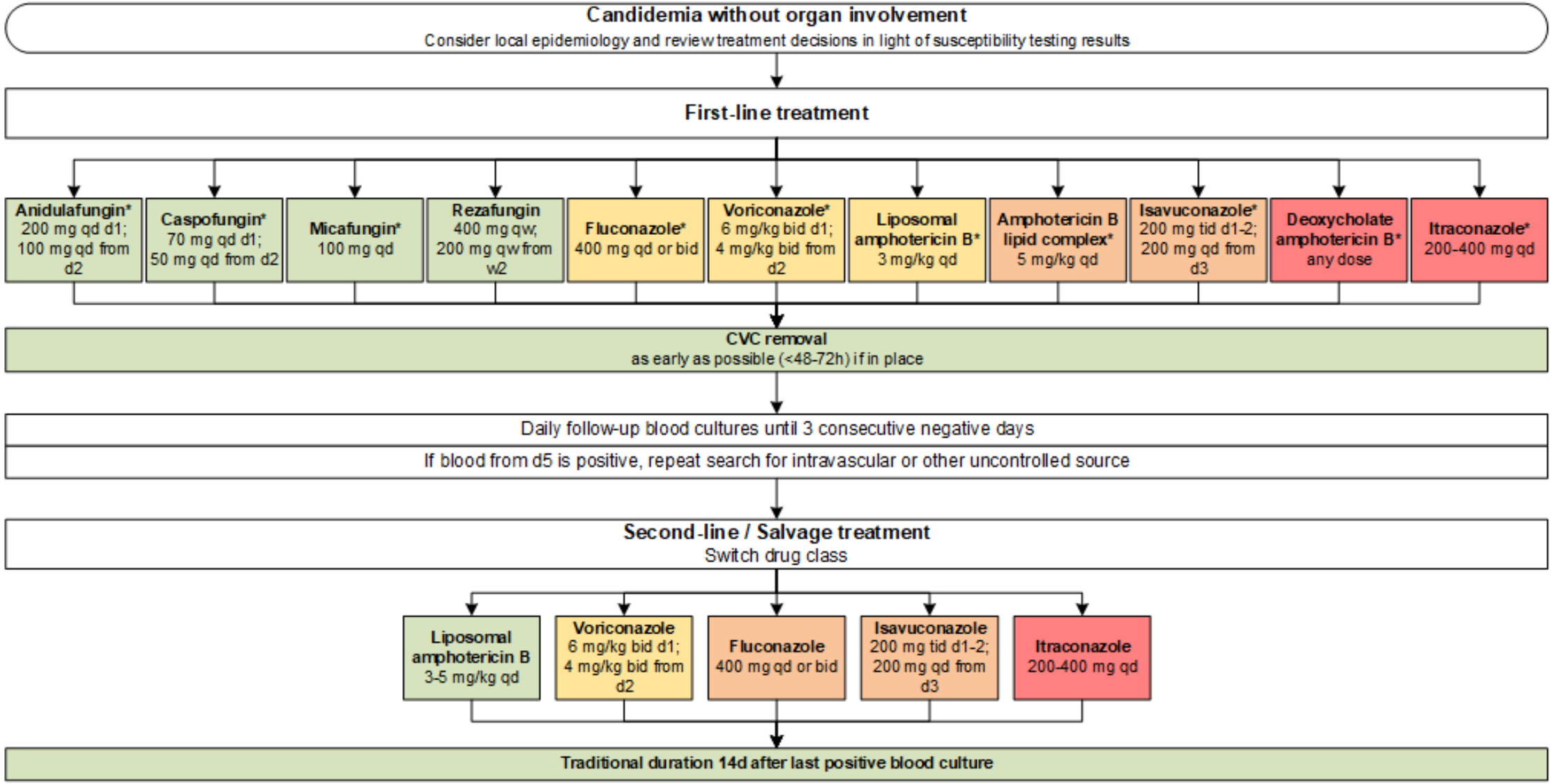
Cornely OA, Sprute R et al. Global Guideline Candida Diseases 2024. Lancet Infect Dis. in press.

Suspected Invasive Candidiasis 2/2



Cornely OA, Sprute R et al. Global Guideline Candida Diseases 2024. Lancet Infect Dis. in press.

Candidemia Management – All Options Available



Cornely OA, Sprute R et al. Global Guideline Candida Diseases 2024. Lancet Infect Dis. in press.

10th EUROPEAN CONFERENCE on INFECTIONS in LEUKAEMIA

An update on primary antifungal prophylaxis

Livio Pagano, Georg Maschmeyer, Frederic Lamoth, Alienor Xhaard,

Ola Blennow, Manuela Spadea, Johan Maertens

Final slide set
Post meeting

CONFERENCE
From September 19th to 21st, 2024

Golden Tulip Sophia Antipolis
Nice, France

AFP in AMLs receiving intensive remission induction/reinduction chemotherapy

Intention	Intervention	SoR	QoE	ECIL 5
Prevent invasive fungal infections in AML patients, excluding allogeneic hematopoietic stem cell transplantation	Posaconazole	A	I[1]	A-I
	Amphotericin B, liposomal, inhalation*[2,3]	B	I	B-I
	Fluconazole[4]	B	I	B-I
	Voriconazole	B	IIu	B-II
	Isavuconazole[2]	B	IIt	NR
	Micafungin	B	II u,t	NR
	Amphotericin B, liposomal, iv[2]	C	II	C-II
	Caspofungin[2]	B	IIt	NR
	Itraconazole, p.o. and i.v.	C	I	B-I
	SUBA-Itraconazole	C	IIt	NR

1 = recommendation for AML under remission induction chemotherapy; 2 = no approval for prophylaxis of invasive fungal infection; 3 = formulation not approved; 4 =Only recommended if the incidence of mould infections is low. Fluconazole may be part of an integrated care strategy together with a mould-directed diagnostic approach

*should be associate to fluconazole;

Footnote: amphotericin deoxycholate is not approved for prophylaxis and should not be considered due to drug-related toxicity

Antifungal Prophylaxis in AMLs Treated with «New Agents» combined with hypomethylating agents (see ECIL 9)

Population	Intention	Intervention	SoR	QoE
Venetoclax	Prevent IFD	Use triazole antifungal prophylaxis, if neutropenia ≥7 days is expected or present	**B**	**IIu,t**
	Prevent toxicity	Reduce dose of venetoclax by at least 75 % in combination with posaconazole or voriconazole and by 50% in combination with fluconazole or isavuconazole	**A**	**IIu,t**
Ivosidenib	Prevent IFD	If neutropenia ≥7 days is expected or present, use triazole antifungal prophylaxis concomitantly to ivosidenib	**B**	**III**
	Prevent toxicity	Reduce ivosidenib dose to 250 mg/day in combination with posaconazole or voriconazole	**B**	**III**

Antifungal prophylaxis in preventing invasive aspergillosis in AML patients undergoing consolidation therapy: SEIFEM

- Cases of IA observed **during consolidation** in adult/paediatric AML patients between 2011 and 2015, retrospectively collected in a multicentre Italian study
- Of **2588 patients**, 56 (2.2%) developed IA [43 probable (1.7%) and 13 proven (0.5%)]
- **IA diagnosed in 34/1137 (2.9%) patients receiving no AP and in 22/1451 (1.5%) who were given AP (p = 0.01)**
- NNT calculation: on average, 71 patients should have received AP (instead of no AP) for 1 additional patient to not have IA
- Overall mortality rate and mortality rate attributable to IA by day 120: 16% and 9%
- Multivariate analysis: **age ≥ 60 years** (OR 12.46, 95% CI 1.13-136.73; p = 0.03) and **high-dose cytarabine** treatment (OR 10.56, 95% CI 1.95-116.74; p = 0.04) **independently affected outcome**
- „AP appears to prevent IA from occurring during consolidation“

An AFP with posaconazole can be considered in consolidation phase of AML, especially in older patients or those receiveing high dose AraC : B IIt

Del Principe et al, J Antimicrob Chemother 2019

Recommendation for MDS, CML, and MPN

Population	Intention	Intervention	SoR	QoE	ECIL 5
MDS low-/ntermediate	No chemotherapy	No prophylaxis	D	I	No recommendation
MDS Intermediate/High	Treated as AML With intensive chemotherapy	Posaconazole prophylaxis	A	I	As for AML
MDS Intermediate/High	Treated with azacytidine	Posaconazole prophylaxis during the first 4 aza courses	B	IIu	No recommendation
CML	Treated with TKI	No prophylaxis	D	I	No recommendation
MPN	No chemotherapy	No prophylaxis	D	I	No recommendation
MPN	Treated with ruxolitinib	No prophylaxis	D	I	No recommendation

Acute lymphoblastic leukemia in adults - Recommendations

Previous recommendations:

ECIL [1]

- Against use of mold-active azoles (hazardous interactions with Vinca alkaloids)
- Cautious use of fluconazole to prevent yeast infection (C III)

ESCMID-ECMM-ERS [2]

- ALL induction: L-AMB D I

AGIHO / DGHO [3]

- ALL induction / re-induction included in «neutropenia >7 days»: posaconazole A I (strong only for AML)

Australasian Antifungal Guidelines Steering Committee [4]

- ALL induction / re-induction included in «high-risk»: A I

Proposed recommendations:

Mold-active azoles (voriconazole and posaconazole) are not recommended (hazardous interactions with Vinca alkaloids). **D II**

Cautious use of fluconazole and isavuconazole to prevent yeast infection (**C III)**

Alternative anti-mold prophylaxis (e.g. L-AMB, echinocandins) might be considered in high risk patients (induction chemotherapy, prolonged neutropenia) but no benefit has been shown

No prophylaxis for patients treated with TKIs **(D III)**

Chronic lymphoid leukemia - Recommendations

Previous recommendations:

ECIL [1]

- AF not recommended (might be considered in case of prolonged neutropenia, unresponsive CLL)

ESCMID-ECMM-ERS [2]

- No recommendation provided

ESCMID-ESGICH [3]

- Ibrutinib: AF not recommended (close monitoring)

ESMO [4]

- AF not recommended

AGIHO / DGHO [5]

- No recommendation provided (only venetoclax in AML: A II)

Australasian Antifungal Guidelines Steering Committee [6]

- Treatment-naïve CLL: no prophylaxis (B II)

Proposed recommendations:

AF prophylaxis not recommended (**D III**) but may be considered in selected cases with refractory CLL and prolonged neutropenia or BTKIs therapy (**C II**).

1. Maertens et al. *J Antimicrob Chemother* 2018; 73:3221-30; 2. Ullmann et al. *Clin Microbiol Infect* 2018; 24: e1-e38; 3. Reinwald et al. *Clin Microbiol Infect* 2018; 24:S53-S70; 4. Eichhorst et al. *Ann Oncol* 2021; 32:23-33; 5. Stemler et al. *J Antimicrob Chemother* 2023; 78:1813-26; 6. Teh et al. *Intern Med J* 2021; 51 Suppl 7:67-88

Non-Hodgkin Lymphoma - Recommendations

Previous recommendations:

ECIL [1]

- AF not recommended (low IFI incidence)

ESCMID-ECMM-ERS [2]

- No recommendation provided

ESCMID-ESGICH [3]

- Ibrutinib: AF not recommended (close monitoring)

AGIHO / DGHO [4]

- No recommendation provided

Australasian Antifungal Guidelines Steering Committee [5]

- Lymphoma intensive/dose-escalated therapy (low risk): FLC (ITZ or echinocandins) B II
- Lymphoma other (very low risk): no AF prophylaxis B II

Proposed recommendations:

AF prophylaxis not recommended (**D II**). Might be considered in selected patients with refractory lymphoma and/or repeated intensive chemotherapies with neutropenia or high doses steroids or BTKis therapy (**C II**)

1. Maertens et al. *J Antimicrob Chemother* 2018; 73:3221-30; 2. Ullmann et al. *Clin Microbiol Infect* 2018; 24: e1-e38; 3. Reinwald et al. *Clin Microbiol Infect* 2018; 24:S53-S70; 4. Stemler et al. *J Antimicrob Chemother* 2023; 78:1813-26; 5. Teh et al. *Intern Med J* 2021; 51 Suppl 7:67-88

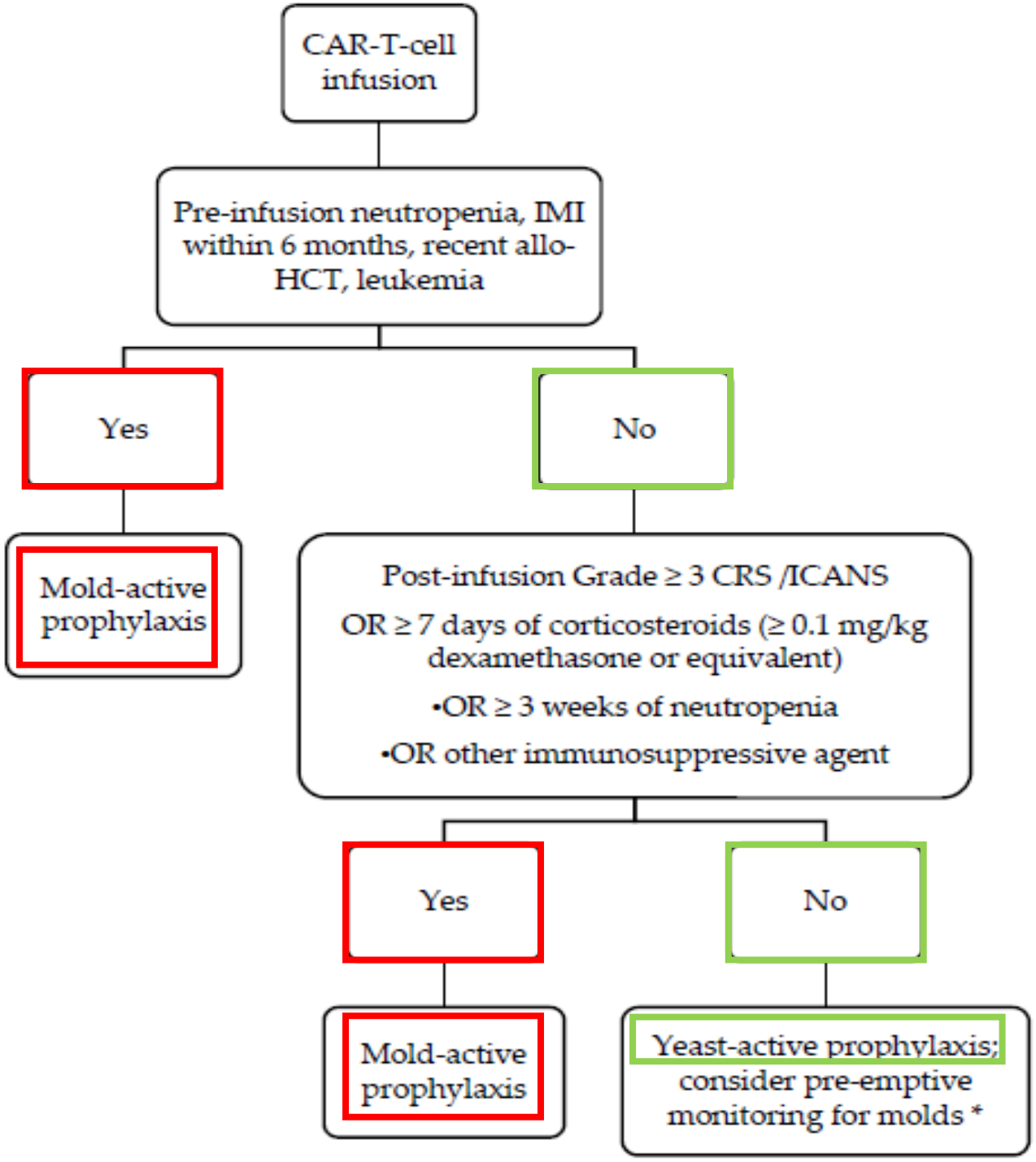
Recommendations for Hodgkin' Lymphoma and Myeloma

- **HD**
  - ECIL 5 and 6: "Patients with lymphoma tend to be at low risk of IFD", with no specific recommendation given. **No change.**

- **Myeloma**
  - Conventional chemotherapy or IMIDs: **No prophylaxis**
  - Bispecific ab:
    - Data insufficient for recommendation
    - Expert panels suggest to consider mold active prophylaxis in high-risk populations such as prolonged neutropenia or prolonged steroid treatment or secondary prophylaxis (no trials)
  - Belantamab
    - Low risk: No antifungal prophylaxis recommended or No recommendations can be made

AntiCD19 CART cells

Panel proposes to **endorse these recommendations (B II)**



Garner et al, J of Fungi 2021

Studio GIMEMA
INF0123

- Tipologia Studio: Osservazionale
- **NCT06025682**

Multicenter retrospective observational study analyzing infective complications and the clinical outcome of patients with acute lymphoblastic leukemia treated with inotuzumab ozogamicin (INO-FIRST)

Sponsor — Fondazione GIMEMA – Franco Mandelli ONLUS
Coordinating Investigator — Livio Pagano
Co-Principal Investigator — Anna Candoni
Principal Investigator of the Coordinating center – Luana Fianchi
Coordinating center — Clinica Ematologica - Fondazione Policlinico Universitario A. Gemelli, IRCCS-Università Cattolica del Sacro Cuore, Roma

Primary objective

To evaluate the clinically or microbiologically documented infectious complications (bacterial, fungal, viral) in patients receiving inotuzumab ozogamicin (INO) up to 60 days after the end of treatment (last dose administered).

Secondary objectives

To evaluate:

- the infection-related mortality in patients receiving inotuzumab ozogamicin (INO) up to 60 days after the end of treatment (last dose administered);
- the impact of infective complications on therapeutic program;
- overall survival (OS);
- hospital admission due to infective and non-infective complications;
- allo-SCT feasibility after INO;
- the mortality attributable to non-infective complications;
- the use of antibacterial, antifungal and antiviral prophylaxis and therapy;
- infectious and non-infectious complications occurring in patients receiving allo-SCT after INO;
- incidence of infective complications according to clinico-biological features of the disease;
- impact of infective complications on the OS.

Study Design

The present study is a multicenter, retrospective, observational clinical-epidemiological study. The study collects data from about 20 Hematologic Centers of the GIMEMA Group treating B-ALL patients with INO over the last 5 years (2018-2023), according to the authorized indications and not included in interventional clinical trials (randomized or not randomized).

Study Duration

Data collection for each single patient will be conducted retrospectively for all cases observed who started INO between May 21st 2018 (AIFA approval) and December 31st 2023. Each patient will be observed for a minimum of 12 months. Data analysis completion is scheduled on June 30th 2024

Sample size

The presumed sample size is of approximately 250 patients

Eligibility criteria

- Adult patients (>18 years old)
- Patients with relapsed/refractory CD-22 positive B-ALL treated with INO or with relapsed/refractory CD22 positive and Ph-positive B-ALL treated with INO after failing at least one TKI inhibitor
- Signed informed consent if applicable.

Non-eligibility criteria

- Patients treated with INO in interventional clinical trials

Laboratorio SEIFEM

Le problematiche infettive nel paziente ematologico

Roma, 12 novembre 2024
Best Western Plus Hotel Universo

Presidente
Livio Pagano

Con il Patrocinio di
SIE - Società Italiana di Ematologia

ADELE SANTONI

Università degli Studi di Siena

Incidenza di complicanze INfettive durante chemioterapia di induzione in pazienti affetti da Leucemia Acuta Mieloide profilassati e non con FLUorchinoloni: studio ossErvazioNale retrospettivo multiCEntrico di Real life (Studio INFLUENCER)

BACKGROUND

Prophylaxis with fluoroquinolones (FQ) during neutropenia is still recommended in most guidelines because it reduces infection rate and febrile episodes, while not affecting infection-related mortality (IRM).

NCCN Guidelines Version 3.2024

Overall Infection Risk in Patients with Cancer[a]	Disease/Therapy Examples	Antimicrobial Prophylaxis
Low	• Standard chemotherapy regimens for most solid tumors • Anticipated neutropenia* <7 days	• Bacterial - None • Fungal - None • Viral - None unless prior HSV episode
Intermediate	• Autologous HCT • Lymphoma[c] • Multiple myeloma[c] • CLL[c] • Purine analog therapy (ie, fludarabine, clofarabine, nelarabine, cladribine) • Anticipated neutropenia* 7–10 days • CAR T-cell therapy	• Bacterial - Consider fluoroquinolone prophylaxis during neutropenia[d] • Fungal - Consider prophylaxis during neutropenia and for anticipated mucositis (INF-2); consider PJP prophylaxis (NF-6) • Viral - During neutropenia and longer depending on risk (INF-3, INF-4, INF-5) • See Immune and Targeted Treatments (INF-A 11 of 13)
High[b]	• Allogeneic HCT including cord blood • Acute leukemia ▸ Induction ▸ Consolidation/maintenance • Alemtuzumab therapy • Moderate to severe GVHD • Anticipated neutropenia* >10 days	• Bacterial - Consider fluoroquinolone prophylaxis during neutropenia[d] • Fungal - Consider prophylaxis during neutropenia (INF-2); consider PJP prophylaxis (INF-6) • Viral - During neutropenia and longer depending on risk (INF-3, INF-4, INF-5) • Length of prophylaxis depends on immune reconstitution.

*Neutropenia: ≤500 neutrophils/mcL or ≤1000 neutrophils/mcL and a predicted decline to ≤500/ mcL over the next 48 hours.

BACKGROUND

- **During last years FQ-resistant bacterial strains rate has increased, especially in Italy.** (Piano Nazionale di Contrasto dell'Antimicrobico-Resistenza (PNCAR) 2017-2020.)

- **For this reason, some centers starting to omit antibiotic prophylaxis in neutropenic hematologic patients, in areas with FQ resistance >30%.** (Ng ES, Leuk Lymphoma, 2011)

- **Since 2014, we also started to omit FQ prophylaxis in neutropenic haematologic patients underwent high-dose chemotherapy.**

AIMS

- **The study aims to verify the efficacy of FQ antibacterial prophylaxis during induction chemotherapy in patients with Acute Myeloid Leukemia**
- **Primary end point: Incidence of microbiologically documented bacterial infectious complications and related mortality during induction in the group with FQ prophylaxis and in the group without FQ prophylaxis**
- **Secondary end point:**
  - **Incidence of fever**
  - **Incidence of FUO**
  - **Bacterial and MDR epidemiology**
  - **OS (40 days)**
  - **Median hospitalization**
  - **Response to induction cht**

STUDY DESIGN

- **Observational, retrospective, multicenter, non commercial (non profit) clinical study.**

- **Retrospective data collection of consecutive AML patients who received high dose induction chemotherapy with or without Fluoroquinolone prophylaxis according to daily clinical practice, between 2018 and 2023.**

- **Starting data: 20.05.2024**

INCLUSION CRITERIA

- **Acute Myeloid Leukemia patients (NO Acute Promyelocitic Leukemia) eligible for high dose induction chemotherapy.**

- **Patients treated with high dose induction chemotherapy with**

  3+7 regimen (+/- inibitori di FLT3)

  fludarabine-based regimens

  CPX-351

  with or without FQ prophylaxis

- **Age ≥ 18 years**

- **Signed informed consent, only requested for alive follow-up patients**

Laboratorio SEIFEM

Le problematiche infettive nel paziente ematologico

Roma, 12 novembre 2024
Best Western Plus Hotel Universo

Presidente
Livio Pagano

Con il Patrocinio di
SIE - Società Italiana di Ematologia

Dott.ssa Elisa Buzzatti

Studio SEIFEM-GilteRInf 2022 (studio osservazionale sull'incidenza di infezioni in pazienti con leucemia mieloide acuta recidivata/refrattaria FLT3+ trattati con Gilteritinib)

OBJECTIVES

- To assess the absolute risk of infection in 'real-world' patients treated with Gilteritinib and compare it to patients receiving chemotherapy
- To assess the type, incidence, and outcome of bacterial, fungal, and viral infections
- To assess the need for hospitalization and its duration
- To analyze the different antifungal prophylaxis policies in various Hematology Centers and correlate them with the incidence of infection
- To analyze the incidence of adverse events associated with the concomitant use of antifungal, antibacterial, and antiviral agents (prophylaxis/therapy) in combination with Gilteritinib

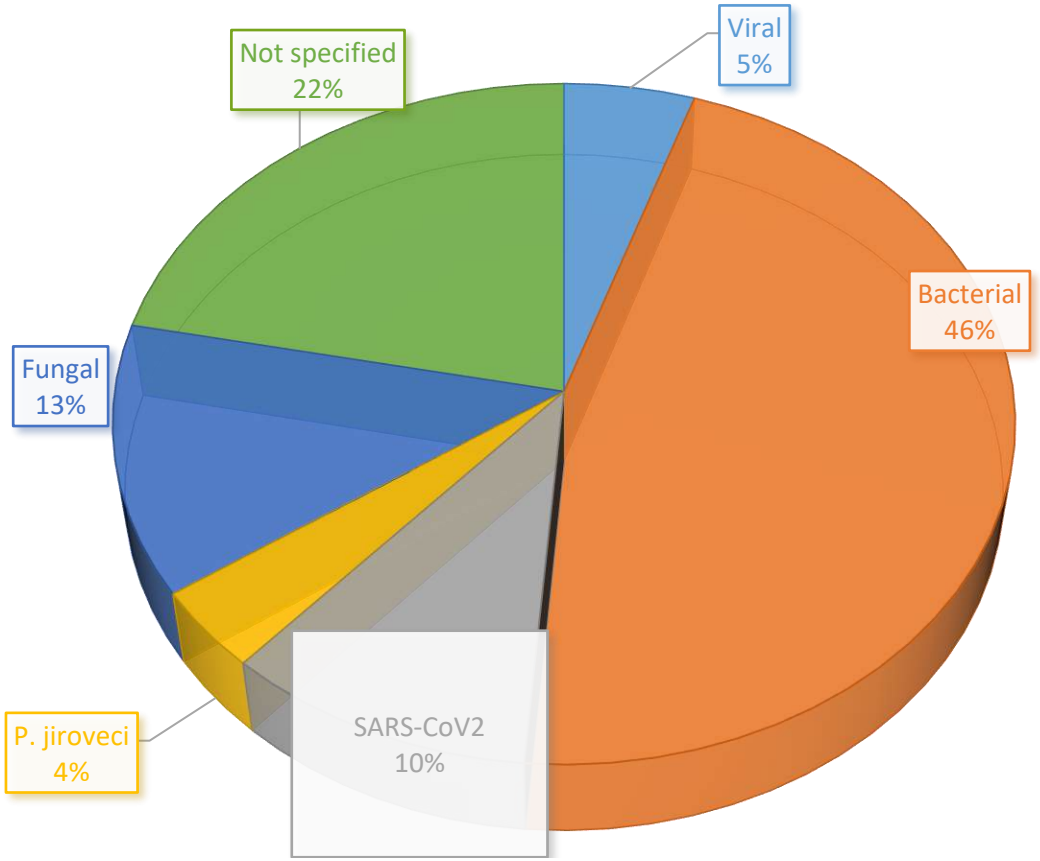
CASE-CONTROL COMPARISON

		GRUPPO			
		Gilteritinib	CT	Totale	
N_infezioni_CATE	nessuna	41	4	45	p=0,031
		91,1%	8,9%	100,0%	
		44,1%	28,6%	42,1%	
	1 infezione	39	4	43	
		90,7%	9,3%	100,0%	
		41,9%	28,6%	40,2%	
	2+ infezione	13	6	19	
		68,4%	31,6%	100,0%	
		14,0%	42,9%	17,8%	
Totale		93	14	107	
		86,9%	13,1%	100,0%	
		100,0%	100,0%	100,0%	

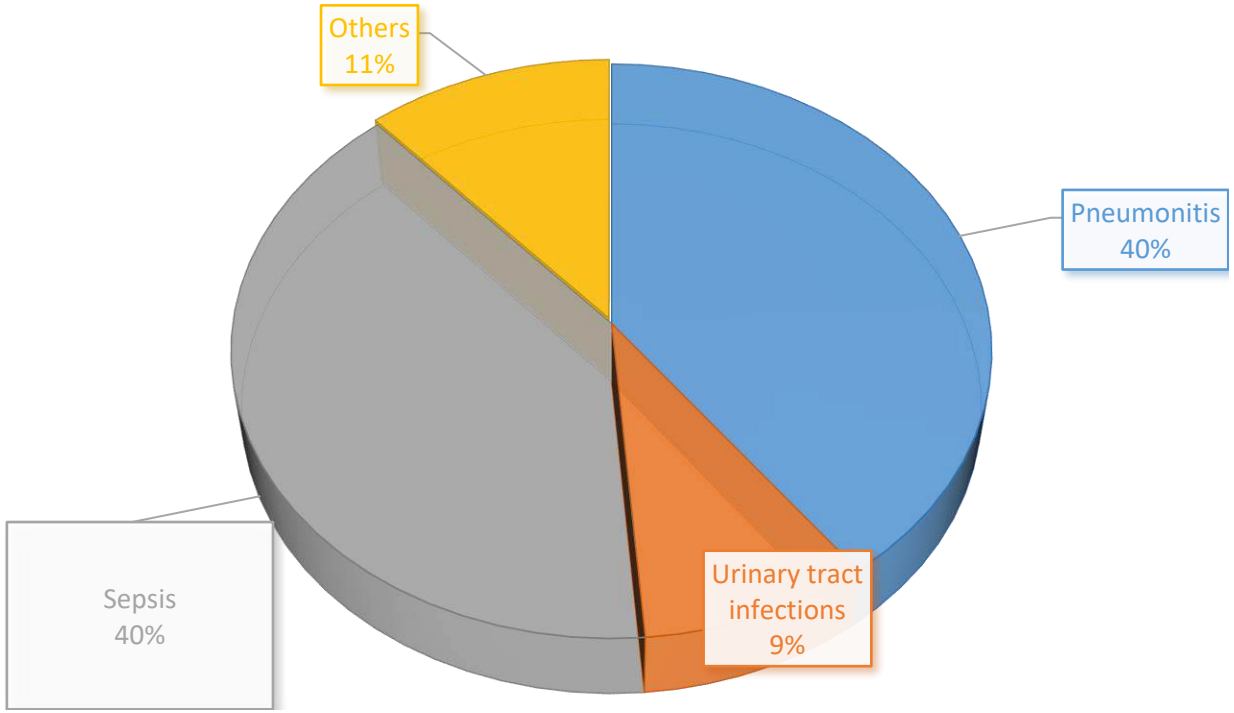
		GRUPPO			
		Gilteritinib	CT	Totale	
infezione_batterica	no	54	6	60	p=0,057
		90,0%	10,0%	100,0%	
		58,1%	42,9%	56,1%	
	si	26	8	34	
		76,5%	23,5%	100,0%	
		28,0%	57,1%	31,8%	
	UK	13	0	13	
		100,0%	0,0%	100,0%	
		14,0%	0,0%	12,1%	
Totale		93	14	107	
		86,9%	13,1%	100,0%	
		100,0%	100,0%	100,0%	

In Gilteritinib group, the number of patients with no infectious event was significantly higher than in the control arm (p=0.031), but no statistical difference was found regarding the grades of the infections according to common toxicity criteria of adverse event (CTCAE) version 5, the number of pts with IFD and fever of undetermined origin (FUO). A trend of significance was observed regarding the number of pts with bacterial events (p=0.057).

TYPES OF INFECTION IN GILTERITINIB ARM 1/2



TYPES OF INFECTION IN GILTERITINIB ARM 2/2



ASSOCIATED DRUGS IN GILTERITINIB ARM

	Cytocrome CYP3A, P-gp inducers	Cytocrome CYP3A, P-gp e/o BCRP inhibitors
	None	
		Voriconazole: 1 patient
		Fluconazole: 1 patient

4 (11%) cases of toxicities, with 1 prolonged QTc e 1 liver toxicity

IN CONCLUSION

- In summary, there is a difference in the incidence of infection between the two arms, but the comparison needs further confirmation by expanding the control group.
- Gilteritinib therapy is not free from infectious complications, but most of the patients recovered within 30 days.
- The mortality rate attributable to infection was not negligible and having at least one infective event emerges as a risk factor for reduced survival.
- Almost all the fatal pneumonitis were fungal, but they occurred in a frail subgroup of pts resistant to Gilteritinib
- The role of prophylaxis needs to be carefully evaluated in this setting of patients, especially given that azoles appear to be quite safe in association with Gilteritinib.

Laboratorio SEIFEM

Le problematiche infettive nel paziente ematologico

Roma, 12 novembre 2024
Best Western Plus Hotel Universo

Presidente
Livio Pagano

Con il Patrocinio di
SIE - Società Italiana di Ematologia

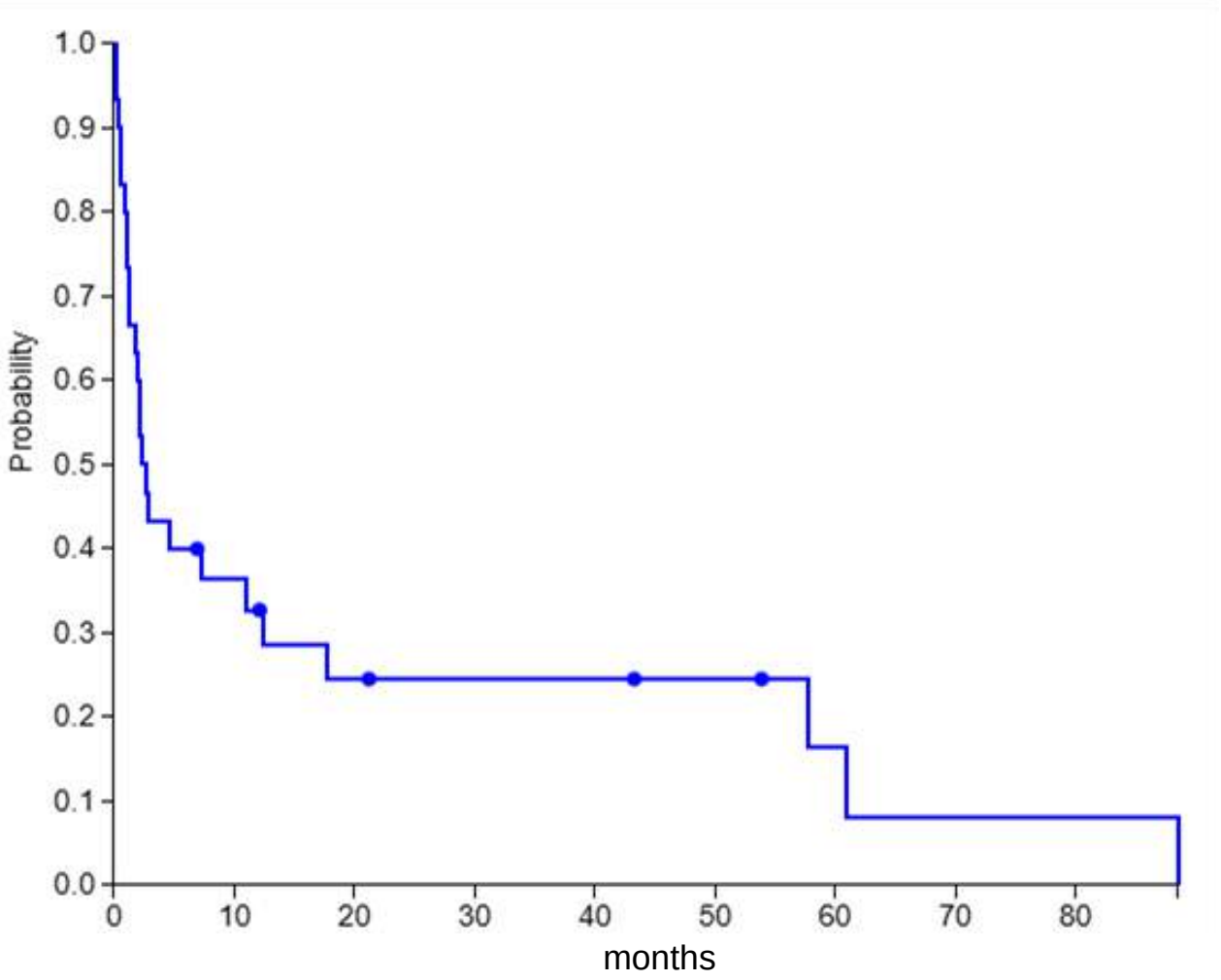
Davide Facchinelli
U.O.C. Ematologia, Ospedale San Bortolo, Vicenza

SEIFEM-GIMEMA, Survey

"Clinical, radiological characteristics and outcome of progressive multifocal leukoencephalopathy (PML) in hematologic patients."

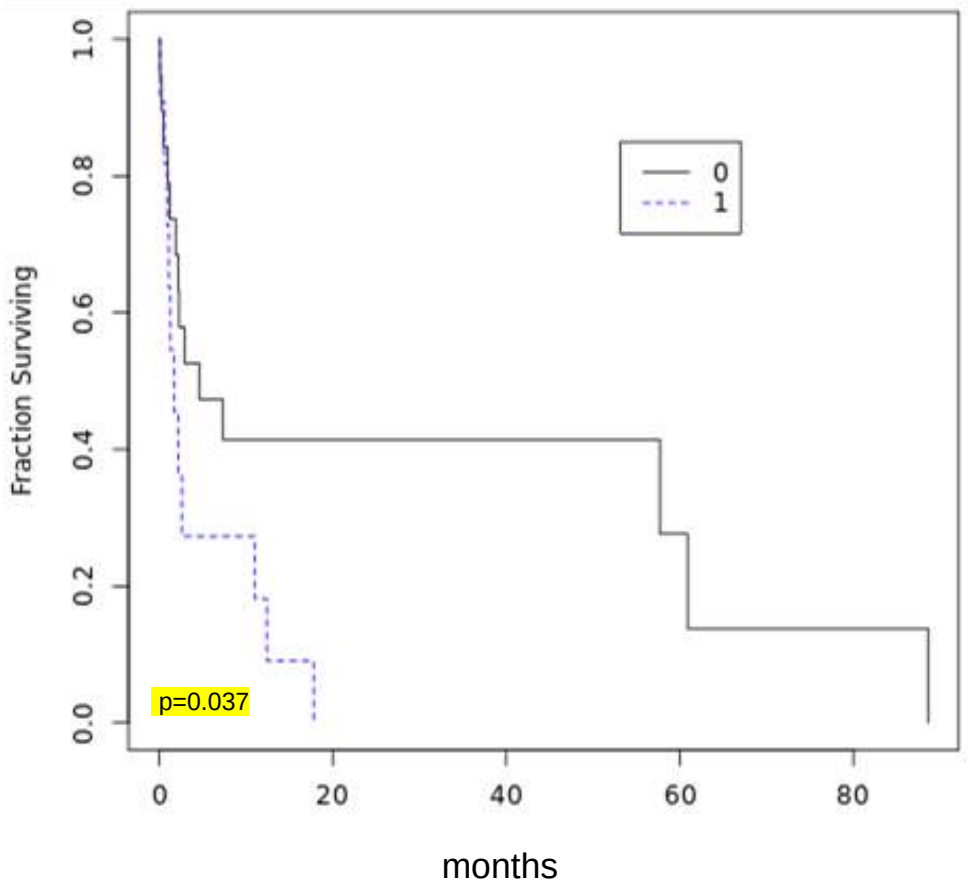
Outcome

- mortality rate 87.3 % (25/30)
- median survival 2.46 months (range 0.07-88.6)

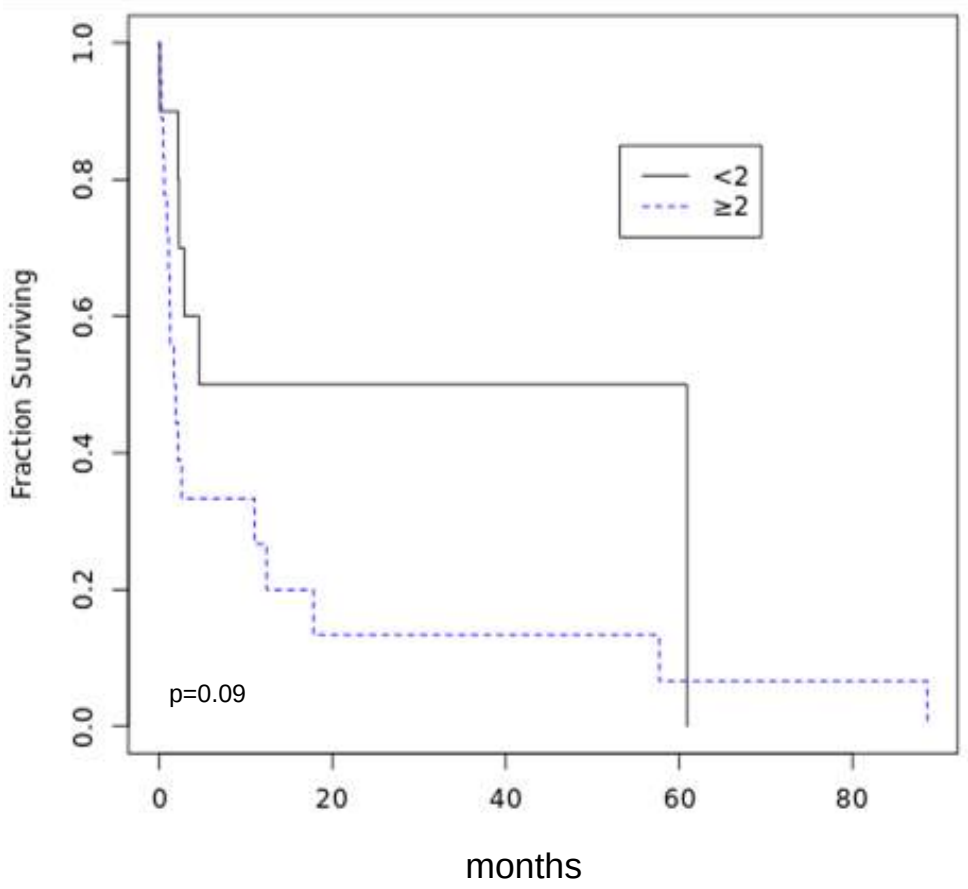


Outcome

Age > 70

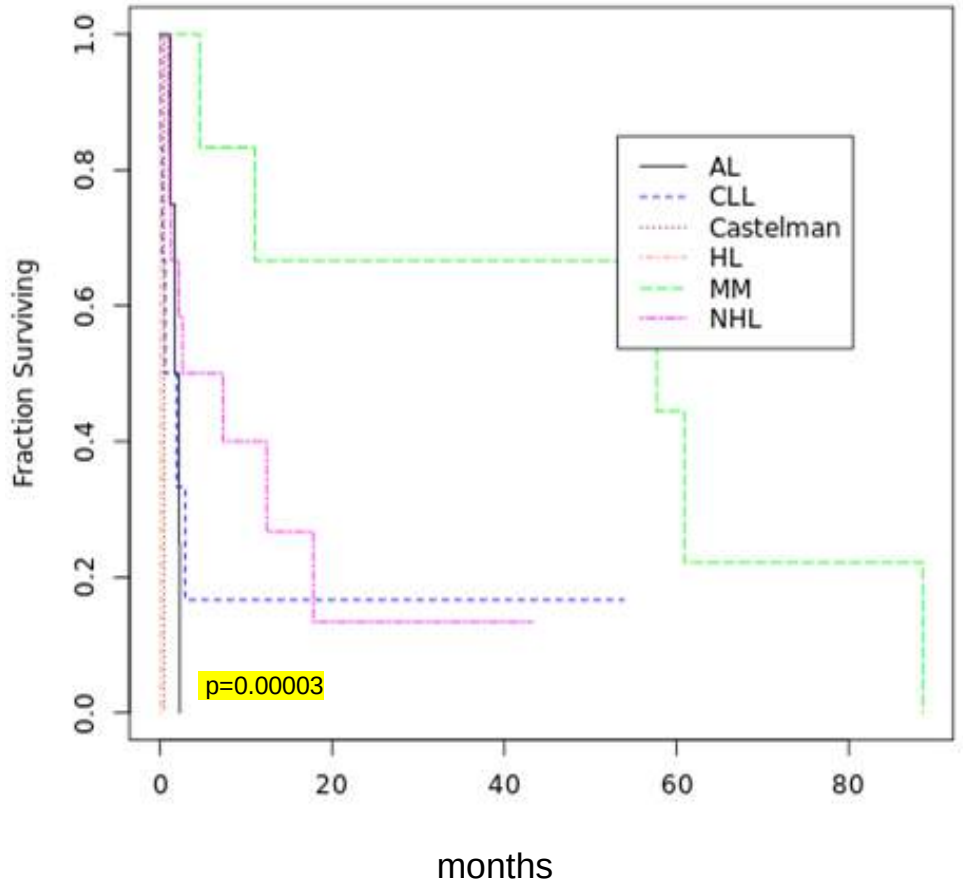


ECOG

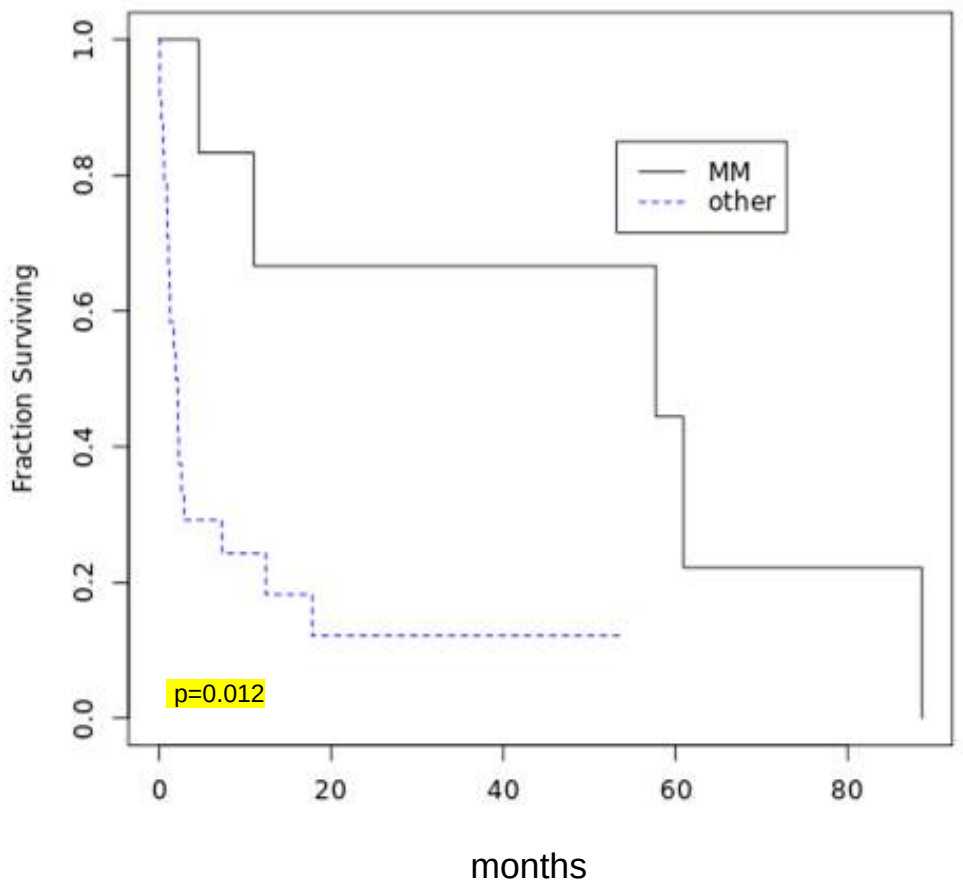


Outcome

Disease

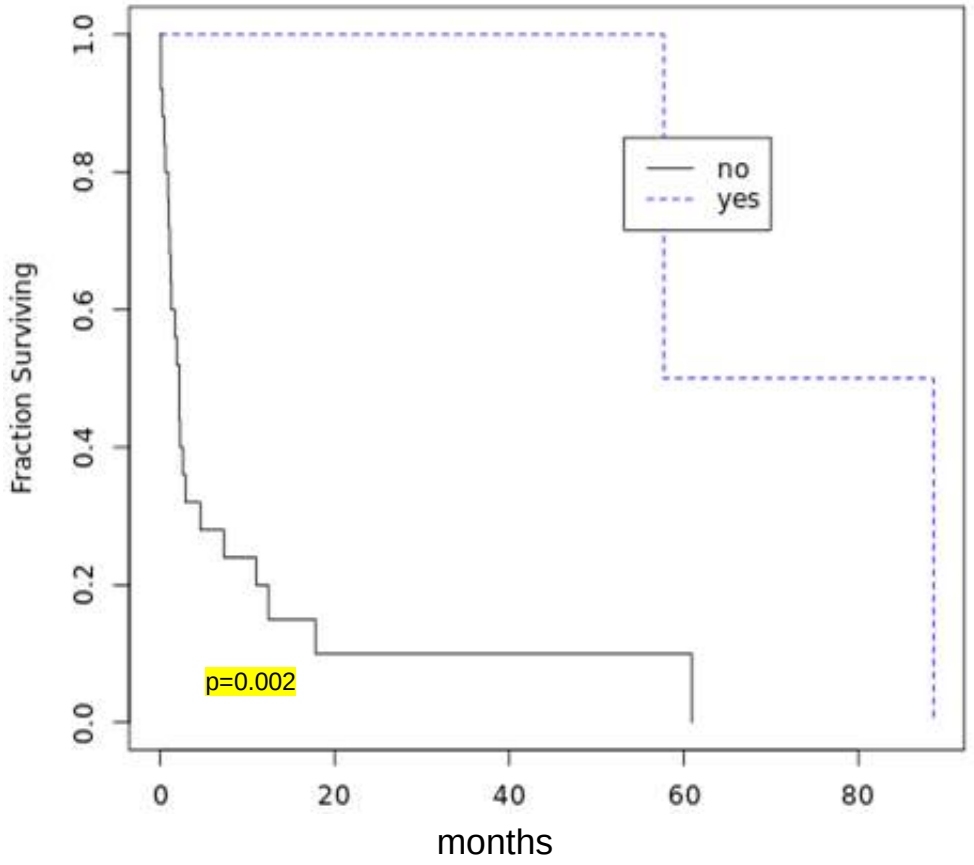


Disease

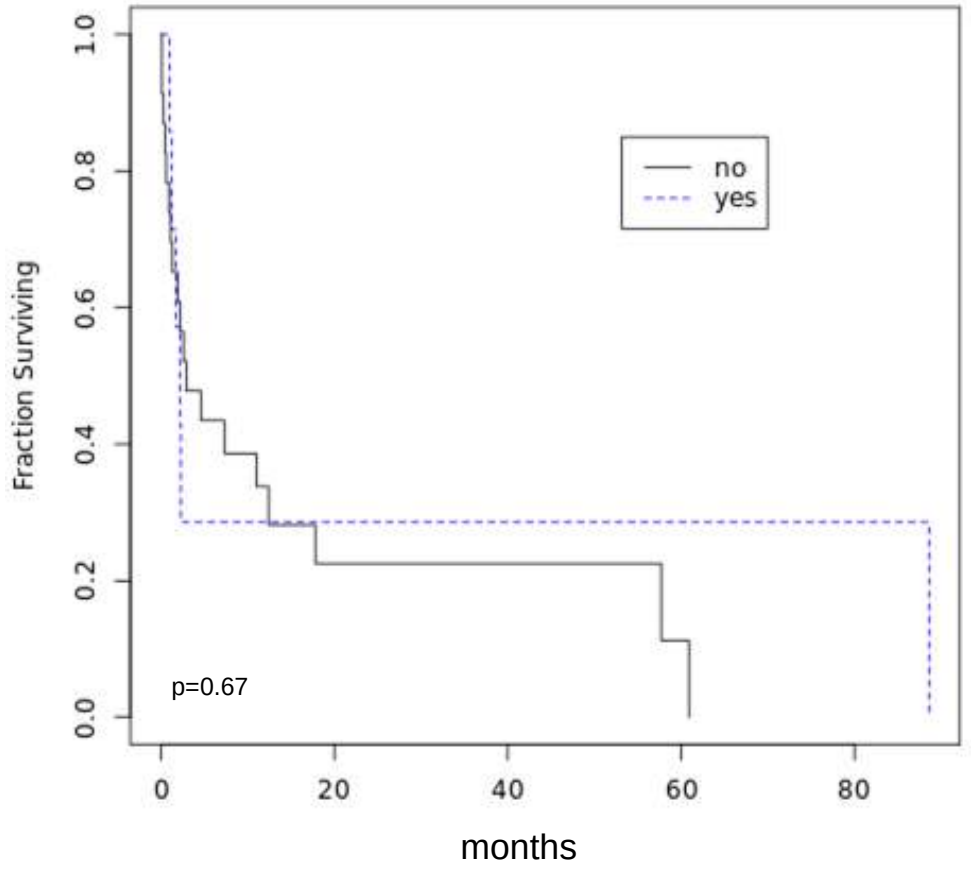


Outcome

ASCT

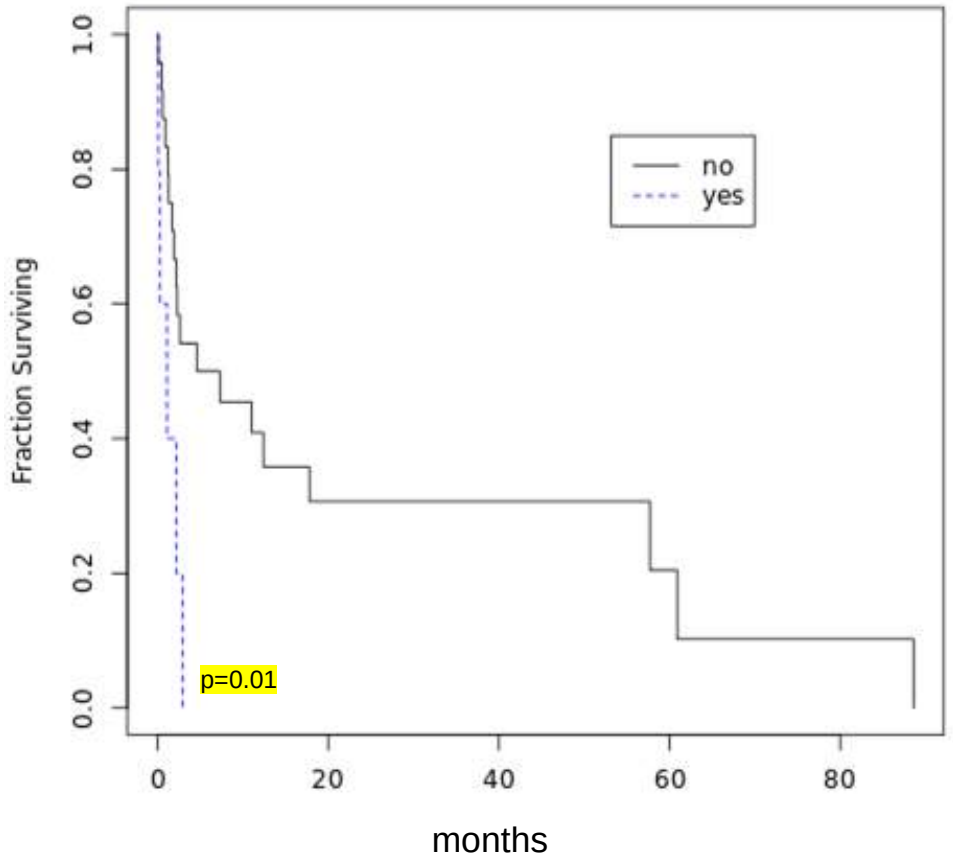


HSCT

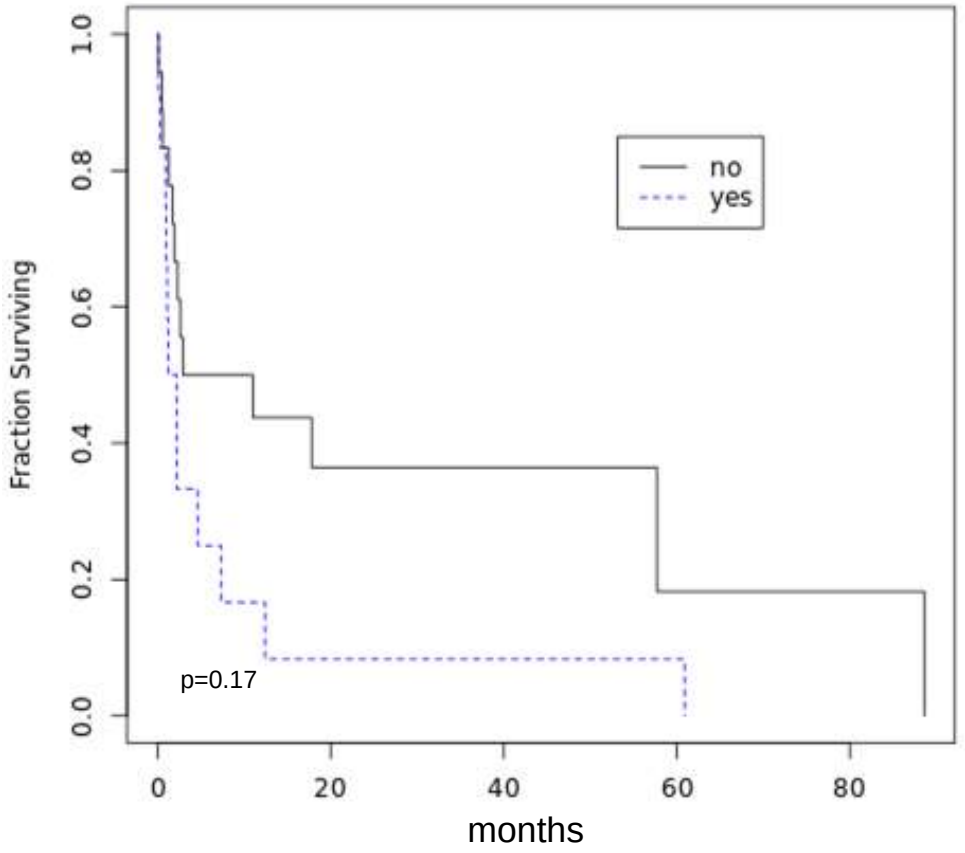


Outcome

neutropenia



lymphopenia



Infectious Complications in Hematological Patients Under Treatment with Bispecific Antibodies. On behalf of European Hematology Association (EHA)

- Dr. Maria S. Infante, University Hospital Infanta Leonor, Madrid, Spain
- Dr. Sigrun Einarsdottir, Sahlgrenska University hospital, Gothenburg, Sweden
- Dr. Jon Salmanton-Garcia, University Hospital of Cologne, Germany
- Dr. Livio Pagano, Fondazione Policlinico Universitario Agostino Gemelli -IRCCS – Università Cattolica del Sacro Cuore, Rome, Italy

Study rationale

- Bispecific therapy: proven efficacy but..
- High infection incidence in trials (gr3 infection 20%)*
- No real world data

*Gemma K Reynolds et al. Blood Adv. 2024 Jul 9;8(13):3555-3559.

Inclusion Criteria

- Adult patients (≥18 years) diagnosed with hematologic malignancies (e.g. multiple myeloma, non-Hodgkin lymphoma) who are receiving treatment with bispecific antibodies
- Patients must have initiated BsAb therapy within 30 days prior to study enrollment
- Ability to provide informed consent

Exclusion Criteria

- Patients with known active infections at the time of BsAb initiation
- Previous treatment with bispecific antibodies in the past 6 months
- Life expectancy of less than 3 months unrelated to infection or malignancy

Objectives

1º objective

-To evaluate **the incidence, type, and severity of infectious complications in hematologic patients undergoing treatment with bispecific antibodies.**

2º objectives

- Identify risk factors associated with infection

- Compare infectious outcomes across different hematologic malignancies and BsAb types

- Assess the impact of infections on overall treatment outcomes.

De-escalation della terapia antibiotica nei pazienti neutropenici con malattia oncoematologica

Marianna Criscuolo

Fondazione Policlinico Universitario A. Gemelli IRCSS

Duration of empiric therapy: NCCN

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2022
Prevention and Treatment of Cancer-Related Infections

NCCN Guidelines Index
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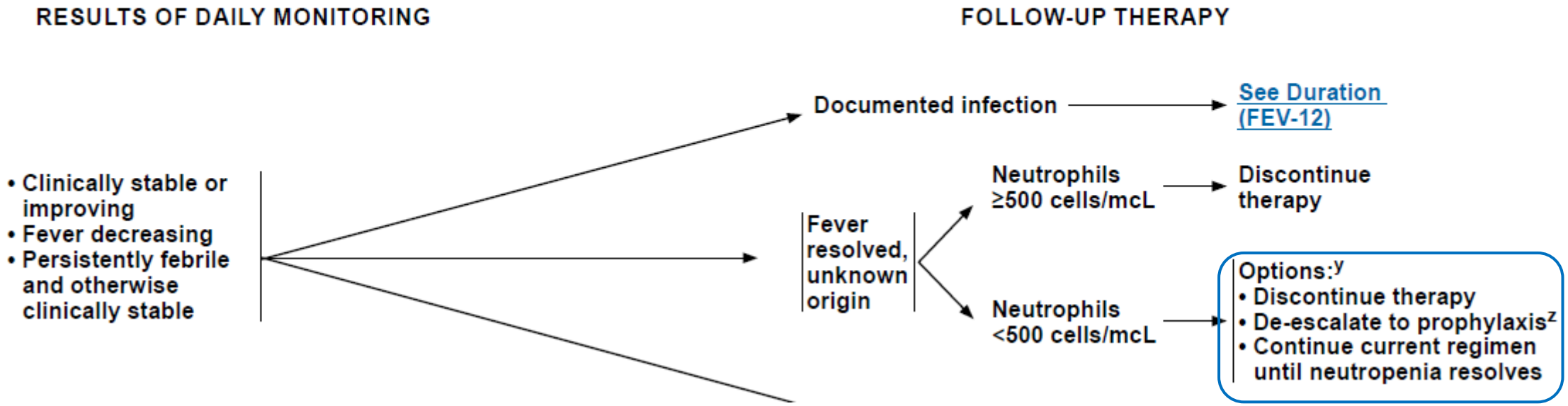
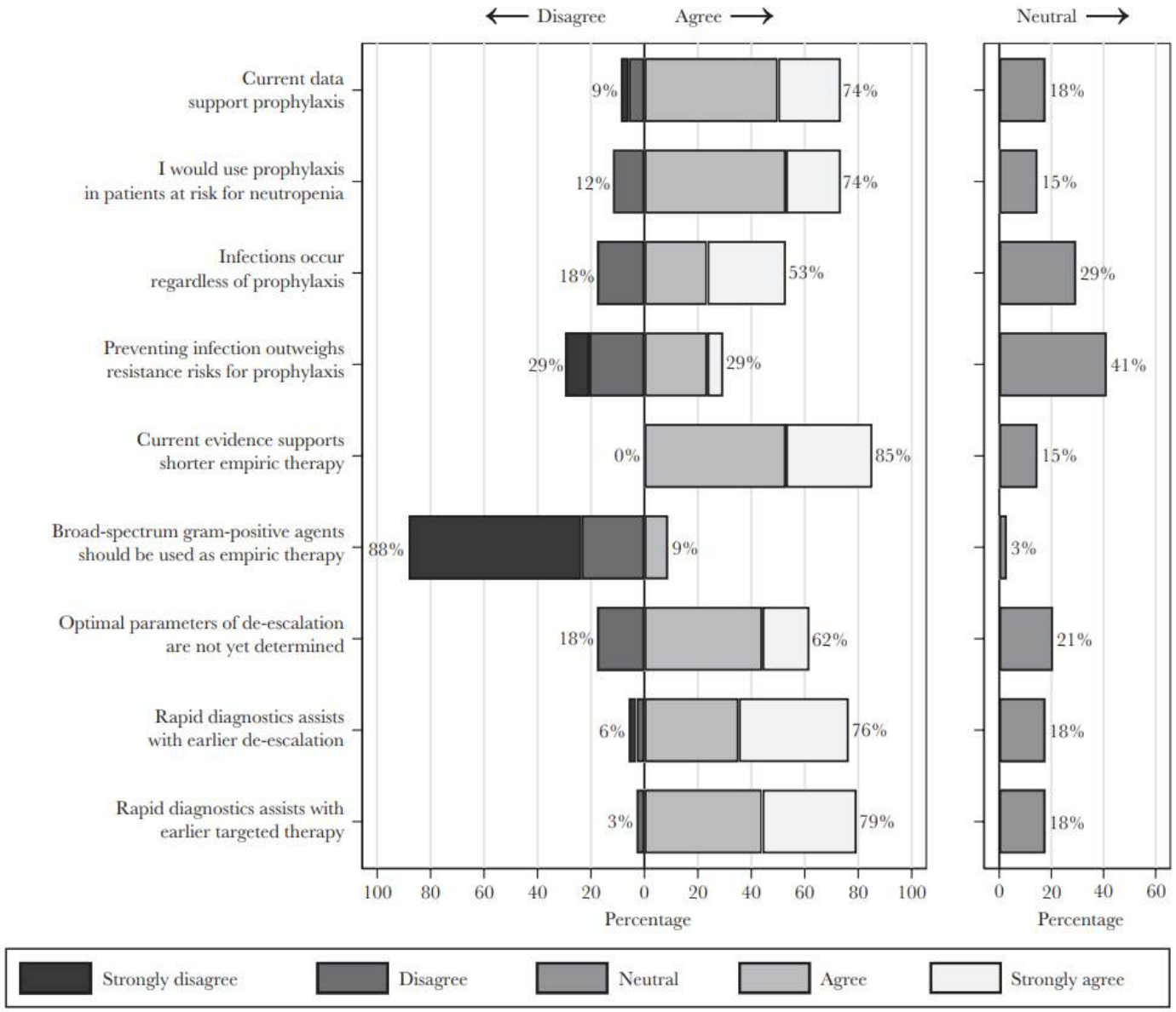
Discussion



https://www.nccn.org/guidelines/category_3



Open Forum Infectious Diseases
MAJOR ARTICLE

Variation in Clinical Practice and Attitudes on Antibacterial Management of Fever and Neutropenia in Patients With Hematologic Malignancy: A Survey of Cancer Centers Across the United States

62% had institutional guidelines from de-escalation of broad spectrum Gram – antibacterial therapy:

83% restarting antibacterial prophylaxis

53% recovery from clinically documented infections without microbiological isolates

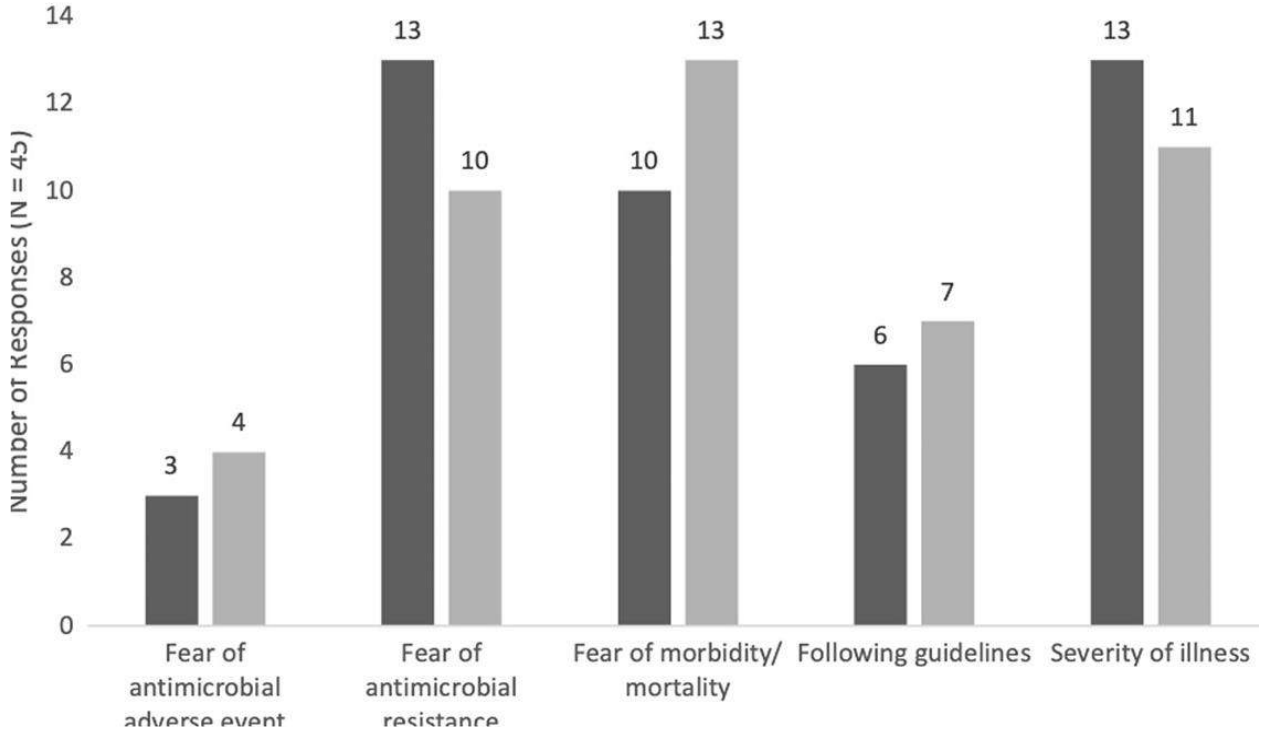
71% clinically stable without source of infection but still neutropenic

8% continue empiric broad spectrum Gram – antibacterial therapy until recovery of neutropenia

Barreto et al. Open Forum Inf Dis 2022

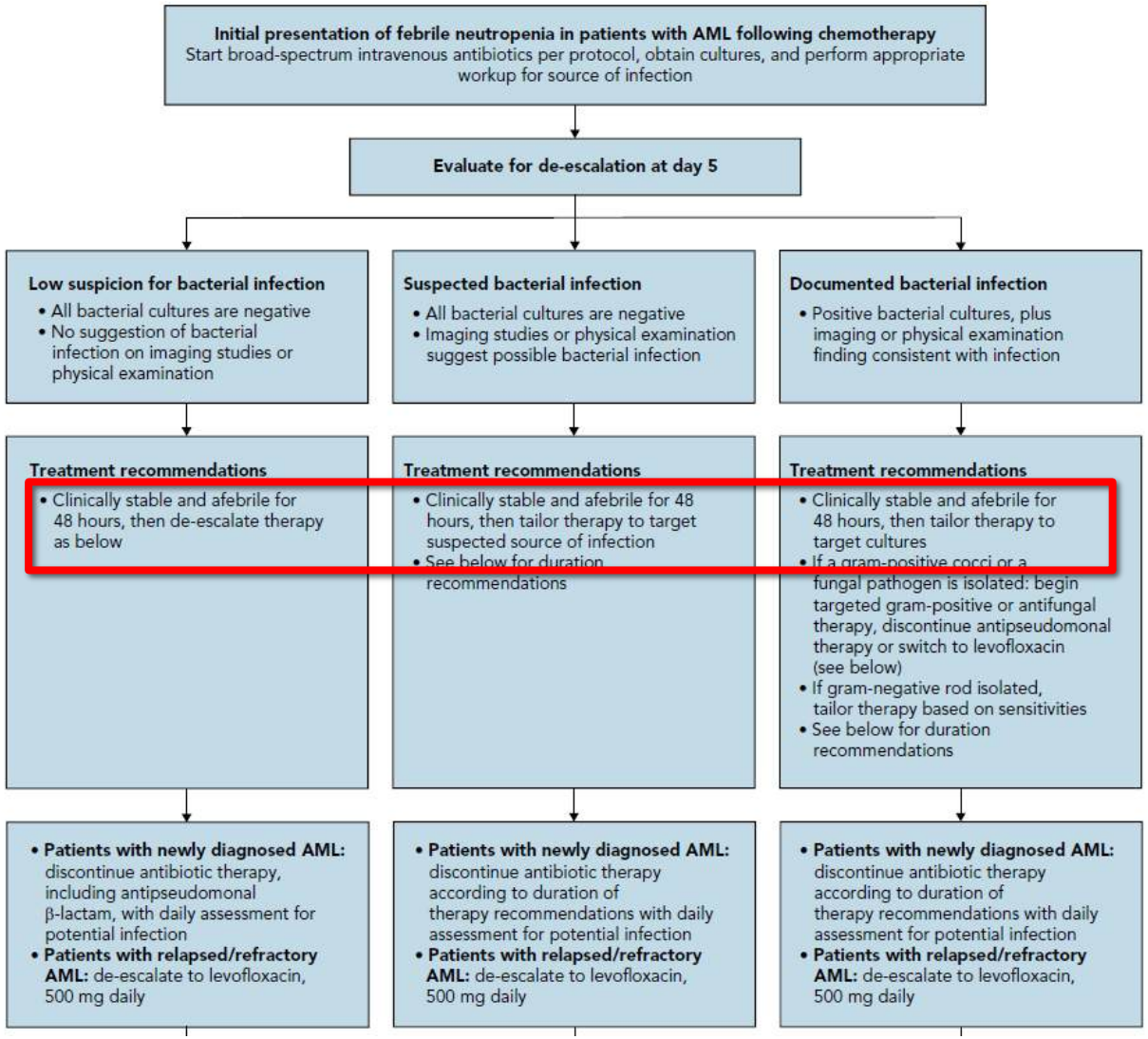
Antimicrobial de-escalation in patients with high-risk febrile neutropenia: Attitudes and practices of adult hospital care providers

"At our center, the hematology–oncology unit in the adult hospital was the highest per-patient user of IV antibiotics"



Gorsline et al. Antimicrob Steward Healthc Epidemiol 2021

Antibiotic De-escalation in AML



The primary efficacy endpoint was the incidence of suspected or documented bacterial infection after antibiotic de-escalation.

Between September 2015 and February 2018, 93 patients were included (40 in the historical group and 53 in the intervention group)

Alegria et al. J Natl Compr Canc Netw 2022

Antibiotic De-escalation in AML

Table 3. Infection- and Treatment-Related Endpoints After De-escalation Intervention

Endpoint	Historical Group n (%)	Intervention Group n (%)	*P* Value
Development of suspected or documented infection after antibiotic de-escalation[a]	18 (45.0)	18 (34.0)	.29
All-cause mortality at 30 d	6 (15.0)	6 (11.3)	.76
Hospital LoS, median (IQR), d	29 (24–37)	27 (24–39)	.47
Incidence of CDI	11 (27.5%)	3 (5.7%)	.007
De-escalation of IV antipseudomonal therapy	3 (7.5%)	38 (71.7%)	<.001
IV antipseudomonal DoT, median	25	14	<.001

High risk patients who met the clinical criteria for discontinuation did not received FQ prophylaxis after interruption of empirical therapy

Duration of antipseudomonal treatment was lower in the intervention group despite a high rate of restart of antibiotics after discontinuation

Alegria et al. J Natl Compr Canc Netw 2022

invasive procedures
device monitoring

patient hygiene, asepsis
and antisepsis measures

control of environmental
biosafety

real-time microbiological
information

updated knowledge of
the local epidemiology

implementation of screening
samples to detect
colonization by multidrug-
resistant organisms

patterns of antimicrobial
prescription and antimicrobial
resistance

Antimicrobial Stewardship

infection severity

organ dysfunctions

changes in
pharmacokinetics

Antimicrobial prophylaxis and
empirical therapy for FN
considering local epidemiology
and different patient risk profiles

surveillance and monitoring
of surgical prophylaxis

de-escalation and
shortening of treatments

Cercenado et al Enfermedades Infecciosas y Microbiología Clínica 2023

De-escalation della terapia antibiotica nei pazienti neutropenici con malattia oncoematologica

Inclusion criteria

-neutropenia in malattia oncoematologica

-recente episodio febbrile con necessità di terapia antibiotica endovenosa ad ampio spettro in regime di ricovero

-assenza di isolamenti microbiologici concomitanti, di segni/sintomi di infezione localizzata, di reperti radiologici suggestivi di infezione

-apiressia da 5 giorni

-stabilità emodinamica

-indici predittivi di sepsi normali

-assenza di pregressi isolamenti microbiologici con caratteristiche di multiresistenza

Exclusion criteria

-pazienti non neutropenici

-pazienti sottoposti a terapia antibiotica ad ampio spettro per via orale e/o in regime ambulatoriale

-isolamento microbiologico documentato

-segni/sintomi di infezione localizzata

-reperti radiologici suggestivi di infezione

-iperpiressia persistente nonostante terapia antibiotica

-instabilità emodinamica

-indici predittivi di sepsi alterati

-pregressi isolamenti microbiologici con caratteristiche di multiresistenza

De-escalation della terapia antibiotica nei pazienti neutropenici con malattia oncoematologica

Studio prospettico multicentrico strutturato in 12 mesi per arruolamento (marzo 205-febbraio 2026) e 6 mesi per elaborazione dei dati (marzo-settembre 2026)

Obiettivo primario:

applicabilità della de-escalation della terapia antibiotica nei pazienti neutropenici con malattia oncoematologica, valutata come percentuale di pazienti con i criteri di inclusione che effettivamente sospendono la terapia antibiotica

Obiettivi secondari:

-sicurezza della procedura, valutata mediante necessità di nuova terapia antibiotica endovenosa, accesso in ICU e mortalità a 30 giorni

-modifica dell'approccio clinico prima e dopo l'attuazione del protocollo (survey pre e post)

Study of Infectious Complications in CLL Patients Treated With Venetoclax…. and other target therapies

Francesco Autore, MD, PhD

Fondazione Policlinico Universitario A. Gemelli IRCCS

Roma 12 novembre 2024

Protocol

PROTOCOLLO DI STUDIO

Titolo dello studio: Studio ambispettico multicentrico sulle complicanze infettive riscontrate nei pazienti affetti da leucemia linfatica cronica trattati con venetoclax

Obiettivo primario

- Valutare l'incidenza di complicanze infettive batteriche, micotiche e virali, clinicamente o microbiologicamente documentate, in pazienti affetti da LLC sottoposti a trattamento con venetoclax.

Obiettivi secondari

- Valutare l'incidenza di ospedalizzazione determinate dalle complicanze infettive e l'impatto delle complicanze più severe in termini di sospensioni del farmaco sul programma terapeutico e sulle risposte;
- Valutare eventuali profilassi antinfettive eseguite da questi pazienti nei diversi centri partecipanti e efficacia delle stesse cercando di identificare le fasi del trattamento con venetoclax a maggiore rischio/incidenza di complicanze infettive;
- Valutare la tipologia di farmaci, soprattutto antifungini, utilizzati nel trattamento delle infezioni riscontrate.
- Calcolare i tempi di Overall Survival (OS) e di Event Free Survival (EFS)

Paper-1

Received: 11 October 2023 | Revised: 20 January 2024 | Accepted: 22 January 2024
DOI: 10.1002/ajh.27247

CORRESPONDENCE

AJH WILEY

Venetoclax infectious risk score to identify patients with chronic lymphocytic leukemia at high infectious risk during venetoclax treatment: A multicenter SEIFEM study

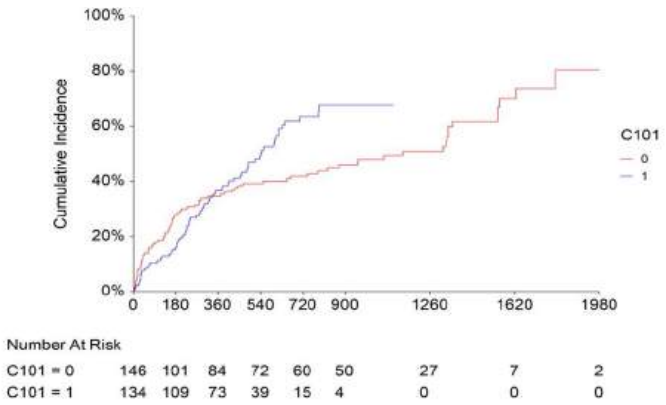
GENERAL	VEN	VEN plus antiCD20
287 pts	151 pts	136 pts

181 infections of grade 1-2 developed in 114 patients (39.7%)

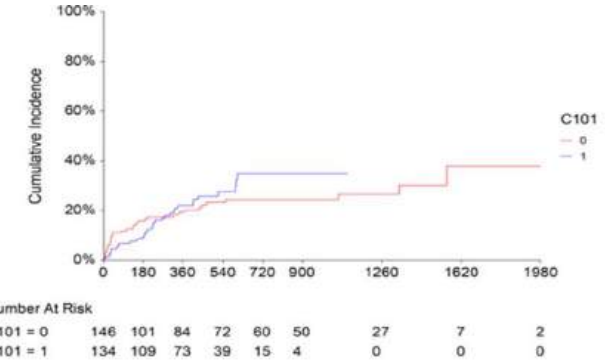
103 infections of grade 3-4, occurred in 73 patients (25.4%).

Site of infection involved the respiratory tract (71 events, 68.9%), then we registered sepsis (13, 12.6%) and gastrointestinal tract infections (7 events, 6.8%).

Of 103 severe infections, 64 (62.1%) were microbiologically proven, of whom 40 were viral, 21 bacterial and 3 fungal.



Time of first infection of any grade between the patients treated with venetoclax and those treated with venetoclax plus antiCD20 antibody.



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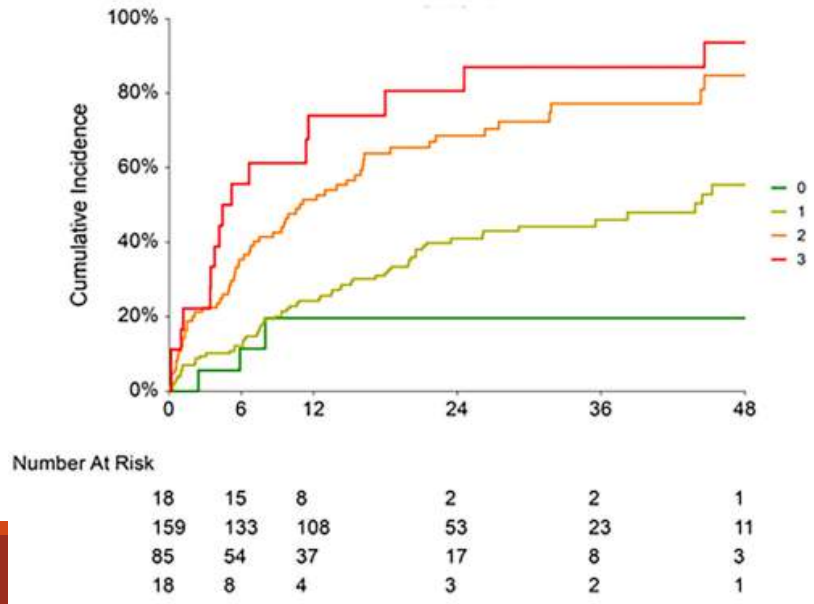
CORRESPONDENCE

AJH WILEY

Venetoclax infectious risk score to identify patients with chronic lymphocytic leukemia at high infectious risk during venetoclax treatment: A multicenter SEIFEM study

Our multivariate analysis identified **COPD**, **previous infections**, and **previous treatments** as risk factors able to stratify patients treated with venetoclax in terms of risk for infections, reaching a cumulative incidence of infection of 74.1% within the 1st year and 80.5% within the 2nd year.



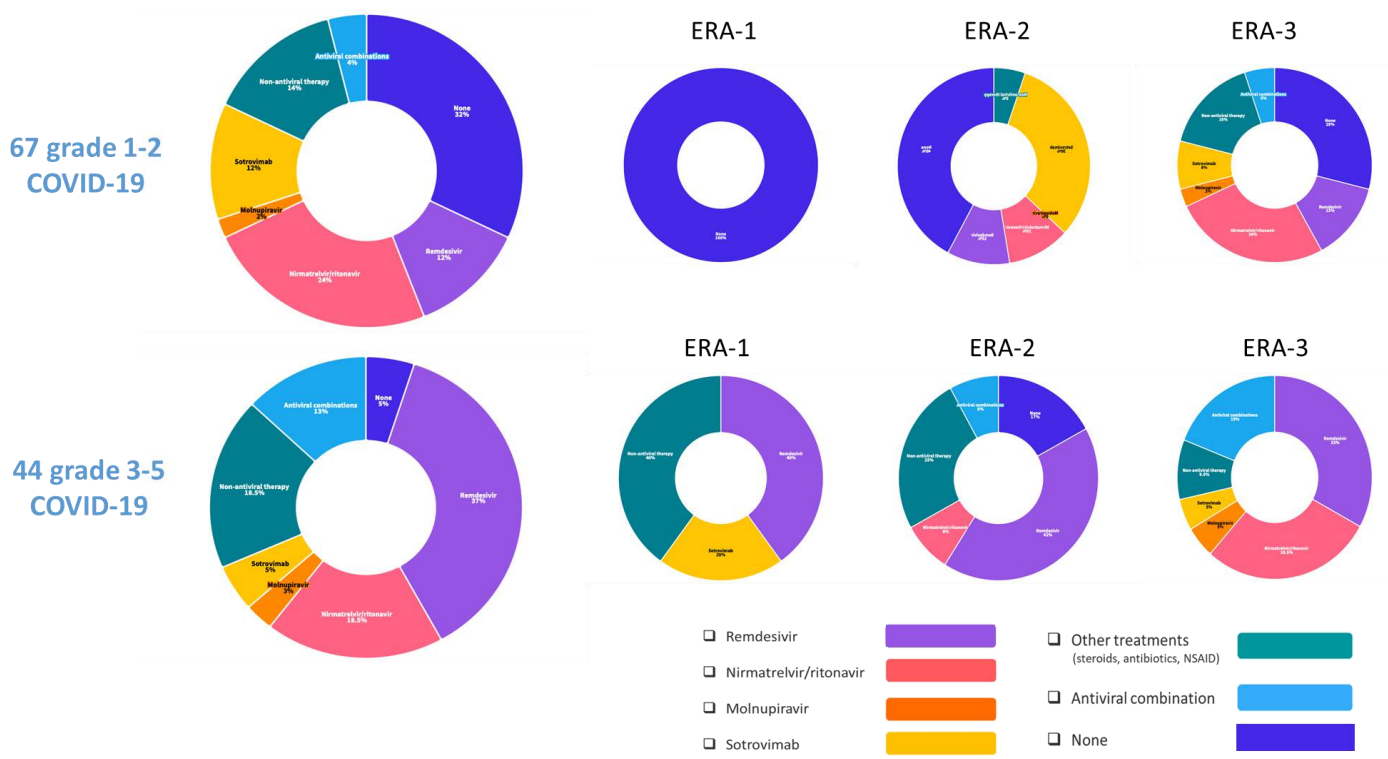
Based on the development of VIRS, we could consider selecting patients on venetoclax therapy with specific risk factors for infection, to be closely monitored and possibly given specific antimicrobial prophylaxis if at high risk.

We could suggest to focus on patients exposed to at least one previous CLL treatment who have COPD and to investigate whether they experienced at least an infection in the 12 months prior to starting venetoclax.

Paper-2

blood advances

COVID-19 in patients with Chronic Lymphocytic Leukemia treated with venetoclax: what is the role of anti-CD20 antibody?



- Multivariable analysis found that **association to anti-CD20** was an independent risk factor for COVID-19 of any grade (OR 1.75 [95% CI 1.01-3.06], p=0.046).
- Our rate of **mortality** due to COVID-19 was 9.6%, but higher (22.7%) among patients with severe grade 3-5 COVID-19.

- Because of the emerging higher risk for severe COVID-19 in CLL patients affected by CLL treated with venetoclax in association with anti-CD20 antibody, **we could suggest to better evaluate a continuos venetoclax administration without the addition of the monoclonal antibodies administrationas a safe treatment in the COVID scenario.**

Protocol: emendament

Titolo dello studio: Studio ambispettico multicentrico sulle complicanze infettive riscontrate nei pazienti affetti da leucemia linfatica cronica trattati con venetoclax **e altre terapie target**

Other BTK inhibitors such as **acalabrutinib** and **zanubrutinib** have arrived in clinical practice and combination therapeutic schemes have been introduced (anti BTK + anti-bcl2 +/- monoclonal antibodies).

Our study fits into this new scenario of CLL treatments by trying to involve a large and representative cohort of patients.
The aim is therefore to collect clinical, laboratory and biological data regarding patients suffering from CLL undergoing treatment with venetoclax and other target therapies such as fixed-term or indefinite-term therapeutic schemes to evaluate the actual real-life infectious risk of each therapeutic scheme. .and evaluate the actual real-life infectious risk of this therapy.

Fondazione IRCCS
San Gerardo dei Tintori

UNIVERSITÀ DEGLI STUDI DI MILANO BICOCCA

HEMPATIMP

critically ill HEMatological PATient Italian Multicenter Protocol

Multicenter prospective observational study on the management of the critical hematology patient

Luisa Verga
Fondazione IRCCS San Gerardo dei Tintori, Monza
Con la partecipazione incondizionata di **Mario Delia**

Intensive care without walls: role of MET

Vergnano B et al, 2023

WHO:

Monocentric, retrospective study
From 2015 to 2019

AIM
To evaluate the role of MET
In this high risk population

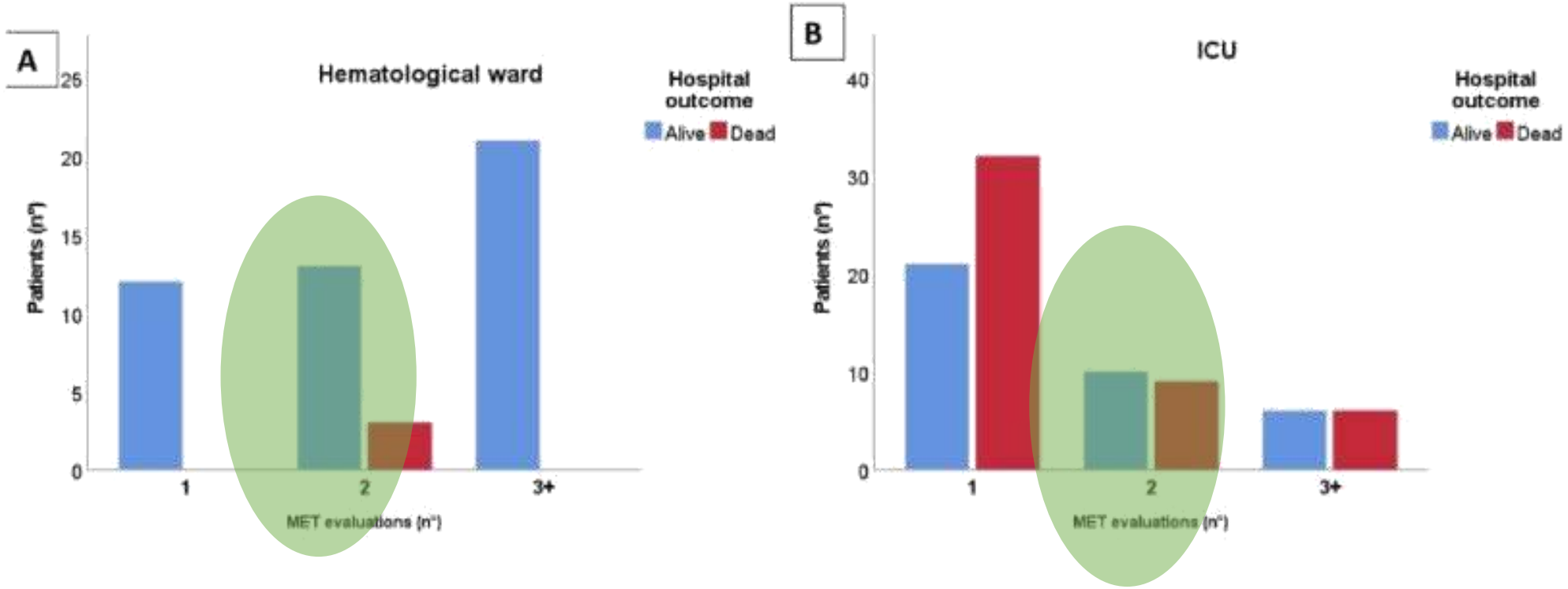
Of these, 84 (63%) → ICU,
49 (37%) → exclusively in the hematological ward

ICU MORTALITY: 56%

	N = 133 (%)
Hematological diagnosis	
- Non-Hodgkin Lymphoma	38 (29)
- Acute myeloid leukemia	36 (27)
- Multiple Myeloma	17 (13)
- Acute lymphocytic leukemia	16 (12)
- Chronic lymphocytic leukemia	5 (4)
- Myelodysplasia	5 (4)
- Bone marrow aplasia	4 (3)
- Hodgkin Lymphoma	3 (2)
- Others	9 (7)
Disease state	
- Onset	55 (42)
- Complete remission	41 (31)
- Relapse < 1 year	5 (4)
- Relapse > 1 year	19 (14)
- Refractory disease	12 (9)
- Unknown	1 (1)
Bone marrow transplant	
- Autologous	5 (4)
- Allogenic	30 (23)
Graft-vs.-host disease	
- Acute	16 (12)
- Chronic	2 (2)
Neutropenia *	46 (35)
Ongoing chemotherapy	76 (57)
Pharmacological immunosuppression	62 (47)

Intensive care without walls: role of MET

Vergnano B et al, 2023



A: FULLY WARD TTM

B: ICU TRANSFER

No difference between the delay of admission of patients who died and those who survived was found (p = 0.214)

68pts:

Helmet Cpap: no difference in the first MET evaluation was evident between those who were admitted to the ICU and those who successfully continued treatments in the medical ward considering PaO2/FiO2 value, SOFA, and MEWS.

53% of the patients who received helmet CPAP support were admitted to the ICU (23 patients),

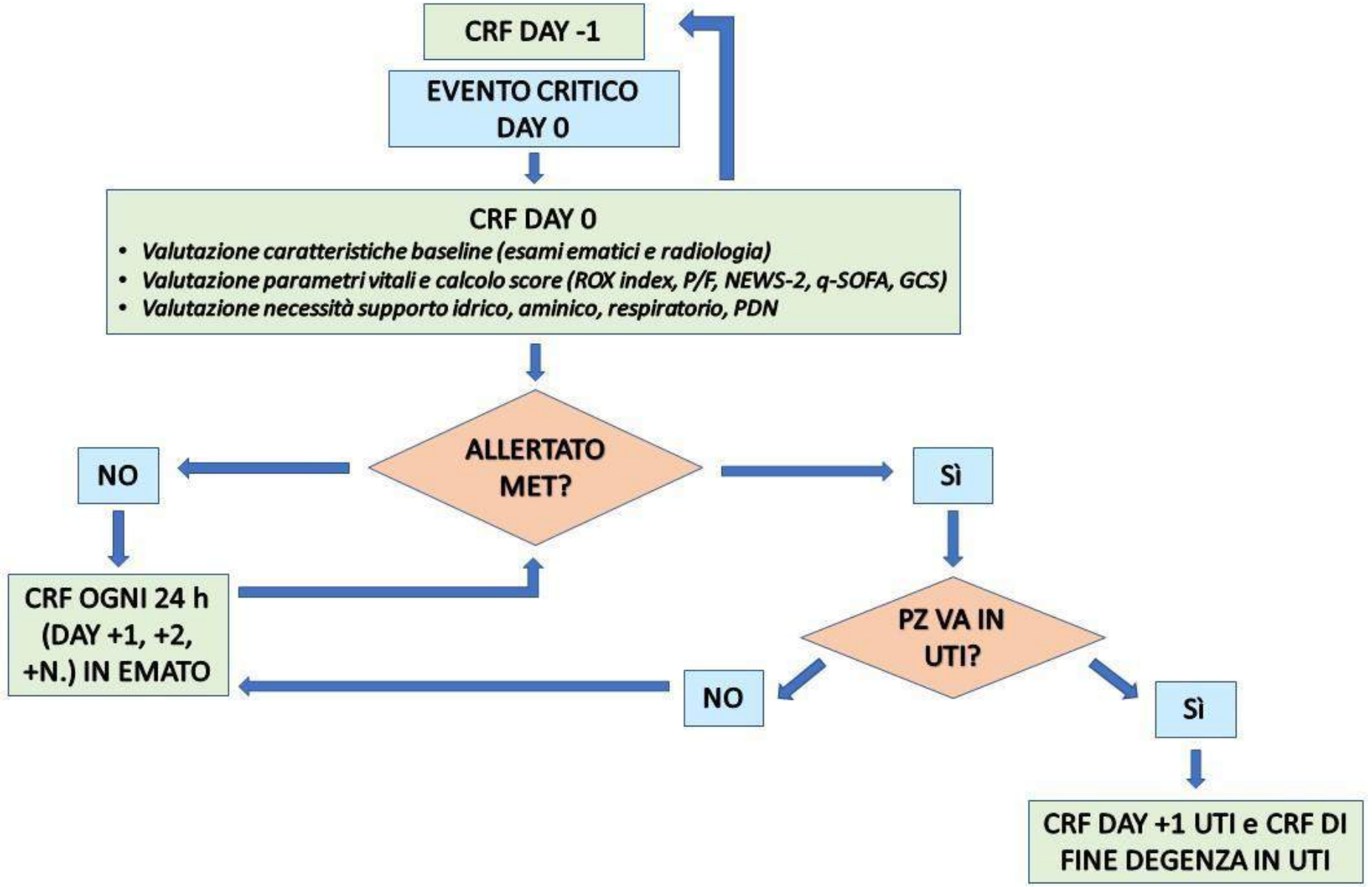
while the ICU admission rate in those without a CPAP trial was 32%.

.. To the HEMPATIMP study

critically ill HEMatological PATient Italian Multicenter Protocol

- **Prospective multicentre observational** clinical study on the management of the critically ill haematological patient
- **Study duration**: *xx months, enrolment period: xx months*
- **from the collaboration** of the Haematology Unit and the Department of Anaesthesia and Intensive Care Unit - of the Fondazione IRCCS San Gerardo dei Tintori (Monza)
- It involves all the centres belonging to SEIFEM
- adhesion and collaboration of **haematologists and intensivists** of all partecipating centre

Study Design



Aim of the Study

Primary objective:
to evaluate the probability of survival of critical haematological patients in different Italian settings at 30 days from the onset of critical event

Secondary objectives:

- to assess the number of critical patients and how they are recognized;
- to describe “baseline” characteristics of disease, causes of critical events and access to ICU;
- to evaluate number of patients requiring MET and timing of activation;
- to quantify probability of survival at 30 and 60 days from onset of critical event in relation to different approaches among involved hospitals;
- to assess the probability of keeping on haematological treatments post-ICU and 6 months survival;
- to evaluate the concordance of opinion between hematologists and intensivists regarding management of the critically ill haematological patient

Inclusion Criteria: WHO is the critically ill patient

- Subjects >/= 18 years old with any hematologic or oncohematologic disease receiving any type of treatment
- Informed consent freely given and acquired before the start of the study
- **Patient must be defined "critical" by the referring hematologist**.

The cause of critical event can be:

- ❑ **Cardiovascular system failure**: septic shock
  other causes of distributive shock such as CRS or HLH,
  hypovolemic shock,
  cardiogenic shock
- ❑ **acute respiratory failure**
- ❑ **acute neurological** problems and altered consciousness,
- ❑ **Acute kidney injury**, acute hyperleukocytic leukemia and tumor lysis syndrome
- ❑ Any other situation according to **the hematologist** clinical **judgment**