Efficacy and safety of abemaciclib combined with either LY3023414 or pembrolizumab in stage IV NSCLC


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Background: Abemaciclib (abema), a cyclin D kinase 4 & 6 inhibitor, has single-agent activity and an acceptable safety profile when dosed continuously in patients with previously treated metastatic NSCLC (NCT01394016). In tumor models, CDK inhibition induces an escape pathway involving PI3kinase (PI3K) and abema induces synergistic immune activation with checkpoint inhibitors. We report on activity and safety of abema plus LY3023414 (LY), a PI3K/mTOR dual inhibitor, and abema plus pembrolizumab (pembro), an anti-PD-1 antibody, in an ongoing Phase 1b open-label, 3 + 3 multicenter trial of previously treated advanced NSCLC (NCT02057963).

Methods: For escalation, Abema (100, 150 mg, or 200 mg (cohort D only)) was given orally on a continuous schedule every 12 hours (q12h) with LY at 100, 150, or 200 mg q12h (cohort D) or with pembro at 200 mg IV. infusion q3 weeks (cohort E). Confirmatory cohorts were given 150 mg abema with 150 mg ly or 200 mg pembro. Pts were treated until progression or other discontinuation criteria were met. Responses were evaluated with RECIST v1.1. Safety assessments followed the NCI-CTCAE v4.0.

Results: As of 01-Mar-2017, cohort D (n = 29) had 62.1% males, 37.9% ≥65 years of age, median # prior systemic therapies = 3; 86.2% stage IV; 72.4% adenocarcinoma; 62.1% ECOG PS = 1. 9 pts (31%) had stable disease (SD), 3 pts had progressive disease (PD), and the status for the remaining 17 pts was unknown or under evaluation. There were 5 deaths unrelated to study drug (2 disease related and 1 stroke). 24/29 pts had a treatment emergent, related AE (TRAE), 10/24 had a Grade 3/4 TRAE. Any grade TRAEs (>30% pts) were nausea (51.7%), diarrhea (51.7%), vomiting (41.4%), and decreased appetite (31%). Cohort E had 19 pts entered (42.1% male, 42.1% ≥65 years of age, median # prior systemic therapies = 2; 52.6% stage IV; 89.5% adenocarcinoma; 57.9% ECOG PS = 1). 8 pts (42.1%) had SD, 1 had PD, and the status for the remaining 10 pts was unknown or under evaluation. There were 3 disease related deaths. 15/19 pts had a TRAE, 5/15 had a G3/4 TRAE. Any grade TRAEs (>30% pts) were fatigue (n = 47.4%) and diarrhea (36.8%).

Conclusions: To date, stable disease as best response and acceptable safety have been observed using combinations of abema and either LY or pembro in advanced NSCLC.

Clinical trial identification: NCT02057963

Legal entity responsible for the study: Eli Lilly and Company

Funding: Eli Lilly and Company