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GUARDANT

Guardant360
基因檢測服務報告

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送檢編號：47729953

檢測次數：第一次

提醒

基因數據乃屬個人隱私，切勿輕易向任何個人、團體或非您的授權者透漏本報告內容。若您有任何疑慮，歡迎來電洽詢，我們很樂意為您提供更詳細的諮詢服務。若因郵遞錯誤收此檔，請予銷毀，多謝合作。

詳細資訊

康誠生技股份有限公司 客戶服務中心

諮詢時間｜週一～週五 9:00～17:00 （國定假日除外）

諮詢專線｜02-55696099

客服信箱｜service.gb@healthconn.com

REPORTING

Report Date:	JUN-26-2024
Receipt Date:	JUN-22-2024
Collection Date:	JUN-21-2024
Specimen:	Blood
Status:	FINAL

PHYSICIAN

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Additional Recipient: N/A

Complete Tumor Response Map on page 2

Summary of Detected Somatic Alterations, Immunotherapy Biomarkers & Associated Treatment Options

KEY ✓ Approved in indication ~ Approved in other indication ⊗ Lack of response

Detected Alteration(s) / Biomarker(s)	Associated FDA-approved therapies	Clinical trial availability (see page 3)	% cfDNA or Amplification
KRAS G12V	None	Yes	0.2%
TP53 V272M	None	Yes	0.1%

Comments

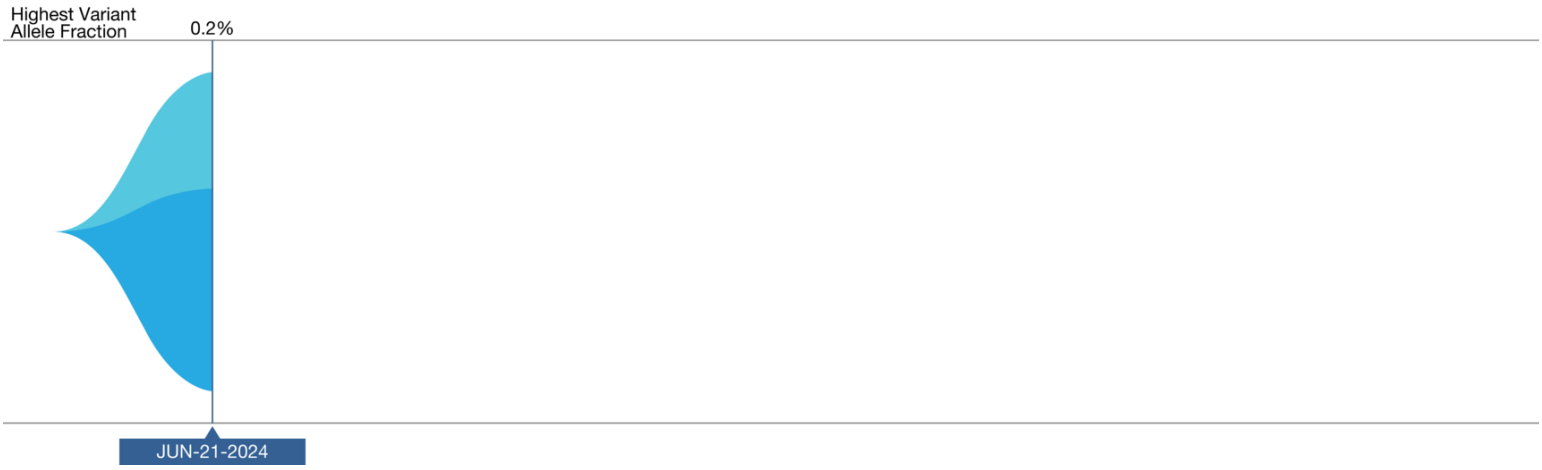
Reported by: JP1

Additional Biomarkers

Biomarker	Additional Details
MSI-High	NOT DETECTED

Guardant360 Tumor Response Map

The Guardant360 Tumor Response Map illustrates the variant allele fraction (% cfDNA) of observed somatic variants at each sample submission. Amplifications are not plotted, and only the first and last five test dates are plotted. Please see the Physician Portal (portal.guardanthealth.com) for the Tumor Response Map with all test dates.



Detected Alteration(s) / Biomarker(s)	% cfDNA or Amp
KRAS G12V	0.2%
TP53 V272M	0.1%

The table above annotates the variant allele fraction (% cfDNA) detected in this sample, listed in descending order.
§ See definitions section for more detail

Available Clinical Trials (within the same state as the ordering physician)

There may be additional trials not listed here. Visit: **portal.guardanthealth.com** or email **clientservices@guardanthealth.com** with A1077218 in the subject line of the email, for additional trials.

Alteration	Trial ID / Contact	Title	Phase	Site(s)
TP53 V272M	NCT04768868 Jian Wang,Jian. wang@impacttherapeutics.com,+86 18613056501	The Safety and Pharmacokinetics Preliminary Efficacy of IMP7068 in Patients With Advanced Solid Tumors	Phase 1	Taipei, Taiwan Taoyuan, Taiwan Taichung, Taiwan Tainan, Taiwan (2)
	Visit **portal.guardanthealth.com** for trials not within the same state as the physician's office			
KRAS G12V	Visit **portal.guardanthealth.com** for trials not within the same state as the physician's office			

More clinical trial options available at **portal.guardanthealth.com**

Definitions

Interpretation

Somatic alterations were detected in the circulating cell-free DNA isolated from this patient's blood specimen. These genomic alterations are cancer-associated somatic variants, some of which have been associated with either increased or reduced clinical response to specific treatments. The percentage of altered cell-free DNA circulating (% cfDNA) in blood is related to the unique tumor biology of each patient. Factors that may affect the % cfDNA of detected somatic alterations include tumor growth, turn over, size, heterogeneity, vascularization, disease progression, and treatment.

Method and Limitations

Guardant360 sequences 74 cancer-associated genes to identify somatic alterations. Cell-free DNA (cfDNA) is extracted from plasma, enriched for targeted regions, and sequenced using the Illumina platform and hg19 as the reference genome. All exons are sequenced in some genes; only clinically significant exons are sequenced in other genes. The types of genomic alterations detected by Guardant360 include single nucleotide variants, gene amplifications, fusions, short insertions/deletions (longest detected, 70 base pairs), and splice site disrupting events (see Table 1). Microsatellite Instability (MSI) is assessed for all cancer types by evaluating somatic changes in the length of repetitive sequences on the Guardant360 panel. A "Not Detected" result in samples where the highest % cfDNA is < 0.2% is an inconclusive result because it does not preclude MSI-High status in tissue. MSI status is currently not reported for earlier panel versions. This version of the Guardant360 test is not validated for the detection of other types of genomic alterations, such as complex rearrangements or gene deletions. Certain sample or variant characteristics, such as low cfDNA concentration, may result in reduced analytic sensitivity. Guardant360 cannot discern the source of circulating cfDNA, and for some variants in the range of ~40 to 60% cfDNA, the test cannot easily distinguish germline variants from somatic alterations. Guardant360 is not validated for the detection of germline or de novo variants that are associated with hereditary cancer risk. Tissue genotyping should be considered when plasma genotyping is negative, if clinically appropriate.

Table 1: Genes on the Guardant360 Panel

Guardant360 reports single nucleotide variants, splice site mutations, and insertion and deletion variants (indels) in all clinically relevant exons in 74 genes and reports other variant types in select genes as indicated below.

AKT1	*ALK* #	*APC*	*AR* †	*ARAF*	*ARID1A*	*ATM*	*BRAF* †	*BRCA1*
BRCA2	*CCND1* †	*CCND2* †	*CCNE1* †	*CDH1*	*CDK12*	*CDK4* †	*CDK6* †	*CDKN2A*
CTNNB1	*DDR2*	*EGFR* †	*ERBB2* †	*ESR1*	*EZH2*	*FBXW7*	*FGFR1* †	*FGFR2* † #
FGFR3 #	*GATA3*	*GNA11*	*GNAQ*	*GNAS*	*HNF1A*	*HRAS*	*IDH1*	*IDH2*
JAK2	*JAK3*	*KIT* †	*KRAS* †	*MAP2K1*	*MAP2K2*	*MAPK1*	*MAPK3*	*MET* †
MLH1	*MPL*	*MTOR*	*MYC* †	*NF1*	*NFE2L2*	*NOTCH1*	*NPM1*	*NRAS*
NTRK1 #	*NTRK3*	*PDGFRA* †	*PIK3CA* †	*PTEN*	*PTPN11*	*RAF1* †	*RB1*	*RET* #
RHEB	*RHOA*	*RIT1*	*ROS1* #	*SMAD4*	*SMO*	*STK11*	*TERT* ‡	*TP53*
TSC1	*VHL*							

‡ Guardant360 reports alterations in the promoter region of this gene.

† Guardant360 reports amplifications of this gene.

Guardant360 reports fusion events involving this gene.

About the Test

The Guardant360 assay was developed and its performance characteristics were determined by Guardant Health, Inc. This test has not been cleared or approved by the U.S. Food and Drug Administration (FDA). The FDA has determined that such clearance or approval is not necessary. This test may be used for clinical purposes and should not be regarded as investigational or for research only. Guardant Health's clinical reference laboratory is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) as qualified to perform high complexity clinical laboratory testing. The laboratory report should be interpreted in the context of other clinical information and laboratory, pathology, and imaging studies by a qualified medical professional prior to initiating or changing a patient's treatment plan. The selection of any, all, or none of the drugs associated with potential clinical benefit (or potential lack of clinical benefit) is entirely at the discretion of the treating medical professional. Drug and trial information are based on the diagnosis written on the submitted test request form; this information is not based on any supplemental information provided by the requesting medical professional, including pathology reports or other molecular studies. Some drugs listed in this report may not be approved or cleared by the FDA for the indicated use. Guardant Health makes no endorsement, express or implied, of any product, physician, or procedure contained in this report. This report makes no promises or guarantees that a particular medication will affect (or not affect) the clinical outcome of any patient.

Testing Performed at: Guardant Health

Laboratory Director: Martina Lefterova, MD PhD | CLIA ID: 05D2070300 | CAP #: 8765297 | 505 Penobscot Drive, Redwood City, CA, 94063, USA

Additional information is available

Any therapeutic annotations are based on publicly available information. This information is described in the "Detailed Therapy Results" and "Relevance of Detected Alterations" sections.

Visit **portal.guardanthealth.com** or email **clientservices@guardanthealth.com** with A1077218 in the subject line of the email for:

- Additional clinical trials
- Detailed Therapy Results
- Relevance of Detected Alterations
- References

If you would like to receive this additional information with every Guardant360 report, please call client services at **855.698.8887** to opt-in.

Additional information begins on the next page.

List of Available Clinical Trials

Alteration	Trial ID / Contact	Title	Phase	Site (number in parenthesis is count of trial sites)
TP53 V272M	NCT02769962 Danielle F Pinkiert, R.N.,danielle.pinkiert@nih.gov,(240) 858-7566	Trial of EP0057, a Nanoparticle Camptothecin With Olaparib in People With Relapsed /Refractory Small Cell Lung Cancer	Phase 1 /Phase 2	Bethesda, MD
	NCT03968653 Debiopharm International S.A, clinicaltrials@debiopharm.com,+41 21 321 01 11	Study of Oral Debio 0123 in Combination With Carboplatin in Participants With Advanced Solid Tumors	Phase 1	Spain; Netherlands (3)
	NCT04005690 See https://clinicaltrials.gov/ct2/show/NCT04005690	Targeted Pathway Inhibition in Patients With Pancreatic Cancer	Early Phase 1	Portland, OR
	NCT04768868 Jian Wang,Jian.wang@impacttherapeutics.com,+86 18613056501	The Safety and Pharmacokinetics Preliminary Efficacy of IMP7068 in Patients With Advanced Solid Tumors	Phase 1	Louisville, KY; Boston, MA; Atlanta, GA; Dallas, TX; Fairway, KS; San Antonio, TX; China (4); Taiwan (5)
	NCT05109975 Debiopharm International S.A, clinicaltrials@debiopharm.com,+41 21 321 01 11	A Study to Evaluate Safety and Preliminary Anti-tumor Activity of Debio 0123 as Monotherapy in Adult Participants With Advanced Solid Tumors	Phase 1	Grand Rapids, MI; San Antonio, TX; Switzerland; Spain (7)
KRAS G12V	NCT03190941 NCI SB Immunotherapy Recruitment Center,IRC@nih.gov,(866) 820-4505	Administering Peripheral Blood Lymphocytes Transduced With a Murine T-Cell Receptor Recognizing the G12V Variant of Mutated RAS in HLA-A*11:01 Patients	Phase 1 /Phase 2	Bethesda, MD
	NCT04117087 Colleen Apostol, RN,GIClinicalTrials@jhmi.edu,410-614-3644	Pooled Mutant KRAS-Targeted Long Peptide Vaccine Combined With Nivolumab and Ipilimumab for Patients With Resected Mismatch Repair Protein (MMR-p) Colorectal and Pancreatic Cancer	Phase 1	Baltimore, MD
	NCT04132505 Shubham Pant,spant@mdanderson.org,713-792-2828	Binimetinib and Hydroxychloroquine in Treating Patients With KRAS Mutant Metastatic Pancreatic Cancer	Phase 1	Houston, TX
	NCT04146298 Shiwei Guo, Doctor,gestwa@163.com,+8618621500666	Mutant KRAS G12V-specific TCR Transduced T Cell Therapy for Advanced Pancreatic Cancer	Phase 1 /Phase 2	China
	NCT06445062 Revolution Medicines,CT-inquiries@RevMed.com,650-779-2300	Study of RAS(ON) Inhibitors in Patients With Gastrointestinal Solid Tumors	Phase 1 /Phase 2	Irving, TX; Fairfax, VA

Detailed Therapy Results

Alteration	Drug	Trade Name	Target	Current Status
KRAS G12V	Anti-KRAS G12V mTCR cells		Peripheral blood lymphocytes transduced with a murine T-Cell receptor recognizing K-Ras G12V.	Phase 2 (Cancer)
	ASN007		ERK1/2 kinase inhibitor.	Phase 1 (Solid Tumor)
	ASTX029		ERK1/2 kinase inhibitor.	Phase 2 (Solid Tumor)
	Avutometinib		Dual Raf/MEK kinase inhibitor.	Phase 1 (Pancreatic carcinoma) Phase 2 (Non-small cell lung carcinoma (NSCLC), Uveal melanoma, Ovarian carcinoma)
	BBP-398		Shp-2 inhibitor.	Phase 1 (Solid Tumor)
	BDTX-4933		Braf class 1, 2, and 3 inhibitor.	Phase 1 (Solid Tumor)
	BI 1701963		Pan-K-Ras inhibitor targeting the interaction of K-Ras and SOS-1.	Phase 1 (Solid Tumor) Phase 1 (Brain and Central Nervous System Tumors)
	BI 3011441		MEK1,2 inhibitor.	Phase 1 (Solid Tumor)
	Binimetinib	Mektovi	MEK1,2 inhibitor.	Phase 2 (Pancreatic carcinoma) FDA Approved in other indications (Melanoma with BRAF V600E/K mutation)
	BMF-219		Covalent menin inhibitor.	Phase 1 (Pancreatic carcinoma) Phase 2 (Diabetes)
	Brimarafenib		Braf class 1, 2, and 3 inhibitor.	Phase 1 (Pancreatic ductal adenocarcinoma) Phase 2 (Solid Tumor)
	Cobimetinib	Cotellic	MEK1,2 inhibitor.	Phase 2 (Pancreatic carcinoma) FDA Approved in other indications (Melanoma with BRAF V600E/K mutation, Histiocytic and dendritic cell neoplasms)
	Defactinib		Focal adhesion kinase (FAK) inhibitor, upstream of MAPK pathway.	Phase 2 (Pancreatic carcinoma) Phase 2 (Lymphoma, Solid Tumor, Multiple myeloma (MM))
	E6201		MEK1,2, Mekk1, and Flt3 inhibitor.	Phase 1 (Solid Tumor) Phase 1 (Acute myeloid leukemia (AML))
	ERAS-601		Shp-2 inhibitor.	Phase 2 (Solid Tumor)
	ET0038		Shp-2 inhibitor.	Phase 1 (Solid Tumor)
	GI-4000		Mutant K-Ras vaccine.	Phase 2 (Pancreatic carcinoma) Phase 2 (Non-small cell lung carcinoma (NSCLC), Colorectal carcinoma (CRC))
	HBI-2376		Shp-2 inhibitor.	Phase 1 (Solid Tumor)
	HMPL-295		ERK1/2 kinase inhibitor.	Phase 1 (Solid Tumor)
	IMM-1-104		MEK1,2 inhibitor.	Phase 2 (Pancreatic ductal adenocarcinoma) Phase 2 (Melanoma, Non-small cell lung carcinoma (NSCLC))
	JAB-3068		Shp-2 inhibitor.	Phase 1 (Solid Tumor) Phase 2 (Non-small cell lung carcinoma (NSCLC), Head and neck squamous cell carcinoma (HNSCC), Esophageal carcinoma)
	JAB-3312		Shp-2 inhibitor.	Phase 1 (Solid Tumor) Phase 1 (Brain and Central Nervous System Tumors)

Detailed Therapy Results

Alteration	Drug	Trade Name	Target	Current Status
	KRAS G12V-specific T-cells		Mutant KRAS G12V-specific TCR transduced autologous T-cells.	Phase 2 (Pancreatic carcinoma)
	LTT462		ERK1/2 kinase inhibitor.	Phase 1 (Solid Tumor)
	LUNA18		Ras peptide inhibitor.	Phase 1 (Solid Tumor)
	Mirdametinib		MEK1,2 inhibitor.	Phase 1 (Pancreatic carcinoma) Phase 2 (Glioma, Non-small cell lung carcinoma (NSCLC), Neurofibroma, Breast carcinoma, Glioneuronal tumor, Neurofibromatosis type 1, Lung cancer, Colorectal carcinoma (CRC))
	MK-8353		ERK1/2 kinase inhibitor.	Phase 1 (Solid Tumor)
	MRTX0902		Pan-K-Ras inhibitor targeting the interaction of K-Ras and SOS-1.	Phase 1 (Solid Tumor)
	PF-07284892		Shp-2 inhibitor.	Phase 1 (Solid Tumor) Phase 1 (Brain and Central Nervous System Tumors)
	PF-07799544		MEK Brain Penetrant Inhibitor.	Phase 1 (Glioma, Melanoma, Non-small cell lung carcinoma (NSCLC), Thyroid carcinoma, Colorectal carcinoma (CRC))
	Pimasertib		MEK1,2 inhibitor.	Phase 2 (Pancreatic ductal adenocarcinoma) Phase 2 (Melanoma, Ovarian carcinoma, Hematologic malignancies, Colorectal carcinoma (CRC))
	Pooled mutant KRAS-targeted long peptide vaccine		KRAS G12-mutant targeted vaccine.	Phase 1 (Non-small cell lung carcinoma (NSCLC))
	RMC-6236		Multispecific K-Ras inhibitor.	Phase 1 (Solid Tumor)
	RSC-1255		Ras inhibitor.	Phase 1 (Solid Tumor)
	Selumetinib	Koselugo	MEK1,2 inhibitor.	Phase 2 (Pancreatic carcinoma) FDA Approved in other indications (NF1-related plexiform neurofibroma)
	SHR7390		MEK1,2 inhibitor.	Phase 1 (Solid Tumor)
	Temuterkib		ERK1/2 kinase inhibitor.	Phase 1 (Pancreatic ductal adenocarcinoma) Phase 1 (Solid Tumor)
	Tizaterkib		ERK1/2 kinase inhibitor.	Phase 1 (Solid Tumor) Phase 1 (Hematologic malignancies)
	TNO155		Shp-2 inhibitor.	Phase 1 (Solid Tumor) Phase 2 (Non-small cell lung carcinoma (NSCLC), Colorectal carcinoma (CRC))
	Trametinib	Mekinist	MEK1,2 inhibitor.	Phase 2 (Pancreatic carcinoma) FDA Approved in other indications (Melanoma with BRAF V600 mutation)
	Ulixertinib		ERK1/2 kinase inhibitor.	Phase 1 (Pancreatic carcinoma) Phase 2 (Gastric carcinoma, Melanoma, Histiocytic and dendritic cell neoplasms, Langerhans cell histiocytosis (LCH), Uveal melanoma, Acute myeloid leukemia

Detailed Therapy Results

Alteration	Drug	Trade Name	Target	Current Status
				(AML), Gastrointestinal carcinoma, Non-Hodgkin lymphoma (NHL), Myelodysplastic Syndrome (MDS))
	V941		Mutant K-Ras vaccine.	Phase 1 (Pancreatic carcinoma) Phase 1 (Non-small cell lung carcinoma (NSCLC), Colorectal carcinoma (CRC))
	Vociprotafib		Shp-2 inhibitor.	Phase 2 (Solid Tumor)
TP53 V272M	Adavosertib		Wee1 tyrosine kinase inhibitor.	Phase 2 (Pancreatic carcinoma) Phase 2 (Lymphoma, Embryonal tumor with multi-layered rosettes (ETMR), Medulloblastoma, Small cell lung carcinoma (SCLC), Solid Tumor, Primary myelofibrosis (PMF), Ovarian carcinosarcoma, Acute myeloid leukemia (AML), MDS/MPN, unclassifiable, Chronic myelomonocytic leukemia (CMML), Peritoneal papillary serous carcinoma, Myelodysplastic Syndrome (MDS))
	AL8326		Aurora kinase B/VEGFRs/Fgfr multi-kinase inhibitor.	Phase 1 (Solid Tumor) Phase 3 (Small cell lung carcinoma (SCLC))
	Alisertib		Aurora kinase A inhibitor.	Phase 1 (Pancreatic carcinoma) Phase 3 (Peripheral T-cell lymphoma (PTCL))
	ATO	Trisenox	PML-RARA inhibitor. Inhibits multiple signaling pathways, including the Hedgehog pathway.	Phase 2 (Pancreatic carcinoma) FDA Approved in other indications (Acute myeloid leukemia (AML), Acute promyelocytic leukemia (APL))
	AZD2811		Nanoparticle formulation of Aurora kinase B inhibitor barasertib (AZD1152).	Phase 1 (Solid Tumor) Phase 2 (Acute myeloid leukemia (AML), Myelodysplastic Syndrome (MDS))
	Azenosertib		Wee1 tyrosine kinase inhibitor.	Phase 2 (Pancreatic adenocarcinoma) Phase 2 (High-grade serous ovarian carcinoma, Uterine serous/clear cell carcinoma, Osteosarcoma, Ovarian epithelial carcinoma, Colorectal adenocarcinoma, Acute myeloid leukemia (AML), Fallopian tube carcinoma, Peritoneal carcinoma)
	Debio 0123		Wee1 tyrosine kinase inhibitor.	Phase 1 (Solid Tumor)
	EP0042		Aurora kinase A/B and Flt3 inhibitor.	Phase 2 (Acute myeloid leukemia (AML), Chronic myelomonocytic leukemia (CMML), Myelodysplastic Syndrome (MDS))
	IMP7068		Wee1 tyrosine kinase inhibitor.	Phase 1 (Solid Tumor)
	JAB-2485		Aurora kinase A inhibitor.	Phase 2 (Solid Tumor)
	LY3295668		Aurora kinase A inhibitor.	Phase 1 (Solid Tumor) Phase 2 (Head and neck squamous cell carcinoma (HNSCC), Small cell lung carcinoma (SCLC), Breast carcinoma (triple negative), Breast carcinoma (hormone receptor +, HER2-))
	SGT-53		TP53 gene therapy delivered via transferrin-targeted nanoparticles.	Phase 2 (Pancreatic carcinoma) Phase 2 (Glioblastoma, Glioma)
	SY-4835		Wee1 tyrosine kinase inhibitor.	Phase 1 (Solid Tumor)
	TAS-119		Aurora kinase A inhibitor.	Phase 1 (Solid Tumor)
	Tinengotinib		Aurora kinase A/B inhibitor.	Phase 1 (Solid Tumor) Phase 1 (Breast carcinoma (triple negative))

Relevance of Detected Alterations

Alteration	Role in Disease	Effect on Drug Sensitivity	Effect on Drug Resistance
KRAS G12V	The KRAS gene is one of the most commonly mutated genes in human malignancies, with high incidences in pancreatic, colorectal, and lung cancers. [1-3]. Oncogenic KRAS mutations are common drivers of pancreatic tumorigenesis, with mutations detected as an early event in intraepithelial neoplasms and found to be involved in transformation to pancreatic carcinoma. [4-11]. KRAS mutation has also been found to be critical to pancreatic tumor maintenance; ablation of KRAS mutation in pancreatic cancer cell lines and xenograft models has been found to result in inhibition of tumor growth. [12-16].	Many of the current attempts to target K-Ras are directed against its downstream signaling pathways, Raf /MEK/ERK and PI3K/Akt/mTOR. [17,18]. Clinical studies have suggested limited efficacy of MEK inhibitors in KRAS mutant tumors; however, combinations of MEK inhibitors with other targeted therapies may still be relevant. [19-28]. Other clinical approaches are being investigated preclinically and clinically in the context of KRAS-mutant tumors, including FAK and Shp-2 inhibitors. [29-34]. In addition, inhibitors specifically targeting KRAS G12C and cell-based therapies targeting KRAS G12V and G12D are being investigated clinically and preclinically. [35-38]. Sotorasib and adagrasib have been FDA-approved in patients with locally advanced or metastatic non-small cell lung carcinoma harboring a KRAS G12C mutation, as determined by an FDA-approved test, following treatment with at least one prior systemic therapy. [39-43]. In addition, combinations of adagrasib or sotorasib with cetuximab or panitumumab have been reported to provide clinical benefit in CRC patients with KRAS G12C mutation. [44-47]. Adagrasib plus cetuximab has been FDA-approved for treatment of adults with KRAS G12C-mutated locally advanced or metastatic colorectal cancer, as determined by an FDA-approved test, who have received prior treatment with fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy. [46,48].	In some cancer types, such as colorectal cancer (CRC) and non-small cell lung cancer (NSCLC), activating KRAS mutations and KRAS amplification have been associated with resistance to Egfr-targeted therapies. [49-57]. A preclinical study of 29 pancreatic cancer cell lines reported that cell lines harboring a KRAS G12V mutation or copy number alterations, either gain or loss, were approximately ten-fold more resistant to binimetinib as compared with cell lines with a G12D or no mutation. [58,59].
TP53 V272M	Loss of tumor suppressor p53, which is encoded by the TP53 gene, is common in aggressive advanced cancers. [60]. Carriers of a germline mutation in TP53 have Li-Fraumeni Syndrome, an inherited cancer syndrome resulting in multiple tumors in early adulthood, including breast cancer, brain tumors, and leukemias. [61-63]. Expression of p53 in normal cells is low; however, TP53 alterations, including those that result in loss of p53 tumor suppressor function, may lead to stabilization and increased expression of p53, particularly in the nucleus, and several studies have shown that it may have oncogenic gain-of-function effects. [64-68]. TP53 has	At present, there are no approved therapies targeting TP53 alterations, despite their high prevalence in cancer. Therapeutic approaches under investigation include gene therapy for TP53 and (dendritic cell-based) TP53 vaccines. [79-81]. Inhibition of components of the DNA damage checkpoint, including Wee1, has been reported to enhance the activity of DNA-damaging agents in preclinical cancer models with deficiency of p53 function. [82-84]. Clinical trials of the Wee1 inhibitor adavosertib (MK-1775) are currently underway for patients with solid tumors and hematologic malignancies. Studies have reported Aurora kinase A to be activated in cells harboring TP53 mutation, and Aurora	Mutations in TP53 may increase resistance to ionizing radiation therapy. [91,92].

Relevance of Detected Alterations

Alteration	Role in Disease	Effect on Drug Sensitivity	Effect on Drug Resistance
	been shown to play a key role in pancreatic carcinogenesis; inactivation of TP53 has been reported in up to 85% of pancreatic cancers, and TP53 deletion and mutation have been detected in both high-grade pancreatic intraepithelial neoplasia (PanIN) lesions and pancreatic ductal adenocarcinoma (PDAC). [4,69-73]. Preclinical studies have reported that p53 inactivation is associated with initiation and progression of PanIN lesions and pancreatic cancer in animal models of disease. [74-78].	kinase A and B inhibitors have been reported to activate wild-type p53 in cellular assays; thus, tumors retaining a wild-type TP53 allele may benefit from Aurora kinase inhibitors. [85-90].	

References

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