

## AFT-15: A Phase I Study of Ibrutinib (PCI-32765) in Combination with Revlimid/dexamethasone (Rd) in Relapsed/Refractory Multiple Myeloma

Yvonne A. Efebera, MD, MPH, Ohio State University  
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rationale/  
objective

study  
schema

trial details

follow up

In the last decade, significant progress has been made in the treatment of Multiple Myeloma (MM), primarily due to the introduction of proteasome inhibitors (PI) and immunomodulatory drugs (IMiDs). However, nearly all patients ultimately relapse and require further therapy, making development of new compounds for MM therapy an important priority.

Preclinical studies suggest synergism between lenalidomide and ibrutinib in MM. The anti-myeloma effects of lenalidomide have been previously described, and include caspase-8-dependent apoptosis of MM cells, inhibition of angiogenesis, and activation of NK and T effector cells. Both ibrutinib and lenalidomide downregulate IRF4, a master transcriptional factor that mediates myeloma cell survival, and both exert effects on the BM microenvironment with overlapping yet distinct targets that influence MM cell growth and survival. The combination of lenalidomide and ibrutinib is thus an attractive therapeutic strategy not only as a potent anti-MM regimen but also in terms of positively impacting bone disease.

### Primary

- To determine the maximum tolerated dose and recommended dose in extension cohort of ibrutinib in combination with lenalidomide and dexamethasone
- To examine the safety profile of ibrutinib in combination with lenalidomide and dexamethasone

### Secondary

- To determine the following:
  - Progression-free survival (PFS)
  - Overall survival (OS)
  - Overall response rate
  - Duration of response
  - Safety Profile: The CTC-CAE version 4.0 will be used to grade and assign attribution to each adverse event reported.

### Correlative Science

- To perform select immunologic studies with this combination therapy

RATIONALE

OBJECTIVE

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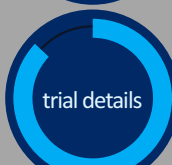
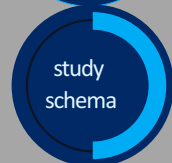
**\*Other reasons or D/C of  
Protocol Tx:**

- Patient Decision
- Unacceptable AEs
- Tx delay >4 weeks

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Study Number  
**AFT-15**

Study Phase  
**Phase I**

Clinical Indication  
**Relapsed/Refractory Multiple Myeloma**

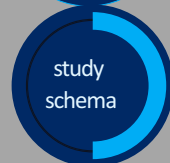
Number of Trial Patients  
**28**

Study Design  
**Dose escalation, followed by dose expansion**

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Study Chairs

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**FUNDING SUPPORT**

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