Results of a Completed Phase 1 Study of LAM-002 (Apilimod Dimesylate), a First-in-Class Phosphatidylinositol-3-Phosphate 5 Kinase (PIKfyve) Inhibitor, Administered as Monotherapy or With Rituximab or Atezolizumab to Patients with Previously Treated Follicular Lymphoma or Other B-cell Cancers


New York University, New York, NY; Winship Cancer Institute, Emory University, Atlanta, GA; Horizon Oncology Center, Lafayette, LA; Mayo Clinic, Rochester, MN; The University of Texas MD Anderson Cancer Center, Houston, TX; Massachusetts General Hospital Cancer Center, Boston, MA; Cancer and Hematology Centers of Western Michigan, Grand Rapids, MI; Clearview Cancer Institute, Huntsville, AL; Mayo Clinic Jacksonville, FL; Virginia Cancer Specialists, Fairfax, VA; Virginia Mason Medical Center, Seattle, WA; Al Therapeutics, Inc, Gulfport, CT; Celgene, Inc, Gulfport, CT; Well Call Medical College, New York, NY

LAM-002 is a Novel, Selective Inhibitor of PIKfyve that Causes Tumor Cell Death By Modulation of Lysosomal Homeostasis

- **PIKfyve**
  - Lipid kinase that regulates endosomal membrane trafficking (left panel)
  - **LAM-002** (apilimod dimesylate)
  - Orally bioavailable, small molecule with selective selectivity for PIKfyve inhibition
  - Dysregulates lysosomal homeostasis, promoting death of non-Hodgkin lymphoma (NHL) cells (right panel)
  - Does not inhibit RTKs, β, γ, or δ (ie, distinctfrom drugs like idelalisib, copanlisib, duvelisib or umbralisib)

In Animal Models, LAM-002 Demonstrated Antitumor Activity Alone or in Combination with Anti-CD20 or Anti-PD-L1 Antibodies

- **Patient Characteristics Were Typical for Those with NHL:** Long Durations of Therapy and Excellent Compliance Were Achieved
  - **10** patients were enrolled (49% women), median age 69 (range 49-81), with a median of 3 prior lines of therapy among lymphoma subtypes.
  - **Tumor Types:** 5 (50%) Follicular lymphoma (FL), 4 (40%) Mantle cell lymphoma (MCL), 1 (10%) Marginal zone lymphoma (MZL)

Durable LAM-002 Antitumor Activity Was Observed in Patients with Previously Treated Follicular Lymphoma

- **Regimen**
  - LAM-002 monotherapy (n=10)
  - LAM-002/rituximab (n=5)
  - LAM-002/atezolizumab (n=1)

- **Duration of therapy:** median 7.5 months (range 1.1-14.0)
- **LAM-002 Compliance:** median 96%

Transient, Reversible Gastrointestinal Events Were the Primary Toxicities, Usually at Doses Exceeding the RDR

- **Adverse Events (AEs) in Patients by FL Monotherapy Regimen**
  - **NHL**
    - **FL Monotherapy (n=10)**
    - **FL Dose Escalation (n=9)**
  - **Tumor Types**
    - **FL**
    - **MCL**
    - **MZL**

Time-to-Event Data Confirmed the Potential for Rapid and Durable Treatment Benefit

- **ClinicalTrials.gov Identifier:** NCT0259438
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**Abbreviations**
- ASCT = autologous stem cell transplantation
- AUC0-8 = area under the concentration-time curve to 8 hours postdose
- BID = 2 times daily
- B-cell = B-lymphocyte
- BLR = baseline
- BV = bone marrow
- CD = cluster of differentiation
- CR = complete response
- CTCAE = Common Terminology Criteria for Adverse Events
- DLBCL = diffuse large B-cell lymphoma
- DOR = duration of response
- ECOG = Eastern Cooperative Oncology Group
- FL = follicular lymphoma
- IP = intraperitoneally
- IV = intravenously
- MCL = mantle cell lymphoma
- MedDRA = Medical Dictionary for Regulatory Activities
- MTD = maximum tolerated dose
- NLR = neutrophil to lymphocyte ratio
- NHL = non-Hodgkin lymphoma
- PO = orally
- PFS = progression-free survival
- PD = progressive disease
- PDL1 = programmed death ligand 1
- PI3K = phosphoinositide 3-kinase
- PR = partial response
- Q1W = weekly
- Q3W = every 3 weeks
- Q8W = every 8 weeks
- RDR = recommended dosing regimen
- TLS = tumor lysis syndrome
- Tmax = time of maximum concentration
- TTR = time to response
- VPR = viral load

References


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LAM-002 Conclusions and Next Steps

- LAM-002, the first clinical PIKfyve inhibitor (distinct from PI3K inhibitors), was studied as a novel oral therapy in 65 patients with B-cell NHL
- During dose escalation, regimens of 150 mg BD or 75 mg BD caused gastrointestinal symptoms precluding effective compliance; no other DLTs were observed
- With the recommended dosing regimen (RDR) of 125 mg BD, LAM-002 has been well tolerated for periods to >12 weeks when given as monotherapy or with rituximab or atezolizumab
- Median dosing compliance was >95%
- Only 10% of patients requested dose modification to 100 mg BD (for gastrointestinal symptoms)
- LAM-002 therapy was not associated with drug-induced myelosuppression or immune adverse events (as with lenalidomide or PD1 inhibitors)
- ORR of 81% (33%), with durable PRs and CRs, supports Phase 2 and 3 studies of LAM-002 monotherapy and LAM-002/rituximab combination therapy for patients with previously treated follicular lymphoma