ALLIANCE FOUNDATION TRIALS, LLC

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

Kami Maddocks, MD, Ohio State University Medical Center

TAP TO RETURN TO KIOSK MENU

Mantle cell lymphoma (MCL) is a distinct B-cell lymphoma comprising 5-10% of all non-Hodgkin lymphomas 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 progression-free survival (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, and based on the pre-clinical and clinical data, we propose a phase II study to further assess efficacy in a multi-center setting. We believe this combination will be well tolerated and improve upon the single agent ibrutinib depth of response and duration of response.

RATIONALE

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.

OBJECTIVE

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Study Number
AFT-32

Study Phase
Phase II

Clinical Indication
Previously Treated Mantle Cell Lymphoma

Number of Trial Patients
61

Estimated Duration
42 Months

STUDY DETAILS

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rationale/ objective
study details
study design
key eligibility criteria
follow up

The proposed study is a single-arm, multi-center, open-label phase II study of the combination of palbociclib and ibrutinib in patients with previously treated MCL to evaluate efficacy. Subjects will be enrolled and treated with palbociclib and ibrutinib with each cycle of therapy being 28 days. Treatment will consist of:

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

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

Response will be assessed by PET/CT and/or CT every 3 cycles while on therapy for the first year and then every 6 cycles thereafter until disease progression or at the investigator's discretion if otherwise indicated.

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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Study Chair
Kami Maddocks, MD
Ohio State University
Kami.Maddocks@osumc.edu

AFT32@alliancefoundation.org

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