

ANTIFUNGAL PROPHYLAXIS IN 771 PATIENTS (PTS) WITH HEMATOLOGICAL MALIGNANCIES: IS THERE A PERFECT DRUG ?

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In our most recent report, 30% of our acute myelogenous leukemia (AML) and high-risk myelodysplastic syndrome (MDS) pts undergoing induction chemotherapy (IC) died due to IFI by autopsy. In an effort to prevent IFI, antifungal prophylaxis (AFP) has been used routinely in our center in this pts since 1992. **Objectives:** To compare the efficacy and safety of regimens used as AFP in pts with AML and MDS undergoing IC 2) To develop a predictive model to more aptly adapt AFP to pts needs. **Methods:** Retrospective review of pts with newly diagnosed AML/MDS that underwent IC and received AFP. **Definitions:** Proven IFI: pts who fulfilled the EORTC/MSG criteria and pts with typical IFI findings on CT with a + culture for mold from bronchoalveolar lavage. Pts with new findings on CXR compatible with pneumonia (Pn) or with persistent fever despite broad-spectrum antibiotics were classified as possible IFI. Outcome of pts on AFP was categorize as: a) completed, no proven or possible IFI or toxicity that required discontinuation of AFP; b) fungal, IFI during AFP as described above; c) Pn, if sign/ symptoms of Pn, new infiltrates by CXR and negative cultures d) Fever, febrile despite 72 hrs on broad spectrum antibiotics + negative cultures e) toxicity, if toxicity required discontinuation of the AFP.

Results: Baseline characteristics of 771 pts included in the analysis and distribution on 8 AFP regimens are shown in Table 1

	ABLC (n=132)	AMBI (n=70)	FL200 (n=132)	FL400 (n=38)	FL+I (n=73)	CASPO IV (n=106)	ITRA VORI (n=182)	p-value
Median age (range)	65 (21- 87)	63 (36- 83)	58 (13- 84)	53 (19- 83)	57 (19- 84)	65 (22- 82)	62 (17- 89)	60 (23-79) 0.0009
Female/Male	46/86	28/41	53/78	13/25	27/46	37/69	69/113	14/24 0.98
Perf. Status, n (%) 0 ≤ 2	128(97)	69(100)	115(88)	36(97)	71(97)	101(95)	171(94)	38(100) 0.002
Diagnosis, n (%)								0.0005
AML	68(52)	52(75)	94(72)	23(62)	47(64)	77(73)	137(75)	27(71)
MDS	64(48)	17(25)	37(28)	14(38)	26(36)	29(27)	45(25)	11(29)
Protected Environment (%)	108(82)	53(77)	64(49)	25(68)	51(70)	93(88)	148(81)	35 (92) <0.0001
Febrile at starting (%)	29(22)	16(23)	46(35)	7(19)	20(27)	18(17)	41(23)	7(18) 0.053

There were no significant differences in the number of pts that completed AFP or that developed IFI (p = 0.95 and p=0.18, respectively). Given pts that had IFI there was a significant difference in the incidence of yeast and mold between the groups, **p=0.021**(Table 2)

	ABLC (6/132)	AMBI (3/70)	FL200 (12/131)	FL400 (4/37)	FL+I (3/73)	CASPO (9/106)	IV ITRA (15/182)	VORI (0/38)
IFI/Total pts								
Mold, n(%)	4(67)	0	11(92)	2(50)	2(67)	7(78)	6(40)	0
Yeast, n(%)	2(33)	3(100)	1(8)	2(50)	1(33)	2(22)	9(60)	0

There was also a significant difference in the number of pts that needed discontinuation of AFP due to toxicity, **p<0.0001** (Table 3)

	ABLC (n=132)	AMBI (n=70)	FL200 (n=132)	FL400 (n=38)	FL+I (n=73)	CASPO (n=106)	IV ITRA (n=182)	VORI (n=38)
D/C Toxicity, n(%)	24(18)	10(15)	1(0.8)	0	5(7)	3(3)	19(10)	9(24)

When we compared the IFI incidence of our standard AFP (IV ITRA) versus the other 7 regimens, there was a marginal significant difference between IV ITRA and VORI (p=0.08). For pts that had IFI we founded no significant differences, except for the FL200 group (yeast :FL200= 8% vs. IV ITRA= 60%, p=0.021; mold: FL200 = 92% vs. IV ITRA 40%, p = 0.021). In regards of toxicity, IV ITRA was significantly better tolerated than VORI (p=0.03); while CASPO, FL200 and FL400 were significantly better tolerate than IV ITRA (p= <0.001, p= <0.001 and p= 0.02, respectively).

Conclusions: 1) VORI tends to be the best AFP with respect to preventing IFI. However, there is not enough power to detect the significance given the small sample size 2) When compare to IV ITRA, Caspo tends to be the less toxic AFP 3) We are currently developing a predictive model to adapt AFP to pts needs.