

AFT-32: A Phase II Study of Palbociclib (PD-0322991) in Combination with Ibrutinib in Patients with Previously Treated Mantle Cell Lymphoma

ALLIANCE
FOUNDATION TRIALS, LLC

Kami Maddocks, MD, Ohio State University Medical Center

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rationale/
objective

study
details

study
design

key eligibility
criteria

follow up

- Mantle cell lymphoma (MCL) is a distinct B-cell lymphoma comprising 5-10% of all NHL that often follows an aggressive clinical course, and is considered incurable with standard chemoimmuno-therapy.
- MCL is characterized by overexpression of cyclin D1 and cyclin-dependent kinase 4 (CDK4), resulting in dysregulation of the cell cycle and proliferation.
- Palbociclib (PD-0332991) is an oral, highly selective, reversible inhibitor of CDK4 and CDK6. Palbociclib induces prolonged early G1 cell cycle arrest (pG1), sensitizing tumor cells to killing by a partner drug *in vitro* and *in vivo*.
- Ibrutinib is an oral selective small molecule irreversible inhibitor of Bruton's tyrosine kinase, which is critical in the B-cell receptor signaling pathway. Ibrutinib has a single-agent response rate of 68% in relapsed MCL, with a 24-month PFS of ~ 30%.
- Pre-clinical data demonstrated these agents to have synergistic activity. A phase I study of the combination confirmed safety and tolerability along with early efficacy.
- We believe this combination will be well tolerated and improve upon the single agent ibrutinib depth of response and duration of response.

Primary

- Evaluate efficacy of palbociclib in combination with ibrutinib in terms of progression-free survival (PFS) in patients with previously treated MCL.

Secondary

- Evaluated efficacy of palbociclib in combination with ibrutinib in terms of overall response rate, complete response rate, duration of response, and overall survival.

Correlative Science

- Several correlative studies will be performed including serial core needle biopsies of involved tissue.

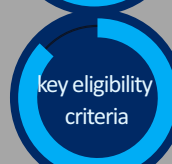
RATIONALE

OBJECTIVE

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Study Number
AFT-32

Study Phase
Phase II

Clinical Indication
**Previously Treated Mantle Cell
Lymphoma**

Number of Trial Patients
55

Estimated Duration
42 Months

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Single-arm, multi-center, open-label phase II study of palbociclib and ibrutinib in patients with previously treated MCL

study
details

Subjects will be enrolled and treated with palbociclib and. Treatment will consist of:

study
design

- Palbociclib administered at 100 mg oral once daily for 21 days on followed by 7 days off
- Ibrutinib administered at 560 mg oral continuously

key eligibility
criteria

Patients will continue to receive study drugs until disease progression, unacceptable toxicity, or withdrawal of consent.

follow up

Response will be assessed by PET/CT and/or CT every 3 cycles for the first year and then every 6 cycles thereafter

STUDY DESIGN

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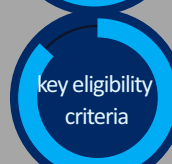
- Histologically/cytologically confirmed MCL with either t(11;14) by karyotype or FISH, or positive IHC
- Measurable disease with 1 lesion of 1.5 cm by radiographic image or 5,000 circulating MCL cells
- At least one prior systemic therapy
- No prior BTK or CDK4/6 inhibitor

KEY ELIGIBILITY CRITERIA

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Pharmacylics, Inc.

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FUNDING SUPPORT

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