Protocol

"Epidemiology of Secondary Prophylaxis of Invasive Fungal Infection"

from the Infectious Disease Working Group of the German Society for Hematology and Oncology

Introduction

Primary Prophylaxis. The antifungal primary prophylaxis in cancer patients has been examined in numerous trials[1]. For patients undergoing allogeneic bone marrow transplantation a reduction of the incidence and mortality could be shown[2-4]. These benefits were achieved under fluconazole 400mg qd. However, fluconazole is not effective against *Aspergillus spp.* and has no satisfying efficacy against certain *Candida spp.* At the moment the clinical value of other antifungals for primary antifungal prophylaxis is ill-defined[1].

Secondary Prophylaxis. Patients, who survived an invasive fungal infection, and undergo another deeply neutropenic treatment phase, a high risk for recurrent fungal infection must be reckoned with. Reliable prospective evaluations defining this risk are not yet available. Currently, diverse antifungal prophylactic regimens are applied an clinicians rely on personal experience. Valid descriptions of the type and effectivity of the regimens applied are not available.

Objectives

The objective of this evaluation is to describe the methods and the success rates of current antifungal secondary prophylactic strategies by focusing on the following topics:

1. To determine the relative frequency of relapses of invasive fungal infections in the subsequent neutropenic phase.
2. To describe the secondary prophylactic regimens applied in the participating centers.
3. To determine the efficacy of the secondary prophylactic regimens.

Study period

The study begins on October 1, 2001.

The study will end after inclusion of 500 evaluable patients.

Patient definition (see Amendments 1 & 2)

Inclusion criteria.

- history of proven or probable invasive fungal infection
- acute myelogenous leukemia (AML), i.e. de novo, relapse, or secondary
  In the beginning phase of the evaluation patients with acute lymphatic leukemia, lymphoma, and solid tumor will not be included.
- on secondary prophylaxis after October 1, 2001

Amendment 1:

From January 1, 2002 the inclusion of patients with acute lymphatic leukemia is allowed.

Amendment 2:

From February 1, 2002 patients with proven invasive fungal infection can be included retrospectively and will be evaluated separately.

Exclusion criteria.

- history of possible invasive fungal infection, but not of proven or probable invasive fungal infection

Case report from

The CRF is an internet based form to be accessed under www.neutropen.de. Pull-down menus and data transfer via email simplify its use. Data will automatically be incorporated into a Filemaker Pro 4.0™ database[5]. Data evaluated comprise:

- demographic data
- underlying malignancy
- concerning first invasive fungal infection (IFI):
  fungal species, organs involved, treatment, treatment results of IFI and of malignancy, treatment delay attributable to IFI
- concerning the secondary prophylaxis:
  identical to first IFI, plus: start and end of prophylaxis, antifungals used
- Risk factors

  room conditions, i.e. laminar air flow, HEPA filter use, exposition to construction work and dust, status of the underlying malignancy at the beginning of the secondary prophylaxis, duration of neutropenia, mucositis grade 3-4 (CTC), diabetes mellitus, central venous catheter, total parenteral nutrition, high dose cytosine arabinoside, steroids >2mg/kg >7 days, anti-thymocyte-, -lymphocyte- or CD3-antibodies, purine analogues, number of antibiotics, and number of days with antibiotics

- concerning any second IFI: yes/no, species, organ involvement, treatment result of underlying malignancy and second IFI, survival, if applicable cause of death, and results of post mortem examination.

Evaluation and statistical considerations

The evaluation will be descriptive. For differences between subgroups χ^2-test or exact test of Fisher will be used with a $p<0.05$ as limit for statistical significance.

Budgetary information

For evaluable CRFs a compensation of € 130 will be paid for each evaluable documentation.

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References

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3. Marr KA, Seidel K, Slavin MA, et al. Prolonged fluconazole prophylaxis is associated with persistent protection against candidiasis-related death in allogeneic marrow transplant recipients: long-term follow-up of a randomized, placebo-controlled trial. Blood. 2000; 96:2055-61.
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