Background CFI-402411, a potent HPK1 inhibitor, may promote T-cell response to tumors through a variety of mechanisms that enhance T-cell function in the cancer immunity cycle, and potentially in settings where antigens are expressed poorly and heterogeneously. Preliminary results demonstrated tolerable safety profile with efficacy signals in select tumor types. 

Methods In this ongoing phase 1/2 study, part A evaluates CFI-402411 daily dose (3+3 design) and dose expansion; part B evaluates CFI-402411 in combination with pembrolizumab (200mg) as BOIN design and dose expansion in pembrolizumab eligible tumors. Dose limiting toxicity (DLT) is any grade 3 toxicity in cycle 1. Starting dose was 80mg.

Results At 02-May-2023 the study enrolled 59 patients (pts; A, 40pts; B, 19pts). In US, checkpoint inhibitor (CPI) pretreated patients were eligible. Diagnoses in ≥ 2pts for A: colorectal (11pts), melanoma (6pts), pancreatic (5pts) and non-small cell lung and prostate (2pts each) cancers; for B: head and neck squamous cell (HNSCC; 3pts) and esophageal, non-small cell lung and small cell lung cancers (2pts each). Part A tested 9 dose levels (80 - 800mg). B tested 5 dose levels (60 - 400mg) to date. Immune-related AEs (irAE) were reported in 7 pts (A; 18%) and 5 pts (B; 26%). Grade ≥ 3 AEs occurred in 25 pts (A: 63%) and 10 pts (B: 53%). SAE’s occurred in 21 pts (A: 53%) and 11 pts (B: 58%). Diarrhea was the most common TEAE (A: 73%; B: 47%), related AE (A: 63%; B: 42%), irAE (A: 15%; B: 11%), and grade ≥ 3 AE in A (18%). Most common grade ≥ 3 AE in B was pulmonary embolism (PE) and AST increase (11% both). The most common SAE was sepsis (A: 15%) and PE (B: 11%). Diarrhea was the most common DLT occurring at 400mg+pembro; 800mg, 720mg, 640mg monotherapy doses. Disease control rates (CR, PR, or SD ≥ 6 weeks from baseline) at 3 months were 18% (A) and 29% (B). Two HNSCC pts achieved a PR (A: 400mg) and confirmed CR (B: 60mg+pembro). A third HNSCC pt’s (B: 400mg+pembro) tumor lesion size reduced 16% at week 5 and pt remains on study. One RCC pt achieved long term SD, 2 years. All 4 pts had prior CPI exposure.

Conclusions CFI-402411 is well-tolerated with a manageable AE profile. Responses as monotherapy and in combination with CPI in CPI exposed patients were seen. Monotherapy part A expansion at 560 mg is underway in HNSCC and RCC.

Acknowledgements Treadwell Therapeutics would like to thank both the patients and the research staff at enrolling centers who have helped to bring this novel therapy to the clinic.

Trial Registration NCT04521413

REFERENCES

Ethics Approval This study obtained ethics approvals; Papadopoulos; ID: Pro00051609 Fu; ID2020–0678 Hamilton; ID: Pro00051611 Spira; ID: Pro00043629 Laurie; CTO Project ID 3320 Wang; ID: Pro00051611 Ma; CREC Ref: 2020.367-T Spreatico; CTO Project ID 3320 Sharma; ID Pro00051609 Chu; ID: HREBA.CC-20-0504 REN1 Hamid; IRB: 2020236

Consent As evidenced by verified clinical database information all subjects gave informed consent before taking part in this clinical trial.

http://dx.doi.org/10.1136/jitc-2023-SITC2023.0741