Regulatory Considerations for Antifungal Drug Development —Perspective from Japan

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Current situation in Japan

- There are no guideline for development of Antifungal drugs issued by regulatory authorities.
- The development of antifungal agents is not so active.
- NDA approved within 5yrs: 4 products
  - —Nail ringworm: 2 products
  - —Oral candida: 1 product
  - —Prophylaxis of deep mycosis, treatment of the mycoses:1 product

Example from most recent approval product

[Brand name] Noxafil Tablets 100 mg, Noxafil for Intravenous Infusion 300 mg

[Non-proprietary name] Posaconazole

[Type] Azole antifungal

[indication]

- prophylaxis of deep mycosis in hematopoietic stemcell transplantation recipients or patients with hematologic malignancy who are predicated to decrease neutrophil.
- treatment of the following mycoses: Fusariosis, mucormycosis, coccidioidomycosis, chromoblastomycosis, and mycetoma.

[Note]

2013: Approved in US.
2014: Approved in EU.

[Clinical data package]

- Foreign clinical trial results (including 3 phase III study) submitted in the application to EMA and FDA
- Phase 3 Japanese clinical trial result conducted in Japan

Sponsor explained that foreign clinical trial can be utilized for evaluation of efficacy in Japanese because…

There are no difference in

- susceptible to clinical isolate between Japan and foreign countries.
- medical environment, treatment algorithm for deep mycosis between Japan and foreign countries .
- Pharmacokinetic profile between Japanese and non-Japanese

[Summary of Japanese clinical study]

- Active controlled open-label trial
- Study population: Systemic and internal organ mycosis
- Primary efficacy endpoint

  —Invasive aspergillosis, mucormycosis:
  comprehensive evaluation of clinical symptoms, radiographic assessments and mycological activities at day42

  —Chronic pulmonary aspergillosis:
  comprehensive evaluation of clinical symptoms and radiographic assessments at day 84