
# Invasive mycoses (IM) in patients (pts) with Hematopoietic Stem Cell Transplant (HSCT): RIFI study

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P0360

## Background

IM represents a major complication in pts with HSCT. The incidence of IM may differ depending on the geographic region. The objective of this study was to estimate the rate of IM among HSCT recipients.

## Material/methods

Multicenter prospective observational study of IM (RIFI - NCT01519648) was performed from Feb 2012 till Mar 2014. All pts were followed up for 6 months. IM in allo HSCT were analyzed in pre-engraftment and engraftment periods.

## Results

A total of 808 pts were included in RIFI study of which 306 were HSCT pts from 10 hematological centers in Russia. Main underlying disease in auto HSCT was multiple myeloma (53%), in allo HSCT – acute leukemia (74%), table 1. The stem cell sources in allo HSCT recipients were bone marrow (55%) and peripherial blood (45%). Most pts with allo HSCT had non-myeloablative conditioning regimen (62.3%).

IM before allo HSCT and auto HSCT had 21% pts. Mismatched related HSCT prevailed in recipients with pre-existing IA (12% vs 3%, p=0.04).

The incidence of IM (proven, probable, possible) and the 6 month cumulative incidence (CI) of IM (proven, probable) are presented in table 2,3 and in fig. 1. Risk factors of IA in engraftment period in allo HSCT were treatment with steroids (p=0.006) with dose > 1 mg/kg (p=0.01). IA prevailed among IM (fig. 2). Overall survival was higher in allo HSCT recipients without pre-existing IA compared with pts with pre–existing IA (75.6% vs 54.5%, p=0.04), fig. 3. The incidence of IA was comparable in allo HSCT recipients with pre-existing IA and without IA (12% vs 11.5%). The main cause of mortality in allo HSCT recipients with pre-existing IA was uncontrolled hematological malignancy (91% vs 48%, p=0.02), table 5.

## Conclusion

IM prevailed in pts with allo HSCT in engraftment period and were caused mainly by IA. The rate of IA was comparable in allo HSCT recipients with and without pre-existing IA. The main cause of mortality in allo HSCT recipients with pre-existing IA was uncontrolled hematological malignancy.

## Results

Prospective multicenter study 2012 (February) – 2014 (March)
138 allogeneic (allo) and 168 autologous (auto) HSCT recipients

**TABLE 1. Characteristic of HSCT recipients**

| Variable | Allo | Auto |
|---|---|---|
| No of pts | 138 | 168 |
| No of centers | 6* | 9 |
| Gender (male/female) | 74/64 | 83/85 |
| Age, median, years | 29 (1-59) | 45 (2-66) |
| < 18 years | 25 (18%) | 19 (11%) |
| > 60 years | - | 10 (6%) |
| Neutropenia, median, days | 17 (3-113) | 11 (2-42) |
| Underlying disease | | |
| Acute leukemia** | 102 (74%) | 8 (4.8%) |
| Multiple myeloma | 3 (2.2%) | 90 (54%) |
| Lymphoma | 6 (4.4%) | 49 (29%) |
| Other | 27 (19.4%) | 21 (13%) |
| Type of HSCT | | |
| Matched, related | 50 (36%) | - |
| Matched, unrelated | 75 (54%) | - |
| Mismatched, related | 6 (4%) | - |
| Mismatched, unrelated | 7 (5%) | - |
| GVHD | 71 (51.5%) | - |
| IM before HSCT | 29 (21%) | 3 (2%) |
| - IA | 25 (18%) | 3 (2%) |
| - Yeasts | 4 (3%) | - |
| Time from diagnosis of IA to HCST, month | 4.5 (1-38) | 12.5 (4-25) |

*90% of pts were enrolled from 2 centers
**68 (49%) AML and 34 (25%) ALL

**TABLE 2. Incidence (6 month) of IM in HSCT recipients**

| IM | Allo N=138 | Auto N=168 | OR | p |
|---|---|---|---|---|
| IA | 16 (11.6%) | 7 (4.2%) | 3 | 0.01 |
| Proven | - | - | | |
| Probable | 14 (10.1%) | 4 (2.4%) | | |
| Possible | 2 (1.5%) | 3 (1.8%) | | |
| Other molds | 1 (0.7%)* | - | - | 0.27 |
| Yeasts | 3 (2.2%) | - | - | 0.06 |
| **Total** | **20 (14.5%)** | **7 (4.2%)** | **3.9** | **0.002** |

* *Fusarium* spp.

**TABLE 3. Incidence (6 month) of IM in pre-engraftment and engraftment periods in allo HSCT recipients**

| IM | Pre-engraftment N=138 | Engraftment N=117 | OR | p |
|---|---|---|---|---|
| IA | 4 (2.9%) | 12 (10.3%) | 3.83 | 0.02 |
| Proven | - | - | | |
| Probable | 4 (2.9%) | 10 (8.6%) | | |
| Possible | - | 2 (1.7%) | | |
| Other molds | - | 1 (0.8%)* | | 0.28 |
| Yeasts | 1 (0.7%) | 2 (1.7%) | 2.3 | 0.47 |
| **Total** | **5 (3.6%)** | **15 (12.8%)** | **2.73** | **0.006** |

* *Fusarium* spp.

**FIG.1 Cumulative incidence of IM (proven, probable) in allo and auto HSCT**

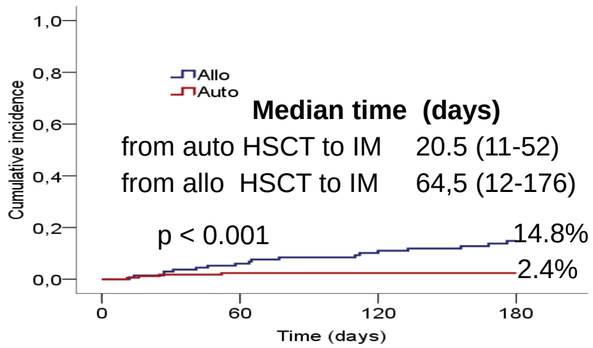


**FIG.2 Etiology of IM in HSCT recipients**

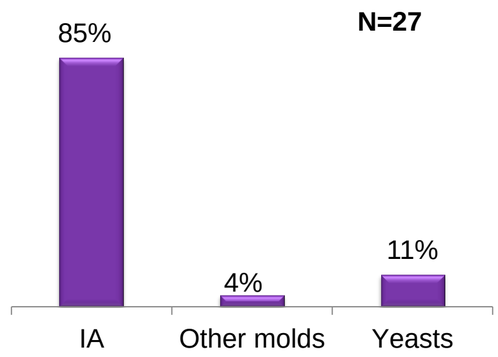


**FIG.3 Overall survival of allo HSCT recipients with and without pre-existing IA**

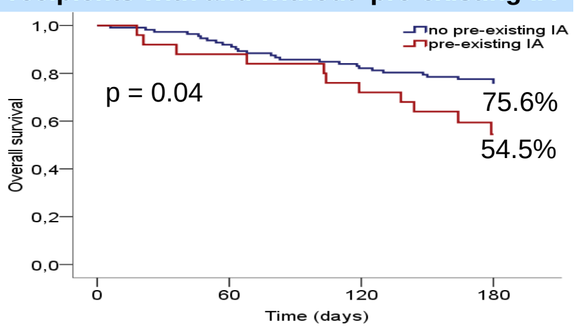


**TABLE 5. Causes of mortality in allo HSCT recipients with and without pre-existing IA**

| Cause of mortality | Pre-existing IA Yes N=11 | No N=27 | p |
|---|---|---|---|
| Uncontrolled malignancy + infection (other then IA) | 10 (91%) | 13 (48%) | 0.02 |
| Infection (other then IA) | - | 8 (30%) | 0.04 |
| **IA** | **1 (9%)** | **6 (22%)** | **0.34** |

**TABLE 4. Incidence of IA in allo HSCT recipients with and without pre-existing IA**

| Variable | Pre-existing IA Yes N=25 | No N=113 |
|---|---|---|
| IA | 3 (12%) | 13 (11.5%) |
| Time from allo HSCT to IA, days | 16 (12-176) | 58 (14-168) |
| **Mortality in pts with IA** | **1/3 (33%)** | **6/13 (46%)** |

ClinicalTrials.gov Protocol Registration System NCT01519648

*The study was supported by research grant of MSD*

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