Abstract Submission

**30. Infectious diseases**

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**ISAVUCONAZOLE IN HEMATOLOGICAL PATIENTS: FINAL RESULTS OF A REAL-LIFE MULTICENTER SEIFEM (SORVEGLIANZA EPIDEMIOLOGICA DELLE INFEZIONI NELLE EMOPATIE) STUDY**

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Does the study abide by applicable national and international regulations and guidelines, including but not limited to ethical committees, data protection and privacy regulations, informed consent and off-label use of drugs?: Yes

**Background:** Isavuconazole (ISV) has been reported as safe and effective in the SECURE trial (Maertens 2016).

**Aims:** To confirm the efficacy and safety of ISV in hematological patients in a clinical care setting.

**Methods:** We planned a multicenter retrospective study, collecting all cases of invasive fungal infections (IFI) occurring in hematological patients (pts) treated with ISV in 17 Centers between Jul-16 and Nov-18. IFI were categorized as possible (PS), probable (PB) or proven (PV) according to EORTC/MSG criteria. The impact of age, gender, type and status of disease at IFI diagnosis [Dx], complete and partial remission [CR/PR], relapse/refractory [r/r], type of IFI, allogeneic stem cell transplantation (alloSCT), neutropenia and timing of ISV treatment were evaluated.

**Results:** One-hundred and twenty-eight pts were enrolled (M/F ratio: 76/52, median age 57y, range 18-80). AL were 88 (68%) (myeloid 57%; lymphoblastic 12%), lymphoma 28 (22%), myeloma 4 (3%), aplastic anemia 3 (2%) and myelodysplastic syndromes 5 (4%) pts. Thirty-one (24%) patients developed IFI at Dx, 54 (42%) while on CR/PR and 43 (34%) with r/r disease; alloSCT pts were 50 (39%). IFI were PS in 54 (42%), PB in 61 (48%) and PV in 13 (10%) cases. *Aspergillus* spp was responsible for 67 (91%) of PB/PV IFI; in the remaining 7 cases, 1 *Rhizomucor* and 1 *Fusarium* spp were isolated and in 5 histologically PV IFI no specific agent was identified. Lung was the more frequent site of IFI (110, 86%), followed by paranasal sinuses (13, 10%). ISV was employed as 1st line therapy in 44 (34%) and as subsequent line in 84 (66%) pts. The median duration of previous treatments was 18d (range 3-1110). Reasons for ISV use were failure in 45 (54%) and intolerance in 17 (20%) of 84 cases. In 17 (20%) ISV was chosen because of the need to switch to oral antifungal agent and in 5 (6%) for a favorable drug-interaction profile. Median duration of ISV treatment was 50d (2-375). Clinical and radiological overall response rate (ORR) was 82 of 118 evaluable pts (69%); it was similar when using ISV as 2nd line with refractory IFI or not (respectively: 67% vs 77%). In multivariate analysis, underlying disease status was confirmed as a predictive factor for ORR to ISV (rec/ref HR 0.259, CI 0.111-0.604). After a median follow-up of 4.2mo, 44 (34%) pts died; IFI-attributable mortality was 13/128 (10%). The estimated 1-year overall survival (OS) from IFI diagnosis of the entire cohort was 50% (CI 0.22-0.45); figures were similar for PS vs PB/PV IFI (52.8% vs 48.7%), AL vs no AL (49% vs 51%) and first vs subsequent line use of ISV (49% vs 51%). OS was significantly lower for pts with refractory IFI (36% vs 58%, p=0.05) (Fig. 1), with r/r hematological disease (r/r 19% vs CR/PR 71%, p=0.0007, or vs Dx 59%, p=0.016) and in alloSCT pts (38% vs 58%, p=0.029).

Response to ISV was associated to better OS (HR 0.102, CI 0.04-0.26), while r/r disease showed a trend toward statistically
significant negative impact on OS (rel/ref HR 2.344, CI 0.932-5.899). Adverse events (AE) were reported in 15/128 pts (11.7%) (hepatic in 5, cutaneous in 3, gastroenteric in 7 and hypokaliemia in 3); grade 3-4 AE were reported in 5 (4%) cases and led to permanent ISV discontinuation.

Summary/Conclusion: ISV is used in hematological pts also in diseases other than acute myeloid leukemia and it is overall well tolerated. ORR to ISV is at least comparable with other antifungal agents. Having an IFI refractory to other antifungal agents does not seem to compromise the response to ISV, although this condition, together with a r/r underlying disease, negatively impacts on survival.

Keywords: Fungal infection, Hematological malignancy, Treatment