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 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.

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
55

Estimated Duration
42 Months

STUDY DETAILS

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rationale/ objective

study details

study design

key eligibility criteria

follow up

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

Subjects will be enrolled and treated with palbociclib and. 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 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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