

# MUCORMYCOSIS & TREATMENT

# Treatment

## General principles

- ▶ Early diagnosis (Chamilos et al.)
- ▶ Early administration of active antifungal agents
- ▶ Reversal of underlying factors
- ▶ Complete removal of all infected tissues
- ▶ Use of various adjunctive therapies

# Treatment


## Primary Antifungal Therapy

- ▶ Liposomal Amphotericin-B first line recommended agent
- ▶ Fluconazole, Voriconazole – No reliable activity, Itraconazole – *Absidia* species
- ▶ Posaconazole, Isavuconazole can also be used as first line therapy

# Treatment

## Liposomal Amphotericin B

- ▶ 2016 ECIL & ESCMID/ECMM liposomal form as first line
- ▶ Can be given as 5mg/kg/day to 10mg/kg/day, if CNS involved
- ▶ Surgery + Lip Amp B increases survival rates and cure rates

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- ▶ Use of Amphotericin Deoxycholate is discouraged (ESCMID/ECMM)
  - ▶ ABLC can also be used- if no CNS involvement (B)
  - ▶ Alternate routes – ABLC aerolised with Respigard II nebulizer, Direct instillation of Amphotericin B into pulmonary cavities or pleural space


# Treatment

## Azoles

- ▶ Posaconazole 800mg/day in 2 or 4 divided doses – first line (ESCMID/ECMM), Salvage therapy (ECIL-6)
- ▶ Isavuconazole (Cornely OA et al) – 200mg OD. But VITAL study showed higher mortality rates and poor response



# Treatment



## Duration of Treatment

- ▶ Highly individualized
- ▶ Near normalization of radiograph, negative biopsy specimens and cultures, recovery from immunosuppression

# Treatment - Surgery

- ▶ Removal of necrotic tissue – Increases penetration of antifungals
- ▶ Lobectomy, Pneumonectomy or wedge resection
- ▶ Surrounding infected healthy-looking tissues should be removed
- ▶ Groll A et al. – Mortality reduced by 79%



# Treatment - Salvage Therapy

- ▶ If disease is refractory or intolerance towards previous antifungal therapy.
  - ▶ Posaconazole(A)
  - ▶ Polyenes + Posaconazole(B)
  - ▶ Lipid complex, liposomal, Colloidal dispersion (B)
  - ▶ Polyenes + Caspofungin(C)

# Treatment – Adjunctive Therapies

- ▶ Hyperbaric Oxygen – 100% O<sub>2</sub> at 2atm pressure for 90 min twice a day (C)
- ▶ Cytokine therapy in hematological malignancy – GCSF(A), Granulocyte transfusion +/- IFN $\gamma$  (C)
- ▶ Lovastatin
- ▶ VT-1161(otesaconazole) – Inhibits fungal CYP51
- ▶ Nivolumumab and IFN $\gamma$

# Treatment – Adjunctive Therapies

## Iron chelators – Deferasirox

- ▶ Deferasirox-AmBisome Therapy for Mucormycosis (DEFEAT Mucor) study
- ▶ First randomized trial for any treatment of mucormycosis
- ▶ 45%(5) mortality at 30 days, 82%(9) mortality at 90 days
- ▶ Deferasirox cannot be recommended as part of an initial combination regimen for the treatment of mucormycosis.

## Iron chelators – Deferasirox

- ▶ Hematological malignancy – ECIL-6 and ESCMID/ECMM recommended against its use.
- ▶ Other than hematological malignancy – ESCMID/ECMM marginally supports its use(C)



# Conclusion

- ▶ More common in immunocompromised
- ▶ Suspected in patients already on anti-aspergillus treatment
- ▶ No specific clinical or radiological features making diagnosis more difficult and challenging
- ▶ Diagnostic options are limited with variable results
- ▶ Invasive diagnostics have more yield which is not possible in some patients

# Conclusion

- ▶ Early diagnosis means early treatment and leading to less mortality rates
- ▶ Reversal of underlying factors, Surgery and Liposomal amphotericin B increases cure rates
- ▶ Duration of treatment is highly individualized
- ▶ Posaconazole, Isavuconazole can also be tried
- ▶ Salvage therapy in refractory or intolerant pts
- ▶ Adjunctive therapies need to be proved in large trials and standardized



# References

- ▶ Fishman's Pulmonary Diseases and Disorders, 5<sup>th</sup> edition
- ▶ Pilmis B, Lanternier F. Recent advances in understanding and management of mucormycosis 2018, *F1000 research*
- ▶ Challenges in the diagnosis and treatment of mucormycosis  
A. Skiada. *Medical Mycology*, 2018
- ▶ ESCMID and ECMM joint clinical guidelines for the diagnosis and management of mucormycosis 2013, *Clin Microbiol Infect* 2014
- ▶ Mucormycosis and entomophthoromycosis: a review of the clinical manifestations, diagnosis and treatment, R. M. Prabhu and R. Patel, Mayo clinic of medicine, *Clin Microbiol Infect* 2004