



Antifungal therapy: Polyenes, posaconazole, or prayers

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Conflict of Interest Statement

- Lectures/Honoraria
 - None anymore
- Consultant relationships
 - none
- Research
 - Pfizer
- Equity holdings - none
- Other - none

Completing the Carbon Cycle: The reason God created moulds



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Human Zygomycosis:

Review of 929 infections in literature

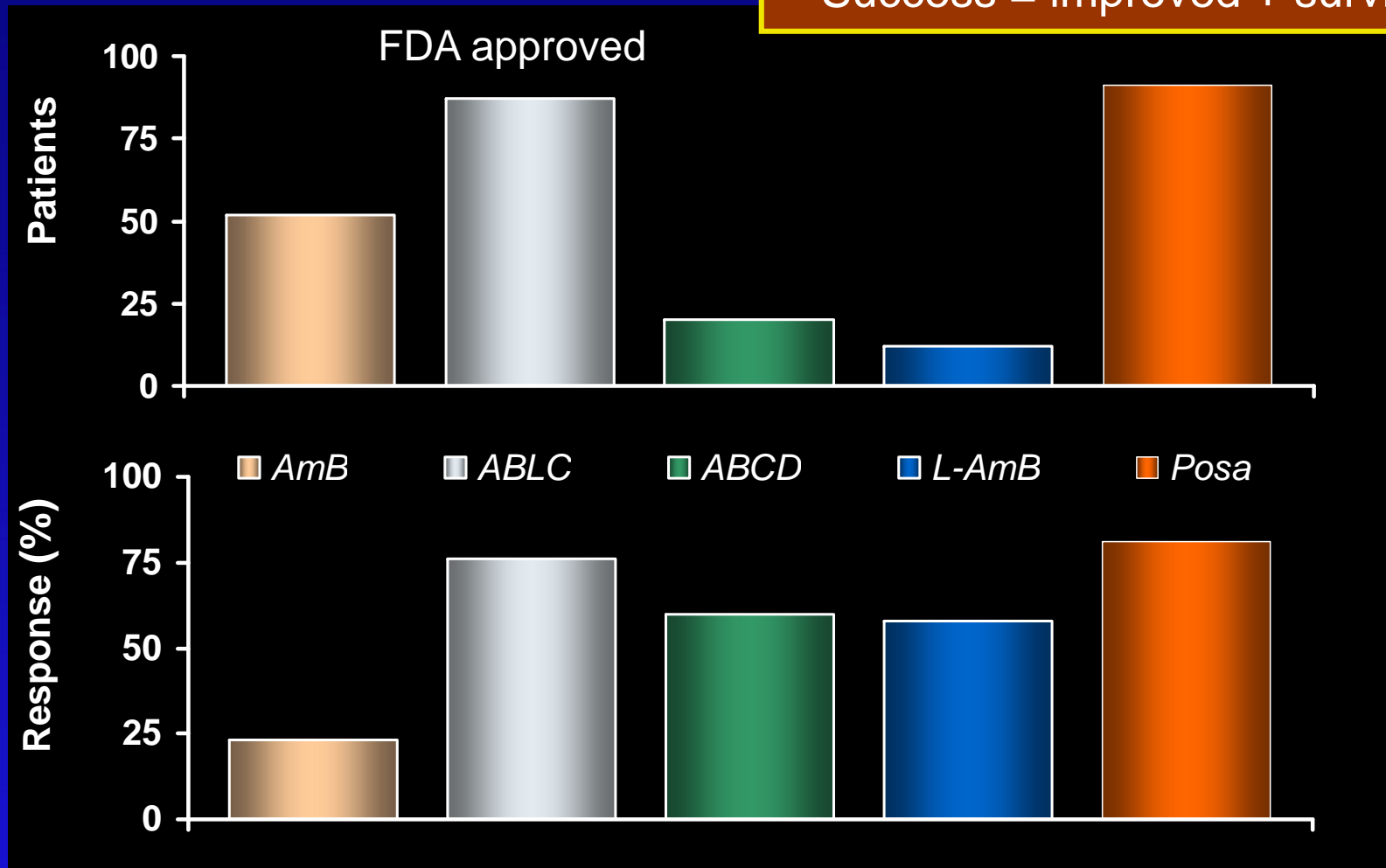
Underlying Conditions	Percent
Diabetes	36
Malignancy	17
Bone marrow transplantation	5
Solid organ transplantation	7
Fe chelation therapy	6
IV drug use	5

Zygomycosis: Sites of Infection

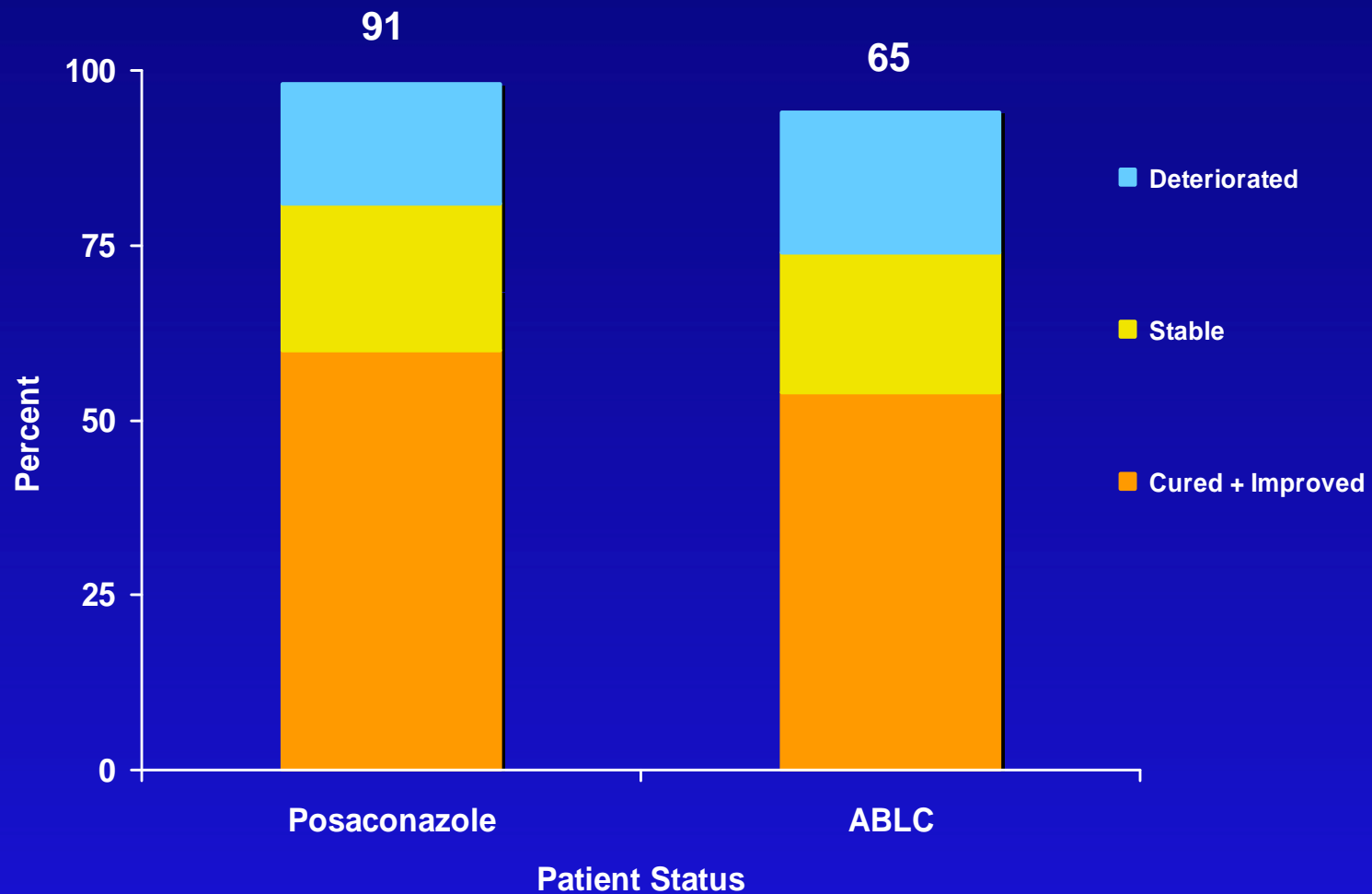
Site of Infection	% of 929 Patients	Mortality (%)
Rhinocerebral	21	62
Sino-orbital	8	24
Sinusitis	8	16
Pulmonary	24	76
Cutaneous	19	31
Disseminated	3	100
Gastrointestinal	7	85
Cerebral	9	79

Zygomycetes: Pooled Outcomes

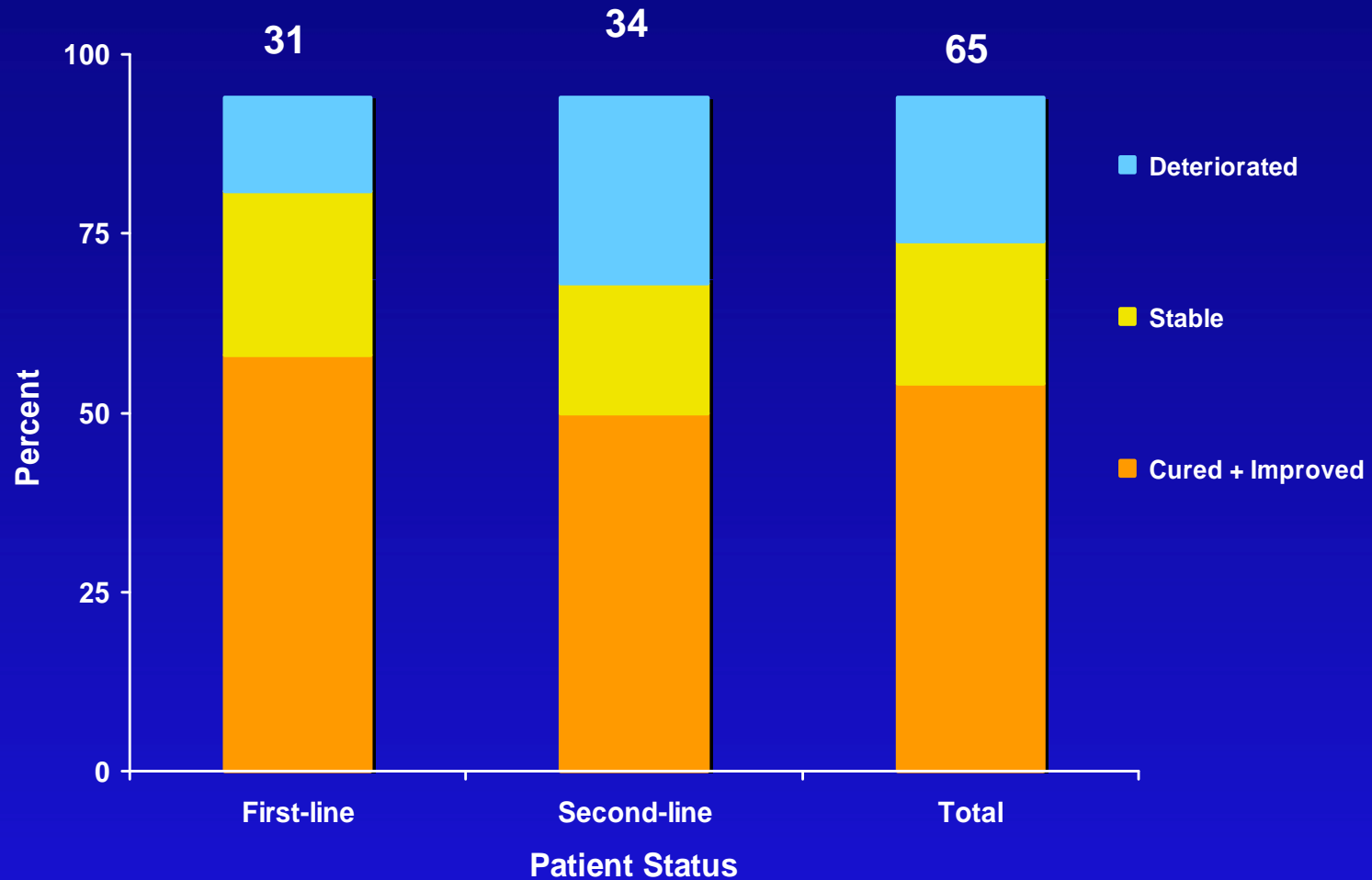
- > 10 subjects/trial
- Success = improved + survived



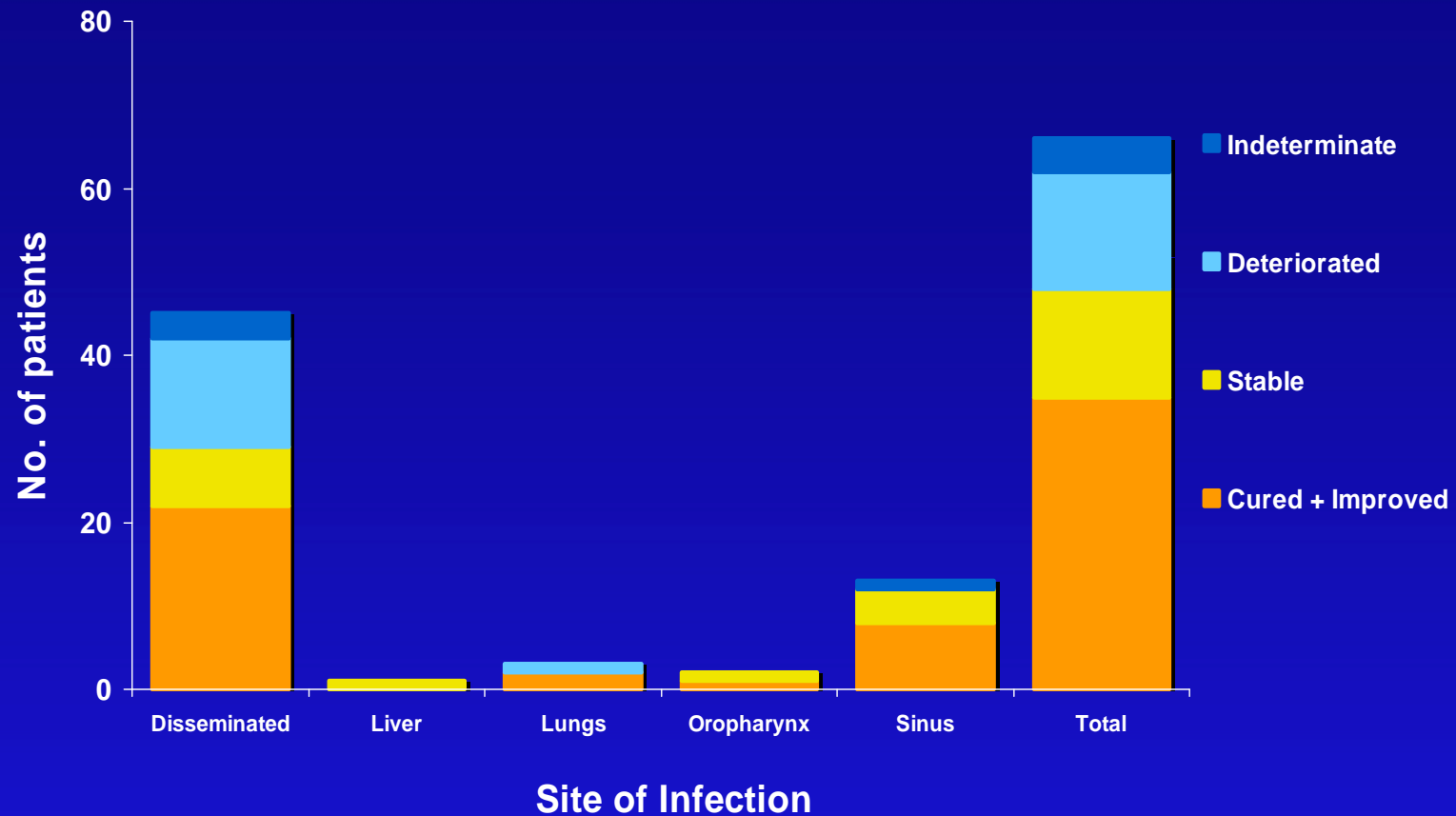
Clinical Responses: ABLC and Posaconazole



Clinical Responses to ABLC At End of Therapy



Clinical Responses to ABLC: End of Therapy



Zygomycosis: Treatment

- Lipid-formulated Ampho B
 - 5 – 7.5 mg/kg IV daily dosing
 - Consensus choice for 1st Rx because only IV choice
- Posaconazole
 - 800 mg divided bid, tid, qid
 - Must be given with fatty food and intact gastric acid production to maximize bioavailability

Zygomycosis: Prayers

Does any of this antifungal outcomes data mean anything?





Zygomycosis: Non - Rx Determinants of Outcomes

- Early Rx with antifungals
 - Chamilos et al., CID 2008 48:503-9
- High pathogen burden/overwhelming infection
- Patient risk factors
 - Immunity is everything (almost)
 - David Stevens, tomorrow 8:35 AM

Zygomycosis: Risk and Immunity: Case #1

38 yo female 3rd induction chemotherapy for relapsed AML.

- Complicated by fever, neutropenia Rx with Abx.
- New L lung nodular infiltrates. Rx with empirical voriconazole for presumptive aspergillosis.
- Eventual progression to total L lung consolidation with CT evidence of necrosis coincident with bone marrow recovery.

Zygomycosis: Risk and Immunity: Case #1 (cont)

38 yo female 3rd induction chemotherapy for relapsed AML.

- Outpatient Rx with voriconazole.
- Four months later, developed hemoptysis. L pneumonectomy by our gutsy chest surgeon.
- Pathology showed mould consistent with zygomycosis (cultures negative).
- Patient doing well one year later on posaconazole despite 4th AML relapse.

Zygomycosis: Risk and Immunity: Case #2

17 yo male with new MDS with excess blasts and “worst combination of multiple poor prognosis tumor genetics ever seen”. Myeloablative chemo followed by MUD allo HSCTx.

- Voriconazole prophylaxis by protocol.
- Complicated by severe skin and GI GVHD leading to prolonged hospital stay and intense anti-GVHD immune suppression.

Zygomycosis: Risk and Immunity: Case #2 (cont)

17 yo male with new MDS with blasts and “worst combination of multiple poor prognosis tumor genetics ever seen”. Myeloablative chemo followed by MUD allo HSCTx.

- Discharged home on immune suppression taper.
- Readmitted one month later in acute respiratory distress. Started immediately on lipid AmB.
- Progressive dyspnea, transfer to MICU, died.
- Autopsy showed widespread zygomycosis.



Zygomycosis and Treatment: Final Comments

- Antifungals are probably important for treatment.
 - Paradoxically, more important but less effective in patients with irreversible immune deficits
 - Immune recovery or, at least, avoidance of more immune suppression is an important Rx goal
- Lipid AmB and posaconazole antifungals of choice
 - Success rates dependent on immune deficiency