Questionnaire

1 1 - Demographics Underlying Diseases

Welcome to the Pediatric Isavuconazole Registry (PedIR)

Thank you for documenting a case in the FungiScope® Pediatric Isavuconazole Registry.

This registry is for **healthcare professionals** and collects **retrospective, anonymized** real-world data on pediatric patients treated with isavuconazole for invasive mold infections.

Please **check eligibility** before proceeding.

Inclusion Criteria

- **Age < 18 years** at the time of isavuconazole administration
- **Underlying condition:** hematologic malignancy and/or HSCT (or comparable immunocompromised state)
- **Infection:** proven or probable or possible invasive mold infection (EORTC/MSG)
- **Treatment:** isavuconazole (IV and/or oral) for treatment of the infection
- **Isavuconazole treatment start:** in 2024 or 2025

Kind regards
Zoi D. Pana, Andreas Groll & Danila Seidel
for the PedIR Study Team

SECTION 1

Patient characteristics I: Demographic data and underlying disease

Please note: The first day of isavuconazole administration is considered day 1. All other days will be calculated based on this day.

Country where the patient was treated

Year in which isavuconazole was administered to the patient:

- ○ 2024
- ○ 2025
- ○ 2026

Sex

- ○ Female
- ○ Male

Age at the time of isavuconazole administration

Months _____ Years _____

Height & Weight

Height [cm] _____ Weight [kg] _____

Underlying disease

- ○ Acute lymphoblastic leukemia (ALL)
- ○ Acute myeloid leukemia (AML)
- ○ Non-Hodgkin Lymphoma (NHL)
- ○ Myelodysplastic syndrome
- ○ Aplastic anemia
- ○ Immunodeficiency
- ○ Thalassemia
- ○ Sickle cell disease
- ○ Other, please specify:

_____

ALL risk stratification:

- ○ High risk
- ○ Medium risk
- ○ Low risk

Year of diagnosis of underlying disease

Optional, additional information on underlying disease:

_____

Current Treatment Phase of the Underlying Disease

Malignancy

- ○ Yes
- ○ No

If yes, please specify the disease status:

- ○ First diagnosis
- ○ Diagnosis of recurrent disease

Please indicate the oncologic treatment phase:

- ○ Induction chemotherapy
- ○ Consolidation chemotherapy
- ○ Maintenance chemotherapy

Current treatment phase of the underlying disease / Transplant status

- ☐ Post-lung / Post-heart and lung SOT
- ☐ Post-heart SOT
- ☐ Post-liver SOT
- ☐ Post-renal SOT
- ☐ Post-pancreas and/or bowel SOT
- ☐ Post-allogeneic HCT
- ☐ Post-autologous HCT
- ☐ Post CAR T-cell therapy
- ☐ Other, please specify:
- ☐ N/A / Unknown

Co-morbidities at start of isavuconazole administration

(select all that apply)

- [ ] Concomitant cardiac disease
- [ ] Concomitant pulmonary disease
- [ ] Liver impairment
- [ ] Renal impairment
- [ ] Diabetes mellitus
- [ ] Syndromes, if yes please specify:
- [ ] None
- [ ] Other, please specify:

Co-morbidities at start of isavuconazole administration, please specify if applicable:

2 2 - Characteristics at isavuconazole start

SECTION 2

Patient Characteristics II: Clinical Information at the Start of Isavuconazole Administration

Please note: The first day of isavuconazole administration is considered day 1. All other days will be calculated based on this day.

Clinical information at the start of isavuconazole administration

	Yes	No	Unknown
Chemotherapy within the last 4 weeks	☐	☐	☐
Steroids (Prednisone equivalent ≥ 2 mg/kg/day) for ≥14 days within the last 4 weeks	☐	☐	☐
Other Immunosuppressants	☐	☐	☐
Neutropenia (<500 cells/μL) within last 4 weeks	☐	☐	☐
Mucositis within last 4 weeks	☐	☐	☐
Active GvHD receiving treatment	☐	☐	☐
Graft rejection (SOT) receiving treatment	☐	☐	☐
ICU stay at time of isavuconazole start	☐	☐	☐
History of invasive fungal disease within the last 12 months	☐	☐	☐
Prior broad spectrum antibiotic use within last 4 weeks	☐	☐	☐
CVC in place within last 4 weeks	☐	☐	☐

Other immunosuppressants at start of isavuconazole administration:

- ☐ Cyclosporine
- ☐ Tacrolimus
- ☐ Sirolimus
- ☐ Other (please specify

Neutropenia (<500 cells/μL) within last 4 weeks prior to isavuconazole administration:

- ☐ Total days with <500 cells/uL:

Mucositis within last 4 weeks prior to isavuconazole administration:
Grade:

- ○ I
- ○ II
- ○ III
- ○ IV
- ○ Unknown

Active GvHD receiving treatment at start of isavuconazole administration:
Details:

- ☐ Acute
- ☐ Chronic

Acute GvHD receiving treatment at start of isavuconazole administration
Grade:

- [ ] I
- [ ] II
- [ ] III
- [ ] IV
- [ ] Unknown

Chronic GvHD receiving treatment at start of isavuconazole administration
Grade:

- [ ] mild
- [ ] moderate
- [ ] severe
- [ ] Unknown

History of invasive fungal disease within the last 12 months:

EORTC/MSG classification:

- [ ] Proven
- [ ] Probable
- [ ] Possible

Type of fungal infection:

- [ ] Invasive pulmonary aspergillosis
- [ ] Candidemia
- [ ] Other, please specify:

Provide the infectious fungal agent(s) causing that previous infection, if identified:

3 3 + 4 - Laboratory finding at isavuconazole start, during isavuconazole, EO-isavuconazole

SECTION 3: Laboratory Findings

- At the Start of isavuconazole Administration
- During isavuconazole Administration
- At End of isavuconazole Administration

Baseline value at isavuconazole start (±3 days), most pathological value during isavuconazole treatment, and at end of isavuconazole treatment (±3 days)

Abbrev. ALP: Alkaline Phosphatase, ANC: Absolute Neutrophil Count, CRP: C-Reactive Protein, γGT: Gamma-Glutamyl Transferase, GOT: Glutamate Oxaloacetate Transaminase (Aspartate Aminotransferase, AST), GPT: Glutamate Pyruvate Transaminase (Alanine Aminotransferase, ALT), Hb: Hemoglobin, PLT: Platelet Count

	BASELINE	MOST PATHOLOGICAL	END OF TREATMENT
Leukocytes [/µl; ×10⁹/L]			
ANC [/µl; ×10⁹/L]			
Hb [g/dL]			
PLT [10³/µL; ×10⁹/L blood]			
Creatinine [mg/dL]			
Urea [mg/dL]			
γGT [U/L]			
Total Bilirubin [mg/dL]			
GPT [U/L]			
GOT [U/L]			
ALP [U/L]			
CRP [mg/L]			

SECTION 4

Diagnosis of Invasive Mold Disease (IMD)

Diagnosis per EORTC/MSG 2020 criteria

	Done	Not done
CT	☐	☐
MRI	☐	☐
Ultrasound	☐	☐
Other imaging	☐	☐
Biopsy	☐	☐

CT findings

CT: please select region(s) and specify findings relevant for the documented IMD

- ☐ Head
- ☐ Thorax
- ☐ Abdomen
- ☐ Musculoskeletal
- ☐ Other, please specify

MRI findings

MRI: please select region(s) and specify findings relevant for the documented IMD

- [ ] CNS
- [ ] ENT / Orbital
- [ ] Thorax
- [ ] Cardiovascular
- [ ] Abdomen
- [ ] Musculoskeletal / Soft Tissue
- [ ] Whole-body
- [ ] Other, please specify

US findings

Ultrasound: please select region(s) and specify findings relevant for the documented IMD

- [ ] Cardiac
- [ ] Abdomen
- [ ] Other, please specify

Other findings, please specify the procedure and findings relevant for the documented IMD:

Biopsy, from which site?

Histopathological evidence (tissue invasion)?

- ◯ Yes, tissue invasion seen
- ◯ No tissue invasion seen
- ◯ Not done

Histopathological evidence (tissue invasion) from which site?

Fungal biomarker and molecular diagnostics for IMD

	Positive	Negative	Not done
GM in serum	☐	☐	☐
GM in bronchoalveolar fluid	☐	☐	☐
GM in cerebrospinal fluid	☐	☐	☐
GM in other fluids	☐	☐	☐
PCR	☐	☐	☐
Next generation sequencing (NGS)	☐	☐	☐
Other sequencing	☐	☐	☐

GM in other fluids, please specify:

PCR, from which site:

NGS, from which site:

Other sequencing, from which site:

Definition of Invasive Mold Disease (IMD):

- ◯ Proven
- ◯ Probable
- ◯ Possible

Location (Type) of IMD

	Yes	No
Localized disease	☐	☐
Disseminated disease	☐	☐

Localized IMD, which site:

Disseminated IMD, which sites:

Etiological infectious agent (causing the IMD)

- ○ Organism was isolated
- ○ No organism isolated

Name of the organism(s):	
Source of the organism(s):	

Was antifungal susceptibility testing performed for the isolate

- ○ Susceptibility performed
- ○ Not performed
- ○ Not available / unknown

Method used for antifungal susceptibility testing of this isolate

Reference standard

- ○ EUCAST broth microdilution
- ○ CLSI broth microdilution

Non-reference / commercial methods

- ○ Gradient strip (e.g. Etest®)
- ○ Automated system (e.g. VITEK® 2, Phoenix™)
- ○ Disk diffusion

Other / unknown

- ○ Other (specify):
- ○ Unknown

Antifungal susceptibility testing results

S = Susceptible
I = Susceptible, increased exposure
R = Resistant
ATU = Area of Technical Uncertainty (interpretation unreliable)

	MIC [mg/L]	Interpretation (S/I/R/ATU)
Amphotericin B		
Anidulafungin		
Caspofungin		
Fluconazole		
Flucytosine		
Fosmanogepix		
Ibrexafungerp		
Isavuconazole		
Itraconazole		
Micafungin		
Olorofim		
Posaconazole		
Rezafungin		
Terbinafine		
Voriconazole		

4 5 - AF Treatment

SECTION 5

Antifungal Treatment Prior and During isavuconazole Administration

Please note: The first day of isavuconazole administration is considered day 1. All other days will be calculated based on this day.

5.1. Treatment prior to the initiation of isavuconazole administration

Antifungal prophylaxis within 4 weeks prior to isavuconazole administration

- ○ Yes
- ○ No
- ○ Unknown

If yes, please select which antifungals:

- ☐ Amphotericin B
- ☐ Isavuconazole
- ☐ Posaconazole
- ☐ Voriconazole
- ☐ Echinocandin
- ☐ Other:

Antifungals for empirical, pre-emptive or definite treatment of IMD within 4 weeks prior to isavuconazole administration

- ☐ Yes, empirically
- ☐ Yes, pre-emptively
- ☐ Yes, definite treatment
- ☐ No
- ☐ Unknown

If yes, which antifungals:

- [ ] Liposomal amphotericin B
- [ ] Lipid-complex amphotericin B
- [ ] Amphotericin B deoxycholate
- [ ] Anidulafungin
- [ ] Caspofungin
- [ ] Fluconazole
- [ ] Flucytosine
- [ ] Fosmanogepix
- [ ] Ibrexafungperp
- [ ] Isavuconazole
- [ ] Itraconazole
- [ ] Micafungin
- [ ] Olorofim
- [ ] Posaconazole
- [ ] Rezafungin
- [ ] Terbinafine
- [ ] Voriconazole
- [ ] Other:

For how many days overall:

(antifungals prior to isavuconazole administration)

_____ days

Combination or monotherapy?

	Monotherapy	Combination therapy	Not applicable/Not given		
Empirically	○	○	○	○	○
Pre-emptively	○	○	○	○	○
Definite treatment	○	○	○	○	○

Primary reason for switch to isavuconazole

- ◯ Lack of response to last regimen
- ◯ IMD progression with last regimen
- ◯ Intolerance to last regimen
- ◯ Drug-drug interactions with last regimen
- ◯ Step-down from combination therapy
- ◯ Step-up to combination therapy including isavuconazole
- ◯ Hospital discharge to outpatient setting
- ◯ Other, please specify:

Was isavuconazole started as mono- or as combination therapy?

- ◯ Monotherapy
- ◯ Combination therapy

Which drugs were administered together with isavuconazole as combination therapy.
For how many days during isavuconazole administration for each drug separately.

- [ ] Liposomal amphotericin B [days]
- [ ] Lipid-complex amphotericin B [days]
- [ ] Amphotericin B deoxycholate [days]
- [ ] Anidulafungin [days]
- [ ] Caspofungin [days]
- [ ] Fluconazole [days]
- [ ] Flucytosine [days]
- [ ] Fosmanogepix [days]
- [ ] Ibrexafungperp [days]
- [ ] Itraconazole [days]
- [ ] Micafungin [days]
- [ ] Olorofim [days]
- [ ] Posaconazole [days]
- [ ] Rezafungin [days]
- [ ] Terbinafine [days]
- [ ] Voriconazole [days]

☐ Other, which and how many days:

5.2. Isavuconazole administration

Please indicate if you refer to isavuconazole OR isavuconazole sulfate

- ○ Isavuconazole
- ○ Isavuconazole sulfate

Did you provide an isavuconazole loading dose?

- ○ Yes
- ○ No

Isavuconazole loading dose

Please provide details.

Dose [mg/kg] (e.g., 200)	
Number of doses administered per day (e.g., 3)	
Route (IV vs. PO) (e.g., IV)	
Number of days (e.g., 2)	

Isavuconazole maintenance dose

Provide infos for any changes in dose or route during isavuconazole treatment.

(please provide information for isavuconazole only)

	Route (IV vs PO)	Dose [mg/KG]	Start Day	Until Day
1. isavuconazole dose				
2. isavuconazole dose				
3. isavuconazole dose				
4. isavuconazole dose				
5. isavuconazole dose				

If isavuconazole dose was modified during treatment, please select the primary reason:

- ○ Lack of response to last regimen
- ○ IMD progression with last regimen
- ○ Intolerance to last regimen
- ○ Drug-drug interactions with last regimen
- ○ TDM results available
- ○ Other, please specify:

Dose modified based on TDM results:

- ○ Yes model based
- ○ Yes empirical

If isavuconazole was switched from iv to oral, what was the reason:

- ○ De-escalation
- ○ Other, please specify:

5.3. Treatment emergent clinical Adverse Events (AEs) during isavuconazole administration considered to be at least possibly associated

(Categorization according to current Common Terminology Criteria for Adverse Events (CTCAE) v6.0)

Where there any AEs considered possibly associated with isavuconazole administration?

- ○ Yes, please specify below
- ○ No AE
- ○ Unknown

Details on AEs considered possibly related to isavuconazole administration

If a row is left blank, N/A will be assumed

	N/A	Mild	Moderate	Severe/Life-threatening	Death
Elevated liver chemistry tests	○	○	○	○	○
Nausea	○	○	○	○	○
Vomiting	○	○	○	○	○
Dyspnoea	○	○	○	○	○
Abdominal pain	○	○	○	○	○
Diarrhoea	○	○	○	○	○
Injection site reaction	○	○	○	○	○
Headache	○	○	○	○	○
Hypokalaemia	○	○	○	○	○
Rash	○	○	○	○	○
Confusional state	○	○	○	○	○
Acute renal failure	○	○	○	○	○
Increased blood bilirubin	○	○	○	○	○
Convulsion	○	○	○	○	○
Epilepsy	○	○	○	○	○
Respiratory failure	○	○	○	○	○

Other AE during isavuconazole administration not mentioned above:

5.4. Final Assessment of isavuconazole Administration Status:

Isavuconazole continued until treatment completed with successful outcome?

- ○ Yes, isavuconazole continued until completed treatment
- ○ No, isavuconazole was discontinued prematurely

Primary reason for premature isavuconazole discontinuation:

- ○ Adverse event or intolerance, please specify:
- ○ Death
- ○ Lack of efficacy
- ○ Other, specify:

5 6 - Outcome

SECTION 6

Invasive Mold Disease (IMD) Outcome at End of Isavuconazole Administration Episode

---

Clinical response at end of isavuconazole treatment

- ○ Complete resolution of all attributable clinical symptoms and physical findings
- ○ Partial resolution of attributable clinical symptoms and physical findings
- ○ No clinical improvement
- ○ Worsening
- ○ Not evaluable

Mycological response at end of isavuconazole treatment

- ○ Eradication (confirmed clearance of pathogen)
- ○ Presumed eradication (clinical and radiological resolution without microbiological proof)
- ○ Persistence (fungal pathogen still detectable)
- ○ Not evaluable

Radiological response at end of isavuconazole treatment

- ○ Complete resolution of radiological signs
- ○ Improvement compared to baseline/screening
- ○ No change
- ○ Progression
- ○ Not evaluable

Overall outcome at end of isavuconazole treatment

- ○ Complete response
- ○ Partial Response
- ○ Stable Disease
- ○ Failure

Overall survival

	Alive	Deceased	Unknown
Alive at End of isavuconazole administration?	○	○	○

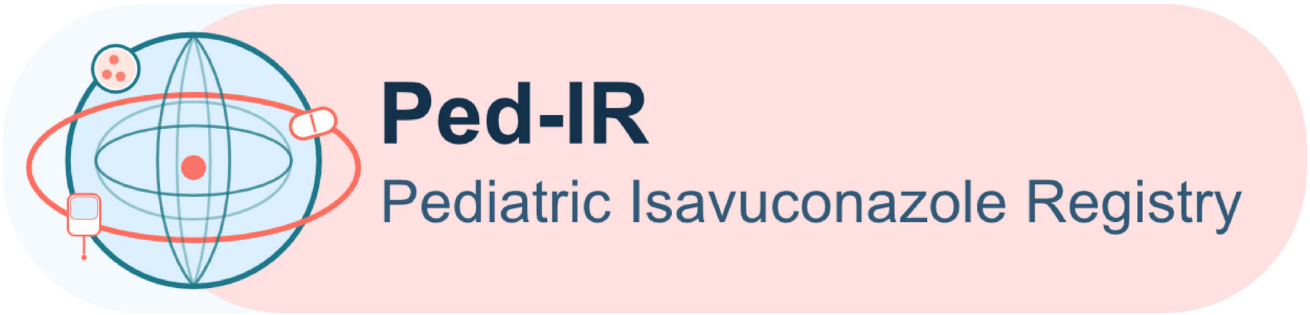
abbrev. ISAV isavuconazole

	Alive	Deceased	Lost to Follow up	Unknown
Alive at day 28 after start of ISAV (day 1)?	○	○	○	○
Alive at day 42 after start of ISAV (day 1)?	○	○	○	○
Alive at day 84 after start of ISAV (day 1)?	○	○	○	○
Alive at day 180 after start of ISAV (day 1)?	○	○	○	○

6 Final page

Thank you for contributing to the Ped-ISAV study.
We will now validate your case for completeness and will reach out if we identify any inconsistencies.

For further questions please contact the study team in the meantime:
Prof. Zoi Pana panazoi@gmail.com and Dr. Danila Seidel danila.seidel@uk-koeln.de.



Study Team:
Prof. Zoi Dorothea Pana, Cyprus & Dr. Danila Seidel, Cologne, GER
Prof. Andreas Groll, Münster, GER
Prof. Fabianne Carlesse, São Paulo, BRA
Dr. Sarina Butzer, Cologne, GER
Prof. Oliver A. Cornely, Cologne, GER
Prof. Thomas Lehrnbecher, Frankfurt, GER