Approaches for using of antifungal drugs (AFD) in adult patients (pts) with newly diagnosed acute myeloid leukemia (AML) in real clinical practice in Russia: RIFI study

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Background

Invasive mycoses (IM) represent a major complication in pts with HSCT and acute leukemia. The objective of this study was to evaluate approaches for using of AFD in pts with newly diagnosed AML for 6 months of chemotherapy cycles (CC) in real clinical practice in hematological centers (HC) of Russia

Methods

Multicenter prospective observational study RIFI (NCT01519648) was performed between February 2012 and March 2014. All pts were followed up for 6 months. The first two cycles of chemotherapy were assessed as induction I and II, subsequent two cycles in pts in remission were considered as consolidation I and II. Patients without complete remission after two induction cycles were considered as refractory cases and were treated with salvage cycles.

Results

A total 262 adult pts from 14 HC with *de novo* AML were included in RIFI study. Within 6 months, 262 pts received 782 CC. Neutropenia was in 88% of CC with comparable frequency in induction I-II (91,2%-88,2%) and consolidation (84,5%). The median duration of neutropenia was 16 (1-94) days (19 and 14 days in induction I-II, 13 and 15 days in consolidation I – II, p<0.001). AFD were not prescribed in 278 (35,5%) of CC (24% in induction I, 35% in induction II, 48% in consolidation I, 44% in consolidation II, p=0.001). Approaches and AFD are presented on Fig.1 and Tab. 1. For prophylaxis fluconazole was used in 80% of CC, posaconazole in 15%. Secondary prophylaxis was in 2,3% (18) of CC and voriconazole was prescribed in 11 (61%) CC. Fever-driven, diagnosis-driven and targeted treatment approaches were done in 125 (16%), in 48 (6%), in 43 (5,5%) of CC respectively. For fever-driven approaches prevailed treatment with amphotericin B (55%), for diagnosis-driven strategy - amphotericin B (60%) and voriconazole (17%). Treatment of invasive aspergillosis (IA) was performed in 62,5% of cases by voriconazole, invasive candidiasis by caspofungin (4) and voriconazole (2) . IM (proven, probable, possible) was diagnosed in 43 (16,4%) pts. Cumulative incidence of IM, etiology of IM and rate of IM on CC are presented on Fig. 2,3 and tab. 2.

Conclusion

Pts with newly diagnosed acute AML received AFD in 64,5% of CC. Approaches for using of antifungal drugs were primary antifungal prophylaxis (29.5%), secondary antifungal prophylaxis (2,3%), fever-driven (16%), diagnosis-driven (6%) and targeted treatment (5,5%).

RESULTS

262 patients with *de novo* AML — Prospective multicenter study 2012 (February) – 2014 (March)

Total of CC	**782**
- Induction I	262
- Induction II	212
- Consolidation I	148
- Consolidation II	116
- Salvage	44
Neutropenia on CC	688 (88%)
Duration of neutropenia, days	16 (1-94)
Prescription of antibiotics	704 (90%)
Persistent fever ≥72 hours	338 (43%)
Recurrent febrile fever	334 (43%)

FIG. 1 Approaches for using of antifungal drugs in *de novo* AML

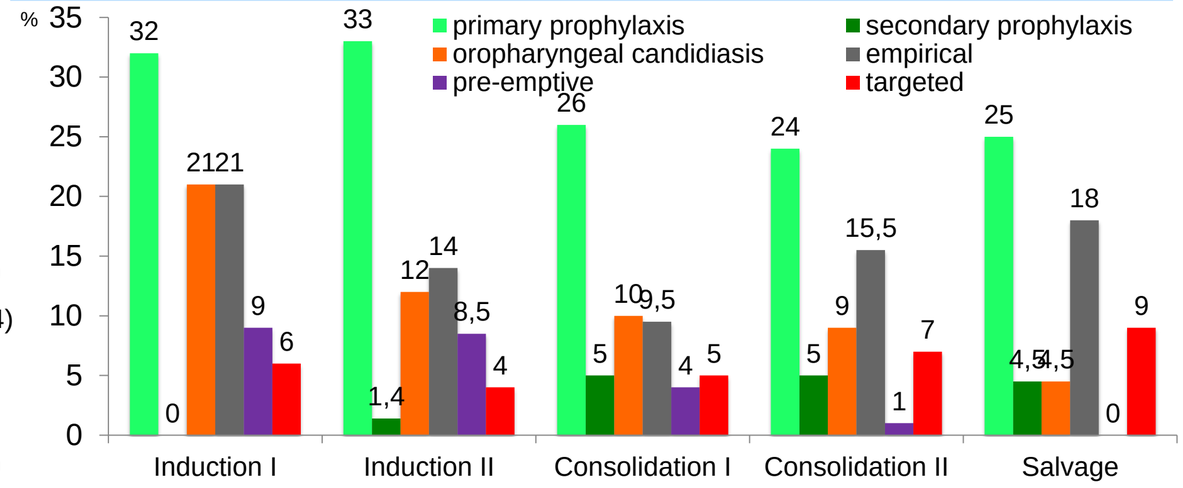


Table 1. Antifungal drugs on chemotherapy cycles in *de novo* AML

Approaches for using of AFD	Cycles n (%)	Drugs n (%)							
		Fluco	Itra	Posa	Vori	Ampho	L-ampho*	Caspo	Mica
Primary prophylaxis	231 (29,5)	184 (80)	2 (1)	34 (15)	7 (3)	4 (2)	-	-	-
Secondary prophylaxis**	18 (2,3)	3 (17)	1 (6)	1 (6)	11 (61)	-	-	-	-
Oropharyngeal candidiasis	108 (14)	104 (96)	1 (1)	-	2 (2)	1 (1)	-	-	-
Empirical	125 (16)	13 (10)	-	-	17 (14)	69 (55)	17 (14)	7 (6)	2 (1,5)
Pre-emptive	48 (6)	2 (4)	-	-	8 (17)	29 (60)	6 (12,5)	2 (4)	1 (2)
Targeted***	43 (5,5)				23 (53)	9 (21)	2 (5)	7 (16)	

* Lipid complex amphotericin B ** Two pts received combination treatment *** One pt received isavuconazole, 1- combination treatment

Fig. 2. Cumulative incidence of IM (proven, probable) in patients with AML

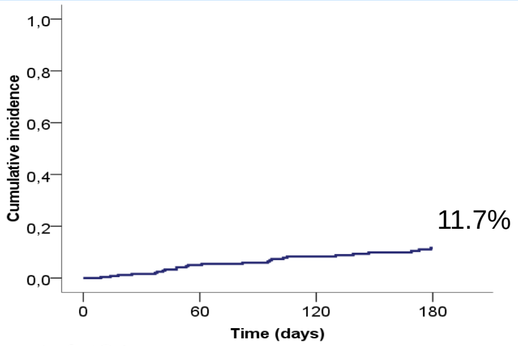
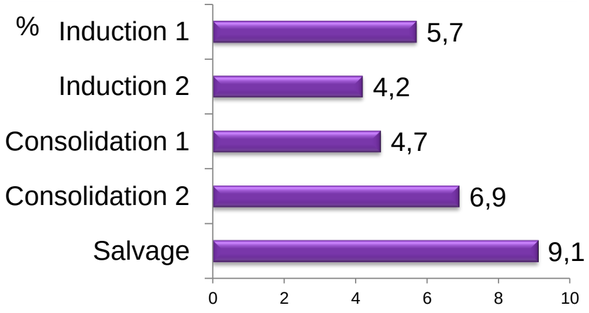


Table 2. Etiology of IM in *de novo* AML (n=262)

IA	32 (12,2%)
- Proven	1
- Probable	16
- Possible	15
Other molds	2 (0,8%)
Yeasts	7 (2,6%)
Mixed infection	2 (0,8%)
Total	**43 (16,4%)**

Fig. 3. Rate of IM on chemotherapy cycles in *de novo* AML



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