

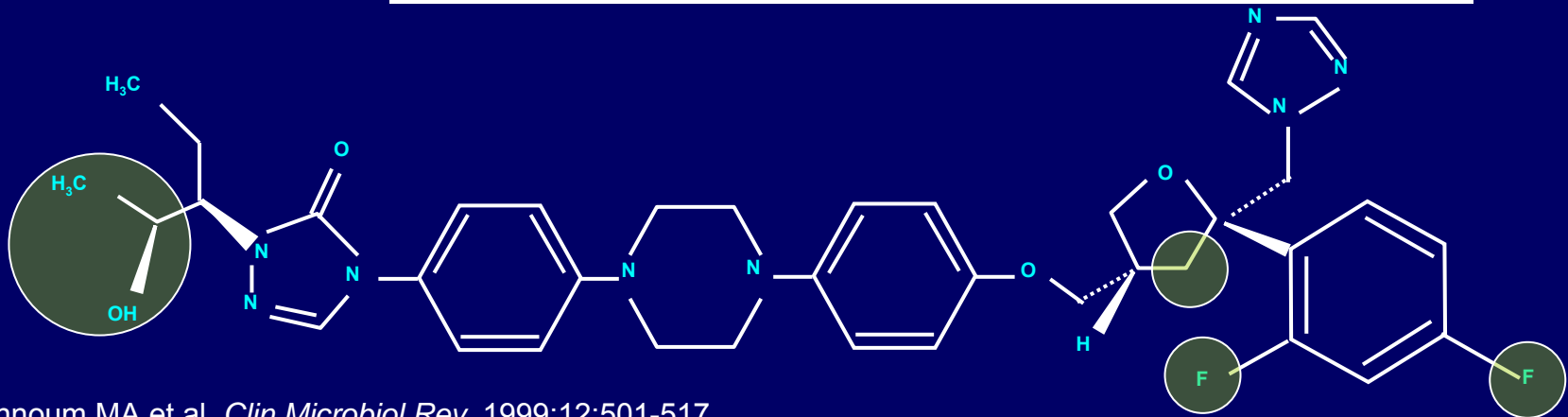
Posaconazole for the Treatment and Prophylaxis of Invasive Fungal infections

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Posaconazole: Mechanism of Action



- Primary mode of action: inhibition of fungal ergosterol biosynthesis (cytochrome P450–dependent enzyme lanosterol 14 α -demethylase [CYP51A1])
- Extended side chain likely result in tighter and more stable binding to receptor sites



Ghannoum MA et al. *Clin Microbiol Rev.* 1999;12:501-517.

Herbrecht R. *Int J Clin Pract.* 2004;58:612-624.

Wexler D et al. *Eur J Pharm Sci.* 2004;21:645-653.

Overview of Posaconazole (Noxafil®)



- **Extended-spectrum triazole**
- **Bioavailable oral suspension**
- ***In vitro* activity against wide range of moulds and yeasts**
- ***In vivo* activity against several moulds and yeasts**
- **Broad activity against several pathogens, including *Aspergillus*, *Fusarium*, *Coccidioides*, agents of chromoblastomycosis and mycetoma, *Candida*, *Cryptococcus*, *Histoplasma*, and Zygomycetes**
- **Well tolerated in clinical studies**

The clinical significance of *in vitro* studies is not established, and results from these studies do not necessarily predict clinical activity.

Noxafil [summary of product characteristics]. Brussels, Belgium; SP Europe; 2006.

Posaconazole Indications in European Union & Turkey

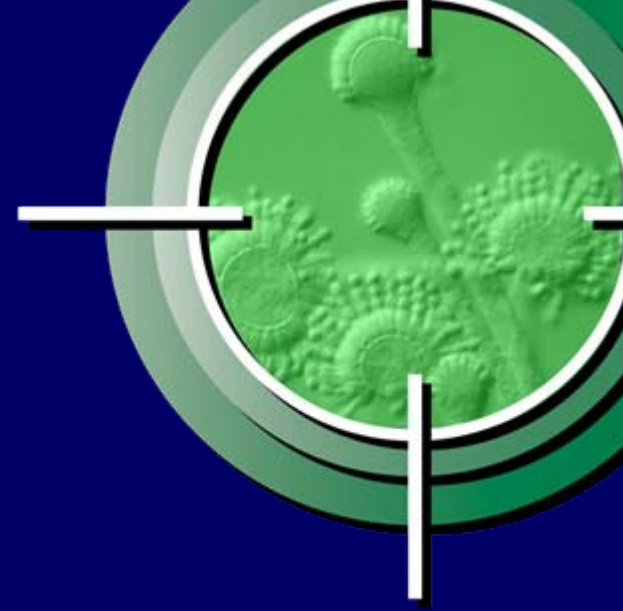


- **Invasive aspergillosis** in patients with disease that is refractory to amphotericin B or itraconazole or in patients who are intolerant of these medicinal products
- **Fusariosis** in patients with disease that is refractory to amphotericin B or in patients who are intolerant of amphotericin B
- **Chromoblastomycosis and mycetoma** in patients with disease that is refractory to itraconazole or in patients who are intolerant of itraconazole
- **Coccidioidomycosis** in patients with disease that is refractory to amphotericin B, itraconazole, or fluconazole or in patients who are intolerant of these medicinal products
- **Oropharyngeal candidiasis:** as first-line therapy in patients who have severe disease or are immunocompromised, in whom response to topical therapy is expected to be poor

Posaconazole Indications in European Union & Turkey



- Noxafil is also indicated for prophylaxis of invasive fungal infections in the following patients:
 - Patients receiving remission-induction chemotherapy for acute myelogenous **leukemia** (AML) or myelodysplastic syndromes (MDS) expected to result in **prolonged neutropenia** and who are at high risk of developing invasive fungal infections;
 - **Hematopoietic stem cell transplant (HSCT) recipients** who are undergoing high-dose immunosuppressive therapy for **graft versus host disease** and who are at high risk of developing invasive fungal infections.



***In Vitro Data
for Posaconazole Compared to
Other Antifungal Agents***

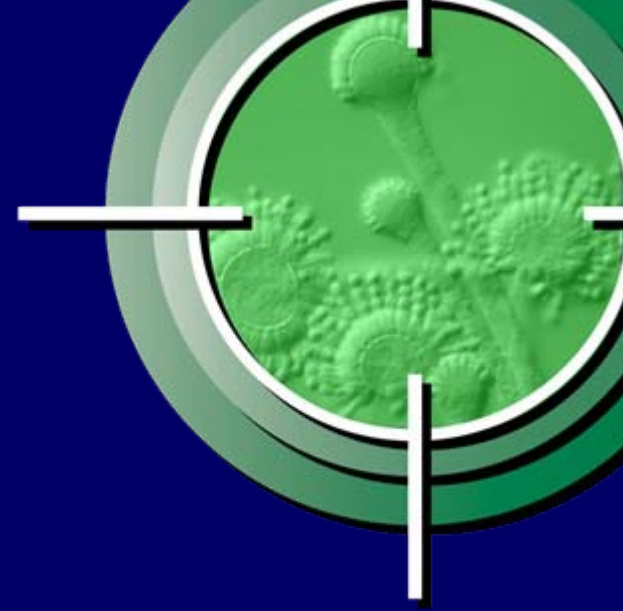
Summary of Posaconazole In Vitro Activity



- Posaconazole has a broad spectrum of *in vitro* activity against many fungi, including:
 - Moulds: including *Aspergillus*, *Fusarium*, and the Zygomycetes
 - Yeasts: including *C albicans*, *C krusei*, and *C glabrata*
 - Dimorphic fungi, including *Coccidioides*, *Histoplasma*, and *Blastomyces*
 - Rare fungi, such as *Scedosporium* (primarily *S apiospermum*) and agents of chromoblastomycosis, mycetoma, and phaeohyphomycosis
- Posaconazole exhibited potent antifungal activity against a wide variety of clinically important fungal pathogens and was frequently **more active than other azoles and amphotericin B**

The clinical significance of *in vitro* studies is not established, and results from these studies do not necessarily predict clinical activity.

Sabatelli F et al. *Antimicrob Agents Chemother.* 2006;2009-2015.



***Posaconazole Treatment of Refractory
Invasive Fungal Infections
Aspergillosis
(MITT Population)***

Posaconazole Treatment of Refractory Invasive Fungal Infections

Baseline Characteristics: Aspergillosis



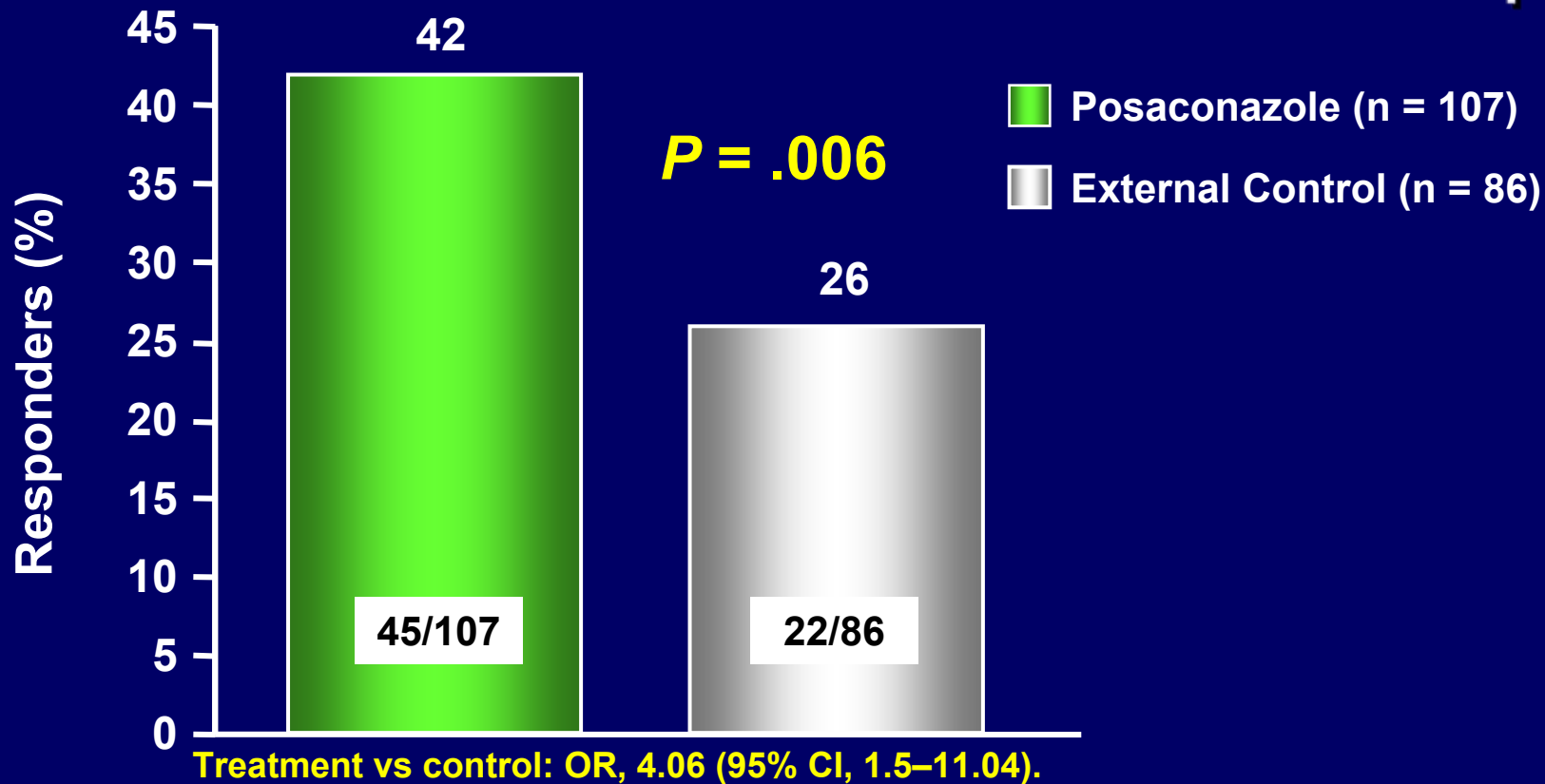
Characteristic, n (%)	Posaconazole (n = 107)	External Control (n = 86)
Hematologic malignancy	79 (74)	70 (81)
Hematopoietic stem cell transplant	55 (51)	38 (44)
Allogeneic	48 (45)	34 (40)
Neutropenia at baseline (ANC <500 cells/mm ³)	21 (20)	26 (30)
Solid organ transplant	12 (11)	7 (8)
Acquired immunodeficiency	28 (26)	19 (22)
Congenital immunodeficiency	2 (2)	3 (3)
Nonhematologic malignancy	13 (12)	5 (6)
Mechanical ventilation at baseline	4 (4)	Not allowed per protocol
Death within 72 hours of baseline	4 (4)	Not allowed per protocol

Study report P02952, pp 60, 61, 80. SPRI, Kenilworth, NJ, USA; March 2004.

Walsh T et al. *Clin Infect Dis*. 2007;44:2-12.

Posaconazole Treatment of Refractory Invasive Fungal Infections

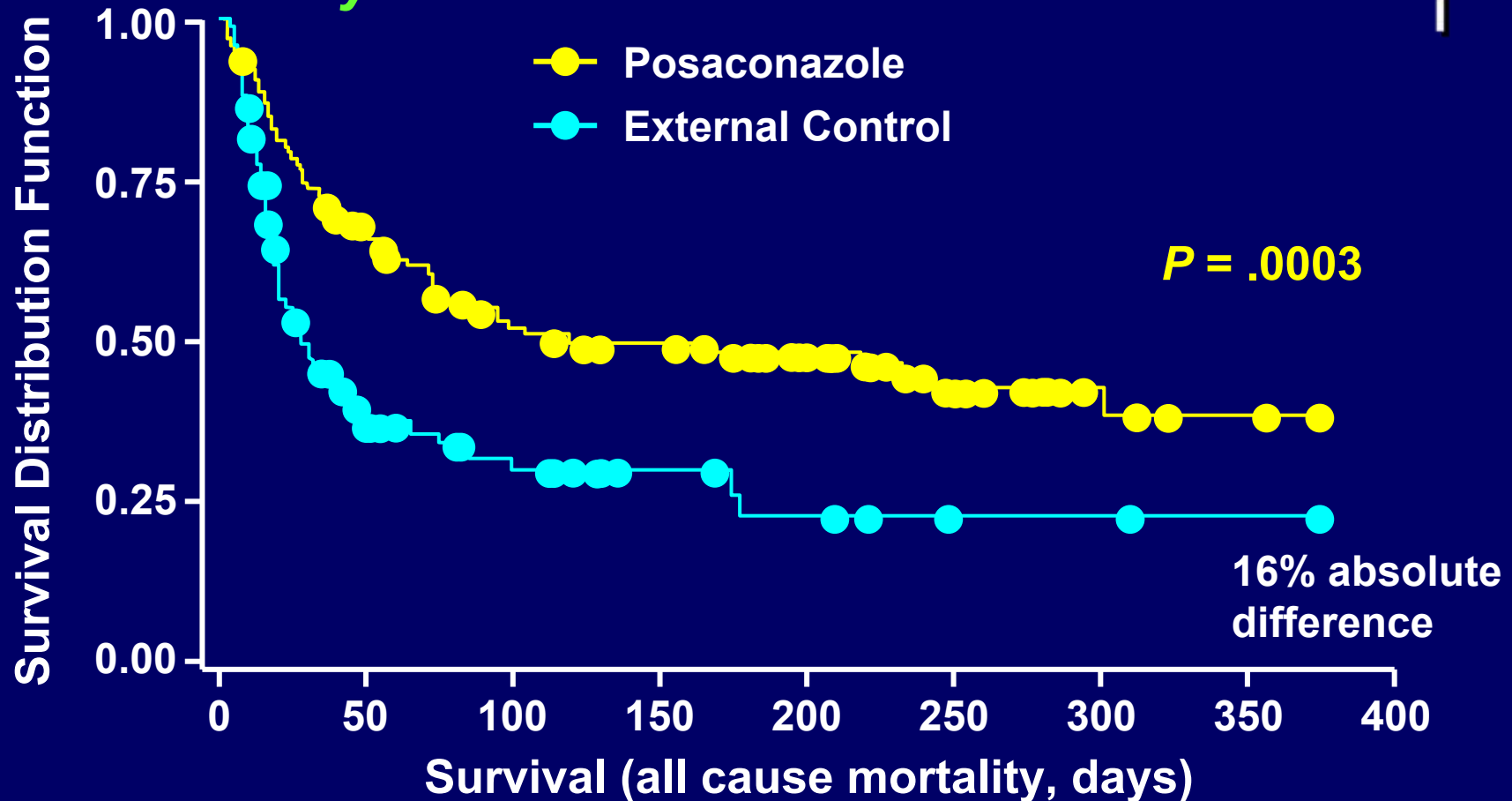
Global Response*: Aspergillosis



*Primary efficacy analysis (logistic regression).

Posaconazole Treatment of Refractory Invasive Fungal Infections

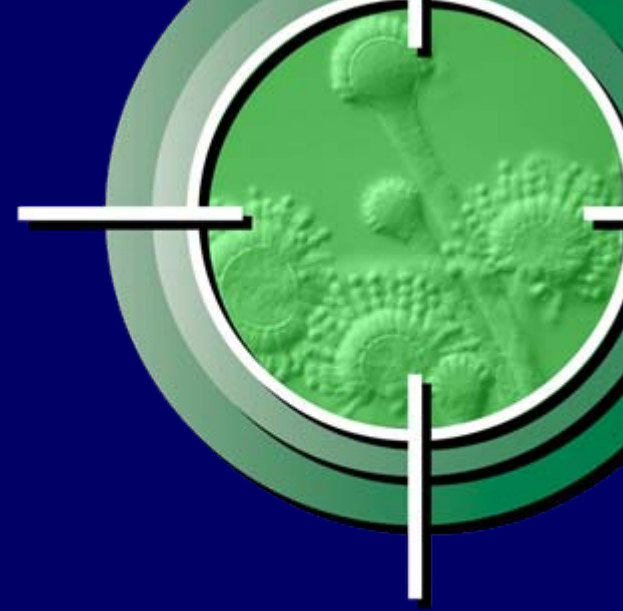
Global Response*: Kaplan-Meier Analysis of All-Cause Mortality



*Global response in MITT subset with *Aspergillus* as primary pathogen.

Walsh T et al. *Clin Infect Dis*. 2007;44:2-12.

Study report P02952, pp 76, 300. SPRI, Kenilworth, NJ, USA; March 2004.



***Posaconazole Registration Data for
Refractory Invasive Fungal Infections
Results for Other Pathogens***

Posaconazole for Zygomycosis

Study Design



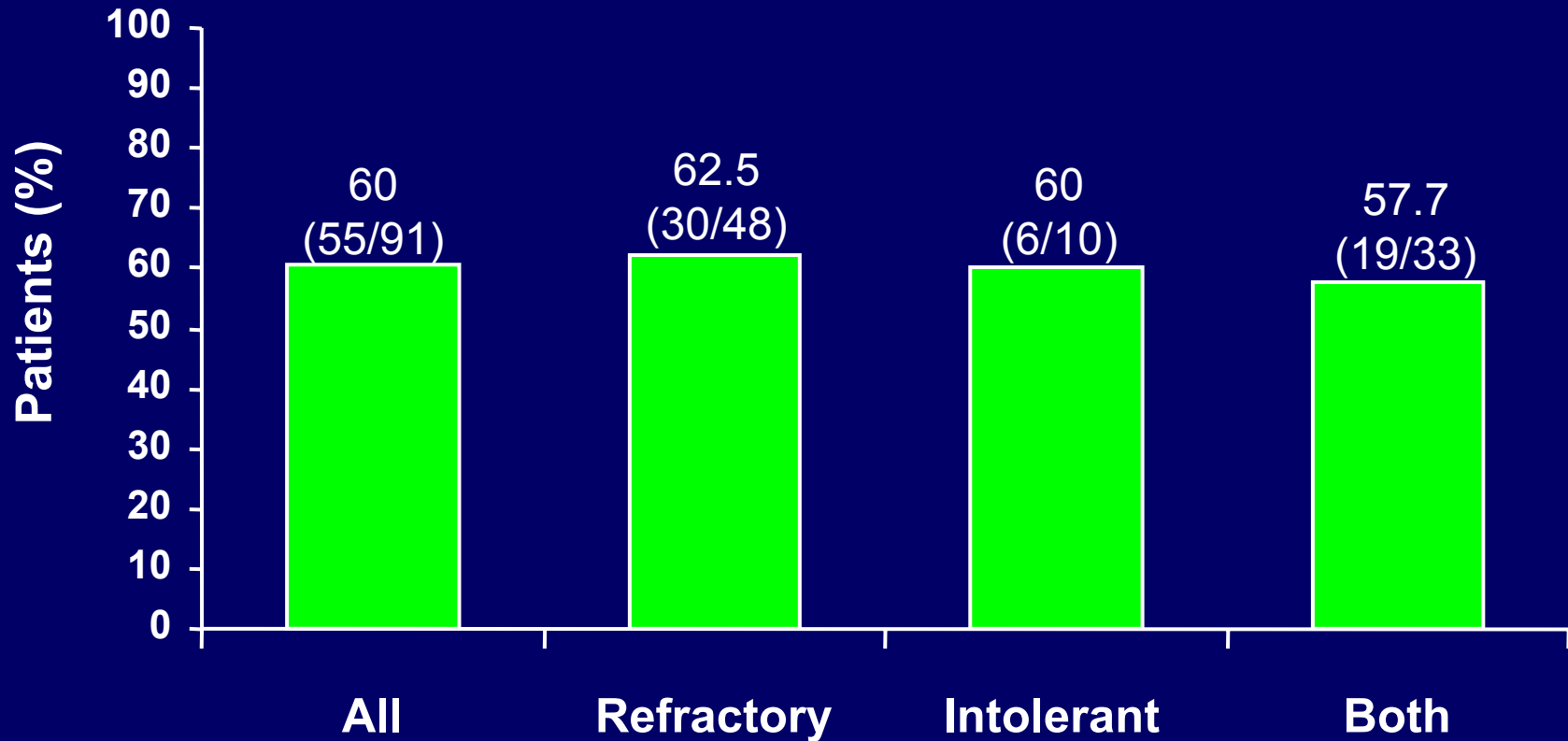
- **Patients identified through enrollment forms from the Schering-Plough compassionate use protocol**
 - Refractory zygomycosis
 - Intolerant of other antifungal therapy
- **91 patients with proven or probable* zygomycosis included in analysis**
- **Team of experts reviewed each case and determined outcome at ≤ 12 weeks after initiation of posaconazole**
 - Complete response: resolution of infection
 - Partial response: clinically meaningful improvement
 - Stable disease: no improvement, but no deterioration
 - Failure: deterioration

*Proven, probable, and possible as defined by the European Organisation for Research and Treatment of Cancer (EORTC) consensus criteria. Ascioglu S et al. *Clin Infect Dis*. 2002;34:7-14.

van Burik J-A et al. *Clin Infect Dis*. 2006;42:e61-e65.

Posaconazole for Zygomycosis

Success Rate by Reason for Enrollment



Posaconazole Activity Against Fusariosis



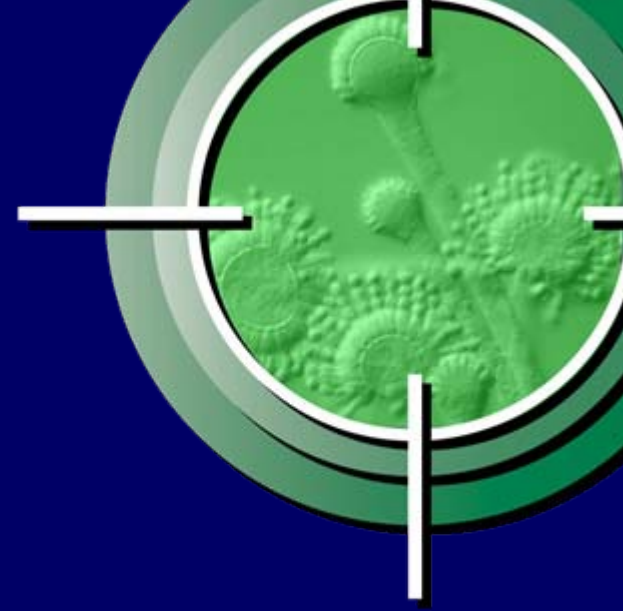
- **Overall success: 46% (11/24)^{1,2}**
 - 18 refractory/intolerant cases
 - 6 proven infections but not refractory/intolerant (4/6 success)
- **Refractory/intolerant infections: 39% (7/18)²⁻⁴**
 - 9 patients had disseminated disease
 - 14 were refractory, 4 were intolerant
 - Prior therapy was amphotericin B
 - 6 patients were neutropenic at baseline, no response in the setting of persistent neutropenia³

1. Noxafil [summary of product characteristics]. Brussels, Belgium; SP Europe; 2006.

2. Raad I et al. ICAAC 2004. Abstract M-669.

3. Study report P00041, p 160-161. SPRI, Kenilworth, NJ, USA; March 2004.

4. Study report P02952, p 91-92. SPRI, Kenilworth, NJ, USA; March 2004.



***Posaconazole Registration Data for
Prophylaxis in High-Risk
Neutropenic Patients***

Posaconazole Prophylaxis in Neutropenic Patients

Study Purpose and Primary Objective



- **Purpose**
 - Evaluate the efficacy, safety, and tolerability of posaconazole as prophylaxis for invasive fungal infections in 602 high-risk patients with acute myelogenous leukemia or myelodysplastic syndrome and prolonged neutropenia
- **Primary objective**
 - Determine efficacy of posaconazole versus pooled standard azoles (fluconazole and itraconazole) in preventing proven or probable invasive fungal infections from randomization to 7 days after last dose

Posaconazole Prophylaxis in Neutropenic Patients

Selected Inclusion Criteria

- **Patients ≥ 13 years of age**
- **Anticipated neutropenia (absolute neutrophil count ≤ 500 cells/mm³) for ≥ 7 days**
- **Treatment with intensive chemotherapy for:**
 - **Newly diagnosed acute myelogenous leukemia**
 - **Relapse of acute myelogenous leukemia**
 - **Myelodysplastic syndrome**



Posaconazole Prophylaxis in Neutropenic Patients

Study Design



- Open-label, evaluator-blinded, **randomized (1:1 ratio) trial**
- Posaconazole 200 mg oral suspension 3x daily
- Standard azole*
 - Fluconazole 400 mg oral suspension 1x daily or
 - Itraconazole 200 mg oral solution 2x daily
- Patients unable to tolerate oral drug could receive intravenous prophylaxis at the same dose for ≤ 3 days per chemotherapy cycle
 - Intravenous alternative for posaconazole: amphotericin B deoxycholate 0.3 to 0.5 mg/kg daily

*Comparator to be used throughout study determined by each center prior to study commencement.

Cornely OA et al. *N Engl J Med.* 2007;356:348-359.

Posaconazole Prophylaxis in Neutropenic Patients

Primary End Point



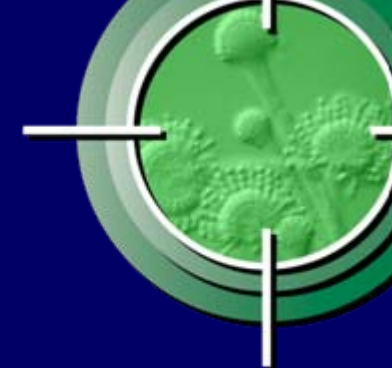
- **Incidence of proven or probable invasive fungal infection during treatment phase*** for the intent-to-treat population (N = 602) versus pooled standard azoles (fluconazole or itraconazole) as evaluated in two stages
 - Noninferiority of posaconazole versus pooled standard azoles and, if demonstrated,
 - Superiority of posaconazole versus pooled standard azoles
- **Invasive fungal infections were adjudicated by an independent data review committee**

*On-treatment period.

Cornely OA et al. *N Engl J Med.* 2007;356:348-359.

Posaconazole Prophylaxis in Neutropenic Patients

Enrollment Summary



602 patients enrolled from
89 centers worldwide

Posaconazole



n = 304

Standard azoles

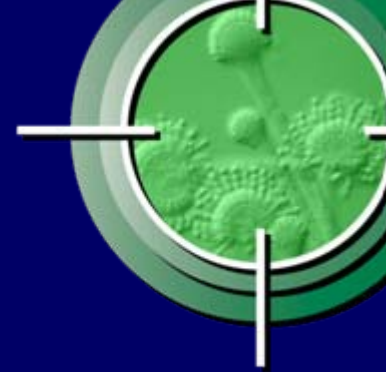


n = 298

Fluconazole (n = 240)
Itraconazole (n = 58)

Posaconazole Prophylaxis in Neutropenic Patients

Summary of Cumulative Prophylaxis and Study Duration



	Posaconazole (n = 304)	Standard Azoles (n = 298)
Duration of prophylaxis, days		
Mean \pm SD^{1,2}	29 \pm 21	25 \pm 17
Median (range)²	23 (1–110)	20 (1–80)
Study duration*, days		
Mean \pm SD^{1,2}	93 \pm 33	90 \pm 33

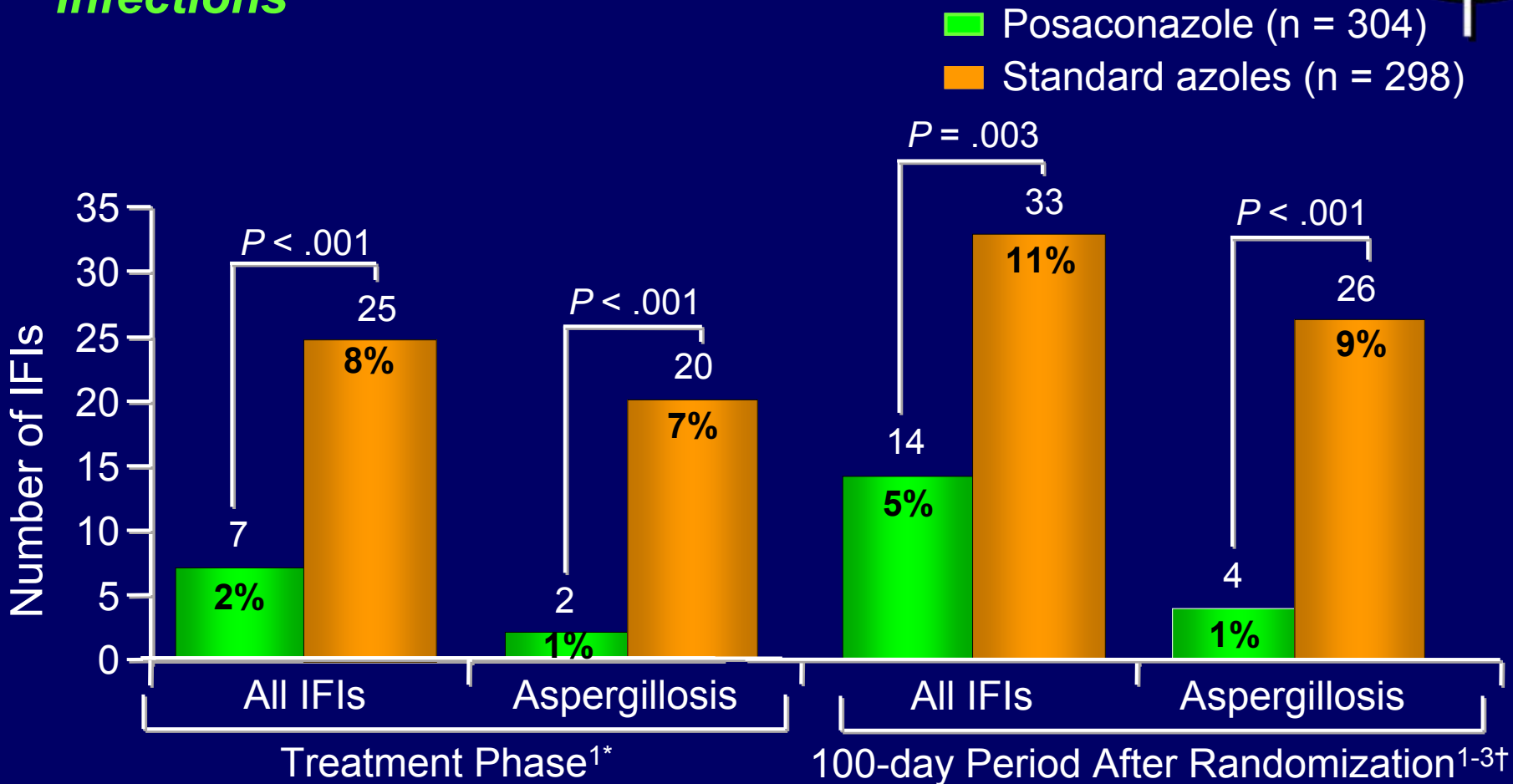
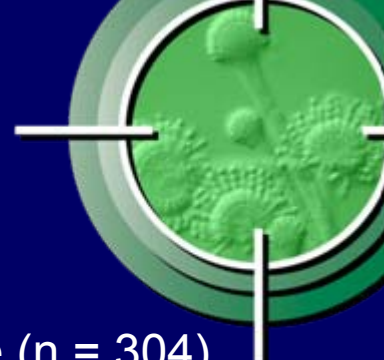
*From randomization to last contact.

1. Cornely OA et al. *N Engl J Med*. 2007;356:348-359.

2. Study report P01899, p 143. SPRI, Kenilworth, NJ, USA; November 2005.

Posaconazole Prophylaxis in Neutropenic Patients

Results – Proven/Probable Invasive Fungal Infections



IFI indicates invasive fungal infection.

1. Noxafil [summary of product characteristics]. Brussels, Belgium; SP Europe; 2006.

2. Cornely OA et al. *N Engl J Med*. 2007;356:348-359.

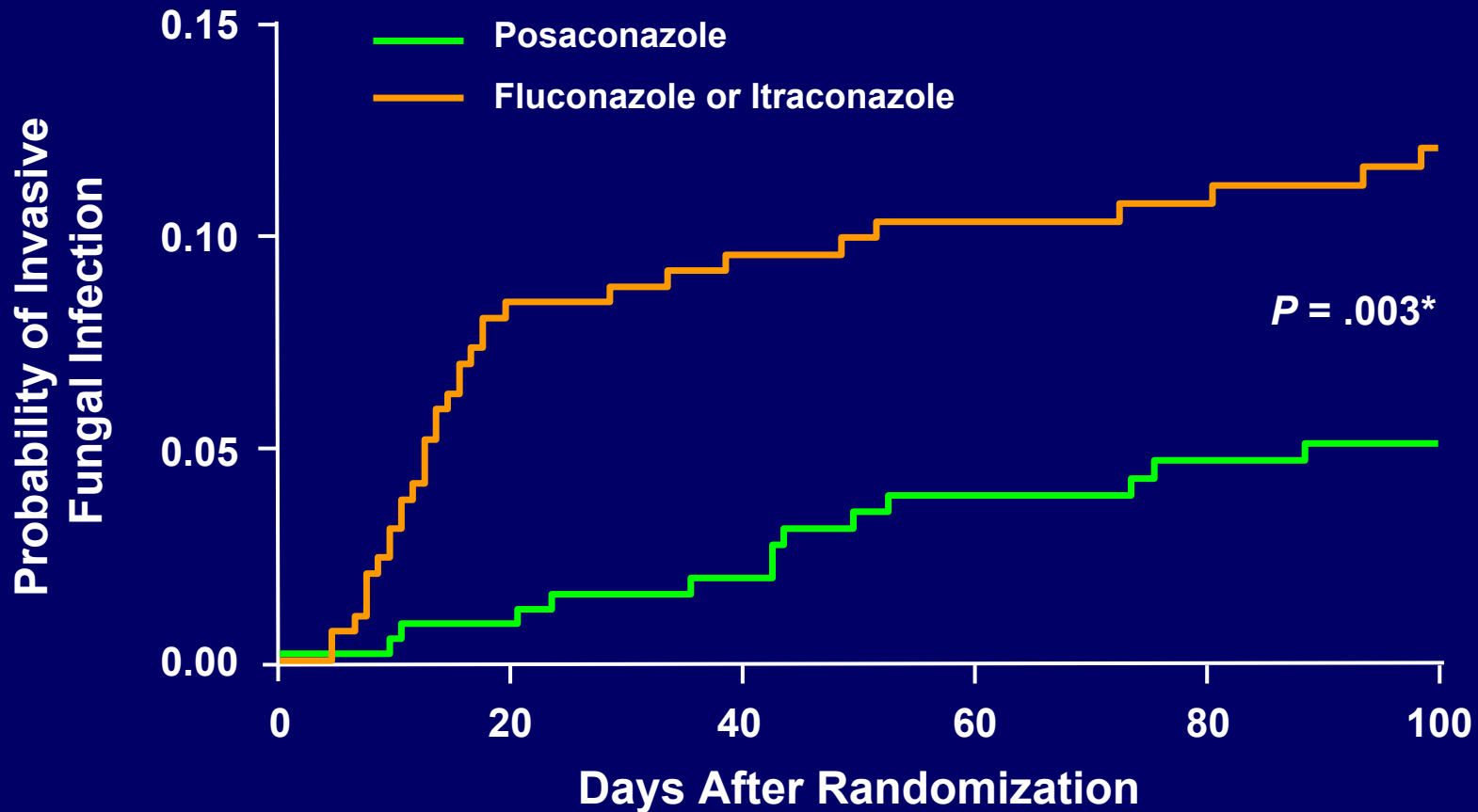
3. Study report P01899, p 106,108,109. SPRI, Kenilworth, NJ, USA; November 2005.

*On-treatment period.

†Fixed-time period.

Posaconazole Prophylaxis in Neutropenic Patients

Results – Time to Invasive Fungal Infection



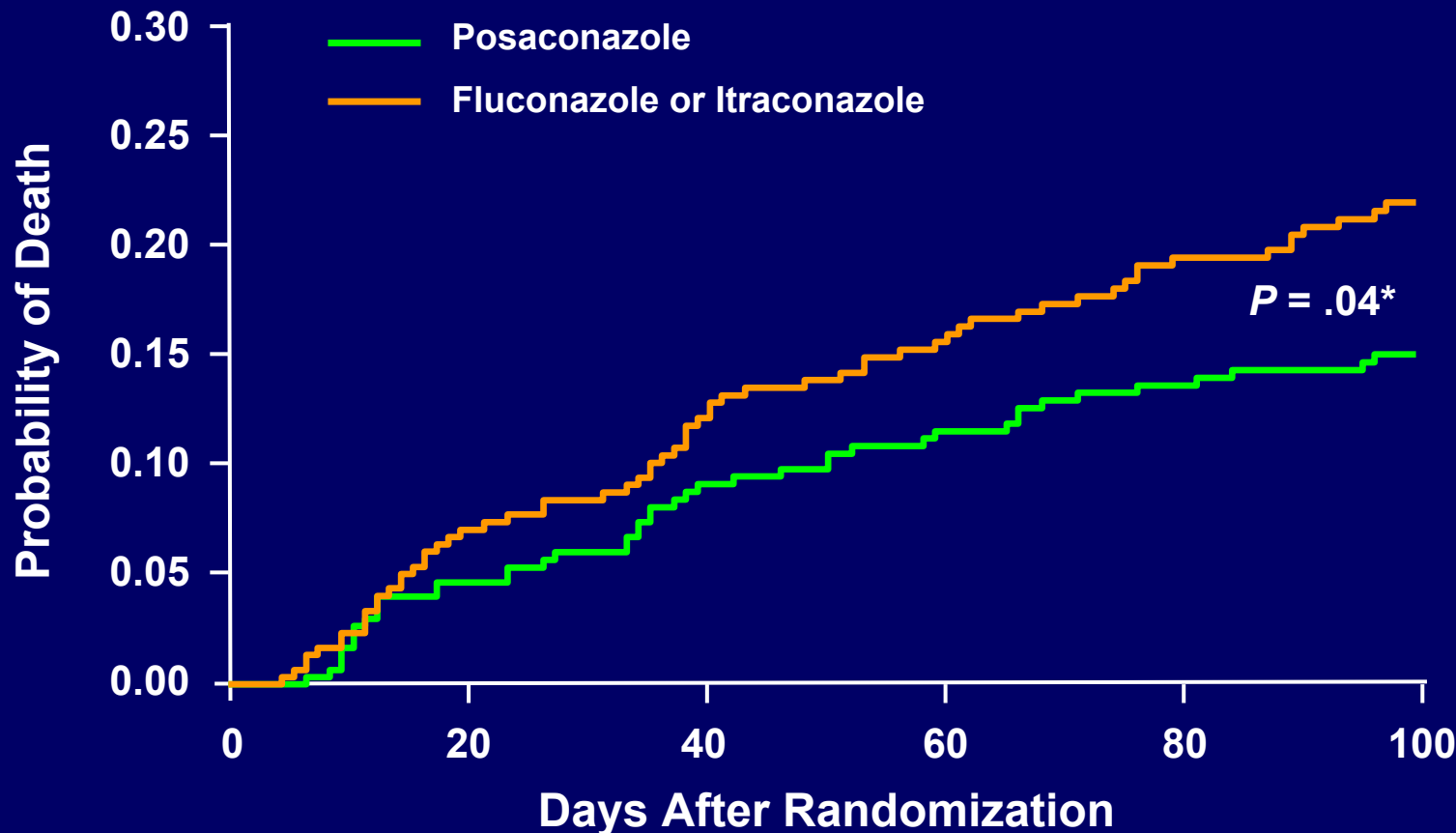
*Estimated using log-rank statistics.

Censoring time is the minimum of the last contact date and day 100.

Cornely OA et al. *N Engl J Med.* 2007;356:348-359.

Posaconazole Prophylaxis in Neutropenic Patients

Results – Death From Any Cause



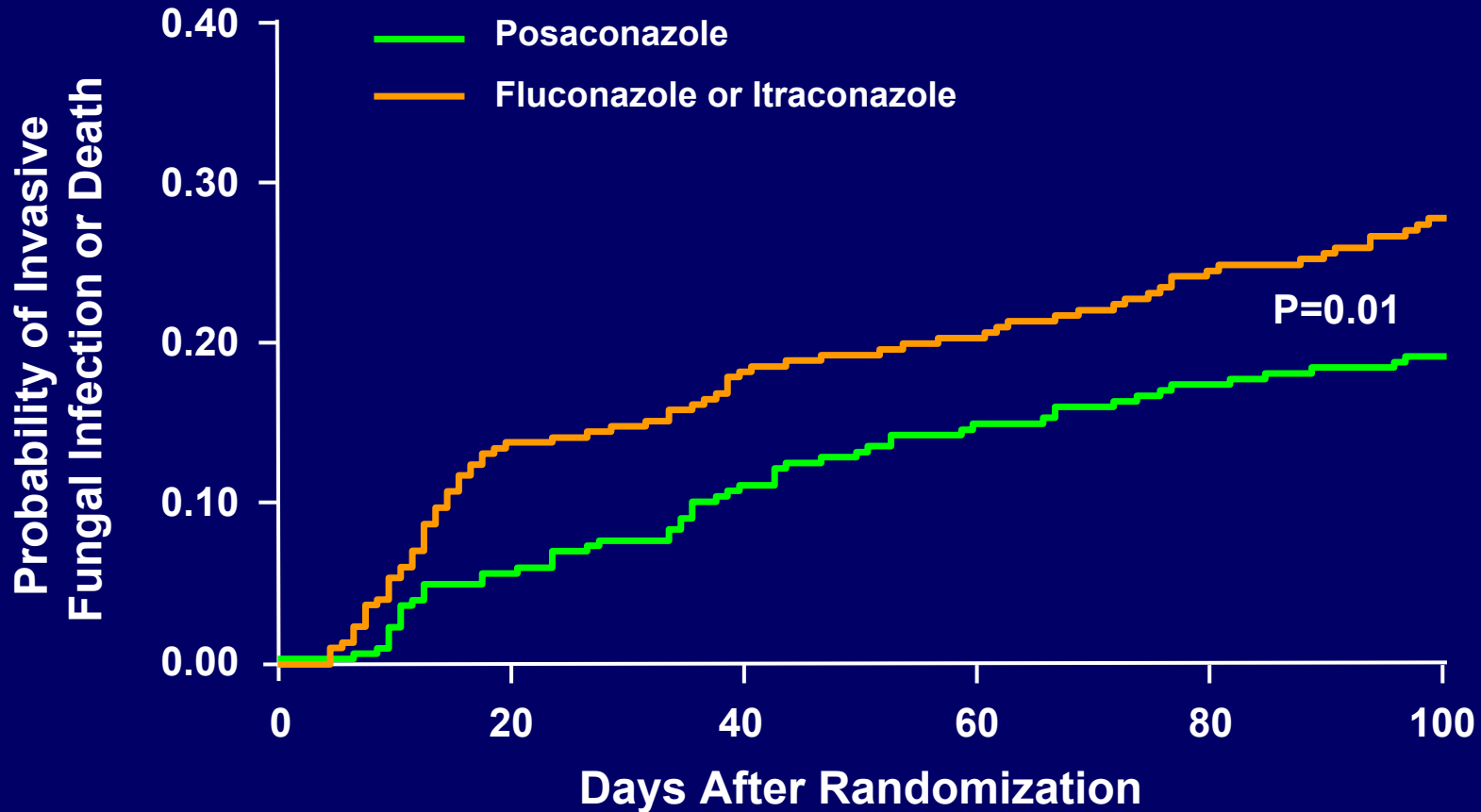
*Estimated using log-rank statistics.

Censoring time is the minimum of the last contact date and day 100.

Cornely OA et al. *N Engl J Med.* 2007;356:348-359.

Posaconazole Prophylaxis in Neutropenic Patients

Results – Time to Invasive Fungal Infection or Death

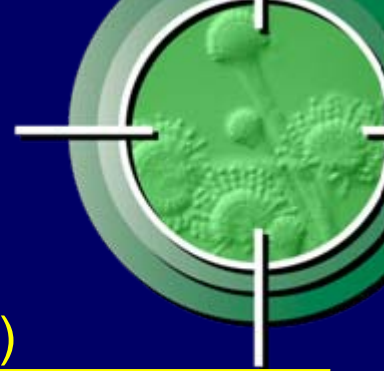


*Estimated using log-rank statistics.

Cornely OA et al. *N Engl J Med.* 2007;356:348-359.

Prophylaxis in Neutropenic Patients

Serious ($\geq 2\%$) AEs*



Event	Patients, n (%)			
	POS (n = 304)	Standard Azoles		
		FLU/ITZ (n = 298)	FLU (n = 240)	ITZ (n = 58)
Any event[†]				
Total	159 (52)	175 (59)	143 (60)	32 (55)
Neutropenia	22 (7)	23 (8)	18 (8)	5 (9)
Gastrointestinal hemorrhage	8 (3)	3 (1)	2 (1)	1 (2)
Bilirubinemia	7 (2)	5 (2)	4 (2)	1 (2)
Hypotension	10 (3)	21 (7)	17 (7)	4 (7)
Cardiac failure	6 (2)	3 (1)	3 (1)	0
Cardiac arrest	4 (1)	6 (2)	5 (2)	1 (2)
Cardiorespiratory arrest	4 (1)	5 (2)	4 (2)	1 (2)
Atrial fibrillation	2 (1)	6 (2)	5 (2)	1 (2)

*Events are listed for the period from randomization until 30 days after the last dose of the study drug had been administered.
Numbers for subentries may not sum to the total numbers because patients could have more than 1 event.

[†]Full list of serious adverse events are available with the publication.

Cornely OA et al. *N Engl J Med.* 2007;356:348-359.

Posaconazole Prophylaxis in Neutropenic Patients

Conclusions



- **Posaconazole was**
 - Superior to standard azoles for prevention of invasive fungal infection
 - Superior to standard azoles for prevention of invasive aspergillosis
 - Associated with a significant survival benefit
- **Safety profile of posaconazole was comparable to that of pooled standard azoles**

Posaconazole Prophylaxis in Allogeneic Hematopoietic Stem Cell Transplant Recipients With Graft-Versus-Host Disease

Study Purpose and Primary Objective



- **Purpose**

- Evaluate the efficacy, safety, and tolerability of posaconazole as prophylaxis for invasive fungal infection in allogeneic hematopoietic stem cell transplant recipients with acute or chronic graft-versus-host disease

- **Primary objective**

- Determine efficacy of posaconazole versus fluconazole in preventing proven or probable invasive fungal infection from randomization to 112 days after first dose (fixed treatment period)*

*Fixed-time period.

Ullmann AJ et al. *N Engl J Med.* 2007;356:335-347.

Posaconazole Prophylaxis in Allogeneic Hematopoietic Stem Cell Transplant Recipients With Graft-Versus-Host Disease

Selected Inclusion Criteria



- **Allogeneic hematopoietic stem cell transplant recipients ≥ 13 years of age**
- **Acute or chronic extensive graft-versus-host disease**
- **Treatment with intensive immunosuppressive therapy**
 - **High-dose corticosteroids**
 - **Antithymocyte globulin**
 - **Steroid-sparing regimen comprising a combination of ≥ 2 immunosuppressive agents or modalities**

Posaconazole Prophylaxis in Allogeneic Hematopoietic Stem Cell Transplant Recipients With Graft-Versus-Host Disease Study Design



- **Double-blind, double-dummy, randomized trial**
- **Posaconazole 200 mg 3x daily or**
- **Fluconazole 400 mg oral capsule 1x daily**
- **Patients unable to tolerate oral study drug:**
 - **Suspension of study drug until oral medication could be tolerated**
 - **Non-azole intravenous prophylaxis could be substituted for no more than 4 days**

Posaconazole Prophylaxis in Allogeneic Hematopoietic Stem Cell Transplant Recipients With Graft-Versus-Host Disease

Primary End Point



- **Incidence of proven or probable invasive fungal infection during the fixed treatment period* for the intent-to-treat population versus fluconazole as evaluated in 2 stages:**
 - Noninferiority of posaconazole versus fluconazole and if demonstrated,
 - Superiority of posaconazole versus fluconazole

*Fixed-time period.

Ullmann AJ et al. *N Engl J Med.* 2007;356:335-347.

Posaconazole Prophylaxis in Allogeneic Hematopoietic Stem Cell Transplant Recipients With Graft-Versus-Host Disease Patient Populations



	Posaconazole	Fluconazole
Intent-to-treat population, n	301	299
All-treated subjects, n	291	288

Intent-to-treat population: all randomized subjects

All-treated subjects: Intent-to-treat subset who received ≥ 1 dose

ITT indicates intent-to-treat.

Ullmann AJ et al. *N Engl J Med.* 2007;356:335-347.

Posaconazole Prophylaxis in Allogeneic Hematopoietic Stem Cell Transplant Recipients With Graft-Versus-Host Disease

Cumulative Duration of Prophylaxis



	Posaconazole (n = 301)	Fluconazole (n = 299)
Duration of prophylaxis, days		
Mean \pm SD^{1,2}	80 \pm 43	77 \pm 43
Median (range)¹	111 (1-138)	108 (1-130)

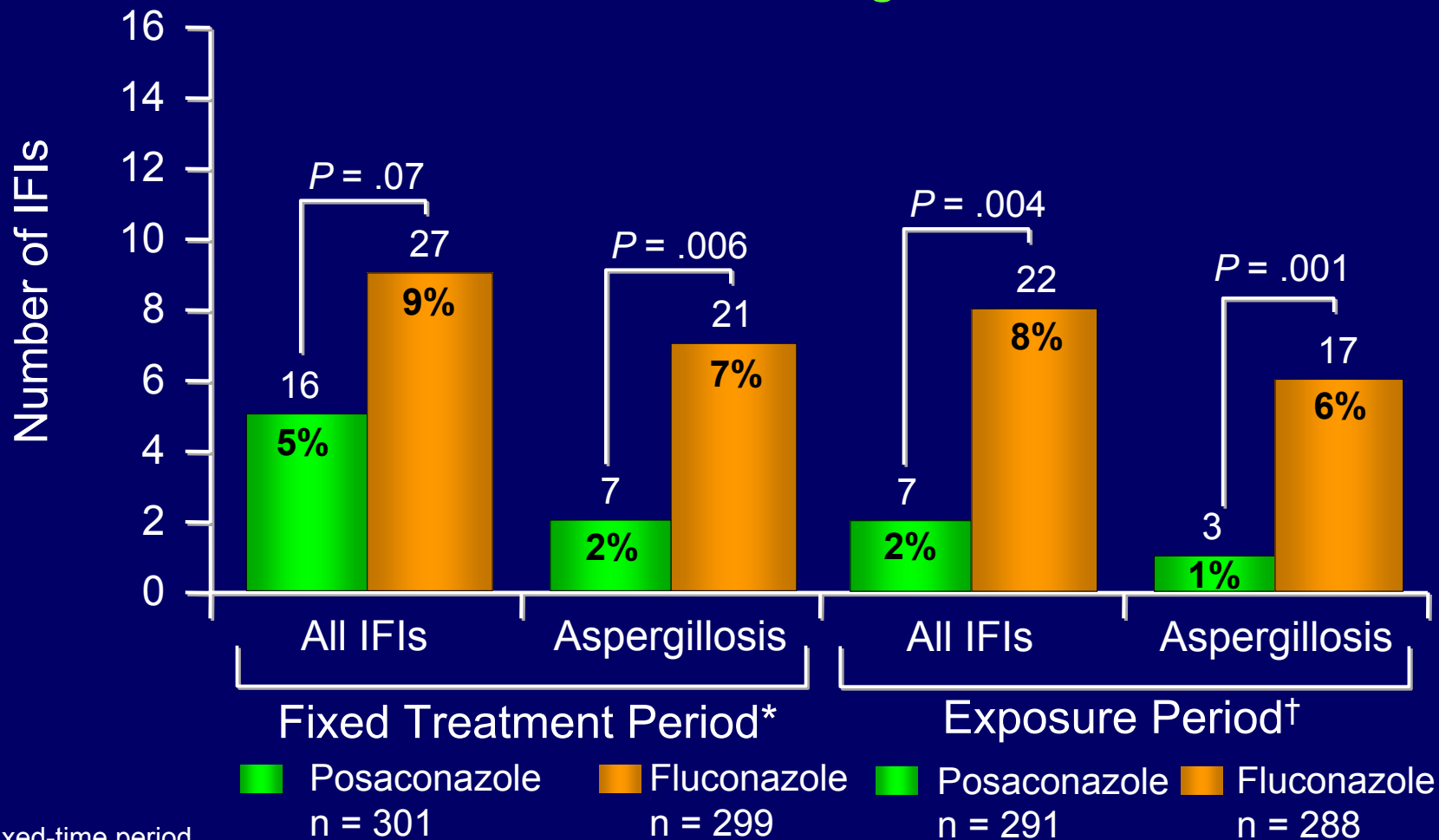
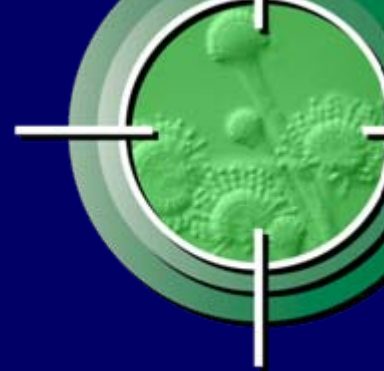
All-treated patients (intent-to-treat subset who received ≥ 1 dose): posaconazole (n = 291); fluconazole (n = 288).

1. Ullmann AJ et al. *N Engl J Med*. 2007;356:335-347.

2. Study report C/198-316, p 153. SPRI, Kenilworth, NJ, USA; June 2005.

Posaconazole Prophylaxis in Allogeneic Hematopoietic Stem Cell Transplant Recipients With Graft-Versus-Host Disease

Results – Proven/Probable Invasive Fungal Infections



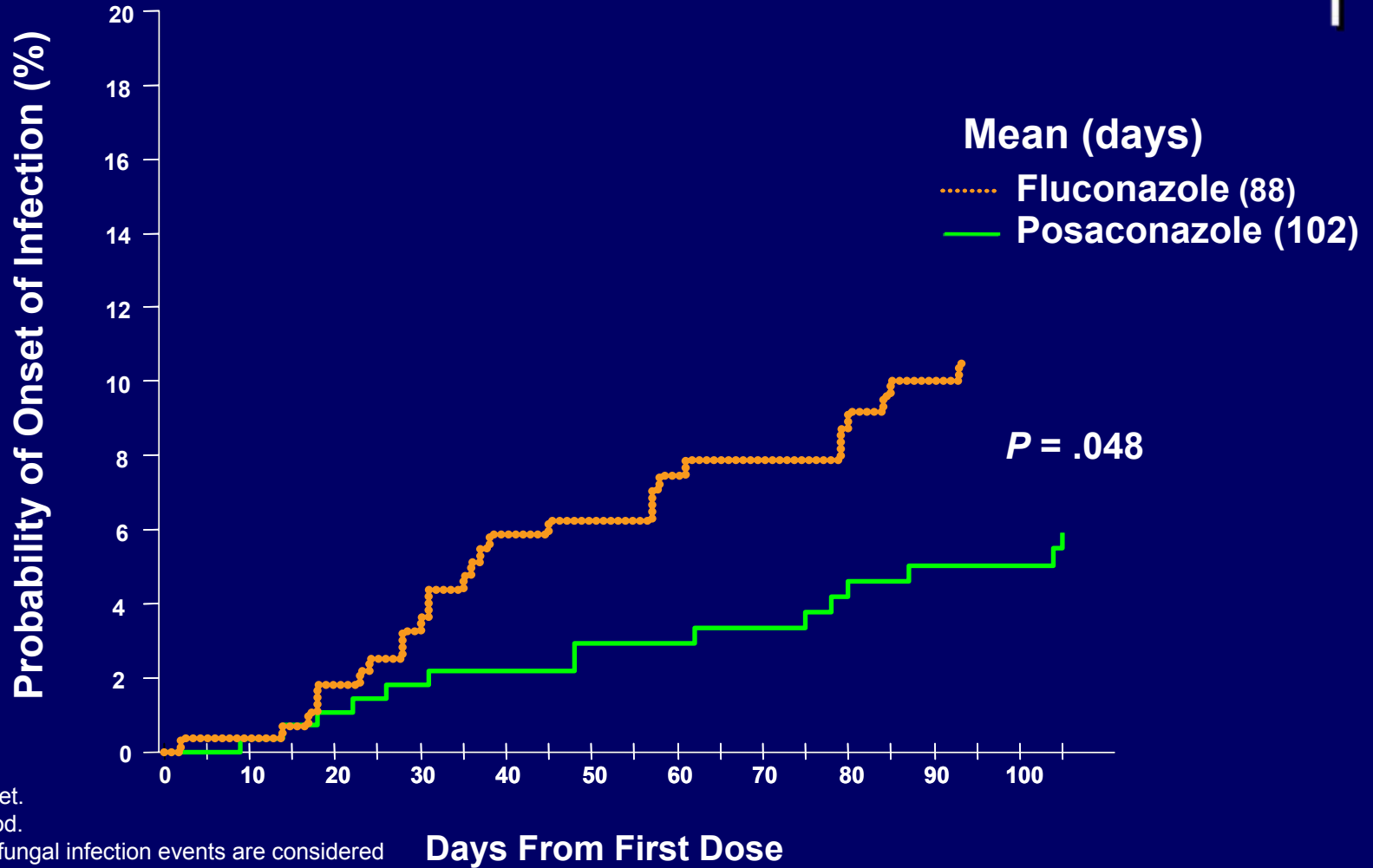
*Fixed-time period.

†On-treatment period.

Ullmann AJ et al. *N Engl J Med.* 2007;356:335-347.

Posaconazole Prophylaxis in Allogeneic Hematopoietic Stem Cell Transplant Recipients With Graft-Versus-Host Disease

Time From First Dose to Invasive Fungal Infection* – Fixed Treatment Period†



*All-treated subset.

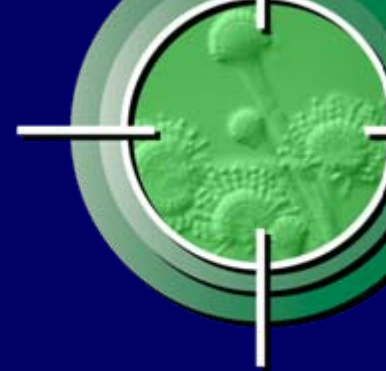
†Fixed-time period.

All non-invasive fungal infection events are considered censored; all subjects censored at the end of prophylaxis phase.

Ullmann AJ et al. *N Engl J Med.* 2007;356:335-347.

Posaconazole Prophylaxis in Allogeneic Hematopoietic Stem Cell Transplant Recipients With Graft-Versus-Host Disease

All-Cause Mortality – Fixed Treatment Period^{1*}



Cause of death (Investigator assessment), n (%)	Posaconazole n = 301	Fluconazole n = 299
Total deaths	76 (25)	84 (28)
Adverse event	39 (13)[†]	37 (12)
Complications related to invasive fungal infection	4 (1)[‡]	12 (4)[†]
Progression of underlying disease/graft-versus-host disease	31 (10)	33 (11)
Other	2 (1)	2 (1)

No significant difference in time to death ($P = .847$) between groups.²

*Fixed-time period.

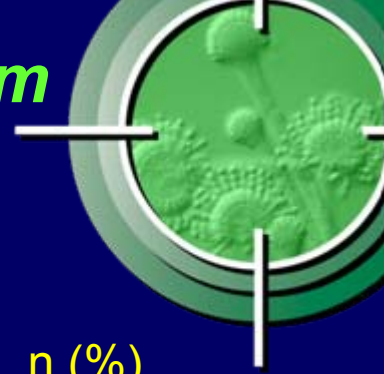
[†] $P = .01$ by Chi-square test.

[‡] $P = .046$ by log-rank test.

1. Study report C/I98-316, p. 134. SPRI Kenilworth, NJ, USA; June 2005.

2. Ullmann AJ et al. *N Engl J Med.* 2007;356:335-347.

Prophylaxis in Allogeneic Hematopoietic Stem Cell Transplant Recipients With Graft Versus Host Disease: Treatment-related Adverse Events ($\geq 2\%$)



Body System/Preferred Term	Patients, n (%)	
	Posaconazole (n = 301)	Fluconazole (n = 299)
Subjects reporting any AE	107 (36)	115 (38)
Body as a whole – General disorders		
Anorexia	3 (1)	7 (2)
Dizziness	4 (1)	5 (2)
Drug level altered	5 (2)	2 (1)
Fatigue	4 (1)	6 (2)
Headache	3 (1)	8 (3)
Weakness	3 (1)	5 (2)
Cardiovascular disorders, general		
Hypertension	2 (1)	5 (2)
Central and peripheral nervous system disorders		
Tremor	4 (1)	6 (2)
Disorders of the eye		
Vision blurred	3 (1)	5 (2)

Prophylaxis in Allogeneic Hematopoietic Stem Cell Recipients With Graft Versus Host Disease: Treatment-related Adverse Events ($\geq 2\%$), continued



Body System/Preferred Term	Patients, n (%)	
	Posaconazole (n = 301)	Fluconazole (n = 299)
Gastrointestinal system disorders		
Abdominal pain	4 (1)	7 (2)
Constipation	1 (<1)	5 (2)
Diarrhea	8 (3)	12 (4)
Dyspepsia	3 (1)	6 (2)
Nausea	22 (7)	28 (9)
Vomiting	13 (4)	15 (5)
Liver and biliary system disorders		
Bilirubinemia	8 (3)	5 (2)
GGT increased	9 (3)	7 (2)
Hepatic enzymes increased	8 (3)	7 (2)
Aspartate aminotransferase increased	8 (3)	3 (1)
Alanine aminotransferase increased	9 (3)	4 (1)

Prophylaxis in Allogeneic-HSCT Recipients With Graft-Versus-Host Disease: Treatment-related AEs ($\geq 2\%$), continued



Body System/Preferred Term	Patients, n (%)	
	Posaconazole (n = 301)	Fluconazole (n = 299)
Metabolic and Nutritional Disorders		
Alkaline phosphatase increased	5 (2)	5 (2)
Renal and urinary system disorders		
Blood creatinine increased	6 (2)	5 (2)
Special senses, other		
Taste perversion	3 (1)	5 (2)

Posaconazole Prophylaxis in Allogeneic Hematopoietic Stem Cell Transplant Recipients With Graft-Versus-Host Disease
Conclusion



- **Posaconazole is effective and safe for the prevention of invasive fungal infections in hematopoietic stem cell transplant recipients during the “at-risk” period for mould and yeast infections and reduces fungal-related mortality**

Summary of Posaconazole Prophylaxis Studies



- **In acute myelogenous leukemia patients with neutropenia due to chemotherapy, posaconazole was**
 - Significantly better than pooled standard azoles for prophylaxis for *Candida* and *Aspergillus* infections
 - Associated with a decrease in all cause mortality at day 100
- **In hematopoietic stem cell transplant recipients with graft versus host disease, posaconazole was**
 - Significantly better than fluconazole for prophylaxis for *Candida* and *Aspergillus* infections during the exposure period*
 - Associated with a reduction in invasive fungal infection-related mortality
- **Posaconazole has a safety profile comparable to fluconazole**

*On-treatment period.

IDSA

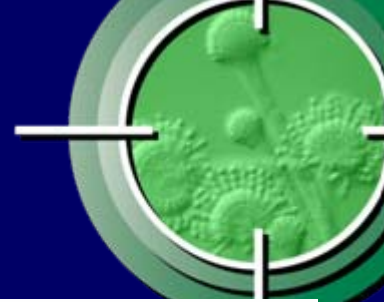


Table 2. (Continued.)

Condition	Therapy ^a		Comments
	Primary	Alternative ^b	
Cutaneous aspergillosis	... ^d	Similar to invasive pulmonary aspergillosis	Surgical resection is indicated where feasible
<i>Aspergillus</i> peritonitis	... ^d	Similar to invasive pulmonary aspergillosis	...
Empirical and preemptive antifungal therapy	For empirical antifungal therapy, L-AMB (3 mg/kg/day IV), caspofungin (70 mg day 1 IV and 50 mg/day IV thereafter), itraconazole (200 mg every day IV or 200 mg BID), voriconazole (6 mg/kg IV every 12h for 1 day, followed by 3 mg/kg IV every 12 h; oral dosage is 200 mg every 12 h)	...	Preemptive therapy is a logical extension of empirical antifungal therapy in defining a high-risk population with evidence of invasive fungal infection (e.g., pulmonary infiltrate or positive galactomannan assay result)
Prophylaxis against invasive aspergillosis	Posaconazole (200 mg every 8h)	Itraconazole (200 mg every 12 h IV for 2 days, then 200 mg every 24 h IV) or itraconazole (200 mg PO every 12 h); micafungin (50 mg/day)	Efficacy of posaconazole prophylaxis demonstrated in high-risk patients (patients with GVHD and neutropenic patients with AML and MDS)
Aspergilloma ^e	No therapy or surgical resection	Itraconazole or voriconazole; similar to invasive pulmonary aspergillosis	The role of medical therapy in treatment of aspergilloma is uncertain; penetration into preexisting cavities may be minimal for AMB but is excellent for itraconazole
Chronic cavitary pulmonary aspergillosis ^f	Itraconazole or voriconazole	Similar to invasive pulmonary aspergillosis	Innate immune defects demonstrated in most of these patients; long-term therapy may be needed; surgical resection may lead to significant complications; anecdotal responses to IFN- γ
Allergic bronchopulmonary aspergillosis	Itraconazole	Oral voriconazole (200 mg PO every 12 h) or posaconazole (400 mg PO BID)	Corticosteroids are a cornerstone of therapy; itraconazole has a demonstrable corticosteroid-sparing effect
Allergic aspergillus sinusitis	None or itraconazole	Few data on other agents	...



Primary antifungal prophylaxis in leukemia patients

- Induction chemotherapy of acute leukemia

Fluconazole 50-400 mg qd iv/oral: CI

Itraconazole oral solution 2.5 mg/kg bid: CI

Posaconazole 200 mg tid oral: AI

Candins iv: insufficient data

Polyene iv: CI

Aerosolized liposomal amphotericin B in combination with oral fluconazole: BI



Primary antifungal prophylaxis in leukemia patients

- Allogeneic hematopoietic stem cell transplantation: GvHD phase

Fluconazole 400 mg qd iv/oral: CI

Itraconazole 200 mg IV followed by oral solution 200 mg bid: BI

Posaconazole 200 mg tid oral: AI

Candins iv: insufficient data

Polyene iv: CI

Voriconazole 200 mg bid oral: provisional AI

Aerosolized liposomal amphotericin B plus fluconazole: insufficient data

