

# Decrease of invasive fungal disease incidence in children with malignancy or undergoing hematopoietic stem cell transplantation after introduction of national program of antifungal prophylaxis with posaconazole

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**BACKGROUND:** Prophylaxis and therapy of invasive fungal disease (IFD) is a key factor in preventing deaths from infectious complications.

**THE OBJECTIVE OF THE STUDY** is the analysis of epidemiology of invasive fungal disease (IFD) over a period of four years in children undergoing chemotherapy (PHO) or HSCT, with respect to national program of antifungal prophylaxis.

**MATERIAL/METHODS:** All children newly diagnosed for malignancy or undergoing HSCT between 1.01.2012-31.12.2015 were analyzed for IFD. Ministry of Health in Poland introduced the refund by National Health System (NFZ) the use of posaconazole for prophylaxis in children on chemotherapy for acute myeloid leukemia (AML), high-risk or relapsed acute lymphoblastic leukemia (ALL), myelodysplastic syndromes (MDS), in graft-versus-host disease (GVHD) after HSCT (1-May-2014), and in secondary prophylaxis after HSCT (1-September-2014). Fungal infections were diagnosed and reported by each center and data were analyzed centrally. The diagnosis of IFD was made according to EORTC/MSG criteria as proven, probable or possible.

**RESULTS:** A total number of 3,614 children with newly diagnosed malignancy and 650 undergoing HSCT were included into the study.

PHO: The number of episodes of probable/proven IFD in all children with malignancy decreased from 0.054/patient in 2012-2013 to 0.033/patient ( $p < 0.01$ ) in 2014-2015.

The number of episodes of probable/proven IFD in patients with AML decreased from 0.26/patient in 2012-2013 to 0.14/patient in 2014-2015 ( $p = ns$ ); and in ALL from 0.09/patient to 0.05/patient ( $p < 0.05$ ) in respective periods.

The incidence of probable/proven IFD in patients with AML decreased from 19.7% in 2012-2013 to 10.8% (ns) in 2014-2015; and in ALL from 6.7% to 4.9% (ns) in respective periods.

HSCT: In the same periods, the number of episodes of probable/proven IFD in patients undergoing allo-HSCT decreased from 0.25/patient to 0.13/patient ( $p = 0.002$ ), and the incidence of probable/proven IFD for patients undergoing allo-HSCT decreased from 15.5% to 11.6% (ns).

INCIDENCE	2012-2013	2014-2015
ALL (PHO)	13,0% (56/430)	14,7% (57/386)
Possible	9,3% (41/430)	11,1% (43/386)
Probable	6,0% (26/430)	2,3% (9/386)
Proven	0,7% (3/430)	2,6% (10/386)
AML (PHO)	43,2% (35/81)	36,5% (27/74)
Possible	34,6% (28/81)	27,0% (20/74)
Probable	14,8% (12/81)	6,7% (5/74)
Proven	4,9% (4/81)	4,1% (3/74)

INCIDENCE	2012-2013	2014-2015
HSCT total	84/308 (27,3%)	79/342 (23,1%)
Possible	44/308 (14,3%)	54/342 (15,8%)
Probable	29/308 (9,4%)	13/342 (3,8%)
Proven	11/308 (3,6%)	20/342 (5,8%)
ALLO	71/232 (30,6%)	71/267 (26,6%)
AUTO	13/76 (17,1%)	8/75 (10,7%)
ALL	21/67 (31,3%)	24/86 (27,9%)
AML	21/47 (44,7%)	20/51 (39,2%)

SURVIVAL	2012-2013	2014-2015
PHO total	90,6% (115/127)	96,0% (192/200) $p = 0.045$
Possible	91,6% (76/83)	96,4% (133/138)
Probable	88,9% (24/27)	92,3% (24/26)
Proven	88,2% (15/17)	97,1% (34/35)

SURVIVAL	2012-2013	2014-2015
HSCT total	77,6% (59/76)	90,8% (89/98) $p = 0.015$
Possible	81,1% (30/37)	95,0% (57/60)
Probable	67,9% (19/28)	87,5% (14/16)
Proven	90,9% (10/11)	81,8% (18/22)

**CONCLUSIONS:** With introduction of prophylactic program with posaconazole, the number of episodes of invasive fungal disease has significantly decreased in children with malignancy or undergoing hematopoietic stem cell transplantation.

