

Invasive mycoses (IM) and prescription of antifungal drugs (AFD) in adult patients (pts) with newly diagnosed acute lymphoblastic leukemia (ALL): RIFI study

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Background

The objective of this study was to estimate the rate of IM and prescription of AFD among pts with newly diagnosed ALL for 6 months of chemotherapy cycles (CC).

Methods

Multicenter prospective observational study RIFI (NCT01519648) was performed between February 2012 and March 2014. Pts with *de novo* ALL were included and followed up for 6 months. CC according to «ALL - 2009» protocol (NCT01193933) received 68 (61%) pts, Fig.1. Patients without complete remission after two induction cycles were considered as refractory cases and were treated with salvage cycles.

Results

A total of 111 pts from 12 hematological centers were enrolled. Within 6 months, 111 pts received 372 CC. Neutropenia was in 47% of CC, more often in induction I than consolidation I-II (74,8% vs 23,5% vs 17,6%, p=0.0001). The median duration of neutropenia was 11 (2-78) days (15 days in induction I, 9 days in consolidation I-II). AFD were not prescribed in 242 (65,1%) of CC (43% induction I, 70,5% induction II, 75,3% consolidation I, 81% consolidation II, p<0.0001). IM (proven, probable, possible) was diagnosed in 10 (9%) pts, tab. 1. The rate of IM on CC and the 6-month cumulative incidence of IM (proven, probable) are presented on Fig. 3,4. Prescription of AFD is presented on Fig.2. The main indications for the using of AFD were prophylaxis (15,3%) and treatment of oropharyngeal candidiasis (11,8%). Fluconazole was the main drug for prophylaxis (89,5%) and treatment of oropharyngeal candidiasis (97,7%). Fever-driven, diagnosis-driven and targeted treatment approaches were done in 11 (3%), in 12 (3,2%), in 10 (2,7%) of CC respectively.

Conclusion

IM were diagnosed in 9% of pts within 6 months of ALL treatment and were caused by molds (5,4%) and yeasts (3,6%). The rate of IM at different CC of treatment for ALL (induction, consolidation) was low and ranged from 3,2-1,2% except of salvage CC. The main indications for the prescription of AFD were prophylaxis and treatment of oropharyngeal candidiasis. Other approaches to the appointment of antifungal drugs did not exceed 3% at all CC. AFD were not used in 65% of CC.

RESULTS

Prospective multicenter study 2012 (February) – 2014 (March)

111 patients with *de novo* ALL

Gender (male/female)	56/55
Age, median, years	32 (18-70)
Total of CC	372
- Induction I	111
- Induction II	95
- Consolidation I	81
- Consolidation II	74
- Salvage	11
Neutropenia on CC	176 (47%)
Duration of neutropenia, days	11 (2-78)
Prescription of antibiotics	195 (52%)
Persistent fever ≥72 hours	45 (12%)
Recurrent of febrile fever	58 (17%)

FIG.1 Algorithm of treatment ALL - "ALL - 2009" (NCT01193933)

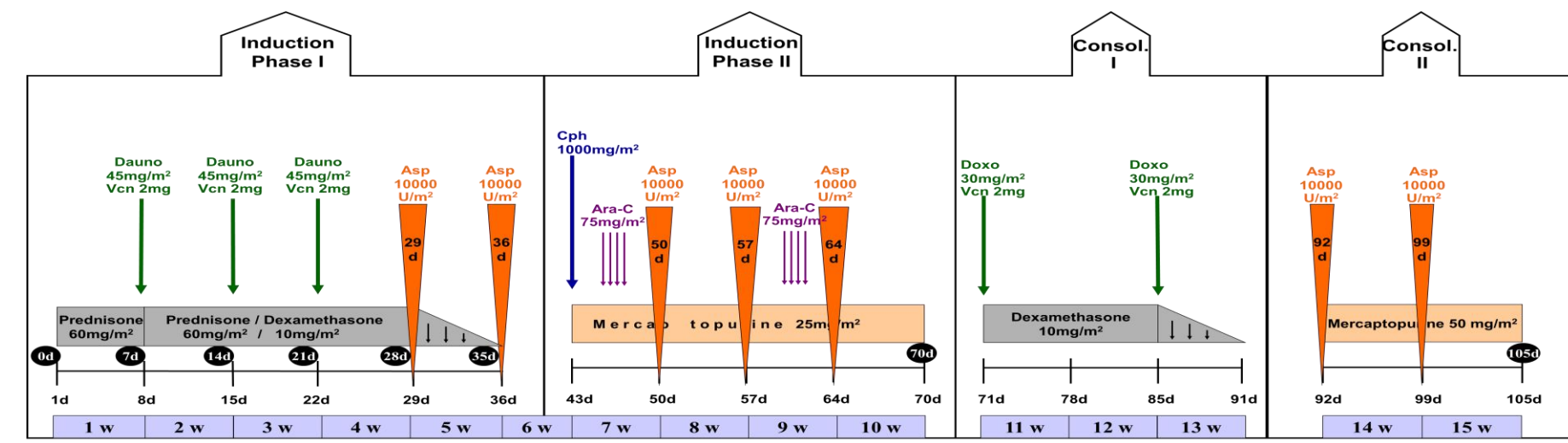


FIG. 2 Prescription of antifungal drugs in *de novo* ALL

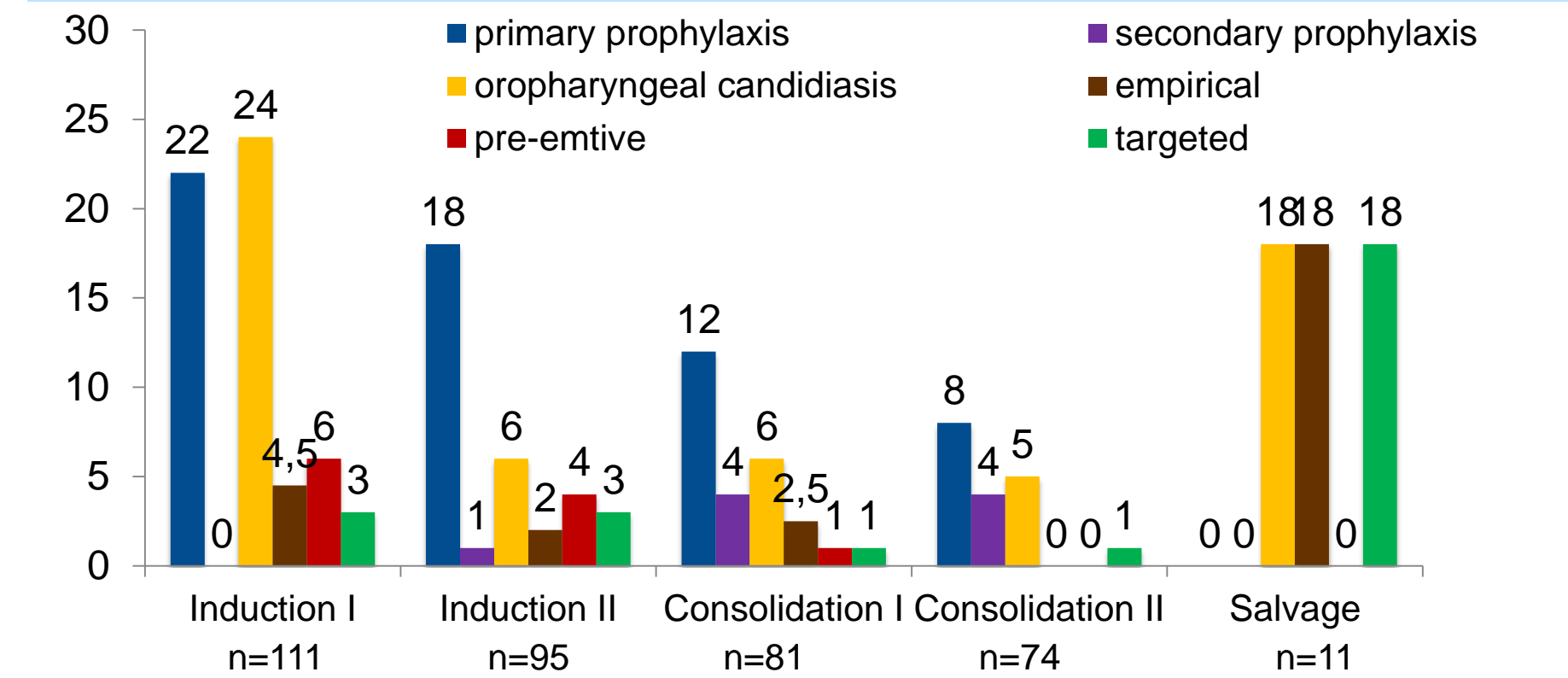


Fig. 3. Cumulative incidence of IM (proven, probable) in patients with ALL

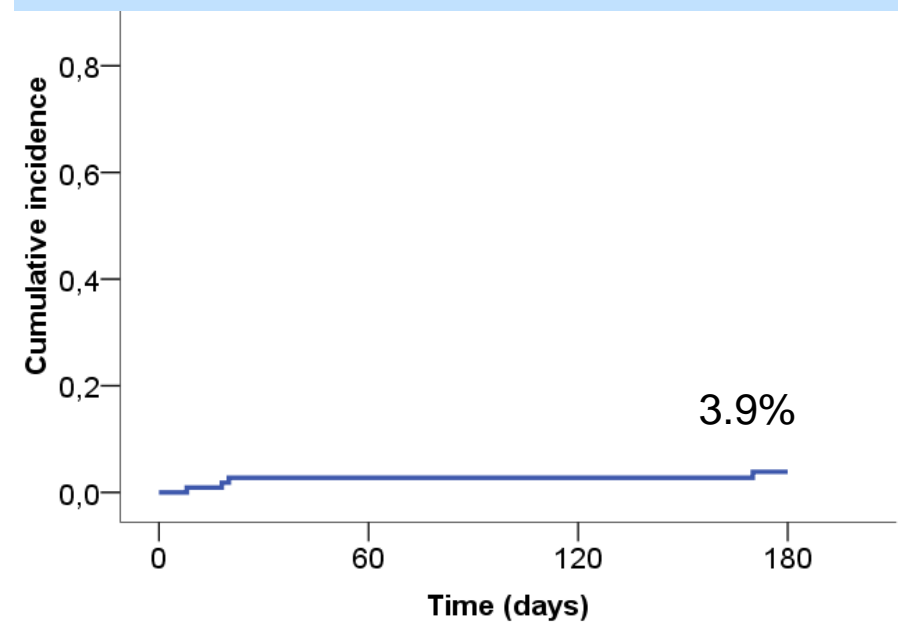


Table 1. Etiology of IM in *de novo* ALL (n=111)

Invasive aspergilosis	5 (4,5%)
- Probable	2
- Possible	3
Other molds	1 (0,9%)
Yeasts	4 (3,6%)
Total	10 (9%)

Fig. 4. Rate of IM on chemotherapy cycles in *de novo* ALL

