CK-101 (RX518), a Third Generation Mutant-Selective Inhibitor of EGFR in NSCLC: Results of an Ongoing Phase I/II Trial

Authors: Melissa Johnson[1], Janet Karlix[1], Howard A. Burris III[1], Suzanne F. Jones[1], Dean Harris[2], Kenneth O'Byrne[3], Virote Sriuranpong[4], Chaiyut Charoentum[5], Naiyarat Prasongsook[6], Wittawat Jitpewngam[7], Kosin Wirasorn[8], Judy Sing-Zan Wang[9], Saiama N. Waqar[10], James Oliviero[11], Leonid Gorelik[11], Xiangping Qian[12]

Affiliations: [1]Sarah Cannon Research Institute, Nashville, TN; [2]Canterbury District Health Board, Christchurch/New Zealand; [3]Princess Alexandra Hospital, Brisbane, QLD/Australia; [4]King Chulalongkorn Memorial Hospital, Bangkok, Thailand; [5]Chiang Mai University, Chiang Mai, Thailand; [6]Phramongkutklao Hospital, Bangkok, Thailand; [7]Naresuan University Hospital, Phitsanulok, Thailand; [8]Khon Kaen University, Khon Kaen, Thailand; [9]Florida Cancer Specialists/SCRI; [10]Washington University School of Medicine; [11]Checkpoint Therapeutics, Inc., New York, NY; [12]NeuPharma, Inc., Foster City, CA.

Background: CK-101 (also known as RX518) is a novel, oral, third-generation, irreversible epidermal growth factor receptor tyrosine kinase inhibitor (EGFR-TKI) that selectively inhibits both EGFR-TKI-sensitizing and resistance mutations, with minimal activity on wild-type EGFR. CK-101 is being studied in an ongoing first-in-human, multicenter, Phase I/II trial in advanced non-small cell lung cancer (NSCLC) patients (pts) with *EGFR* mutations and other advanced malignancies in the US, Australia, New Zealand and Thailand (NCT02926768). Following dose escalation in which 18 pts received CK-101 in dose groups ranging from 100 mg to 1200 mg/day, a first dose-expansion cohort was enrolled at 400 mg bid.

Methods: Eligible pts in dose escalation had a confirmed diagnosis of NSCLC or any advanced solid tumor where targeting *EGFR* was reasonable. Eligible pts in dose-expansion had a confirmed diagnosis of either (1) *EGFR* mutation-positive advanced or metastatic NSCLC without prior exposure to EGFR-TKI therapy, or (2) T790M-positive advanced or metastatic NSCLC with disease progression on previous EGFR-TKI therapy, with no limit on number of prior lines of systemic therapy.

Results: As of 25 June 2018, 37 pts were treated in dose escalation and expansion and evaluable for safety; median age 59 years, 51% male, 51% Asian, 84% ECOG PS 1. No DLTs or treatment-related SAEs were reported. Most common treatment-emergent adverse events: nausea (16%), diarrhea (14%), lacrimation increased (14%) and vomiting (11%), all grade 1/2 except one grade 3 diarrhea; no grade 4. In dose-expansion, 19 pts were treated with CK-101 at a dose of 400 mg bid and evaluable for response; 8/19 (42%) pts were treatment-naïve, 6/19 (32%) pts had brain metastases; 16/19 (84%) pts remained on treatment. Disease control rate was 100% (19/19), with 16/19 pts (84%) experiencing target lesion reduction versus baseline and 8 pts achieving a partial response (7 confirmed, 1 pending confirmation). In treatment-naïve pts, 6/8 (75%) pts achieved a partial response. In pts with brain metastases, 3/6 (50%) pts achieved a partial response. Higher drug exposures were associated with higher response rate with a confirmed ORR of 55% (6/11) in pts achieving Cmax >400 ng/mL. Median duration of response and progression-free survival were not reached as of the data cutoff.

Conclusions: CK-101 was well tolerated with a manageable safety profile. Durable anti-tumor activity was observed, particularly in treatment-naïve pts. Further study is ongoing to establish the optimal dose to maximize therapeutic effect in a planned Phase 3 study in treatment-naïve EGFR-mutant NSCLC pts.