Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

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Supplementary Appendix

Sotorasib for Lung Cancers with *KRAS* p.G12C Mutation

Ferdinandos Skoulidis et al.

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Supplementary Methods

Exploratory biomarker analysis

1. Programmed death-ligand 1 (PD-L1) immunohistochemical (IHC) assay

Immunohistochemical evaluation of programmed death-ligand 1 (PD-L1) expression on tumor cells was performed using the PD-L1 IHC 22C3 pharmDx assay on the BOND III automated staining system (Leica Microsystems), according to the manufacturer's instructions for use (IFU). All slides were reviewed and scored by a board-certified pathologist trained to score the PD-L1 IHC 22C3 pharmDx assay. The reporting of tumor cell PD-L1 expression (% tumor proportion score) and the test result (positive/negative) was conducted in accordance with established companion diagnostic guidelines by the Food and Drug Administration (FDA) for 22C3.

2. Next generation sequencing (NGS) analysis

Tissue-based NGS analysis was performed at Tempus Labs, a CAP/CLIA facility, following approved SOPs. The Tempus xT assay encompasses a targeted 648-gene DNA sequencing panel in addition to a whole transcriptome RNA sequencing assay using FFPE tissue samples. All FFPE tissue samples were reviewed by a board-certified pathologist to evaluate total tumor content and cellularity with a minimum requirement of 20% tumor to normal nuclei. Extraction of total nucleic acids from FFPE tissue sections was performed using Chemagic 360 sample-specific extraction kits (Perkin Elmer) following digestion

by proteinase K. RNA was purified from the total nucleic acid after digestion with DNase-I. For library construction and sequencing, DNA libraries were prepared using the KAPA Hyper Prep Kit, hybridized to the xT probe set, and amplified with the KAPA HiFi HotStart ReadyMix. Library preps were hybridized to the xGEN Exome Research Panel v1.0 (Integrated DNA Technologies) and target recovery was performed using Streptavidin-coated beads, followed by amplification with the KAPA HiFi Library Amplification Kit. The amplified target-captured DNA tumor library was sequenced using 2x126bp paired-end (PE) reads to an average unique on-target depth of 500x (tumor) and 150x (normal) on an Illumina NovaSeq 6000. The amplified target-captured RNA tumor library was sequenced using 2x75bp PE reads to an average of 50M reads on an Illumina Novaseq 6000. The xT DNA panel was used to detect single and multi-nucleotide alterations.

Cell-free DNA (cfDNA) was isolated from plasma samples using the MagMAX™ Cell-Free DNA Isolation Kit (ThermoFisher) automated on the KingFisherTM Flex Purification System (ThermoFisher). Analysis of tumor mutations using the Resolution Bioscience ctDx Lung™ targeted hybrid-capture assay was performed. Briefly, barcoded DNA libraries were hybridized to a panel of short, 40bp probes targeting single nucleotide variants (SNVs) and insertions and deletions (indels). The resulting sequencing data is analyzed on the Resolution Analysis Platform, which includes proprietary error correction and variant callers that evaluate the samples for SNVs, Indels, fusions, and copy number variations (CNV). For SNVs and indels, the panel covers mutations in AKT1, ALK, B2M, BRAF, EGFR, ERBB2, FGFR2, FGFR3, KEAP1, KRAS, MAP2K1, MET, NRAS, PIK3CA, PTEN, RET, ROS1, STK11, and TP53. The panel targets gene fusion regions within ALK, RET, ROS1, NTRK1,

EGFR, FGFR2, and FGFR3 and copy number variations (CNVs) in B2M, EGFR, ERBB2, FGFR1, KRAS, MET, MYC, NTRK1, PTEN, PIK3CA, RICTOR, STK11 and TP53.

3. Combined tissue and plasma analyses of STK11/KEAP1/TP53

For evaluation of the impact of co-occurring genomic alterations in STK11, KEAP1 and TP53 on clinical outcomes with sotorasib, subjects with available tissue-based NGS results from Tempus or plasma cfDNA NGS results from Resolution Biosciences were included in the analysis. Qualifying variants in STK11, KEAP1 and TP53 included nonsense, frameshift, splice site alterations, as well as missense variants that are known or likely to be pathogenic. Subjects with variant of uncertain significance (VUS) in STK11, KEAP1 or TP53 were not included in the corresponding comparisons of mutant versus wild-type for each gene. A subject with any qualifying variant was considered mutated for that gene, and otherwise wild type. Due to platform differences in report content, our filtering approach was customized to each platform. Tempus' filtered molecular master file (MMF) was processed to retain non-synonymous variants (including splice site mutations, deletions, frame shifts), rearrangements, and CNVs. Excluded variants were those not in COSMIC or dbSNP with either non-pathogenic status and allele frequency at least 0.40 or one of the following cases: uncertain significance, benign, likely benign or germline. Germline status was provided by Tempus, based on matched normal samples. Resolution Biosciences' cfDNA NGS results were annotated using SnpEff v4.3t, and variants were further annotated with information from COSMIC (v92) and dbSNP (build 154) using SnpSift v4.3t. Variants were then filtered down to retain non-synonymous variants

(including splice site mutations, deletions, frame shifts), ClinVar clinical significance of at least 4 (likely-pathogenic), indels, CNVs, and variants in at least 3 COSMIC samples. Excluded variants were those not in COSMIC or dbSNP with allele frequency at least 0.40 or ClinVar clinical significance of uncertain, benign or likely benign.

Supplementary Tables

Table S1. List of Additional Baseline Demographics

	Phase 2 NSCLC 960 mg QD Fasted (N = 126)
Weight (kg)	
n	126
Mean	71.08
SD	17.14
Median	70.65
Q1, Q3	57.70, 83.00
Min, Max	36.8, 122.7
Height (cm)	
n	123
Mean	167.83
SD	9.20
Median	168.80
Q1, Q3	161.00, 175.00
Min, Max	146.0, 188.0
Type of cancer - n (%)	
Non-small cell lung	126 (100.0)
Disease stage at initial diagnosis - n (%)	
Stage I	11 (8.7)
Stage II	14 (11.1)
Stage III	22 (17.5)

	Phase 2 NSCLC 960 mg QD Fasted (N = 126)
Stage IV	78 (61.9)
Missing	1 (0.8)
Disease stage at screening - n (%)	
Stage I	0 (0.0)
Stage II	0 (0.0)
Stage III	5 (4.0)
Stage IV	121 (96.0)
Differentiation - n (%)	
Well differentiated	6 (4.8)
Moderately differentiated	15 (11.9)
Poorly differentiated	24 (19.0)
Undifferentiated	0 (0.0)
Other	0 (0.0)
Unknown	81 (64.3)
Histopathology type - n (%)	
Squamous	1 (0.8)
Adenosquamous carcinoma	0 (0.0)
Squamous cell carcinoma	1 (0.8)
Non-squamous	125 (99.2)
Adenocarcinoma	120 (95.2)
Mucinous	8 (6.3)
Large cell carcinoma	3 (2.4)
Bronchoalveolar carcinoma	2 (1.6)
Sarcomatoid	0 (0.0)
Undifferentiated	0 (0.0)
Other	0 (0.0)

	Phase 2 NSCLC 960 mg QD Fasted (N = 126)
Number of body sites of metastatic disease - n (%)	
0	4 (3.2)
1	51 (40.5)
2	30 (23.8)
3	24 (19.0)
> 3	17 (13.5)
Liver metastasis - n (%)	
Yes	26 (20.6)
No	100 (79.4)
Brain metastasis - n (%)	
Yes	26 (20.6)
No	100 (79.4)
Bone metastasis - n (%)	
Yes	61 (48.4)
No	65 (51.6)
Region - n (%)	
North America	79 (62.7)
Europe	30 (23.8)
Asia	12 (9.5)
Rest of the world	5 (4.0)

Table S2. Objective Response Rate by Prior Lines of Therapy and Prior Anti-PD-1/PD-L1 Therapies

	ORR (95% CI)
Prior Lines of Therapy	
1 (53)	39.6 (26.5, 54.0)
≥ 2 (71)	35.2 (24.2, 47.5)
Prior Anti-PD-1/PD-L1 Therapy	
Yes (113)	36.3 (27.4, 45.9)
No (11)	45.5 (16.7, 76.6)

Table S3. Investigator Assessment of Objective Response Rate Associated with Sotorasib

Response	Investigator Assessment (N = 126)
Objective response rate – % (95% CI)	31.0 (23.0, 39.8)
Disease control rate – % (95% CI)	85.7 (78.4, 91.3)
Best response – n (%)	
Complete response	2 (1.6)
Partial response	37 (29.4)
Stable disease	69 (54.8)
Progressive disease	15 (11.9)
Not evaluable	2 (1.6)
Missing scan	1 (0.8)
Duration of response	
Patients with a response – n (%)	39 (31.0)
Median duration of response – months (95% CI)	11.1 (8.4, 12.6)
Kaplan-Meier estimate (95% CI)	
3 months	94.7 (80.6, 98.7)
6 months	78.6 (61.7, 88.7)
9 months	62.0 (44.4, 75.5)

Table S4. Full List of Treatment-Emergent Adverse Events by Preferred Term

Preferred Term	Phase 2 NSCLC 960 mg QD Fasted (N = 126) n (%)
Number of subjects reporting treatment-emergent adverse events	125 (99.2)
Diarrhoea	64 (50.8)
Nausea	39 (31.0)
Fatigue	32 (25.4)
Arthralgia	27 (21.4)
Aspartate aminotransferase increased	27 (21.4)
Alanine aminotransferase increased	26 (20.6)
Constipation	24 (19.0)
Dyspnoea	24 (19.0)
Vomiting	23 (18.3)
Back pain	21 (16.7)
Cough	19 (15.1)
Anaemia	18 (14.3)
Oedema peripheral	18 (14.3)
Blood alkaline phosphatase increased	17 (13.5)
Decreased appetite	16 (12.7)
Pleural effusion	13 (10.3)
Pneumonia	13 (10.3)
Productive cough	13 (10.3)
Pruritus	12 (9.5)
Pyrexia	12 (9.5)
Abdominal pain	11 (8.7)
Fall	11 (8.7)
Headache	11 (8.7)
Hypokalaemia	11 (8.7)
Hypertension	10 (7.9)

Preferred Term	Phase 2 NSCLC 960 mg QD Fasted (N = 126) n (%)
Rash maculo-papular	10 (7.9)
Hyponatraemia	9 (7.1)
Insomnia	9 (7.1)
Pain	9 (7.1)
Pain in extremity	9 (7.1)
Upper respiratory tract infection	9 (7.1)
Urinary tract infection	9 (7.1)
Weight decreased	9 (7.1)
Abdominal pain upper	8 (6.3)
Anxiety	8 (6.3)
Asthenia	8 (6.3)
Dry skin	8 (6.3)
Hypomagnesaemia	8 (6.3)
Myalgia	8 (6.3)
Non-small cell lung cancer	8 (6.3)
Rash	8 (6.3)
Dehydration	7 (5.6)
Lymphocyte count decreased	7 (5.6)
Oropharyngeal pain	7 (5.6)
Rhinorrhoea	7 (5.6)
Haemorrhoids	6 (4.8)
Neck pain	6 (4.8)
Abdominal distension	5 (4.0)
Chills	5 (4.0)
Dizziness	5 (4.0)
Gamma-glutamyltransferase increased	5 (4.0)
Hypotension	5 (4.0)
Muscle spasms	5 (4.0)
Rhinitis allergic	5 (4.0)

Preferred Term	Phase 2 NSCLC 960 mg QD Fasted (N = 126) n (%)
Blood cholesterol increased	4 (3.2)
Blood creatinine increased	4 (3.2)
Chronic obstructive pulmonary disease	4 (3.2)
Depression	4 (3.2)
Drug-induced liver injury	4 (3.2)
Dyspepsia	4 (3.2)
Dysphonia	4 (3.2)
Flatulence	4 (3.2)
Hypoalbuminaemia	4 (3.2)
Hypocalcaemia	4 (3.2)
Nasal congestion	4 (3.2)
Oral candidiasis	4 (3.2)
Platelet count decreased	4 (3.2)
Pulmonary embolism	4 (3.2)
Blood bilirubin increased	3 (2.4)
Deep vein thrombosis	3 (2.4)
Dysgeusia	3 (2.4)
Dysphagia	3 (2.4)
Electrocardiogram QT prolonged	3 (2.4)
Flank pain	3 (2.4)
Haemoptysis	3 (2.4)
Herpes zoster	3 (2.4)
Hyperhidrosis	3 (2.4)
Hyperkalaemia	3 (2.4)
Hypoaesthesia	3 (2.4)
Hypoglycaemia	3 (2.4)
Hypophosphataemia	3 (2.4)
International normalised ratio increased	3 (2.4)
Malaise	3 (2.4)

Preferred Term	Phase 2 NSCLC 960 mg QD Fasted (N = 126) n (%)
Muscular weakness	3 (2.4)
Musculoskeletal chest pain	3 (2.4)
Nasopharyngitis	3 (2.4)
Night sweats	3 (2.4)
Non-cardiac chest pain	3 (2.4)
Oral fungal infection	3 (2.4)
Pneumonitis	3 (2.4)
Pollakiuria	3 (2.4)
Sinus tachycardia	3 (2.4)
Sinusitis	3 (2.4)
Tachycardia	3 (2.4)
Wheezing	3 (2.4)
Activated partial thromboplastin time prolonged	2 (1.6)
Alopecia	2 (1.6)
Ascites	2 (1.6)
Blood creatine phosphokinase increased	2 (1.6)
Breast pain	2 (1.6)
Bronchial obstruction	2 (1.6)
Cancer pain	2 (1.6)
Cardiac failure	2 (1.6)
Cellulitis	2 (1.6)
Chest pain	2 (1.6)
Cholecystitis	2 (1.6)
Contusion	2 (1.6)
Depressed mood	2 (1.6)
Dermatitis acneiform	2 (1.6)
Dry eye	2 (1.6)
Dry mouth	2 (1.6)
Dysuria	2 (1.6)

Preferred Term	Phase 2 NSCLC 960 mg QD Fasted (N = 126) n (%)
Embolism	2 (1.6)
Femoral neck fracture	2 (1.6)
Folliculitis	2 (1.6)
Gastritis	2 (1.6)
Gastrooesophageal reflux disease	2 (1.6)
General physical health deterioration	2 (1.6)
Hepatic function abnormal	2 (1.6)
Hot flush	2 (1.6)
Hypercalcaemia	2 (1.6)
Hyperglycaemia	2 (1.6)
Hyperphosphataemia	2 (1.6)
Hypoxia	2 (1.6)
Influenza	2 (1.6)
Inguinal hernia	2 (1.6)
Lipase increased	2 (1.6)
Liver function test increased	2 (1.6)
Lung neoplasm malignant	2 (1.6)
Memory impairment	2 (1.6)
Pain in jaw	2 (1.6)
Paraesthesia	2 (1.6)
Periorbital oedema	2 (1.6)
Pharyngitis	2 (1.6)
Respiratory failure	2 (1.6)
Respiratory tract congestion	2 (1.6)
Supraventricular tachycardia	2 (1.6)
Systemic inflammatory response syndrome	2 (1.6)
Transaminases increased	2 (1.6)
Vertigo	2 (1.6)
Vision blurred	2 (1.6)

Preferred Term	Phase 2 NSCLC 960 mg QD Fasted (N = 126) n (%)
Weight increased	2 (1.6)
White blood cell count decreased	2 (1.6)
Abdominal discomfort	1 (0.8)
Abdominal mass	1 (0.8)
Abnormal dreams	1 (0.8)
Acute kidney injury	1 (0.8)
Acute myocardial infarction	1 (0.8)
Acute respiratory failure	1 (0.8)
Adenocarcinoma	1 (0.8)
Adjustment disorder with depressed mood	1 (0.8)
Adult failure to thrive	1 (0.8)
Alcoholism	1 (0.8)
Amaurosis fugax	1 (0.8)
Amnesia	1 (0.8)
Amylase increased	1 (0.8)
Anaemia of malignant disease	1 (0.8)
Anaphylactic shock	1 (0.8)
Angiomyolipoma	1 (0.8)
Atrioventricular block second degree	1 (0.8)
Biliary tract infection	1 (0.8)
Bilirubin conjugated increased	1 (0.8)
Blood corticotrophin decreased	1 (0.8)
Blood creatine increased	1 (0.8)
Blood glucose increased	1 (0.8)
Blood potassium decreased	1 (0.8)
Blood triglycerides increased	1 (0.8)
Bone pain	1 (0.8)
Bone swelling	1 (0.8)
Brachial plexopathy	1 (0.8)

Preferred Term	Phase 2 NSCLC 960 mg QD Fasted (N = 126) n (%)
Breath odour	1 (0.8)
Bronchial carcinoma	1 (0.8)
Bronchitis	1 (0.8)
Bursitis	1 (0.8)
C-reactive protein increased	1 (0.8)
COVID-19	1 (0.8)
Cachexia	1 (0.8)
Candida infection	1 (0.8)
Cardiac arrest	1 (0.8)
Cardiac failure congestive	1 (0.8)
Cardiac murmur	1 (0.8)
Cataract	1 (0.8)
Catheter site infection	1 (0.8)
Cell death	1 (0.8)
Cerebellar infarction	1 (0.8)
Cerebrovascular accident	1 (0.8)
Cervical radiculopathy	1 (0.8)
Chylothorax	1 (0.8)
Clostridium difficile infection	1 (0.8)
Clubbing	1 (0.8)
Colitis	1 (0.8)
Compression fracture	1 (0.8)
Confusional state	1 (0.8)
Conjunctival haemorrhage	1 (0.8)
Cortisol decreased	1 (0.8)
Cushingoid	1 (0.8)
Cystitis	1 (0.8)
Decubitus ulcer	1 (0.8)
Dermatitis	1 (0.8)

Preferred Term	Phase 2 NSCLC 960 mg QD Fasted (N = 126) n (%)
Diarrhoea infectious	1 (0.8)
Diverticulitis	1 (0.8)
Drug hypersensitivity	1 (0.8)
Dyslipidaemia	1 (0.8)
Ear pain	1 (0.8)
Ecchymosis	1 (0.8)
Embolic stroke	1 (0.8)
Encephalomalacia	1 (0.8)
Enterocolitis haemorrhagic	1 (0.8)
Epistaxis	1 (0.8)
Erectile dysfunction	1 (0.8)
Eructation	1 (0.8)
Erythema	1 (0.8)
Essential hypertension	1 (0.8)
Eye haemorrhage	1 (0.8)
Eye pain	1 (0.8)
Eye swelling	1 (0.8)
Facial pain	1 (0.8)
Feeling jittery	1 (0.8)
Fibrin D dimer increased	1 (0.8)
Fibromyalgia	1 (0.8)
Fracture	1 (0.8)
Gallbladder disorder	1 (0.8)
Gastric pH decreased	1 (0.8)
Gastric ulcer	1 (0.8)
Gastrointestinal disorder	1 (0.8)
Gastrointestinal haemorrhage	1 (0.8)
Generalised oedema	1 (0.8)
Groin pain	1 (0.8)

Preferred Term	Phase 2 NSCLC 960 mg QD Fasted (N = 126) n (%)
Gynaecomastia	1 (0.8)
Haematochezia	1 (0.8)
Haematuria	1 (0.8)
Haemorrhoidal haemorrhage	1 (0.8)
Hemiparesis	1 (0.8)
Hepatic steatosis	1 (0.8)
Hepatotoxicity	1 (0.8)
Hiatus hernia	1 (0.8)
Hydrocholecystis	1 (0.8)
Hyperlipidaemia	1 (0.8)
Hypermagnesaemia	1 (0.8)
Hypersomnia	1 (0.8)
Hypertriglyceridaemia	1 (0.8)
Hypoproteinaemia	1 (0.8)
Hypovolaemic shock	1 (0.8)
Increased bronchial secretion	1 (0.8)
Infection	1 (0.8)
Influenza like illness	1 (0.8)
Intestinal obstruction	1 (0.8)
Irritability	1 (0.8)
Jaundice	1 (0.8)
Joint range of motion decreased	1 (0.8)
Leukocytosis	1 (0.8)
Leukocyturia	1 (0.8)
Leukopenia	1 (0.8)
Ligament rupture	1 (0.8)
Limb discomfort	1 (0.8)
Lip dry	1 (0.8)
Liver function test abnormal	1 (0.8)

Preferred Term	Phase 2 NSCLC 960 mg QD Fasted (N = 126) n (%)
Localised oedema	1 (0.8)
Lung disorder	1 (0.8)
Lymphoedema	1 (0.8)
Lymphopenia	1 (0.8)
Malignant biliary obstruction	1 (0.8)
Malignant pleural effusion	1 (0.8)
Metabolic acidosis	1 (0.8)
Metastases to bone	1 (0.8)
Metastases to central nervous system	1 (0.8)
Muscle strain	1 (0.8)
Musculoskeletal discomfort	1 (0.8)
Musculoskeletal disorder	1 (0.8)
Musculoskeletal pain	1 (0.8)
Nervous system disorder	1 (0.8)
Neuralgia	1 (0.8)
Neuropathy peripheral	1 (0.8)
Neutropenia	1 (0.8)
Neutrophil count decreased	1 (0.8)
Neutrophil count increased	1 (0.8)
Nipple pain	1 (0.8)
Nocturia	1 (0.8)
Non-small cell lung cancer metastatic	1 (0.8)
Non-small cell lung cancer stage IV	1 (0.8)
Normocytic anaemia	1 (0.8)
Ocular hyperaemia	1 (0.8)
Oesophageal stenosis	1 (0.8)
Onycholysis	1 (0.8)
Oral herpes	1 (0.8)
Oral mucosal blistering	1 (0.8)

Preferred Term	Phase 2 NSCLC 960 mg QD Fasted (N = 126) n (%)
Osteoarthritis	1 (0.8)
Panic attack	1 (0.8)
Papule	1 (0.8)
Pathological fracture	1 (0.8)
Pelvic fracture	1 (0.8)
Pericardial effusion	1 (0.8)
Periodontal disease	1 (0.8)
Peripheral coldness	1 (0.8)
Photosensitivity reaction	1 (0.8)
Pleurisy	1 (0.8)
Pneumonia aspiration	1 (0.8)
Pneumonia bacterial	1 (0.8)
Pneumothorax	1 (0.8)
Polydipsia	1 (0.8)
Polyuria	1 (0.8)
Presyncope	1 (0.8)
Protein deficiency	1 (0.8)
Proteinuria	1 (0.8)
Puncture site erythema	1 (0.8)
Purpura	1 (0.8)
Pyuria	1 (0.8)
Quadrantanopia	1 (0.8)
Rectal haemorrhage	1 (0.8)
Red blood cell count decreased	1 (0.8)
Respiratory tract infection bacterial	1 (0.8)
Restlessness	1 (0.8)
Rhinitis	1 (0.8)
Sciatica	1 (0.8)
Seizure	1 (0.8)

Preferred Term	Phase 2 NSCLC 960 mg QD Fasted (N = 126) n (%)
Sepsis	1 (0.8)
Sinus congestion	1 (0.8)
Skin cancer	1 (0.8)
Skin fissures	1 (0.8)
Skin lesion	1 (0.8)
Skin mass	1 (0.8)
Sleep apnoea syndrome	1 (0.8)
Sleep disorder	1 (0.8)
Speech disorder	1 (0.8)
Spinal compression fracture	1 (0.8)
Spinal cord compression	1 (0.8)
Spinal stenosis	1 (0.8)
Staphylococcal infection	1 (0.8)
Stomatitis	1 (0.8)
Subacute endocarditis	1 (0.8)
Subileus	1 (0.8)
Taste disorder	1 (0.8)
Tendonitis	1 (0.8)
Testicular oedema	1 (0.8)
Thermal burn	1 (0.8)
Thrombocytopenia	1 (0.8)
Thrombocytosis	1 (0.8)
Tooth infection	1 (0.8)
Transaminases abnormal	1 (0.8)
Tremor	1 (0.8)
Troponin increased	1 (0.8)
Tumour pain	1 (0.8)
Type 2 diabetes mellitus	1 (0.8)
Upper-airway cough syndrome	1 (0.8)

Preferred Term	Phase 2 NSCLC 960 mg QD Fasted (N = 126) n (%)
Urinary incontinence	1 (0.8)
Urinary tract infection bacterial	1 (0.8)
Urinary tract infection fungal	1 (0.8)
Urine potassium increased	1 (0.8)
Vertebral foraminal stenosis	1 (0.8)
Viral infection	1 (0.8)
Vulvovaginal pruritus	1 (0.8)
Xeroderma	1 (0.8)
Xerophthalmia	1 (0.8)

Table S5. Full List of Treatment-Emergent Treatment-Related Adverse Events by System Organ Class, Preferred Term and Grade

System Organ Class Preferred Term Worst Grade	Phase 2 NSCLC 960 mg QD Fasted (N = 126) n (%)
Number of subjects reporting treatment-related adverse events	88 (69.8)
Any system organ class	88 (69.8)
Any preferred term	88 (69.8)
Grade 1 or 2	62 (49.2)
Grade 3	25 (19.8)
Grade 4	1 (0.8)
Fatal	0 (0.0)
Blood and lymphatic system disorders	8 (6.3)
Anaemia	6 (4.8)
Grade 1 or 2	5 (4.0)
Grade 3	1 (0.8)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Anaemia of malignant disease	1 (0.8)
Grade 1 or 2	1 (0.8)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Lymphopenia	1 (0.8)
Grade 1 or 2	0 (0.0)
Grade 3	1 (0.8)

System Organ Class Preferred Term Worst Grade	Phase 2 NSCLC 960 mg QD Fasted (N = 126) n (%)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Neutropenia	1 (0.8)
Grade 1 or 2	0 (0.0)
Grade 3	1 (0.8)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Eye disorders	2 (1.6)
Vision blurred	1 (0.8)
Grade 1 or 2	1 (0.8)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Xerophthalmia	1 (0.8)
Grade 1 or 2	1 (0.8)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Gastrointestinal disorders	56 (44.4)
Diarrhoea	40 (31.7)
Grade 1 or 2	35 (27.8)
Grade 3	5 (4.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)

System Organ Class Preferred Term Worst Grade	Phase 2 NSCLC 960 mg QD Fasted (N = 126) n (%)
Nausea	24 (19.0)
Grade 1 or 2	24 (19.0)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Vomiting	10 (7.9)
Grade 1 or 2	10 (7.9)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Abdominal distension	3 (2.4)
Grade 1 or 2	3 (2.4)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Abdominal pain	3 (2.4)
Grade 1 or 2	3 (2.4)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Abdominal pain upper	3 (2.4)
Grade 1 or 2	3 (2.4)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)

System Organ Class Preferred Term Worst Grade	Phase 2 NSCLC 960 mg QD Fasted (N = 126) n (%)
Constipation	2 (1.6)
Grade 1 or 2	2 (1.6)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Dry mouth	2 (1.6)
Grade 1 or 2	2 (1.6)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Dyspepsia	2 (1.6)
Grade 1 or 2	2 (1.6)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Breath odour	1 (0.8)
Grade 1 or 2	1 (0.8)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Flatulence	1 (0.8)
Grade 1 or 2	1 (0.8)
Grade 3	0 (0.0)
Grade 4	0 (0.0)

System Organ Class Preferred Term Worst Grade	Phase 2 NSCLC 960 mg QD Fasted (N = 126) n (%)
Fatal	0 (0.0)
Gastrooesophageal reflux disease	1 (0.8)
Grade 1 or 2	1 (0.8)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Oral mucosal blistering	1 (0.8)
Grade 1 or 2	1 (0.8)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Stomatitis	1 (0.8)
Grade 1 or 2	1 (0.8)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
General disorders and administration site conditions	21 (16.7)
Fatigue	14 (11.1)
Grade 1 or 2	14 (11.1)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Oedema peripheral	5 (4.0)
Grade 1 or 2	5 (4.0)

System Organ Class Preferred Term Worst Grade	Phase 2 NSCLC 960 mg QD Fasted (N = 126) n (%)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Asthenia	3 (2.4)
Grade 1 or 2	3 (2.4)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Malaise	2 (1.6)
Grade 1 or 2	2 (1.6)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Feeling jittery	1 (0.8)
Grade 1 or 2	1 (0.8)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Localised oedema	1 (0.8)
Grade 1 or 2	1 (0.8)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)

System Organ Class Preferred Term Worst Grade	Phase 2 NSCLC 960 mg QD Fasted (N = 126) n (%)
Non-cardiac chest pain	1 (0.8)
Grade 1 or 2	1 (0.8)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Pyrexia	1 (0.8)
Grade 1 or 2	1 (0.8)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Hepatobiliary disorders	5 (4.0)
Drug-induced liver injury	3 (2.4)
Grade 1 or 2	1 (0.8)
Grade 3	2 (1.6)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Hepatic function abnormal	2 (1.6)
Grade 1 or 2	1 (0.8)
Grade 3	1 (0.8)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Hepatotoxicity	1 (0.8)
Grade 1 or 2	0 (0.0)
Grade 3	1 (0.8)
Grade 4	0 (0.0)

System Organ Class Preferred Term Worst Grade	Phase 2 NSCLC 960 mg QD Fasted (N = 126) n (%)
Fatal	0 (0.0)
Immune system disorders	1 (0.8)
Drug hypersensitivity	1 (0.8)
Grade 1 or 2	0 (0.0)
Grade 3	1 (0.8)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Infections and infestations	5 (4.0)
Cellulitis	1 (0.8)
Grade 1 or 2	0 (0.0)
Grade 3	1 (0.8)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Diverticulitis	1 (0.8)
Grade 1 or 2	1 (0.8)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Oral candidiasis	1 (0.8)
Grade 1 or 2	1 (0.8)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)

System Organ Class Preferred Term Worst Grade	Phase 2 NSCLC 960 mg QD Fasted (N = 126) n (%)
Oral fungal infection	1 (0.8)
Grade 1 or 2	1 (0.8)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Upper respiratory tract infection	1 (0.8)
Grade 1 or 2	1 (0.8)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Investigations	30 (23.8)
Alanine aminotransferase increased	19 (15.1)
Grade 1 or 2	11 (8.7)
Grade 3	8 (6.3)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Aspartate aminotransferase increased	19 (15.1)
Grade 1 or 2	12 (9.5)
Grade 3	7 (5.6)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Blood alkaline phosphatase increased	9 (7.1)
Grade 1 or 2	8 (6.3)
Grade 3	1 (0.8)
Grade 4	0 (0.0)

System Organ Class Preferred Term Worst Grade	Phase 2 NSCLC 960 mg QD Fasted (N = 126) n (%)
Fatal	0 (0.0)
Weight decreased	4 (3.2)
Grade 1 or 2	4 (3.2)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Gamma-glutamyltransferase increased	3 (2.4)
Grade 1 or 2	0 (0.0)
Grade 3	3 (2.4)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Lymphocyte count decreased	3 (2.4)
Grade 1 or 2	2 (1.6)
Grade 3	1 (0.8)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Platelet count decreased	3 (2.4)
Grade 1 or 2	3 (2.4)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Blood bilirubin increased	2 (1.6)
Grade 1 or 2	2 (1.6)
Grade 3	0 (0.0)

System Organ Class Preferred Term Worst Grade	Phase 2 NSCLC 960 mg QD Fasted (N = 126) n (%)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Blood cholesterol increased	1 (0.8)
Grade 1 or 2	1 (0.8)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Blood corticotrophin decreased	1 (0.8)
Grade 1 or 2	1 (0.8)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Blood creatinine increased	1 (0.8)
Grade 1 or 2	1 (0.8)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Cortisol decreased	1 (0.8)
Grade 1 or 2	1 (0.8)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Electrocardiogram QT prolonged	1 (0.8)
Grade 1 or 2	1 (0.8)

System Organ Class Preferred Term Worst Grade	Phase 2 NSCLC 960 mg QD Fasted (N = 126) n (%)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Gastric pH decreased	1 (0.8)
Grade 1 or 2	1 (0.8)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Lipase increased	1 (0.8)
Grade 1 or 2	0 (0.0)
Grade 3	1 (0.8)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Liver function test increased	1 (0.8)
Grade 1 or 2	0 (0.0)
Grade 3	1 (0.8)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Neutrophil count decreased	1 (0.8)
Grade 1 or 2	0 (0.0)
Grade 3	1 (0.8)
Grade 4	0 (0.0)
Fatal	0 (0.0)

System Organ Class Preferred Term Worst Grade	Phase 2 NSCLC 960 mg QD Fasted (N = 126) n (%)
Red blood cell count decreased	1 (0.8)
Grade 1 or 2	1 (0.8)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Transaminases abnormal	1 (0.8)
Grade 1 or 2	0 (0.0)
Grade 3	1 (0.8)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Transaminases increased	1 (0.8)
Grade 1 or 2	1 (0.8)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Weight increased	1 (0.8)
Grade 1 or 2	1 (0.8)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
White blood cell count decreased	1 (0.8)
Grade 1 or 2	1 (0.8)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)

System Organ Class Preferred Term Worst Grade	Phase 2 NSCLC 960 mg QD Fasted (N = 126) n (%)
Metabolism and nutrition disorders	15 (11.9)
Decreased appetite	5 (4.0)
Grade 1 or 2	5 (4.0)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Hypokalaemia	5 (4.0)
Grade 1 or 2	4 (3.2)
Grade 3	1 (0.8)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Dehydration	1 (0.8)
Grade 1 or 2	1 (0.8)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Dyslipidaemia	1 (0.8)
Grade 1 or 2	1 (0.8)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Hypertriglyceridaemia	1 (0.8)
Grade 1 or 2	1 (0.8)
Grade 3	0 (0.0)

System Organ Class Preferred Term Worst Grade	Phase 2 NSCLC 960 mg QD Fasted (N = 126) n (%)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Hypoglycaemia	1 (0.8)
Grade 1 or 2	1 (0.8)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Hypomagnesaemia	1 (0.8)
Grade 1 or 2	1 (0.8)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Hypophosphataemia	1 (0.8)
Grade 1 or 2	1 (0.8)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Musculoskeletal and connective tissue disorders	7 (5.6)
Arthralgia	3 (2.4)
Grade 1 or 2	3 (2.4)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)

System Organ Class Preferred Term Worst Grade	Phase 2 NSCLC 960 mg QD Fasted (N = 126) n (%)
Myalgia	2 (1.6)
Grade 1 or 2	2 (1.6)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Muscular weakness	1 (0.8)
Grade 1 or 2	1 (0.8)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Osteoarthritis	1 (0.8)
Grade 1 or 2	1 (0.8)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	1 (0.8)
Angiomyolipoma	1 (0.8)
Grade 1 or 2	1 (0.8)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Nervous system disorders	9 (7.1)
Headache	5 (4.0)
Grade 1 or 2	5 (4.0)
Grade 3	0 (0.0)

System Organ Class Preferred Term Worst Grade	Phase 2 NSCLC 960 mg QD Fasted (N = 126) n (%)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Dysgeusia	2 (1.6)
Grade 1 or 2	2 (1.6)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Hypersomnia	1 (0.8)
Grade 1 or 2	1 (0.8)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Hypoaesthesia	1 (0.8)
Grade 1 or 2	1 (0.8)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Nervous system disorder	1 (0.8)
Grade 1 or 2	1 (0.8)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Psychiatric disorders	2 (1.6)
Confusional state	1 (0.8)

System Organ Class Preferred Term Worst Grade	Phase 2 NSCLC 960 mg QD Fasted (N = 126) n (%)
Grade 1 or 2	1 (0.8)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Insomnia	1 (0.8)
Grade 1 or 2	1 (0.8)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Renal and urinary disorders	2 (1.6)
Leukocyturia	1 (0.8)
Grade 1 or 2	1 (0.8)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Pollakiuria	1 (0.8)
Grade 1 or 2	1 (0.8)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Proteinuria	1 (0.8)
Grade 1 or 2	1 (0.8)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)

System Organ Class Preferred Term Worst Grade	Phase 2 NSCLC 960 mg QD Fasted (N = 126) n (%)
Reproductive system and breast disorders	1 (0.8)
Gynaecomastia	1 (0.8)
Grade 1 or 2	1 (0.8)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Respiratory, thoracic and mediastinal disorders	5 (4.0)
Dyspnoea	2 (1.6)
Grade 1 or 2	1 (0.8)
Grade 3	0 (0.0)
Grade 4	1 (0.8)
Fatal	0 (0.0)
Pneumonitis	2 (1.6)
Grade 1 or 2	0 (0.0)
Grade 3	1 (0.8)
Grade 4	1 (0.8)
Fatal	0 (0.0)
Productive cough	2 (1.6)
Grade 1 or 2	2 (1.6)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Cough	1 (0.8)
Grade 1 or 2	1 (0.8)

System Organ Class Preferred Term Worst Grade	Phase 2 NSCLC 960 mg QD Fasted (N = 126) n (%)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Skin and subcutaneous tissue disorders	19 (15.1)
Rash maculo-papular	7 (5.6)
Grade 1 or 2	7 (5.6)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Dry skin	6 (4.8)
Grade 1 or 2	6 (4.8)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Pruritus	5 (4.0)
Grade 1 or 2	5 (4.0)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Alopecia	2 (1.6)
Grade 1 or 2	2 (1.6)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)

System Organ Class Preferred Term Worst Grade	Phase 2 NSCLC 960 mg QD Fasted (N = 126) n (%)
Dermatitis acneiform	1 (0.8)
Grade 1 or 2	1 (0.8)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Hyperhidrosis	1 (0.8)
Grade 1 or 2	1 (0.8)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Night sweats	1 (0.8)
Grade 1 or 2	1 (0.8)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Onycholysis	1 (0.8)
Grade 1 or 2	1 (0.8)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Photosensitivity reaction	1 (0.8)
Grade 1 or 2	1 (0.8)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)

System Organ Class Preferred Term Worst Grade	Phase 2 NSCLC 960 mg QD Fasted (N = 126) n (%)
Purpura	1 (0.8)
Grade 1 or 2	1 (0.8)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Rash	1 (0.8)
Grade 1 or 2	1 (0.8)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Xeroderma	1 (0.8)
Grade 1 or 2	1 (0.8)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Vascular disorders	2 (1.6)
Hypotension	1 (0.8)
Grade 1 or 2	1 (0.8)
Grade 3	0 (0.0)
Grade 4	0 (0.0)
Fatal	0 (0.0)
Peripheral coldness	1 (0.8)
Grade 1 or 2	1 (0.8)
Grade 3	0 (0.0)

System Organ Class Preferred Term Worst Grade	Phase 2 NSCLC 960 mg QD Fasted (N = 126) n (%)
Grade 4	0 (0.0)
Fatal	0 (0.0)

N = Number of subjects in the analysis set. n = Number of subjects with observed data.
Coded using MedDRA version 23.1. Severity graded using CTCAE version 5.0
Rows are sorted by system organ class (alphabetically) and preferred term within system organ class (in descending order of frequency in the NSCLC column); worst grade is presented.
Grade 5 fatal adverse events may start prior to data cutoff and result in death after cutoff. These events are summarized with grade 5 but the death after data cutoff are not included in analysis.

Table S6. Exploratory Analyses of PD-L1 and Co-Occurring Mutations in *STK11*, *KEAP1*, and *TP53*

					95%CI	
	PD-L1 TPS	**N**	**OR events**	**ORR**	**low**	**high**
	< 1%	44	21	48%	32%	63%
	1-49%	33	13	39%	23%	58%
	≥ 50%	9	2	22%	3%	60%
	all evaluable	86	36	42%	31%	53%
					95%CI	
Gene	**Mutation status**	**N**	**OR events**	**ORR**	**low**	**high**
TP53	wt	20	8	40%	19%	64%
TP53	mut	84	33	39%	29%	51%
STK11	wt	69	27	39%	28%	52%
STK11	mut	35	14	40%	24%	58%
KEAP1	wt	84	37	44%	33%	55%
KEAP1	mut	20	4	20%	6%	44%
					95%CI	
KEAP1	**STK11**	**N**	**OR events**	**ORR**	**low**	**high**
mut	mut	13	3	23%	5%	54%
wt	mut	22	11	50%	28%	72%
mut	wt	7	1	14%	0%	58%
wt	wt	62	26	42%	30%	55%
all evaluable		104	41	39%	30%	49%

TPS denotes tumor proportion score, wt wild type, mut mutant, and ORR objective response rate.

Table S7. Exploratory Analysis of Tumor Mutational Burden and Objective Response to Sotorasib

	ORR (95% CI)
TMB Level	
Low, <10 Mut/Mb (69)	42.0 (30.2, 54.5)
High, ⩾10 Mut/Mb (15)	40.0 (16.3, 67.7)

Supplementary Figures.

Figure S1. Patient Disposition

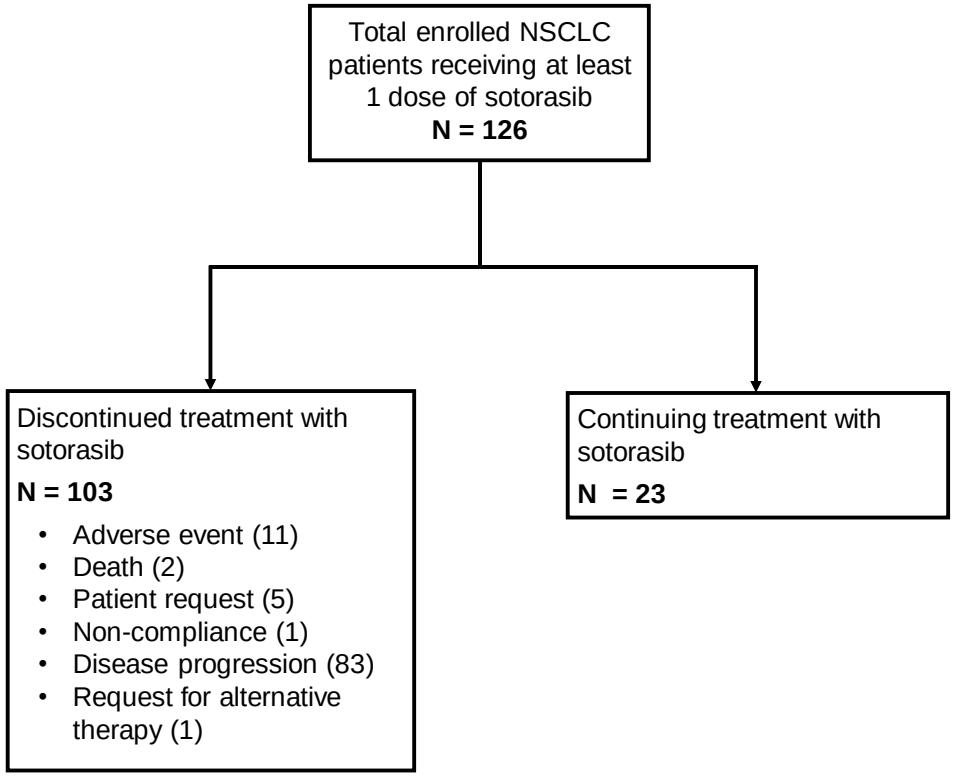


Figure S1 illustrates the patient flow.

Figure S2. Best Tumor Shrinkage by PD-L1 Levels and Co-Occurring Mutations in *STK11*, *KEAP1,* and *TP53*

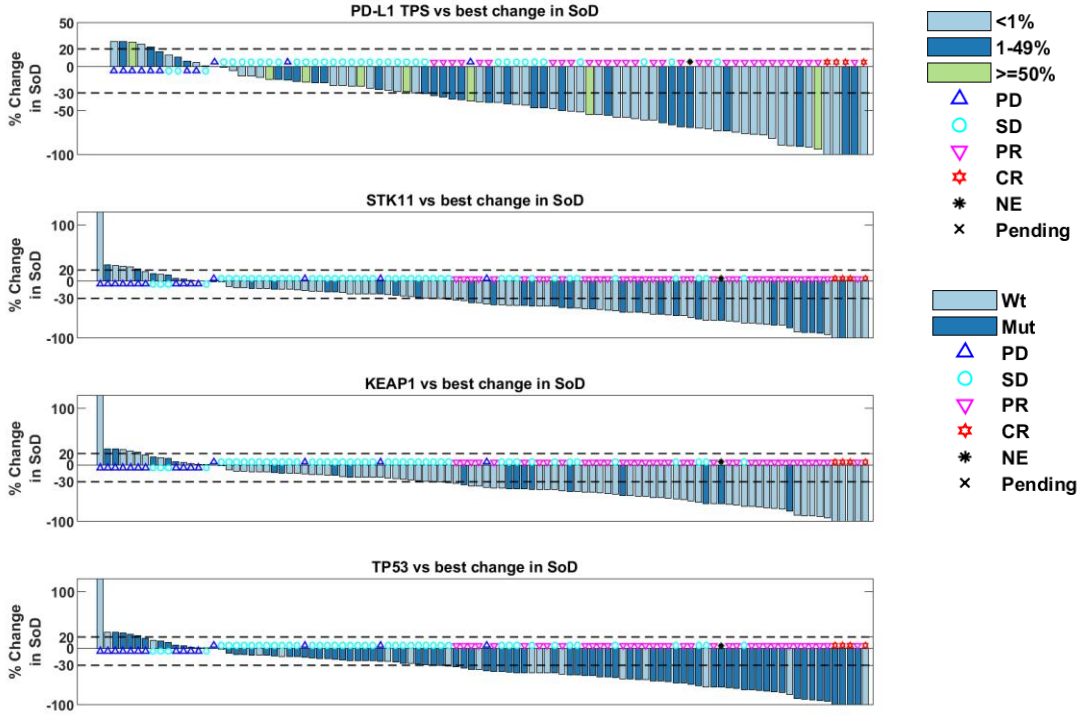
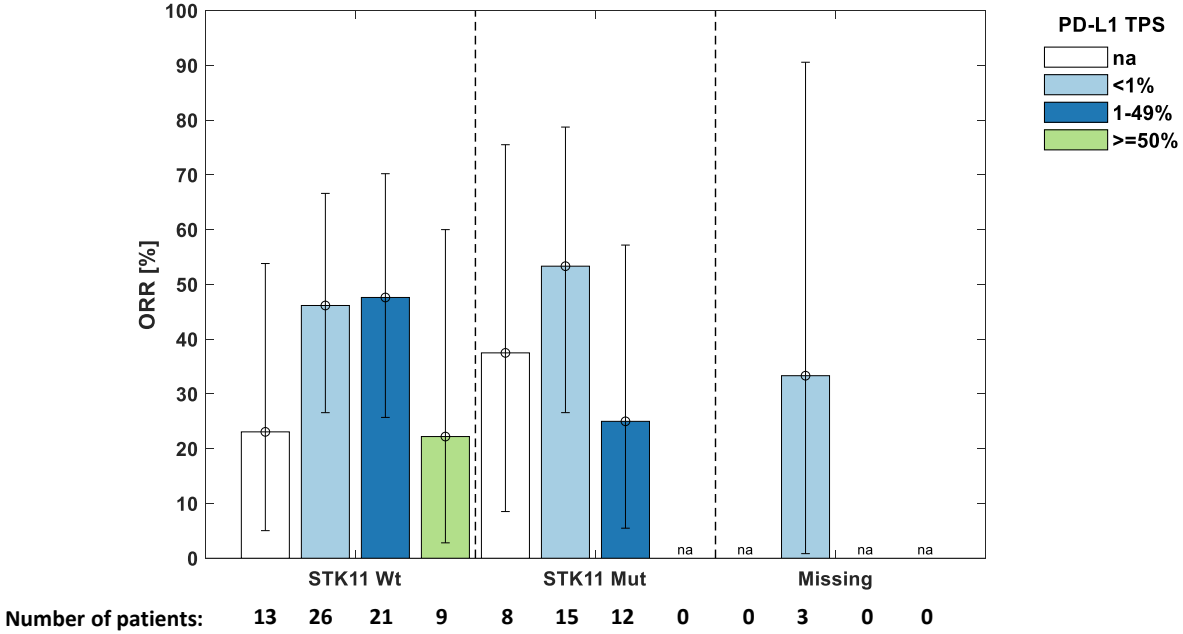
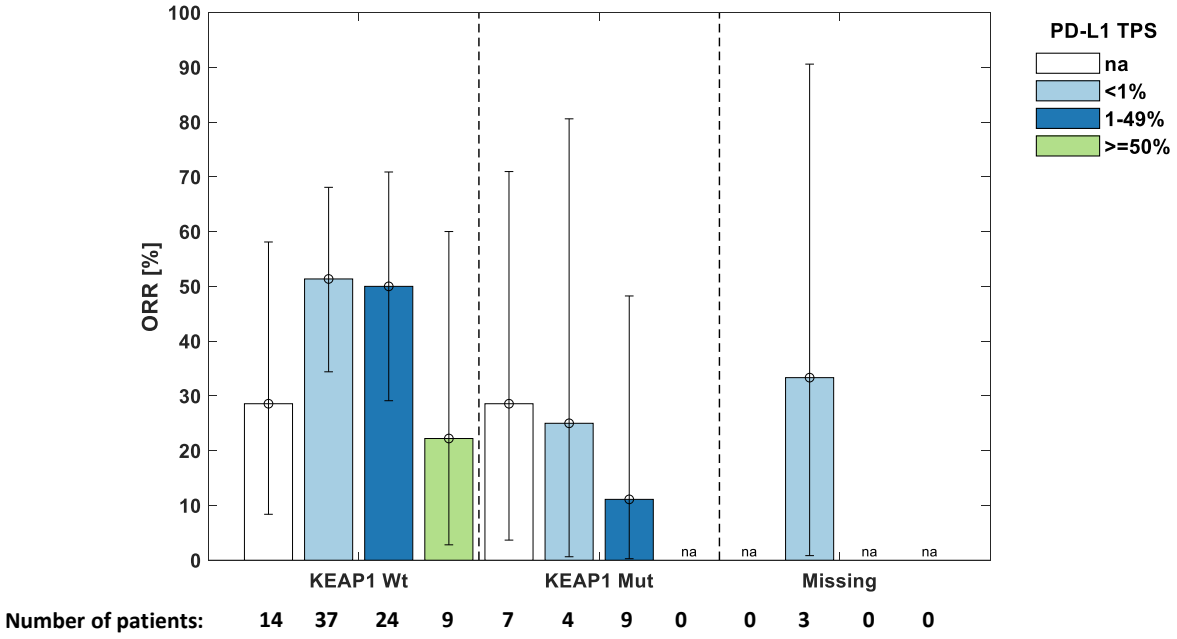


Figure S2 illustrates the best tumor shrinkage in patients stratified by PD-L1 levels (top panel) and co-occurring mutations of *STK11*, *KEAP1*, and *TP53* (bottom panel). SoD denotes sum of diameters, TPS tumor proportion score, PD progressive disease, SD stable disease, PR partial response, CR complete response, NE not evaluable.

Figure S3. Objective Response Rate by PD-L1 Levels Overlaid by Co-Occurring Mutations in *STK11*, *KEAP1*, and *TP53*




PD-L1 TPS
na
<1%
1-49%
>=50%
ORR [%]
100
90
80
70
60
50
40
30
20
10
0
na
na
na
na
KEAP1 Wt
KEAP1 Mut
Missing
Number of patients:
14 37 24 9 7 4 9 0 0 3 0 0

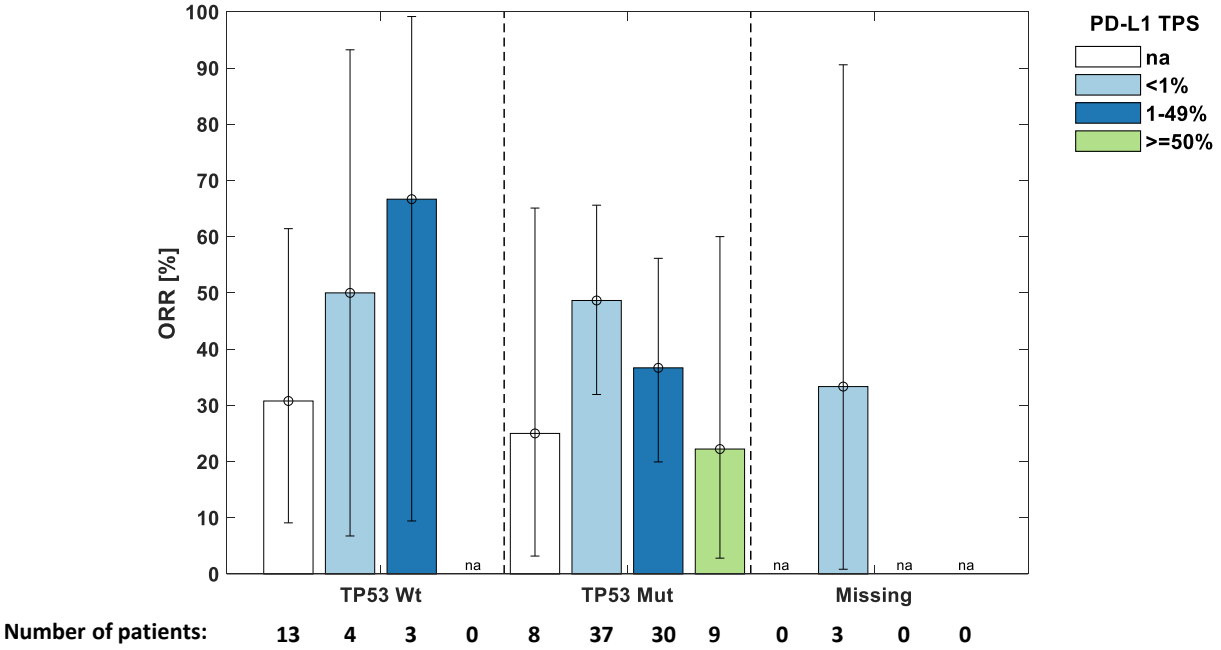


Figure S3 illustrates objective response rate associated with sotorasib by PD-L1 expression levels in the co-occurring mutation profiles of *STK11* (top panel), *KEAP1* (middle panel), and *TP53* (bottom panel), respectively. ORR denotes objective response rate; TPS tumor proportion score; wt wild-type, and mut mutant.