



UNIKLINIK
KÖLN

Pro Management Guidelines of Invasive Fungal Infections



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- Federal Ministry of Research and Education
(BMBF 01KN1106, 01KN0706, 01GH1001E, 01EZ0931)
- Deutsche Forschungsgemeinschaft
- German Center for Infectious Disease Research
- German José Carreras Leukaemia Foundation
- Research Gants, Trial Design, or Speaker for:
Actelion, Astellas, Basilea, Bayer, F2G, Gilead, Menarini,
MSD, Miltenyi, Novartis, Optimer, Pfizer, Quintiles,
Viropharma.



- To serve as a quick reference for clinicians.
- To convey an overview in case there is a vast number of trials.
- To give transparent = traceable information.
- To provide a basis for local guidelines.



Ideally follow these steps OR another catalogue agreed on.

1. Select a target patient population
2. Define a goal of the intervention to be described
3. Characterize intervention
4. Allocate EBM grade

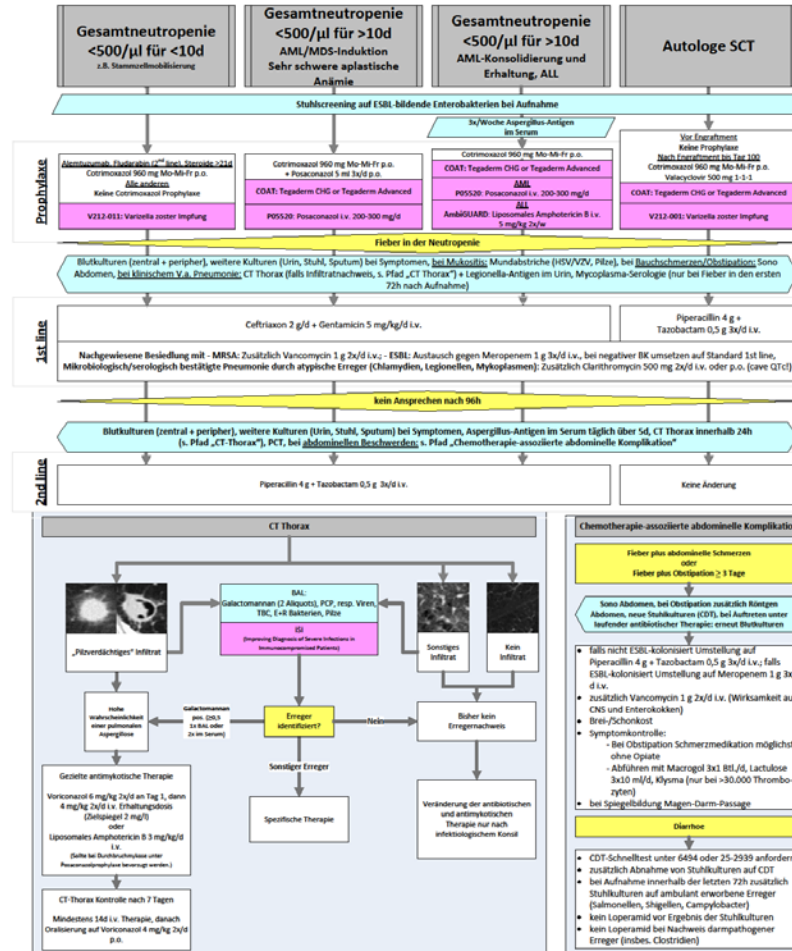
Example

1. Population: Estimated duration of neutropenia >7 days
2. Intention: Reduce attributable mortality
3. Intervention: Antifungal drug X / dosing schedule Y
4. Grading: EBM



- Avoid negative recommendations
 - Is the first step in avoiding ambiguity / double negations
- Strictly adhere to the grading system chosen
 - Every discussant should at any time have it on the table
 - Even consider projecting it with a second LCD
- Fill the key recommendations into a table
- Tabulate essential primary data, so that readers/clinicians can follow your decision process

Behandlungspfad – Fieber in der Neutropenie



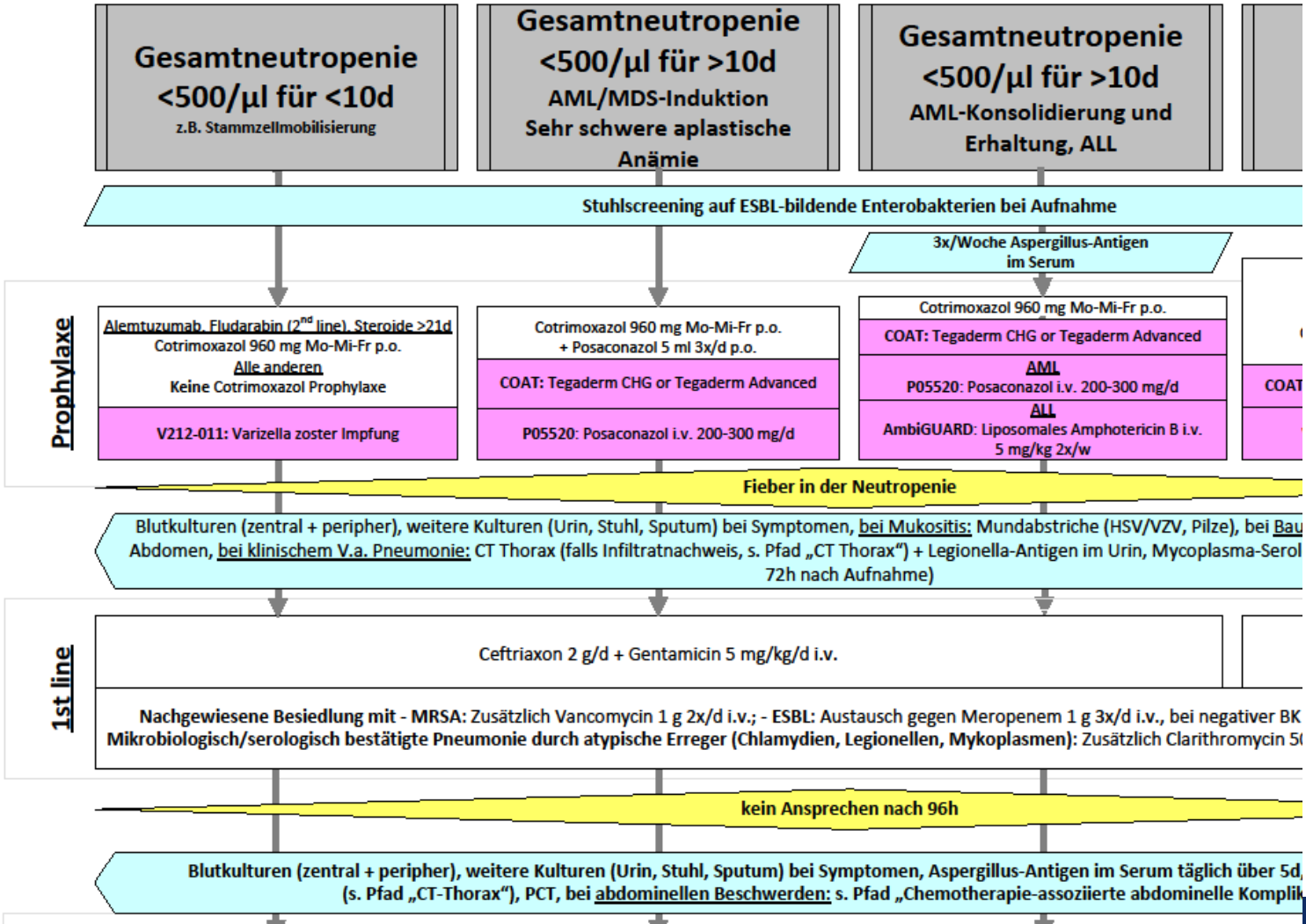
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Behandlungspfad – Fieber in der Neutro



ESCMID / ECMM Guideline Diagnosis & Management of Emerging Invasive Fungal Diseases

Conveners: Oliver A. Cornely, Jacques F. Meis

Structure of the ESCMID/ECMM Recommendations

Two Independent Evaluations

1. Strength of Recommendation = SoR
2. Quality of Evidence = QoE

Strength of Recommendation – Definition

Grade of Recommendation	Definition
Grade A	ESCMID (EFISG) and ECMM <u>strongly</u> support a recommendation for use
Grade B	ESCMID (EFISG) and ECMM <u>moderately</u> support a recommendation for use
Grade C	ESCMID (EFISG) and ECMM <u>marginally</u> support a recommendation for use
Grade D	ESCMID (EFISG) and ECMM support a recommendation <u>against</u> use

Quality of Evidence – Level Definition

Level of Evidence	Definition
Level I	Evidence from at least 1 properly designed randomized, controlled trial
Level II	Evidence from at least 1 well-designed clinical trial, without randomization; from cohort or case-controlled analytic studies (preferably from >1 centre); from multiple time series; or from dramatic results of uncontrolled experiments
Level III	Evidence from opinions of respected authorities, based on clinical experience, descriptive case studies, or reports of expert committees

Added Index – Definition

Added Index	Source of Level II Evidence
r	Meta-analysis or systematic review of RCT
t	Transferred evidence i.e. results from different patients' cohorts, or similar immune-status situation
h	Comparator group: historical control
u	Uncontrolled trials
a	For published abstract presented at an international symposium or meeting

For Biomarkers only: Strength of Recommendation – Definition

Strength of Recommendation	Definition
Highly recommended	Technique is accurate* in >70% of cases
Recommended	Technique is accurate in 50 – 70% of cases
Not recommended	Technique accurate in <50% of cases
No recommendation	No data

$$\text{Accuracy} = \frac{\text{number of true positives} + \text{number of true negatives}}{\text{numbers of true positives} + \text{false positives} + \text{false negatives} + \text{true negatives}}$$

For Biomarkers only: Quality of Evidence – Definition

Level of Evidence	Definition
Level I	Evidence from at least 1 properly designed prospective multicentre cross-sectional or cohort study
Level II	Evidence from at least 1 well-designed prospective single-centre cross-sectional or cohort study, or a properly designed retrospective multicentre cross-sectional or cohort study, or from case-control studies
Level III	Opinions of respected authorities, clinical experience, descriptive case studies, or reports of expert committees

Example

- The following slides give an example from the candida guideline on how the group felt
 - maximum transparency could be preserved throughout the process
 - homogenous manuscripts could be produced

Example: Prophylaxis for Invasive Candidiasis: Which Agents?

Start with an empty 7 column table – 7 steps to follow

Population	Intention	Intervention	SoR	QoE	Reference	Comment

Example: Prophylaxis for Invasive Candidiasis: Which Agents?

Step 1. Define the population addressed

Population	Intention	Intervention	SoR	QoE	Reference	Comment
Recent abdominal surgery AND recurrent gastrointestinal perforations or anastomotic leakages						

Example: Prophylaxis for Invasive Candidiasis: Which Agents?

Step 2. Describe the medical intention

Population	Intention	Intervention	SoR	QoE	Reference	Comment
Recent abdominal surgery AND recurrent gastrointestinal perforations or anastomotic leakages	To prevent intraabdominal candida infection					

Example: Prophylaxis for Invasive Candidiasis: Which Agents?

Step 3. Which intervention is being evaluated

Population	Intention	Intervention	SoR	QoE	Reference	Comment
Recent abdominal surgery AND recurrent gastrointestinal perforations or anastomotic leakages	To prevent intraabdominal candida infection	Fluconazole 400mg/d				

Example: Prophylaxis for Invasive Candidiasis: Which Agents?

Step 4. Find consensus on the Strength of Recommendation

Population	Intention	Intervention	SoR	QoE	Reference	Comment
Recent abdominal surgery AND recurrent gastrointestinal perforations or anastomotic leakages	To prevent intraabdominal candida infection	Fluconazole 400mg/d	B			

Example: Prophylaxis for Invasive Candidiasis: Which Agents?

Step 5. Rate the Quality of published Evidence

Population	Intention	Intervention	SoR	QoE	Reference	Comment
Recent abdominal surgery AND recurrent gastrointestinal perforations or anastomotic leakages	To prevent intraabdominal candida infection	Fluconazole 400mg/d	B	I		

Example: Prophylaxis for Invasive Candidiasis: Which Agents?

Step 6. Give all relevant references in „Name Journal Year“ format

Population	Intention	Intervention	SoR	QoE	Reference	Comment
Recent abdominal surgery AND recurrent gastrointestinal perforations or anastomotic leakages	To prevent intraabdominal candida infection	Fluconazole 400mg/d	B	I	Eggimann CCM 1999	

Example: Prophylaxis for Invasive Candidiasis: Which Agents?

Step 7. Add a comment if felt necessary, e.g. items to be discussed in the manuscript

Population	Intention	Intervention	SoR	QoE	Reference	Comment
Recent abdominal surgery AND recurrent gastrointestinal perforations or anastomotic leakages	To prevent intraabdominal candida infection	Fluconazole 400mg/d	B	I	Eggimann CCM 1999	Placebo, N=43

Example: Prophylaxis for Invasive Candidiasis: Which Agents?

Start with a different population, intention, intervention etc.

Population	Intention	Intervention	SoR	QoE	Reference	Comment
Recent abdominal surgery AND recurrent gastrointestinal perforations or anastomotic leakages	To prevent intraabdominal candida infection	Fluconazole 400mg/d	B	I	Eggimann CCM 1999	Placebo, N=43
	As above	Caspofungin 70/50mg/d	C	II _u	Senn ICM 2009	Single arm, N=19
Critically ill surgical patients with an expected length of ICU stay \geq 3d	To delay the time to fungal infection	Fluconazole 400mg/d	C	I	Pelz Ann Surg 2001	Placebo, N=260

THE TEAM

