REPORTING

Report Date:	MAY-03-2024
Receipt Date:	APR-25-2024
Collection Date:	APR-23-2024
Specimen:	Blood
Status:	FINAL

PHYSICIAN

Tien-Hua Chen
Account: Genconn Biotech Co., LTD
Address: F15., No 207-5 Sec 3, Beixin Rd, Xindian Dist, New Taipei City, 23143, Taiwan
Ph: +886 963 820 633 | Fax: N/A
Additional Recipient: N/A

Complete Tumor Response Map on page 3

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 5)	% cfDNA or Amplification
BRAF V600E	✓ Dabrafenib+trametinib ~ Binimetinib, Cobimetinib, Dabrafenib, Encorafenib+binimetinib, Trametinib, Vemurafenib, Vemurafenib+cobimetinib	Yes	2.5%
MSI-High	✓ Pembrolizumab ~ Atezolizumab, Avelumab, Dostarlimab, Durvalumab, Nivolumab, Nivolumab+ipilimumab	Yes	DETECTED
PTEN N323fs	~ Capivasertib	Yes	2.9%
CDK12 M1028fs	~ Olaparib, Talazoparib	Yes	2.6%
FBXW7 W425*	None	Yes	2.1%
ARID1A D1850fs	None	Yes	2.4%
ARID1A G276fs	None	Yes	2.3%
TP53 K373fs	None	Yes	2.2%

Variants of Uncertain Clinical Significance
FGFR2 M734V (3.3%), *ATM* M1484I (2.2%), *BRAF* P403fs (2.2%), *CCND1* R291dup (2.2%)
The functional consequences and/or clinical significance of alterations are unknown. Relevance of therapies targeting these alterations is uncertain.

Comments

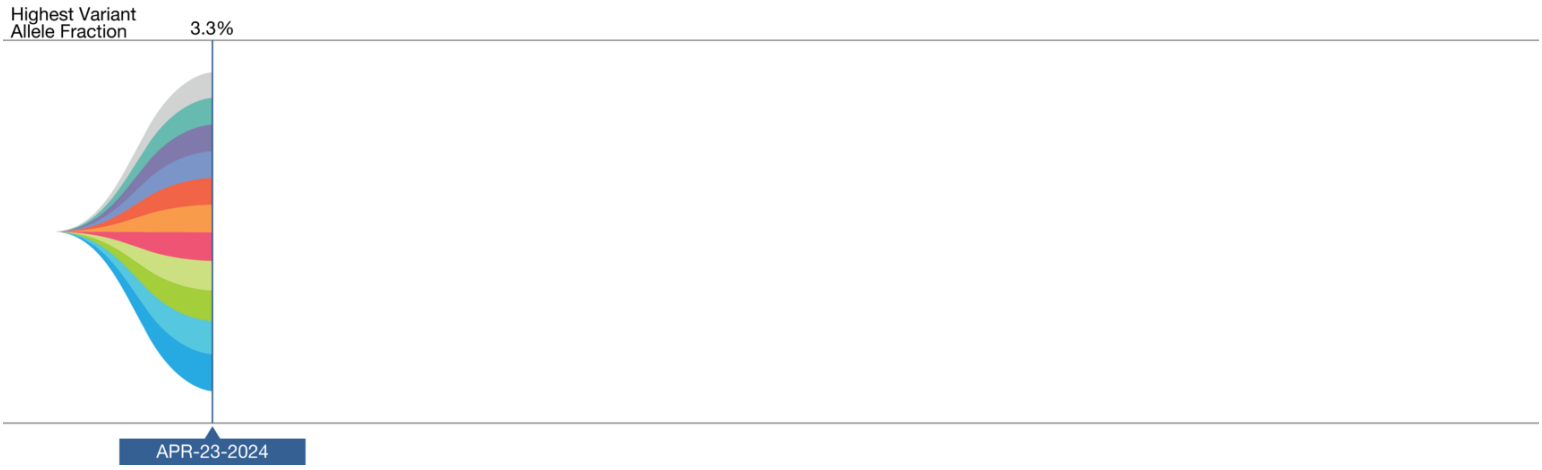
Reported by: JV4

Additional Biomarkers

Biomarker	Additional Details
MSI-High	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	
FGFR2 M734V	3.3%	Variants of Uncertain Clinical Significance §
PTEN N323fs	2.9%	
CDK12 M1028fs	2.6%	
BRAF V600E	2.5%	
ARID1A D1850fs	2.4%	
ARID1A G276fs	2.3%	
TP53 K373fs	2.2%	
ATM M1484I	2.2%	Variants of Uncertain Clinical Significance §
BRAF P403fs	2.2%	Variants of Uncertain Clinical Significance §
CCND1 R291dup	2.2%	Variants of Uncertain Clinical Significance §

Detected Alteration(s) / Biomarker(s)	% cfDNA or Amp
FBXW7 W425*	2.1%

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 A1025854 in the subject line of the email, for additional trials.

Alteration	Trial ID / Contact	Title	Phase	Site(s)
MSI-High	NCT03821935 ABBVIE CALL CENTER, abbvieclinicaltrials@abbvie.com,844-663-3742	Study to Determine the Safety, Tolerability, Pharmacokinetics and Recommended Phase 2 Dose (RP2D) of Livmoniplimab (ABBV-151) as a Single Agent and in Combination With Budigalimab (ABBV-181) in Participants With Locally Advanced or Metastatic Solid Tumors	Phase 1	Kaohsiung, Taiwan Taipei City, Taiwan Taipei, Taiwan Taichung, Taiwan
	NCT04083599 Genmab A/S Trial Information, clinicaltrials@genmab.com,+4570202728	GEN1042 Safety Trial and Anti-tumor Activity in Subjects With Malignant Solid Tumors	Phase 1 /Phase 2	Tainan, Taiwan Taoyuan, Taiwan Kaohsiung City, Taiwan (2) Taipei, Taiwan (2) Additional trial sites available
	NCT04799054 Janet Connolly-Giwa, jcgt@ascendispharma.com,+1 650-512-2153	A Study of TransCon TLR7/8 Agonist With or Without Pembrolizumab in Patients With Advanced or Metastatic Solid Tumors	Phase 1 /Phase 2	Taipei City, Taiwan
	NCT05661578 Reference Study ID Number: GO44096 https://forpatients.roche.com/,global-roche-genentech-trials@gene.com,888-662-6728 (U.S. Only)	A Study to Evaluate the Safety and Pharmacokinetics of the Intravenous Fixed-Dose Combination (IV FDC) of Tiragolumab and Atezolizumab in Participants With Locally Advanced, Recurrent or Metastatic Solid Tumors	Phase 2	Tainan, Taiwan
	NCT05838768 Novartis Pharmaceuticals,novartis. email@novartis.com,1-888-669-6682	Study of HRO761 Alone or in Combination in Cancer Patients With Specific DNA Alterations Called Microsatellite Instability or Mismatch Repair Deficiency.	Phase 1	Taipei, Taiwan
	Visit portal.guardanthealth.com for trials not within the same state as the physician's office			
CDK12 M1028fs	NCT04434482 Min Song,min.song@impacttherapeutics.com,021 68411121	IMP4297 in Combination With Temozolomide in Patients With Advanced Solid Tumors and Small Cell Lung Cancer	Phase 1 /Phase 2	Taipei, Taiwan Taoyuan, Taiwan Taichung, Taiwan Tainan, Taiwan (2)
	NCT05269316 Xiangna Chen,xiangna.chen@impacttherapeutics.com,+86-021-68411121	Study to Evaluate IMP9064 as a Monotherapy or in Combination in Patients With Advanced Solid Tumors	Phase 1	Taipei, Taiwan
	NCT05797168 AstraZeneca Clinical Study Information Center,information.center@astrazeneca.com,1-877-240-9479	Phase I/IIa Study for AZD5335 as Monotherapy and in Combination With Anti-cancer Agents in Participants With Solid Tumors	Phase 1 /Phase 2	Tainan City, Taiwan Taichung, Taiwan Taipei, Taiwan (2)
	Visit portal.guardanthealth.com for trials not within the same state as the physician's office			
ARID1A D1850fs	NCT04434482 Min Song,min.song@impacttherapeutics.com,021 68411121	IMP4297 in Combination With Temozolomide in Patients With Advanced Solid Tumors and Small Cell Lung Cancer	Phase 1 /Phase 2	Taipei, Taiwan Taoyuan, Taiwan Taichung, Taiwan Tainan, Taiwan (2)
	NCT05269316 Xiangna Chen,xiangna.chen@impacttherapeutics.com,+86-021-68411121	Study to Evaluate IMP9064 as a Monotherapy or in Combination in Patients With Advanced Solid Tumors	Phase 1	Taipei, Taiwan
	NCT05797168 AstraZeneca Clinical Study Information Center,information.center@astrazeneca.com,1-877-240-9479	Phase I/IIa Study for AZD5335 as Monotherapy and in Combination With Anti-cancer Agents in Participants With Solid Tumors	Phase 1 /Phase 2	Tainan City, Taiwan Taichung, Taiwan Taipei, Taiwan (2)
	Visit portal.guardanthealth.com for trials not within the same state as the physician's office			

Alteration	Trial ID / Contact	Title	Phase	Site(s)
ARID1A G276fs	NCT04434482 Min Song,min.song@impacttherapeutics.com,021 68411121	IMP4297 in Combination With Temozolomide in Patients With Advanced Solid Tumors and Small Cell Lung Cancer	Phase 1 /Phase 2	Taipei, Taiwan Taoyuan, Taiwan Taichung, Taiwan Tainan, Taiwan (2)
	NCT05269316 Xiangna Chen,xiangna.chen@impacttherapeutics.com,+86-021-68411121	Study to Evaluate IMP9064 as a Monotherapy or in Combination in Patients With Advanced Solid Tumors	Phase 1	Taipei, Taiwan
	NCT05797168 AstraZeneca Clinical Study Information Center,information.center@astrazeneca.com,1-877-240-9479	Phase I/IIa Study for AZD5335 as Monotherapy and in Combination With Anti-cancer Agents in Participants With Solid Tumors	Phase 1 /Phase 2	Tainan City, Taiwan Taichung, Taiwan Taipei, Taiwan (2)
	Visit **portal.guardanthealth.com** for trials not within the same state as the physician's office			
TP53 K373fs	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			
BRAF V600E	Visit **portal.guardanthealth.com** for trials not within the same state as the physician's office			
PTEN N323fs	Visit **portal.guardanthealth.com** for trials not within the same state as the physician's office			
FBXW7 W425*	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

Variants of Uncertain Clinical Significance: The functional consequences and/or clinical significance of alterations are unknown. Relevance of therapies targeting these alterations is uncertain.

Insertion (Ins): The following alteration was detected in this patient: *ARID1A* D1850fs; *CCND1* R291dup; *CDK12* M1028fs. Guardant360 detects short insertions in exons of certain genes (see Table 1).

Deletion (Del): The following alteration was detected in this patient: *ARID1A* G276fs; *BRAF* P403fs; *PTEN* N323fs; *TP53* K373fs. Guardant360 detects short deletions in exons of certain genes (see Table 1), including potential splice site-disrupting events.

***Nonsense mutation:** A point mutation that results in a premature stop codon.

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 fusion events involving this gene.

† Guardant360 reports amplifications of 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 A1025854 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)
MSI-High	NCT02693535 Pam Mangat, MS,tapur@asco.org,www.tapur.org	TAPUR: Testing the Use of Food and Drug Administration (FDA) Approved Drugs That Target a Specific Abnormality in a Tumor Gene in People With Advanced Stage Cancer	Phase 2	Phoenix, AZ; Manchester, NH; Charlotte, NC; Portland, OR; Fargo, ND; Concord, NH; Houston, TX; Chapel Hill, NC; Cedar City, UT; Omaha, NE; Birmingham, AL; Portsmouth, NH; Hilton Head Island, SC; Nashville, TN; Fairfax, VA; Kettering, OH; Sioux Falls, SD; Saint George, UT; Chicago, IL; Seattle, WA; Indianapolis, IN; Cincinnati, OH; Salt Lake City, UT; West Chester, OH; Bismarck, ND; Bluffton, SC (3); FL (37); NY (5); WI (16); ME (19); GA (6); MI (11); CA (21); PA (5); CT (7); NM (5)
	NCT03568656 Tomasz Knurowski, MD, MFPM,Tomasz.Knurowski@cellcentric.com,07882 871299	Study to Evaluate CCS1477 in Advanced Tumours	Phase 1 /Phase 2	United Kingdom (10)
	NCT03821935 ABBVIE CALL CENTER, abbvieclinicaltrials@abbvie.com,844-663-3742	Study to Determine the Safety, Tolerability, Pharmacokinetics and Recommended Phase 2 Dose (RP2D) of Livmoniplimab (ABBV-151) as a Single Agent and in Combination With Budigalimab (ABBV-181) in Participants With Locally Advanced or Metastatic Solid Tumors	Phase 1	Saint Louis, MO; New York, NY; New Haven, CT; Columbus, OH; Celebration, FL; San Antonio, TX; Indianapolis, IN (2); Puerto Rico; Belgium; Japan (2); Taiwan (4); Korea, Republic of (5); Israel (5); Australia (2); Spain (2)
	NCT04083599 Genmab A/S Trial Information, clinicaltrials@genmab.com,+4570202728	GEN1042 Safety Trial and Anti-tumor Activity in Subjects With Malignant Solid Tumors	Phase 1 /Phase 2	Louisville, KY; Hinsdale, IL; Saint Louis, MO; Winston-Salem, NC; Newark, DE; New Haven, CT; Columbia, MD; Charlotte, NC; Portland, OR; Los Alamitos, CA; Miami Beach, FL; Seattle, WA; Kingwood, TX; San Diego, CA; Ocala, FL; Spokane, WA; Salt Lake City, UT; Nashville, TN; Lexington, KY; Fairfax, VA; Anchorage, AK; Philadelphia, PA (2); Moldova, Republic of; Georgia; Taiwan (7); Korea, Republic of (7); Denmark (2); Italy (4); Israel (2); France (3); Spain (19)
	NCT04799054 Janet Connolly-Giwa, jcgt@ascendispharma.com,+1 650-512-2153	A Study of TransCon TLR7/8 Agonist With or Without Pembrolizumab in Patients With Advanced or Metastatic Solid Tumors	Phase 1 /Phase 2	Louisville, KY; Iowa City, IA; Chicago, IL; Orange, CA; San Francisco, CA; Los Angeles, CA; Knoxville, TN; Houston, TX; Duarte, CA; Cleveland, OH; Pittsburgh, PA; Cincinnati, OH; Canton, OH; Tampa, FL; Fairfax, VA; Dallas, TX (2); Taiwan; Netherlands (2); Korea, Republic of (8); Australia (2); Spain (12)
	NCT04983745 Robin Patterson, RN, rpatterson@westclinic.com,901-683-0055 x63019	Niraparib and Dostarlimab in HRD Solid Tumors	Phase 2	Germantown, TN
	NCT05661578 Reference Study ID Number: GO44096 https://forpatients.roche.com/,global-roche-genentech-trials@gene.com,888-662-6728 (U.S. Only)	A Study to Evaluate the Safety and Pharmacokinetics of the Intravenous Fixed-Dose Combination (IV FDC) of Tiragolumab and Atezolizumab in Participants With Locally Advanced, Recurrent or Metastatic Solid Tumors	Phase 2	Pikeville, KY; Omaha, NE; Spokane, WA; Fort Worth, TX; Taiwan; Greece (6); Canada (2); Turkey (10); Cyprus (2); Korea, Republic of (4); Serbia (6); Spain (10); Croatia (2)

List of Available Clinical Trials

Alteration	Trial ID / Contact	Title	Phase	Site (number in parenthesis is count of trial sites)
	NCT05700721 Timothy Yap, MBBS,PHD, tyap@mdanderson.org,(713) 563-1784	Phase II Trial of the PARP Inhibitor Niraparib and PD-1 Inhibitor Dostarlimab in Patients With Advanced Cancers With Active Progressing Brain Metastases (STARLET)	Phase 2	Houston, TX
	NCT05722886 Aida Sarmiento Castro,determine@cancer.org.uk,+442034695101	DETERMINE (Determining Extended Therapeutic Indications for Existing Drugs in Rare Molecularly Defined Indications Using a National Evaluation Platform Trial) - Master Screening Protocol	Phase 2 /Phase 3	United Kingdom (25)
	NCT05838768 Novartis Pharmaceuticals,novartis.email@novartis.com,1-888-669-6682	Study of HRO761 Alone or in Combination in Cancer Patients With Specific DNA Alterations Called Microsatellite Instability or Mismatch Repair Deficiency.	Phase 1	Los Angeles, CA; Houston, TX; New York, NY (2); Singapore; Belgium; Norway; Japan; Taiwan; Korea, Republic of; Israel; France (2); Germany (2); Spain (3)
CDK12 M1028fs	NCT03568656 Tomasz Knurowski, MD, MFPM,Tomasz.Knurowski@cellcentric.com,07882 871299	Study to Evaluate CCS1477 in Advanced Tumours	Phase 1 /Phase 2	United Kingdom (10)
	NCT03682289 Early Phase Clinical Trials Recruitment, EarlyPhaseClinicalTrials@ucsf.edu,877-827-3222	Ceralasertib (AZD6738) Alone and in Combination With Olaparib or Durvalumab in Patients With Solid Tumors	Phase 2	San Francisco, CA
	NCT04434482 Min Song,min.song@impacttherapeutics.com,021 68411121	IMP4297 in Combination With Temozolomide in Patients With Advanced Solid Tumors and Small Cell Lung Cancer	Phase 1 /Phase 2	Evergreen Park, IL; Canton, OH; Columbus, OH; Tennessee, TN; China (4); Taiwan (5); Korea, Republic of (4); Australia (4)
	NCT04983745 Robin Patterson, RN, rpatterson@westclinic.com,901-683-0055 x63019	Niraparib and Dostarlimab in HRD Solid Tumors	Phase 2	Germantown, TN
	NCT05038839 See https://clinicaltrials.gov/ct2/show/NCT05038839	Cabozantinib and Pamiparib for the Treatment of Advanced of Refractory Solid Tumors	Phase 1	Houston, TX
	NCT05269316 Xiangna Chen,xiangna.chen@impacttherapeutics.com,+86-021-68411121	Study to Evaluate IMP9064 as a Monotherapy or in Combination in Patients With Advanced Solid Tumors	Phase 1	Greenville, SC; New York, NY; Dallas, TX; Hackensack, NJ; China; Taiwan; Australia (2)
	NCT05338346 Edwin Hoe,edwin.hoe@antengene.com, +61 497 390477	A Study of ATG-018 (ATR Inhibitor) Treatment in Patients With Advanced Solid Tumors and Hematological Malignancies	Phase 1	Australia (5)
	NCT05797168 AstraZeneca Clinical Study Information Center,information.center@astrazeneca.com,1-877-240-9479	Phase I/IIa Study for AZD5335 as Monotherapy and in Combination With Anti-cancer Agents in Participants With Solid Tumors	Phase 1 /Phase 2	Houston, TX; Duarte, CA; Louisville, KY; Boston, MA; Columbus, OH; Irvine, CA; Portland, OR; Aurora, CO; Providence, RI (2); Canada (5); Japan (2); China (5); Taiwan (4); United Kingdom (4); Israel (2); Australia (2); Spain (4)
ARID1A D1850fs	NCT03568656 Tomasz Knurowski, MD, MFPM,Tomasz.Knurowski@cellcentric.com,07882 871299	Study to Evaluate CCS1477 in Advanced Tumours	Phase 1 /Phase 2	United Kingdom (10)
	NCT03682289 Early Phase Clinical Trials Recruitment, EarlyPhaseClinicalTrials@ucsf.edu,877-827-3222	Ceralasertib (AZD6738) Alone and in Combination With Olaparib or Durvalumab in Patients With Solid Tumors	Phase 2	San Francisco, CA

List of Available Clinical Trials

Alteration	Trial ID / Contact	Title	Phase	Site (number in parenthesis is count of trial sites)
	NCT04434482 Min Song,min.song@impacttherapeutics.com,021 68411121	IMP4297 in Combination With Temozolomide in Patients With Advanced Solid Tumors and Small Cell Lung Cancer	Phase 1 /Phase 2	Evergreen Park, IL; Canton, OH; Columbus, OH; Tennessee, TN; China (4); Taiwan (5); Korea, Republic of (4); Australia (4)
	NCT05038839 See https://clinicaltrials.gov/ct2/show/NCT05038839	Cabozantinib and Pamiparib for the Treatment of Advanced of Refractory Solid Tumors	Phase 1	Houston, TX
	NCT05269316 Xiangna Chen,xiangna.chen@impacttherapeutics.com,+86-021-68411121	Study to Evaluate IMP9064 as a Monotherapy or in Combination in Patients With Advanced Solid Tumors	Phase 1	Greenville, SC; New York, NY; Dallas, TX; Hackensack, NJ; China; Taiwan; Australia (2)
	NCT05338346 Edwin Hoe,edwin.hoe@antengene.com,+61 497 390477	A Study of ATG-018 (ATR Inhibitor) Treatment in Patients With Advanced Solid Tumors and Hematological Malignancies	Phase 1	Australia (5)
	NCT05687136 See https://clinicaltrials.gov/ct2/show/NCT05687136	Testing the Combination of Two Anti-cancer Drugs, Peposertib (M3814) and M1774 for Advanced Solid Tumors	Phase 1	Boston, MA; Bethesda, MD (2)
	NCT05797168 AstraZeneca Clinical Study Information Center,information.center@astrazeneca.com,1-877-240-9479	Phase I/IIa Study for AZD5335 as Monotherapy and in Combination With Anti-cancer Agents in Participants With Solid Tumors	Phase 1 /Phase 2	Houston, TX; Duarte, CA; Louisville, KY; Boston, MA; Columbus, OH; Irvine, CA; Portland, OR; Aurora, CO; Providence, RI (2); Canada (5); Japan (2); China (5); Taiwan (4); United Kingdom (4); Israel (2); Australia (2); Spain (4)
ARID1A G276fs	NCT03568656 Tomasz Knurowski, MD, MFPM,Tomasz.Knurowski@cellcentric.com,07882 871299	Study to Evaluate CCS1477 in Advanced Tumours	Phase 1 /Phase 2	United Kingdom (10)
	NCT03682289 Early Phase Clinical Trials Recruitment, EarlyPhaseClinicalTrials@ucsf.edu,877-827-3222	Ceralasertib (AZD6738) Alone and in Combination With Olaparib or Durvalumab in Patients With Solid Tumors	Phase 2	San Francisco, CA
	NCT04434482 Min Song,min.song@impacttherapeutics.com,021 68411121	IMP4297 in Combination With Temozolomide in Patients With Advanced Solid Tumors and Small Cell Lung Cancer	Phase 1 /Phase 2	Evergreen Park, IL; Canton, OH; Columbus, OH; Tennessee, TN; China (4); Taiwan (5); Korea, Republic of (4); Australia (4)
	NCT05038839 See https://clinicaltrials.gov/ct2/show/NCT05038839	Cabozantinib and Pamiparib for the Treatment of Advanced of Refractory Solid Tumors	Phase 1	Houston, TX
	NCT05269316 Xiangna Chen,xiangna.chen@impacttherapeutics.com,+86-021-68411121	Study to Evaluate IMP9064 as a Monotherapy or in Combination in Patients With Advanced Solid Tumors	Phase 1	Greenville, SC; New York, NY; Dallas, TX; Hackensack, NJ; China; Taiwan; Australia (2)
	NCT05338346 Edwin Hoe,edwin.hoe@antengene.com,+61 497 390477	A Study of ATG-018 (ATR Inhibitor) Treatment in Patients With Advanced Solid Tumors and Hematological Malignancies	Phase 1	Australia (5)
	NCT05687136 See https://clinicaltrials.gov/ct2/show/NCT05687136	Testing the Combination of Two Anti-cancer Drugs, Peposertib (M3814) and M1774 for Advanced Solid Tumors	Phase 1	Boston, MA; Bethesda, MD (2)
	NCT05797168 AstraZeneca Clinical Study Information Center,information.center@astrazeneca.com,1-877-240-9479	Phase I/IIa Study for AZD5335 as Monotherapy and in Combination With Anti-cancer Agents in Participants With Solid Tumors	Phase 1 /Phase 2	Houston, TX; Duarte, CA; Louisville, KY; Boston, MA; Columbus, OH; Irvine, CA; Portland, OR; Aurora, CO; Providence, RI (2); Canada (5); Japan

List of Available Clinical Trials

Alteration	Trial ID / Contact	Title	Phase	Site (number in parenthesis is count of trial sites)
				(2); China (5); Taiwan (4); United Kingdom (4); Israel (2); Australia (2); Spain (4)
TP53 K373fs	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)
	NCT05253053 Caixia Sun, Ph.D., clinicaltrial@transtherabio.com,025-58216298	To Evaluate Efficacy and Safety of TT-00420 (Tinengotinib) as Monotherapy and Combination Therapy in Patients With Advanced Solid Tumors	Phase 1 /Phase 2	China (9)
	NCT05291182 Yinghui Sun, PhD,yhsun@centaurusbio.com,86-10-88858616	A Phase I Study of SY-4835 in Patients With Advanced Solid Tumors	Phase 1	China
	NCT05490472 Jacobio Pharmaceuticals, clinicaltrials@jacobiopharma.com,(781) 918-6670	JAB-2485 Activity in Adult Patients With Advanced Solid Tumors	Phase 1 /Phase 2	Dallas, TX; Salt Lake City, UT; China (3)
BRAF V600E	NCT02407509 Taleen Shakouri, PhD,DDU3808@icr.ac.uk,02034376629	Phase I Trial of VS-6766 Alone and in Combination With Everolimus	Phase 1	United Kingdom (3)
	NCT04965220 Zhang Li, leading PI,zhangli@sysucc.org.cn,13902282893	HLX208 (BRAF V600E Inhibitor) in Combination With Trametinib in Patients With Advanced Solid Tumors	Phase 1	China
	NCT05159245 Tanja Juslin,tanja.juslin@hus.fi, +358405597415	The Finnish National Study to Facilitate Patient Access to Targeted Anti-cancer Drugs	Phase 2	Finland (4)
	NCT05641493 Shun Lu, Dr.,shunlu@sjtu.edu.cn,021-22200000	A Phase Ib/II Clinical Trial to Evaluate the Safety and Efficacy of HLX208+HLX10 in NSCLC With BRAF V600E Mutation	Phase 1 /Phase 2	China
	NCT05722886 Aida Sarmiento Castro,determine@cancer.org.uk,+442034695101	DETERMINE (Determining Extended Therapeutic Indications for Existing Drugs in Rare Molecularly Defined Indications Using a National Evaluation Platform Trial) - Master Screening Protocol	Phase 2 /Phase 3	United Kingdom (25)
PTEN N323fs	NCT03568656 Tomasz Knurowski, MD, MFPM,Tomasz.Knurowski@cellcentric.com,07882 871299	Study to Evaluate CCS1477 in Advanced Tumours	Phase 1 /Phase 2	United Kingdom (10)
	NCT03682289 Early Phase Clinical Trials Recruitment, EarlyPhaseClinicalTrials@ucsf.edu,877-827-3222	Ceralasertib (AZD6738) Alone and in Combination With Olaparib or Durvalumab in Patients With Solid Tumors	Phase 2	San Francisco, CA
	NCT03742895 Toll Free Number,Trialsites@merck.com, 1-888-577-8839	Efficacy and Safety of Olaparib (MK-7339) in Participants With Previously Treated, Homologous Recombination Repair Mutation (HRRm) or Homologous Recombination Deficiency (HRD) Positive Advanced Cancer (MK-7339-002 / LYNK-002)	Phase 2	Harrison, NY; Seattle, WA; New York, NY; Baltimore, MD; Middletown, NJ; Colombia; Argentina; United Kingdom; Switzerland; Ireland; Denmark; Israel; Australia; Spain (2); Canada (2); Turkey (7); Korea, Republic of (2); Guatemala (4); Mexico (3); France (2); Peru (5)
	NCT04983745 Robin Patterson, RN, rpatterson@westclinic.com,901-683-0055	Niraparib and Dostarlimab in HRD Solid Tumors	Phase 2	Germantown, TN

List of Available Clinical Trials

Alteration	Trial ID / Contact	Title	Phase	Site (number in parenthesis is count of trial sites)
	x63019			
	NCT05700721 Timothy Yap, MBBS,PHD, tyap@mdanderson.org,(713) 563-1784	Phase II Trial of the PARP Inhibitor Niraparib and PD-1 Inhibitor Dostarlimab in Patients With Advanced Cancers With Active Progressing Brain Metastases (STARLET)	Phase 2	Houston, TX
FBXW7 W425*	NCT03065062 Geoffrey Shapiro, MD, Geoffrey_Shapiro@dfci.harvard.edu,617-632-4942	Study of the CDK4/6 Inhibitor Palbociclib (PD-0332991) in Combination With the PI3K/mTOR Inhibitor Gedatolisib (PF-05212384) for Patients With Advanced Squamous Cell Lung, Pancreatic, Head & Neck and Other Solid Tumors	Phase 1	Boston, MA (3)
	NCT03994796 Priscilla Brastianos, MD, pbrastianos@partners.org,617-724-1074	Genetic Testing in Guiding Treatment for Patients With Brain Metastases	Phase 2	Oklahoma City, OK; Deerfield Beach, FL; Minneapolis, MN; Edina, MN; Bremerton, WA; Midlothian, VA; Worcester, MA; Jacksonville, FL; Colorado Springs, CO; Kennewick, WA; Pennington, NJ; Kearney, NE; Jackson, MS; Berlin, VT; Rochester, MN; Neptune, NJ; Vancouver, WA; Boston, MA; Richmond, VA; Atlanta, GA; Burlington, VT; Summit, NJ; Salt Lake City, UT; Lexington, KY; Coral Gables, FL; NY (5); WI (19); IA (12); OH (17); ID (6); MI (46); CA (6); OR (5); IL (19); MT (7); PA (6); NC (5)
	NCT04851119 See https://clinicaltrials.gov/ct2/show/NCT04851119	Tegavivint for the Treatment of Recurrent or Refractory Solid Tumors, Including Lymphomas and Desmoid Tumors	Phase 1 /Phase 2	Philadelphia, PA; Saint Louis, MO; Minneapolis, MN; New York, NY; Chicago, IL; Orange, CA; San Francisco, CA; Memphis, TN; Los Angeles, CA; Seattle, WA; Houston, TX; Boston, MA; Indianapolis, IN; Atlanta, GA; Pittsburgh, PA; Cincinnati, OH; Washington, DC; Birmingham, AL; Aurora, CO; Ann Arbor, MI

Detailed Therapy Results

Alteration	Drug	Trade Name	Target	Current Status	
MSI-High	ABL503			antiPD-L1/4-1BB bispecific antibody.	Phase 1 (Solid Tumor) Phase 1 (Brain and Central Nervous System Tumors)
	Adebrelimab			Anti-PD-L1 monoclonal antibody.	Phase 1 (Solid Tumor) Phase 3 (Small cell lung carcinoma (SCLC))
	AK129			Anti-PD-1/LAG-3 bispecific antibody.	Phase 1 (Solid Tumor) Phase 1 (Brain and Central Nervous System Tumors)
	AMG 404			Anti-PD-1 monoclonal antibody.	Phase 1 (Solid Tumor) Phase 1 (Brain and Central Nervous System Tumors)
	AP203			anti-CD137/PD-L1 bispecific antibody.	Phase 1 (Solid Tumor) Phase 2 (Non-small cell lung carcinoma (NSCLC), Head and neck squamous cell carcinoma (HNSCC), Esophageal squamous cell carcinoma)
	Atezolizumab		Tecentriq	Anti-PD-L1 monoclonal antibody.	Phase 2 (Carcinoma of unknown primary (CUP)) FDA Approved in other indications (Non-small cell lung carcinoma (NSCLC), Small cell lung carcinoma (SCLC), Alveolar soft part sarcoma)
	ATG-101			anti-PD-L1/4-1BB bispecific antibody.	Phase 1 (Solid Tumor) Phase 1 (Non-Hodgkin lymphoma (NHL))
	Avelumab		Bavencio	Anti-PD-L1 monoclonal antibody.	Phase 1 (Solid Tumor) FDA Approved in other indications (Merkel cell carcinoma, Urothelial carcinoma, Bladder carcinoma)
	AZD2936			Anti-PD-1/TIGIT bispecific antibody.	Phase 2 (Non-small cell lung carcinoma (NSCLC))
	AZD7789			Anti-PD-1/TIM-3 bispecific antibody.	Phase 2 (Hodgkin lymphoma (HL), Non-small cell lung carcinoma (NSCLC))
	Balstilimab			Anti-PD-1 monoclonal antibody.	Phase 1 (Solid Tumor) Phase 2 (Cervical carcinoma, Soft tissue sarcoma)
	BAT1306			Anti-PD-1 monoclonal antibody.	Phase 2 (Colorectal carcinoma (CRC))
	BAT1308			Anti-PD-1 monoclonal antibody.	Phase 1 (Solid Tumor) Phase 1 (Brain and Central Nervous System Tumors)
	Benmelstobart			Anti-PD-L1 monoclonal antibody.	Phase 1 (Solid Tumor) Phase 3 (Head and neck squamous cell carcinoma (HNSCC))
	Bintrafusp alfa			Fusion protein targeting PD-L1 and TGF-beta-1.	Phase 1 (Solid Tumor) Phase 2 (Pancreatic carcinoma, Prostate carcinoma, Colorectal carcinoma (CRC))
	BJ-005			Anti-PD-L1/TGFbetaRII fusion protein.	Phase 1 (Solid Tumor) Phase 1 (Lymphoma)
	BS-006				Phase 1 (Solid Tumor) Phase 1 (Brain and Central Nervous System Tumors)
	Budigalimab			Anti-PD-1 monoclonal antibody.	Phase 1 (Solid Tumor) Phase 1 (Small cell lung carcinoma (SCLC), Brain and Central Nervous System Tumors)
	Cadonilimab			Anti-PD-1/CTLA-4 bispecific antibody.	Phase 1 (Solid Tumor) Phase 2 (Gastric carcinoma, Gastroesophageal junction carcinoma, Nasopharyngeal carcinoma)

Detailed Therapy Results

Alteration	Drug	Trade Name	Target	Current Status
	Camrelizumab		Anti-PD-1 monoclonal antibody.	Phase 1 (Solid Tumor) Phase 3 (Non-small cell lung carcinoma (NSCLC), Esophageal carcinoma, Nasopharyngeal carcinoma)
	Cemiplimab	Libtayo	Anti-PD-1 monoclonal antibody.	Phase 1 (Solid Tumor) FDA Approved in other indications (NSCLC with high PD-L1 expression, Non-small cell lung carcinoma (NSCLC), Cutaneous squamous cell carcinoma, Basal cell carcinoma)
	Cetrelimab		Anti-PD-1 monoclonal antibody.	Phase 1 (Solid Tumor) Phase 2 (Prostate carcinoma, Urothelial carcinoma)
	Cosibelimab		Anti-PD-L1 monoclonal antibody.	Phase 1 (Hodgkin lymphoma (HL), Melanoma, Merkel cell carcinoma, Non-small cell lung carcinoma (NSCLC), Endometrial carcinoma, Head and neck squamous cell carcinoma (HNSCC), Small cell lung carcinoma (SCLC), Urothelial carcinoma, Cutaneous squamous cell carcinoma, Non-Hodgkin lymphoma (NHL), Colorectal carcinoma (CRC), Mesothelioma)
	Dostarlimab	Jemperli	Anti-PD-1 monoclonal antibody.	Phase 1 (Solid Tumor) FDA Approved in other indications (Endometrial carcinoma with dMMR, Solid tumor with dMMR, Endometrial carcinoma with MSI-H or dMMR)
	Durvalumab	Imfinzi	Anti-PD-L1 monoclonal antibody.	Phase 2 (Solid Tumor) FDA Approved in other indications (Gallbladder carcinoma, Non-small cell lung carcinoma (NSCLC), Small cell lung carcinoma (SCLC), Cholangiocarcinoma)
	Durvalumab+tremelimumab	Imfinzi+Imjudo	Anti-PD-L1 monoclonal antibody + anti-CTLA-4 monoclonal antibody combination.	FDA Approved in other indications (Hepatocellular carcinoma (HCC), Non-small cell lung carcinoma (NSCLC))
	EMB-02		Anti-PD-1/LAG-3 bispecific antibody.	Phase 1 (Solid Tumor) Phase 2 (Melanoma)
	Envafolimab		Injectable anti-PD-L1 monoclonal antibody.	Phase 1 (Solid Tumor) Phase 3 (Gallbladder carcinoma, Cholangiocarcinoma)
	Ezabenlimab		Anti-PD-1 monoclonal antibody.	Phase 1 (Solid Tumor) Phase 2 (Colorectal carcinoma (CRC))
	FAZ053		Anti-PD-L1 monoclonal antibody.	Phase 1 (Solid Tumor)
	FS118		anti-PD-L1/LAG-3 bispecific antibody.	Phase 1 (Solid Tumor) Phase 1 (Lymphoma, Hematologic malignancies)
	GEN1046		Anti-PD-L1/anti-4-1BB (CD137) bispecific antibody.	Phase 1 (Solid Tumor) Phase 2 (Non-small cell lung carcinoma (NSCLC))
	HB0025		Anti-PD-L1/VEGFR-1 fusion protein.	Phase 1 (Solid Tumor)
	HB0036		anti-TIGIT/anti-PD-L1 bispecific antibody.	Phase 1 (Solid Tumor) Phase 2 (Non-small cell lung carcinoma (NSCLC))

Detailed Therapy Results

Alteration	Drug	Trade Name	Target	Current Status
	IBI315		Anti-PD-1/Her2 bispecific antibody.	Phase 1 (Solid Tumor) Phase 2 (Gastric carcinoma, Gastroesophageal junction carcinoma)
	IBI323		Anti-PD-L1/LAG-3 bispecific antibody.	Phase 1 (Solid Tumor) Phase 2 (Non-small cell lung carcinoma (NSCLC))
	INBRX-105		anti-PD-L1/4-1BB bispecific antibody.	Phase 2 (Solid Tumor) Phase 2 (Head and neck squamous cell carcinoma (HNSCC), Gastric adenocarcinoma, Nasopharyngeal carcinoma, Esophageal adenocarcinoma)
	INCA32459		Anti-PD-1/LAG-3 bispecific antibody.	Phase 1 (Solid Tumor) Phase 2 (Melanoma, Head and neck squamous cell carcinoma (HNSCC))
	INCB086550		Anti-PD-L1 monoclonal antibody.	Phase 1 (Solid Tumor) Phase 2 (Hepatocellular carcinoma (HCC), Melanoma, Non-small cell lung carcinoma (NSCLC), Renal cell carcinoma, Urothelial carcinoma)
	Ipilimumab	Yervoy	Anti-CTLA-4 monoclonal antibody.	Phase 2 (Carcinoma of unknown primary (CUP)) FDA Approved in other indications (Melanoma, Head and neck squamous cell carcinoma (HNSCC), CRC with MSI-H or dMMR)
	Ivonescimab		Anti-PD-1/VEGF-A bispecific antibody.	Phase 1 (Solid Tumor) Phase 3 (Non-small cell lung carcinoma (NSCLC))
	Lorigerlimab		Anti-PD-1/CTLA-4 dual-affinity re-targeting (DART) protein.	Phase 1 (Solid Tumor) Phase 1 (Brain and Central Nervous System Tumors)
	LVGN3616		Anti-PD-1 monoclonal antibody.	Phase 1 (Solid Tumor)
	LY3300054		Anti-PD-L1 monoclonal antibody.	Phase 1 (Solid Tumor)
	MCLA-145		anti-CD137/PD-L1 bispecific antibody.	Phase 1 (Solid Tumor) Phase 1 (Brain and Central Nervous System Tumors, B-cell lymphoma)
	mRNA-4359		mRNA-derived IDO/PD-L1-targeted vaccine.	Phase 1 (Solid Tumor) Phase 2 (Melanoma, Non-small cell lung carcinoma (NSCLC))
	Nivolumab	Opdivo	Anti-PD-1 monoclonal antibody.	Phase 2 (Malignant neoplasm of unknown primary) FDA Approved in other indications (Gastric carcinoma, Hodgkin lymphoma (HL), Melanoma, Non-small cell lung carcinoma (NSCLC), Renal cell carcinoma, Head and neck squamous cell carcinoma (HNSCC), Gastroesophageal junction carcinoma, Urothelial carcinoma, Bladder carcinoma, Esophageal carcinoma, CRC with MSI-H or dMMR)
	Nivolumab+ipilimumab	Opdivo+Yervoy	Anti-PD-1 monoclonal antibody + anti-CTLA-4 monoclonal antibody combination.	Phase 2 (Carcinoma of unknown primary (CUP)) FDA Approved in other indications (NSCLC with high PD-L1 expression, Hepatocellular carcinoma (HCC), Melanoma, Non-small cell lung carcinoma (NSCLC), Renal cell carcinoma,

Detailed Therapy Results

Alteration	Drug	Trade Name	Target	Current Status
				Esophageal squamous cell carcinoma, CRC with MSI-H or dMMR, Mesothelioma)
	ONO-4685		Anti-PD-1/CD3 bispecific antibody.	Phase 1 (T-cell lymphoma)
	Pacmilimab		Protease-activated anti-PD-L1 monoclonal antibody.	Phase 1 (Solid Tumor) Phase 1 (Lymphoma, Brain and Central Nervous System Tumors)
	Pembrolizumab	Keytruda	Anti-PD-1 monoclonal antibody.	Phase 2 (Malignant neoplasm of unknown primary) FDA Approved in other indications (Gastric carcinoma, HER2+ Gastric carcinoma, HER2+ Gastroesophageal junction carcinoma, Solid tumor with TMB-H, Endometrial carcinoma with MSI-H or dMMR, Gastric carcinoma with MSI-H or dMMR, Small bowel adenocarcinoma with MSI-H or dMMR, Cholangiocarcinoma with MSI-H or dMMR, Gallbladder carcinoma with MSI-H or dMMR, HNSCC with PD-L1 expression, HER2- Gastric carcinoma, HER2- Gastroesophageal junction carcinoma, Hepatocellular carcinoma (HCC), Hodgkin lymphoma (HL), Melanoma, Merkel cell carcinoma, Non-small cell lung carcinoma (NSCLC), Renal cell carcinoma, Head and neck squamous cell carcinoma (HNSCC), Gastroesophageal junction carcinoma, Urothelial carcinoma, Bladder carcinoma, Cutaneous squamous cell carcinoma, Breast carcinoma (triple negative), Esophageal carcinoma, Cervical carcinoma, Primary mediastinal (thymic) large B-cell lymphoma, Solid tumor with MSI-H or dMMR, CRC with MSI-H or dMMR)
	Penpulimab		Anti-PD-1 monoclonal antibody.	Phase 2 (Solid Tumor) Phase 2 (Hodgkin lymphoma (HL), Head and neck squamous cell carcinoma (HNSCC), Small cell lung carcinoma (SCLC), Brain and Central Nervous System Tumors, Nasopharyngeal carcinoma)
	Pimivalimab		Anti-PD-1 monoclonal antibody.	Phase 1 (Solid Tumor) Phase 2 (Non-small cell lung carcinoma (NSCLC))
	Pucotenlimab		Anti-PD-1 monoclonal antibody.	Phase 2 (Solid Tumor) Phase 3 (Gastric carcinoma, Non-small cell lung carcinoma (NSCLC))
	QL1604		Anti-PD-1 monoclonal antibody.	Phase 1 (Solid Tumor) Phase 2 (Hepatocellular carcinoma (HCC))
	QL1706		Mixture of anti-PD-1 and anti-CTLA-4 monoclonal antibodies.	Phase 1 (Solid Tumor) Phase 3 (Non-small cell lung carcinoma (NSCLC), Cervical carcinoma, Nasopharyngeal carcinoma)
	Retifanlimab	Zynyz	Anti-PD-1 monoclonal antibody.	Phase 1 (Solid Tumor) FDA Approved in other indications (Merkel cell carcinoma)

Detailed Therapy Results

Alteration	Drug	Trade Name	Target	Current Status	
	RO7121661			Anti-PD-1/TIM-3 bispecific antibody.	Phase 1 (Solid Tumor) Phase 1 (Small cell lung carcinoma (SCLC))
	RO7247669			anti-PD-1/LAG-3 bispecific antibody.	Phase 1 (Solid Tumor) Phase 2 (Hepatocellular carcinoma (HCC), Melanoma, Esophageal squamous cell carcinoma)
	RO7284755			PD-1-targeted IL-2 variant antibody fusion protein.	Phase 1 (Solid Tumor) Phase 1 (Brain and Central Nervous System Tumors)
	SAR445877			Anti-PD-L1 antibody with IL-15/IL-15 receptor sushi-domain complex.	Phase 1 (Solid Tumor) Phase 2 (Gastric carcinoma, Hepatocellular carcinoma (HCC), Non-small cell lung carcinoma (NSCLC), Gastroesophageal junction adenocarcinoma)
	Sasanlimab			Anti-PD-1 monoclonal antibody.	Phase 1 (Solid Tumor)
	SCT-I10A			Anti-PD-1 monoclonal antibody.	Phase 3 (Hepatocellular carcinoma (HCC))
	Serplulimab			Anti-PD-1 monoclonal antibody.	Phase 2 (Solid Tumor) Phase 3 (Gastric carcinoma, Non-small cell lung carcinoma (NSCLC), Small cell lung carcinoma (SCLC), Esophageal squamous cell carcinoma, Colorectal carcinoma (CRC))
	SG001			Anti-PD-1 monoclonal antibody.	Phase 1 (Solid Tumor) Phase 3 (Cervical carcinoma)
	SHR-1701			Anti-PD-L1 antibody fused with the extracellular domain of TGF-beta receptor II.	Phase 1 (Solid Tumor) Phase 3 (Gastric carcinoma, Non-small cell lung carcinoma (NSCLC), Gastroesophageal junction carcinoma, Cervical carcinoma, Colorectal carcinoma (CRC))
	SHR-1901			Anti-PD-1 monoclonal antibody.	Phase 1 (Solid Tumor) Phase 1 (Brain and Central Nervous System Tumors)
	Sintilimab			Anti-PD-1 monoclonal antibody.	Phase 2 (Solid Tumor) Phase 3 (Gastric carcinoma, Hepatocellular carcinoma (HCC), Non-small cell lung carcinoma (NSCLC), Gastroesophageal junction carcinoma, Nasopharyngeal carcinoma, Esophageal squamous cell carcinoma)
	Spartalizumab			Anti-PD-1 monoclonal antibody.	Phase 1 (Solid Tumor) Phase 2 (Neuroendocrine carcinoma, Hepatocellular carcinoma (HCC), Nasopharyngeal carcinoma)
	STI-3031			Anti-PD-L1 monoclonal antibody.	Phase 1 (Solid Tumor) Phase 2 (Gastric carcinoma, Hepatocellular carcinoma (HCC), Esophageal carcinoma, NK/T-cell lymphoma)
	Sugemalimab			Anti-PD-L1 monoclonal antibody.	Phase 1 (Solid Tumor) Phase 3 (Gastric carcinoma, Non-small cell lung carcinoma (NSCLC), Gastroesophageal junction carcinoma, Esophageal squamous cell carcinoma)
	Sym021			Anti-PD-1 monoclonal antibody.	Phase 1 (Solid Tumor) Phase 1 (Lymphoma)

Detailed Therapy Results

Alteration	Drug	Trade Name	Target	Current Status	
	T3011			Oncolytic HSV expressing IL-12 and anti-PD-1 antibody.	Phase 2 (Solid Tumor) Phase 2 (Head and neck squamous cell carcinoma (HNSCC), Brain and Central Nervous System Tumors)
	Tebotelimab			Anti-PD-1/anti-LAG-3 dual-affinity re-targeting (DART) protein.	Phase 1 (Solid Tumor) Phase 3 (Gastric carcinoma, Gastroesophageal junction carcinoma)
	TG-1501			Anti-PD-L1 monoclonal antibody.	Phase 1 (Hodgkin lymphoma (HL), Chronic lymphocytic leukemia (CLL), Non-Hodgkin lymphoma (NHL))
	Tislelizumab	Tevimbra		Anti-PD-1 monoclonal antibody.	Phase 2 (Solid Tumor) FDA Approved in other indications (Esophageal squamous cell carcinoma)
	Toripalimab			Anti-PD-1 monoclonal antibody.	Phase 1 (Solid Tumor) FDA Approved in other indications (Nasopharyngeal carcinoma)
	TQB2868			Anti-PD-1/anti TGF-beta bifunctional fusion protein.	Phase 1 (Solid Tumor) Phase 2 (Cervical carcinoma)
	TY101			Anti-PD-1 monoclonal antibody.	Phase 1 (Solid Tumor) Phase 2 (Lymphoma)
	Volrustomig			Anti-PD-L1/CTLA-4 bispecific antibody.	Phase 2 (Solid Tumor) Phase 3 (Non-small cell lung carcinoma (NSCLC))
	Vudalimab			Anti-PD-1/CTLA4 bispecific antibody.	Phase 1 (Gastric carcinoma, Neuroendocrine carcinoma, Hepatocellular carcinoma (HCC), Melanoma, Non-small cell lung carcinoma (NSCLC), Endometrial carcinoma, Renal cell carcinoma, Head and neck squamous cell carcinoma (HNSCC), Gastroesophageal junction carcinoma, Urothelial carcinoma, Breast carcinoma, Anal carcinoma, Cervical carcinoma, Colorectal carcinoma (CRC), Mesothelioma)
	Zimberelimab			Anti-PD-1 monoclonal antibody.	Phase 2 (Non-small cell lung carcinoma (NSCLC), Prostate carcinoma)
BRAF V600E	ABM-1310			Braf (V600E) kinase inhibitor.	Phase 1 (Solid Tumor)
	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 (Solid Tumor) Phase 2 (Non-small cell lung carcinoma (NSCLC), Uveal melanoma, Ovarian carcinoma)
	BDTX-4933			Braf class 1, 2, and 3 inhibitor.	Phase 1 (Solid Tumor)
	Belvarafenib			Pan-Raf kinase inhibitor.	Phase 1 (Solid Tumor)
	BI 3011441			MEK1,2 inhibitor.	Phase 1 (Solid Tumor)
	Binimetinib	Mektovi		MEK1,2 inhibitor.	Phase 1 (Solid Tumor) FDA Approved in other indications (Melanoma with BRAF V600E/K mutation)

Detailed Therapy Results

Alteration	Drug	Trade Name	Target	Current Status
	Brimarafenib		Braf class 1, 2, and 3 inhibitor.	Phase 2 (Solid Tumor) Phase 1 (Pancreatic ductal adenocarcinoma, Colorectal carcinoma (CRC))
	CFT1946		Braf class 1 inhibitor and degrader.	Phase 1 (Solid Tumor) Phase 2 (Melanoma, Non-small cell lung carcinoma (NSCLC))
	CMAB009		Anti-Egfr monoclonal antibody.	Phase 3 (Colorectal carcinoma (CRC))
	Cobimetinib	Cotellic	MEK1,2 inhibitor.	Phase 2 (Malignant neoplasm of unknown primary) FDA Approved in other indications (Melanoma with BRAF V600E /K mutation, Histiocytic and dendritic cell neoplasms)
	Dabrafenib	Tafinlar	Braf (V600E) kinase inhibitor.	FDA Approved in other indications (Melanoma with BRAF V600E)
	Dabrafenib+trametinib	Tafinlar+Mekinist	Braf (V600E) kinase inhibitor + MEK1,2 inhibitor combination.	FDA Approved in other indications (Anaplastic thyroid carcinoma with BRAF V600E, Melanoma with BRAF V600E/K mutation, Solid tumor with BRAF V600E, Low-grade glioma with BRAF V600E, NSCLC with BRAF V600E)
	Defactinib		Focal adhesion kinase (FAK) inhibitor, upstream of MAPK pathway.	Phase 2 (Solid Tumor) Phase 2 (Lymphoma, Multiple myeloma (MM))
	E6201		MEK1,2, Mekk1, and Flt3 inhibitor.	Phase 1 (Solid Tumor) Phase 1 (Acute myeloid leukemia (AML))
	Encorafenib	Braftovi	Braf (V600E/K) kinase inhibitor.	Phase 2 (Solid Tumor) Phase 3 (Melanoma, Colorectal carcinoma (CRC))
	Encorafenib+binimetinib	Braftovi+Mektovi	Braf (V600E/K) kinase inhibitor + MEK1,2 inhibitor combination.	FDA Approved in other indications (Melanoma with BRAF V600E/K mutation, NSCLC with BRAF V600E)
	HLX208		Braf (V600E) inhibitor.	Phase 2 (Solid Tumor) Phase 2 (Erdheim Chester Disease (ECD), Anaplastic thyroid carcinoma, Langerhans cell histiocytosis (LCH), Brain and Central Nervous System Tumors)
	HMPL-295		ERK1/2 kinase inhibitor.	Phase 1 (Solid Tumor)
	IMM-1-104		MEK1,2 inhibitor.	Phase 1 (Solid Tumor) Phase 2 (Melanoma, Non-small cell lung carcinoma (NSCLC), Pancreatic ductal adenocarcinoma)
	JZP815		pan-Raf kinase inhibitor.	Phase 1 (Solid Tumor)
	KIN-2787		Pan-Raf kinase inhibitor.	Phase 1 (Solid Tumor) Phase 1 (Brain and Central Nervous System Tumors)
	KL-140		Anti-Egfr monoclonal antibody.	Phase 3 (Colorectal carcinoma (CRC))
	Lifirafenib		Dual Braf/Egfr inhibitor.	Phase 1 (Solid Tumor) Phase 1 (Brain and Central Nervous System Tumors)
	LTT462		ERK1/2 kinase inhibitor.	Phase 1 (Solid Tumor)

Detailed Therapy Results

Alteration	Drug	Trade Name	Target	Current Status
	Mirdametinib		MEK1,2 inhibitor.	Phase 1 (Solid Tumor) 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)
	Naporafenib		Pan-Raf kinase inhibitor.	Phase 1 (Solid Tumor)
	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 1 (Solid Tumor) Phase 2 (Melanoma, Pancreatic ductal adenocarcinoma, Ovarian carcinoma, Hematologic malignancies, Colorectal carcinoma (CRC))
	Plixorafenib		Braf mutant kinase inhibitor.	Phase 2 (Solid Tumor) Phase 2 (Glioma, Hairy cell leukemia)
	QLH11906		pan-Raf kinase inhibitor.	Phase 1 (Solid Tumor)
	RSC-1255		Ras inhibitor.	Phase 1 (Solid Tumor)
	Selumetinib	Koselugo	MEK1,2 inhibitor.	Phase 1 (Solid Tumor) FDA Approved in other indications (NF1-related plexiform neurofibroma)
	SHR7390		MEK1,2 inhibitor.	Phase 1 (Solid Tumor)
	Temuterkib		ERK1/2 kinase inhibitor.	Phase 1 (Solid Tumor) Phase 1 (Pancreatic ductal adenocarcinoma)
	Tizaterkib		ERK1/2 kinase inhibitor.	Phase 1 (Solid Tumor) Phase 1 (Hematologic malignancies)
	Tovorafenib	Ojemda	Pan-Raf kinase inhibitor.	Phase 1 (Solid Tumor) FDA Approved in other indications (Low-grade glioma with BRAF V600 mutation or BRAF fusion /rearrangement)
	Trametinib	Mekinist	MEK1,2 inhibitor.	Phase 2 (Solid Tumor) FDA Approved in other indications (Melanoma with BRAF V600 mutation)
	Ulixertinib		ERK1/2 kinase inhibitor.	Phase 1 (Solid Tumor) Phase 2 (Gastric carcinoma, Melanoma, Histiocytic and dendritic cell neoplasms, Langerhans cell histiocytosis (LCH), Uveal melanoma, Acute myeloid leukemia (AML), Gastrointestinal carcinoma, Non-Hodgkin lymphoma (NHL), Myelodysplastic Syndrome (MDS))
	Vemurafenib	Zelboraf	Braf (V600E) kinase inhibitor.	Phase 2 (Carcinoma of unknown primary (CUP)) FDA Approved in other indications (Erdheim Chester Disease (ECD), Melanoma with BRAF V600E)
	Vemurafenib+cobimetinib	Zelboraf+Cotellic	Braf (V600E) kinase inhibitor + MEK1,2 inhibitor combination.	FDA Approved in other indications (Melanoma with BRAF V600E/K mutation)
	XP-102		pan-Raf kinase inhibitor.	Phase 2 (Melanoma, Non-small cell lung

Detailed Therapy Results

Alteration	Drug	Trade Name	Target	Current Status
				carcinoma (NSCLC), Thyroid carcinoma, Colorectal carcinoma (CRC))
ARID1A D1850fs G276fs	ABBV-744		Bromodomain and extra-terminal domain (BET) inhibitor.	Phase 1 (Prostate carcinoma, Acute myeloid leukemia (AML))
	AMXI-5001		Dual PARP1/2 and microtubule polymerization inhibitor.	Phase 2 (Solid Tumor)
	ART0380		Atr inhibitor.	Phase 2 (Solid Tumor) Phase 2 (Brain and Central Nervous System Tumors)
	ATG-018		Atr inhibitor.	Phase 1 (Solid Tumor) Phase 1 (Marginal zone lymphoma (MZL), Diffuse large B-cell lymphoma (DLBCL))
	ATRN-119		Atr inhibitor.	Phase 2 (Solid Tumor) Phase 2 (Brain and Central Nervous System Tumors)
	AZD5153		Bromodomain and extra-terminal domain (BET) inhibitor.	Phase 1 (Solid Tumor) Phase 1 (Brain and Central Nervous System Tumors)
	AZD9574		PARP1 inhibitor (brain penetrant).	Phase 2 (Glioma, Pancreatic carcinoma, Prostate carcinoma, Ovarian carcinoma, Breast carcinoma)
	Berzosertib		Atr inhibitor.	Phase 1 (Solid Tumor) Phase 2 (Gastric carcinoma, Neuroendocrine carcinoma, Small cell carcinoma, Osteosarcoma, Non-small cell lung carcinoma (NSCLC), Prostate carcinoma, Ovarian carcinoma, Small cell lung carcinoma (SCLC), Gastroesophageal junction carcinoma, Urothelial carcinoma, Bladder carcinoma, Leiomyosarcoma, Renal pelvis carcinoma, Lung cancer)
	BMS-986158		Bromodomain and extra-terminal domain (BET) inhibitor.	Phase 2 (Solid Tumor)
	Camonsertib		Atr inhibitor.	Phase 1 (Solid Tumor) Phase 1 (Brain and Central Nervous System Tumors)
	Ceralasertib		Atr inhibitor.	Phase 1 (Solid Tumor) Phase 3 (Non-small cell lung carcinoma (NSCLC), Lung cancer)
	DS-3201b		Ezh1/2 inhibitor.	Phase 2 (Small cell lung carcinoma (SCLC), Adult T-cell leukemia/lymphoma (ATLL))
	Elimusertib		Atr inhibitor.	Phase 1 (Solid Tumor) Phase 1 (Head and neck squamous cell carcinoma (HNSCC))
	Fluzoparib		PARP inhibitor.	Phase 1 (Solid Tumor) Phase 3 (Pancreatic carcinoma, Ovarian carcinoma, Breast carcinoma)
	HH2853		Ezh1/2 inhibitor.	Phase 2 (Solid Tumor) Phase 2 (Non-Hodgkin lymphoma (NHL))
	IDX-1197		PARP inhibitor.	Phase 2 (Solid Tumor) Phase 2 (Brain and Central Nervous System Tumors)
	IMP9064		Atr inhibitor.	Phase 1 (Solid Tumor)
	INCB057643		Bromodomain and extra-terminal domain (BET) inhibitor.	Phase 1 (Solid Tumor) Phase 1 (Lymphoma, Hematologic malignancies)
	JAB-8263		Bromodomain and extra-terminal domain (BET) inhibitor.	Phase 1 (Solid Tumor)
	Niraparib	Zejula	PARP inhibitor.	Phase 1 (Solid Tumor) FDA Approved in other indications (Prostate carcinoma with BRCA1/2

Detailed Therapy Results

Alteration	Drug	Trade Name	Target	Current Status
				mutation, Ovarian carcinoma with BRCA1/2 mutation)
	NMS-03305293		PARP inhibitor.	Phase 1 (Solid Tumor) Phase 2 (Glioblastoma)
	NUV-868		Bromodomain and extra-terminal domain (BET) inhibitor.	Phase 1 (Solid Tumor) Phase 2 (Pancreatic carcinoma, Prostate carcinoma, Ovarian carcinoma, Breast carcinoma (triple negative))
	Olaparib	Lynparza	PARP inhibitor.	Phase 2 (Carcinoma of unknown primary (CUP)) FDA Approved in other indications (Pancreatic adenocarcinoma with germline BRCA1/2 mutation, Prostate cancer with HRR gene mutation, Ovarian carcinoma with BRCA1/2 mutation, Breast carcinoma with germline BRCA1 /2 mutation)
	Pamiparib		PARP inhibitor.	Phase 1 (Solid Tumor) Phase 3 (Gastric carcinoma, Gastroesophageal junction carcinoma)
	Pelabresib		Bromodomain and extra-terminal domain (BET) inhibitor.	Phase 1 (Lymphoma, Multiple myeloma (MM), Myelodysplastic Syndrome (MDS))
	PF-06821497		Ezh2 inhibitor.	Phase 1 (Prostate carcinoma, Small cell lung carcinoma (SCLC), Follicular lymphoma (FL), Diffuse large B-cell lymphoma (DLBCL))
	PLX2853		Bromodomain and extra-terminal domain (BET) inhibitor.	Phase 2 (Solid Tumor) Phase 2 (Uveal melanoma, Small cell lung carcinoma (SCLC), Brain and Central Nervous System Tumors, Non-Hodgkin lymphoma (NHL))
	RNK05047		Brd4 protein degrader.	Phase 2 (Solid Tumor) Phase 2 (Diffuse large B-cell lymphoma (DLBCL))
	RP12146		PARP inhibitor.	Phase 1 (Gastric carcinoma, Pancreatic carcinoma, Prostate carcinoma, Endometrial carcinoma, Ovarian carcinoma, Small cell lung carcinoma (SCLC), Breast carcinoma, Cholangiocarcinoma, Colorectal carcinoma (CRC))
	Rucaparib	Rubraca	PARP inhibitor.	Phase 1 (Solid Tumor) FDA Approved in other indications (Prostate carcinoma with BRCA1/2 mutation, Ovarian carcinoma)
	Saruparib		PARP1 inhibitor.	Phase 2 (Solid Tumor)
	Senaparib		PARP inhibitor.	Phase 1 (Solid Tumor) Phase 2 (Small cell lung carcinoma (SCLC))
	SHR2554		Ezh2 inhibitor.	Phase 2 (Pancreatic carcinoma, Non-small cell lung carcinoma (NSCLC), Breast carcinoma, Gastrointestinal carcinoma, Cholangiocarcinoma, B-cell lymphoma)
	Stenoparib		PARP inhibitor.	Phase 1 (Pancreatic carcinoma, Non-small cell lung carcinoma (NSCLC), Endometrial carcinoma, Ovarian carcinoma, Breast carcinoma, Colorectal carcinoma (CRC))
	Talazoparib	Talzenna	PARP inhibitor.	Phase 1 (Solid Tumor) FDA Approved in other indications (Prostate cancer with HRR gene mutation, Breast carcinoma with germline BRCA1 /2 mutation)
	Tazemetostat	Tazverik	Ezh2 inhibitor.	Phase 1 (Solid Tumor) FDA Approved in other

Detailed Therapy Results

Alteration	Drug	Trade Name	Target	Current Status
				indications (Follicular lymphoma with EZH2 mutation, Epithelioid sarcoma, Follicular lymphoma (FL))
	Trotabresib		Bromodomain and extra-terminal domain (BET) inhibitor.	Phase 1 (Solid Tumor) Phase 1 (Non-Hodgkin lymphoma (NHL))
	Tulmimetostat		2nd generation Ezh2 inhibitor.	Phase 2 (Solid Tumor) Phase 2 (Lymphoma)
	Tuvusertib		Atr inhibitor.	Phase 1 (Solid Tumor) Phase 2 (Merkel cell carcinoma, Non-small cell lung carcinoma (NSCLC), Prostate carcinoma, Endometrial carcinoma, Ovarian carcinoma, Colorectal carcinoma (CRC))
	Veliparib		PARP inhibitor.	Phase 1 (Carcinoma of unknown primary (CUP)) Phase 3 (Glioblastoma, Non-small cell lung carcinoma (NSCLC), Ovarian carcinoma, Ovarian carcinosarcoma, Breast carcinoma, Lung cancer)
	ZEN003694		Bromodomain and extra-terminal domain (BET) inhibitor.	Phase 2 (Prostate carcinoma, Breast carcinoma (triple negative))
PTEN N323fs	ABTL0812		Inhibitor of mTORC1/mTORC2 /Dhfr.	Phase 1 (Solid Tumor) Phase 2 (Pancreatic carcinoma, Non-small cell lung carcinoma (NSCLC), Endometrial carcinoma)
	Alpelisib	Piqray	p110-alpha inhibitor.	Phase 1 (Solid Tumor) FDA Approved in other indications (Breast carcinoma (HR+, HER2-) with a PIK3CA mutation, as determined by a validated test)
	Archexin	Archexin	Akt1 antisense oligonucleotide.	Phase 1 (Solid Tumor) Phase 2 (Pancreatic carcinoma, Renal cell carcinoma)
	ARQ 751		Akt inhibitor.	Phase 1 (Solid Tumor)
	AZD8186		p110-beta and p110-delta small molecule inhibitor.	Phase 1 (Solid Tumor) Phase 1 (Breast carcinoma (triple negative), Lung squamous cell carcinoma)
	Buparlisib		PI3K inhibitor.	Phase 2 (Solid Tumor) Phase 3 (Head and neck squamous cell carcinoma (HNSCC), Breast carcinoma)
	Capivasertib	Truqap	Akt inhibitor.	Phase 1 (Solid Tumor) FDA Approved in other indications (Breast carcinoma (HR+, HER2-) with a PIK3CA/AKT1/PTEN mutation)
	CC-115		DNA-PK/dual mTORC1/2 kinase inhibitor.	Phase 1 (Solid Tumor) Phase 2 (Glioblastoma, Glioma)
	Copanlisib	Aliqopa	PI3K inhibitor.	Phase 1 (Solid Tumor) Phase 3 (Non-Hodgkin lymphoma (NHL))
	CYH33		p110-alpha-specific small molecule inhibitor.	Phase 1 (Solid Tumor)
	Everolimus	Afinitor	mTOR inhibitor, immunosuppressant.	Phase 2 (Carcinoma of unknown primary (CUP)) FDA Approved in other indications (TSC associated renal angiomyolipoma and subependymal giant cell astrocytoma, Renal cell carcinoma, Gastrointestinal neuroendocrine carcinoma, Lung carcinoid, Breast carcinoma (hormone receptor +, HER2-), Subependymal giant cell astrocytoma)
	Gedatolisib		Dual PI3K/mTOR inhibitor.	Phase 1 (Solid Tumor) Phase 3 (Breast

Detailed Therapy Results

Alteration	Drug	Trade Name	Target	Current Status
				carcinoma)
	GSK2636771		p110-beta small molecule inhibitor.	Phase 2 (Solid Tumor) Phase 1 (Prostate carcinoma)
	HS-10352		p110-alpha-specific small molecule inhibitor.	Phase 1 (Breast carcinoma)
	Inavolisib		PI3K inhibitor.	Phase 1 (Solid Tumor) Phase 3 (Breast carcinoma)
	Ipatasertib		Akt inhibitor.	Phase 1 (Solid Tumor) Phase 3 (Prostate carcinoma, Breast carcinoma)
	ME-344		Dual mTORC1/mTORC2 inhibitor.	Phase 1 (Solid Tumor) Phase 2 (Ovarian carcinoma, Small cell lung carcinoma (SCLC))
	MEN1611		PI3K inhibitor.	Phase 2 (Metaplastic breast carcinoma, Colorectal carcinoma (CRC))
	Miransertib		Akt inhibitor.	Phase 1 (Solid Tumor)
	MK-2206		Akt inhibitor.	Phase 1 (Solid Tumor) Phase 2 (Gastric carcinoma, Gallbladder carcinoma, Hepatocellular carcinoma (HCC), Pancreatic carcinoma, Hodgkin lymphoma (HL), Lymphoma, Melanoma, Non-small cell lung carcinoma (NSCLC), Carcinoid tumor, Prostate carcinoma, Endometrial carcinoma, Renal cell carcinoma, Ovarian carcinoma, Small cell lung carcinoma (SCLC), Adenoid cystic carcinoma, Head and neck carcinoma, Gastroesophageal junction carcinoma, Gastrointestinal neuroendocrine carcinoma, Mucinous colon adenocarcinoma, Breast carcinoma, Chronic lymphocytic leukemia (CLL), Acute myeloid leukemia (AML), Cholangiocarcinoma, Thymic neoplasm, Peritoneal papillary serous carcinoma, Lung cancer, Colorectal carcinoma (CRC), Diffuse large B-cell lymphoma (DLBCL))
	MSC2363318A		Akt1, Akt3, and p70S6K inhibitor.	Phase 1 (Solid Tumor) Phase 1 (Lymphoma)
	Niraparib	Zejula	PARP inhibitor.	Phase 1 (Solid Tumor) FDA Approved in other indications (Prostate carcinoma with BRCA1/2 mutation, Ovarian carcinoma with BRCA1/2 mutation)
	Olaparib	Lynparza	PARP inhibitor.	Phase 2 (Carcinoma of unknown primary (CUP)) FDA Approved in other indications (Pancreatic adenocarcinoma with germline BRCA1/2 mutation, Prostate cancer with HRR gene mutation, Ovarian carcinoma with BRCA1/2 mutation, Breast carcinoma with germline BRCA1 /2 mutation)
	Onatasertib		Dual mTORC1/mTORC2 inhibitor.	Phase 2 (Solid Tumor) Phase 2 (Bladder neuroendocrine carcinoma, Multiple myeloma (MM), Diffuse large B-cell lymphoma (DLBCL))
	Paxalisib		Dual PI3K/mTOR inhibitor.	Phase 2 (Glioblastoma, Breast carcinoma)
	RLY-2608		p110-alpha-specific small molecule inhibitor.	Phase 1 (Solid Tumor)
	RLY-5836		p110-alpha-specific small molecule inhibitor.	Phase 1 (Solid Tumor)

Detailed Therapy Results

Alteration	Drug	Trade Name	Target	Current Status
	RMC-5552		mTORC1-specific inhibitor.	Phase 1 (Solid Tumor)
	Samotolisib		Dual PI3K/mTOR inhibitor.	Phase 1 (Solid Tumor) Phase 2 (Pancreatic carcinoma, Non-small cell lung carcinoma (NSCLC), Prostate carcinoma)
	Sapanisertib		Dual mTORC1/mTORC2 inhibitor.	Phase 1 (Solid Tumor) Phase 2 (Uterine carcinosarcoma, Hepatocellular carcinoma (HCC), Lymphoma, Merkel cell carcinoma, Anaplastic thyroid carcinoma, Non-small cell lung carcinoma (NSCLC), Pancreatic neuroendocrine tumor, Prostate carcinoma, Endometrial carcinoma, Renal cell carcinoma, Ovarian carcinoma, Urothelial carcinoma, Bladder carcinoma, Breast carcinoma, Multiple myeloma (MM), Non-Hodgkin lymphoma (NHL), Lung cancer, Sarcoma, Acute lymphoblastic leukemia (ALL))
	Serabelisib		PI3K inhibitor.	Phase 1 (Solid Tumor) Phase 2 (Endometrial carcinoma, Renal cell carcinoma, Breast carcinoma (triple negative))
	Talazoparib	Talzenna	PARP inhibitor.	Phase 1 (Solid Tumor) FDA Approved in other indications (Prostate cancer with HRR gene mutation, Breast carcinoma with germline BRCA1 /2 mutation)
	TAS-117		Akt inhibitor.	Phase 2 (Solid Tumor)
	TAS0612		Akt/p70S6K/p90RSK1 multikinase inhibitor.	Phase 1 (Solid Tumor)
	Temsirolimus	Torisel	mTOR inhibitor.	Phase 1 (Solid Tumor) FDA Approved in other indications (Renal cell carcinoma)
	TOS-358		p110-alpha-specific small molecule inhibitor.	Phase 1 (Gastric carcinoma, Non-small cell lung carcinoma (NSCLC), Endometrial carcinoma, Head and neck squamous cell carcinoma (HNSCC), Ovarian carcinoma, Urothelial carcinoma, Breast carcinoma, Cervical carcinoma, Colorectal carcinoma (CRC))
	Triciribine		DNA synthesis and Akt inhibitor.	Phase 1 (Solid Tumor) Phase 2 (Ovarian carcinoma, Breast carcinoma)
	Uprosertib		Akt inhibitor.	Phase 1 (Solid Tumor) Phase 2 (Melanoma, Uveal melanoma, Breast carcinoma, Cervical carcinoma, Acute myeloid leukemia (AML), Multiple myeloma (MM))
	Vistusertib		Dual mTORC1/mTORC2 inhibitor.	Phase 2 (Solid Tumor) Phase 2 (Meningioma, Small cell lung carcinoma (SCLC), Diffuse large B-cell lymphoma (DLBCL))
	WGI-0301		Nanoliposomal Archexin, an Akt1 antisense oligonucleotide.	Phase 1 (Solid Tumor)
CDK12 M1028fs	AMXI-5001		Dual PARP1/2 and microtubule polymerization inhibitor.	Phase 2 (Solid Tumor)
	ATG-018		Atr inhibitor.	Phase 1 (Solid Tumor) Phase 1 (Marginal zone lymphoma (MZL), Diffuse large B-cell lymphoma (DLBCL))
	AZD9574		PARP1 inhibitor (brain penetrant).	Phase 2 (Glioma, Pancreatic carcinoma, Prostate carcinoma, Ovarian carcinoma, Breast carcinoma)

Detailed Therapy Results

Alteration	Drug	Trade Name	Target	Current Status
	Berzosertib		Atr inhibitor.	Phase 1 (Solid Tumor) Phase 2 (Gastric carcinoma, Neuroendocrine carcinoma, Small cell carcinoma, Osteosarcoma, Non-small cell lung carcinoma (NSCLC), Prostate carcinoma, Ovarian carcinoma, Small cell lung carcinoma (SCLC), Gastroesophageal junction carcinoma, Urothelial carcinoma, Bladder carcinoma, Leiomyosarcoma, Renal pelvis carcinoma, Lung cancer)
	Camonsertib		Atr inhibitor.	Phase 1 (Solid Tumor) Phase 1 (Brain and Central Nervous System Tumors)
	Fluzoparib		PARP inhibitor.	Phase 1 (Solid Tumor) Phase 3 (Pancreatic carcinoma, Ovarian carcinoma, Breast carcinoma)
	IDX-1197		PARP inhibitor.	Phase 2 (Solid Tumor) Phase 2 (Brain and Central Nervous System Tumors)
	Ipilimumab	Yervoy	Anti-CTLA-4 monoclonal antibody.	Phase 2 (Carcinoma of unknown primary (CUP)) FDA Approved in other indications (Melanoma, Head and neck squamous cell carcinoma (HNSCC), CRC with MSI-H or dMMR)
	Niraparib	Zejula	PARP inhibitor.	Phase 1 (Solid Tumor) FDA Approved in other indications (Prostate carcinoma with BRCA1/2 mutation, Ovarian carcinoma with BRCA1/2 mutation)
	Nivolumab	Opdivo	Anti-PD-1 monoclonal antibody.	Phase 2 (Malignant neoplasm of unknown primary) FDA Approved in other indications (Gastric carcinoma, Hodgkin lymphoma (HL), Melanoma, Non-small cell lung carcinoma (NSCLC), Renal cell carcinoma, Head and neck squamous cell carcinoma (HNSCC), Gastroesophageal junction carcinoma, Urothelial carcinoma, Bladder carcinoma, Esophageal carcinoma, CRC with MSI-H or dMMR)
	NMS-03305293		PARP inhibitor.	Phase 1 (Solid Tumor) Phase 2 (Glioblastoma)
	Olaparib	Lynparza	PARP inhibitor.	Phase 2 (Carcinoma of unknown primary (CUP)) FDA Approved in other indications (Pancreatic adenocarcinoma with germline BRCA1/2 mutation, Prostate cancer with HRR gene mutation, Ovarian carcinoma with BRCA1/2 mutation, Breast carcinoma with germline BRCA1 /2 mutation)
	Pamiparib		PARP inhibitor.	Phase 1 (Solid Tumor) Phase 3 (Gastric carcinoma, Gastroesophageal junction carcinoma)
	RP12146		PARP inhibitor.	Phase 1 (Gastric carcinoma, Pancreatic carcinoma, Prostate carcinoma, Endometrial carcinoma, Ovarian carcinoma, Small cell lung carcinoma (SCLC), Breast carcinoma, Cholangiocarcinoma, Colorectal carcinoma (CRC))
	Rucaparib	Rubraca	PARP inhibitor.	Phase 1 (Solid Tumor) FDA Approved in other indications (Prostate carcinoma with BRCA1/2 mutation, Ovarian carcinoma)
	Saruparib		PARP1 inhibitor.	Phase 2 (Solid Tumor)
	Senaparib		PARP inhibitor.	Phase 1 (Solid Tumor) Phase 2 (Small cell lung carcinoma (SCLC))

Detailed Therapy Results

Alteration	Drug	Trade Name	Target	Current Status
	Stenoparib		PARP inhibitor.	Phase 1 (Pancreatic carcinoma, Non-small cell lung carcinoma (NSCLC), Endometrial carcinoma, Ovarian carcinoma, Breast carcinoma, Colorectal carcinoma (CRC))
	Talazoparib	Talzenna	PARP inhibitor.	Phase 1 (Solid Tumor) FDA Approved in other indications (Prostate cancer with HRR gene mutation, Breast carcinoma with germline BRCA1 /2 mutation)
	Veliparib		PARP inhibitor.	Phase 1 (Carcinoma of unknown primary (CUP)) Phase 3 (Glioblastoma, Non-small cell lung carcinoma (NSCLC), Ovarian carcinoma, Ovarian carcinosarcoma, Breast carcinoma, Lung cancer)
FBXW7 W425*	ABTL0812		Inhibitor of mTORC1/mTORC2 /Dhfr.	Phase 1 (Solid Tumor) Phase 2 (Pancreatic carcinoma, Non-small cell lung carcinoma (NSCLC), Endometrial carcinoma)
	CC-115		DNA-PK/dual mTORC1/2 kinase inhibitor.	Phase 1 (Solid Tumor) Phase 2 (Glioblastoma, Glioma)
	Gedatolisib		Dual PI3K/mTOR inhibitor.	Phase 1 (Solid Tumor) Phase 3 (Breast carcinoma)
	ME-344		Dual mTORC1/mTORC2 inhibitor.	Phase 1 (Solid Tumor) Phase 2 (Ovarian carcinoma, Small cell lung carcinoma (SCLC))
	Onatasertib		Dual mTORC1/mTORC2 inhibitor.	Phase 2 (Solid Tumor) Phase 2 (Bladder neuroendocrine carcinoma, Multiple myeloma (MM), Diffuse large B-cell lymphoma (DLBCL))
	Paxalisib		Dual PI3K/mTOR inhibitor.	Phase 2 (Glioblastoma, Breast carcinoma)
	RMC-5552		mTORC1-specific inhibitor.	Phase 1 (Solid Tumor)
	Samotolisib		Dual PI3K/mTOR inhibitor.	Phase 1 (Solid Tumor) Phase 2 (Pancreatic carcinoma, Non-small cell lung carcinoma (NSCLC), Prostate carcinoma)
	Sapanisertib		Dual mTORC1/mTORC2 inhibitor.	Phase 1 (Solid Tumor) Phase 2 (Uterine carcinosarcoma, Hepatocellular carcinoma (HCC), Lymphoma, Merkel cell carcinoma, Anaplastic thyroid carcinoma, Non-small cell lung carcinoma (NSCLC), Pancreatic neuroendocrine tumor, Prostate carcinoma, Endometrial carcinoma, Renal cell carcinoma, Ovarian carcinoma, Urothelial carcinoma, Bladder carcinoma, Breast carcinoma, Multiple myeloma (MM), Non-Hodgkin lymphoma (NHL), Lung cancer, Sarcoma, Acute lymphoblastic leukemia (ALL))
	Tegavivint		Wnt/beta-catenin pathway inhibitor.	Phase 1 (Solid Tumor) Phase 2 (Hepatocellular carcinoma (HCC), Wilms tumor, Ewing sarcoma, Desmoid fibromatosis)
	Vistusertib		Dual mTORC1/mTORC2 inhibitor.	Phase 2 (Solid Tumor) Phase 2 (Meningioma, Small cell lung carcinoma (SCLC), Diffuse large B-cell lymphoma (DLBCL))
TP53 K373fs	AL8326		Aurora kinase B/VEGFRs/Fgfr multi-kinase inhibitor.	Phase 1 (Solid Tumor) Phase 3 (Small cell lung carcinoma (SCLC))
	ATO	Trisenox	PML-RARA inhibitor. Inhibits multiple signaling pathways, including the Hedgehog pathway.	FDA Approved in other indications (Acute myeloid leukemia (AML), Acute promyelocytic leukemia (APL))
	Azenosertib		Wee1 tyrosine kinase inhibitor.	Phase 1 (Solid Tumor) Phase 2 (High-grade

Detailed Therapy Results

Alteration	Drug	Trade Name	Target	Current Status
				serous ovarian carcinoma, Uterine serous/clear cell carcinoma, Osteosarcoma, Ovarian epithelial carcinoma, Colorectal adenocarcinoma, Acute myeloid leukemia (AML), Fallopian tube carcinoma, Peritoneal carcinoma, Pancreatic adenocarcinoma)
	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)
	SY-4835		Wee1 tyrosine kinase 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
MSI-High	MSI is associated with the loss or dysfunction of DNA mismatch repair (MMR) proteins that are required for correcting errors that occur during DNA replication or recombination; germline mutations in genes encoding MMR proteins are associated with Lynch syndrome, a hereditary cancer-predisposition syndrome also known as hereditary nonpolyposis colorectal cancer (HNPCC). [1-3]. Tumors exhibiting MSI have been reported to have increased numbers of tumor-infiltrating lymphocytes (TILs) and a significantly higher mutational burden than microsatellite stable (MSS) tumors. [4-7].	MSI has been reported to correlate with high levels of immune checkpoint gene expression in some types of cancer, including colorectal and endometrial carcinoma, and with clinical response to checkpoint inhibition in colorectal carcinoma; thus, immunotherapies may be relevant in tumors exhibiting MSI. [6,9]. Checkpoint inhibitors are currently in clinical development, several of which have received agency approval for certain indications. [10,11]. In fact, pembrolizumab has been FDA-approved as a second or later line of therapy for the treatment of pediatric and adult solid tumors with high microsatellite instability (MSI-H) or that are deficient in mismatch repair (dMMR), as a front-line therapy for colorectal carcinoma patients with MSI-H or dMMR, and endometrial carcinoma patients with MSI-H or dMMR, who are not eligible for curative surgery or radiation, following progression on systemic therapy. [9,13]. In addition, nivolumab and the combination of nivolumab and ipilimumab have been FDA-approved for the treatment of MSI-H or dMMR colorectal carcinoma. [14,15]. Dostarlimab in combination with carboplatin and paclitaxel, followed by dostarlimab as a single agent, has been FDA-approved for the treatment of primary advanced or recurrent dMMR or MSI-H endometrial carcinoma. [16-18]. In contrast, the combination of lenvatinib and pembrolizumab has been FDA-approved for the treatment of advanced endometrial cancer patients with unresectable tumors lacking markers for MSI-H and dMMR following disease progression on systemic therapy. [19].	
BRAF V600E	BRAF activating mutations or amplification have been reported to result in uncontrolled cell growth and tumorigenesis. [20,21].	Braf signals upstream of the MAPK pathway, and BRAF amplification or activating mutations may confer sensitivity to inhibitors of Braf and/or components of the MAPK pathway, including MEK. [22]. The BRAF V600-specific inhibitors vemurafenib and dabrafenib have been approved for the treatment of BRAF V600E-positive melanoma. [23,24]. In addition, the MEK inhibitors trametinib and cobimetinib (in combination with vemurafenib) have been FDA-approved for BRAF V600E-	In some studies, BRAF V600E mutation has been correlated with lack of response to approved anti-Egfr therapies such as cetuximab and panitumumab in CRC; patients with wild-type BRAF experienced a higher response rate when cetuximab was added to chemotherapy, compared to treatment with chemotherapy alone. [45,46]. Several retrospective analyses (including the CRYSTAL and OPUS studies) suggest that while BRAF mutation is a negative prognostic

Relevance of Detected Alterations

Alteration	Role in Disease	Effect on Drug Sensitivity	Effect on Drug Resistance
		and V600K-positive melanoma as has the encorafenib-binimetinib combination. [25-27]. Vemurafenib has additionally been approved for BRAF V600-positive Erdheim-Chester disease. [28]. Encorafenib in combination with cetuximab has been FDA-approved for the treatment of pretreated adult colorectal cancer patients with metastatic disease and harboring a BRAF V600E mutation, as detected by an FDA-approved test. [29-31]. BRAF encodes the signaling protein Braf, which is downstream of Ras and activates the MAPK pathway. [21]. Encorafenib in combination with binimetinib has been approved by the FDA for adult patients with metastatic non–small cell lung carcinoma with a BRAF V600E mutation. [32]. The combination of dabrafenib and trametinib has been FDA-approved for V600E/K-positive melanoma as well as V600E-positive solid tumor (excluding CRC), non-small cell lung carcinoma, anaplastic thyroid carcinoma, and pediatric low-grade glioma. [24,33-39]. The triple combination of atezolizumab plus cobimetinib and vemurafenib has also been FDA-approved for the treatment of V600E/K-positive melanoma. [40]. The pan-Raf inhibitor tovorafenib has been approved by the FDA for the treatment of pediatric patients 6 months of age and older with relapsed or refractory low-grade glioma harboring a BRAF fusion or rearrangement, or a BRAF V600 mutation. [41]. Early clinical data has shown limited activity of Braf inhibitor monotherapy in BRAF-mutant colorectal cancers, possibly due to Egfr activation, suggesting a possible requirement for combination therapy. [42-44].	marker, it is not predictive of response to cetuximab. [47-50].
PTEN N323fs	Loss of PTEN (through mutation or deletion) can lead to uncontrolled cell growth and suppression of apoptosis. [51]. PTEN haploinsufficiency has been associated with tumorigenesis in some tumor types, including astrocytoma and prostate cancer. [52-55]. PTEN germline mutations are found in several cancer-predisposition syndromes, such as Cowden syndrome and Proteus syndrome. [56]. Loss of PTEN has been reported to co-occur with BRAF V600 mutation in melanoma, and the combination has been associated	Because PTEN negatively regulates the PI3K/Akt/mTOR pathway, PTEN loss or mutation leads to activation of the PI3K pathway and may therefore predict sensitivity to inhibitors of the PI3K/Akt /mTOR pathway. [64]. The PI3K inhibitors alpelisib and copanlisib, the Akt inhibitor capivasertib, and the mTOR inhibitors everolimus and temsirolimus have been approved in specific cancer indications. These and other PI3K, Akt, and mTOR inhibitors, as well as dual PI3K/mTOR inhibitors are also currently in clinical trials, alone	Absence of Pten expression was associated with reduced efficacy of pembrolizumab or nivolumab in a cohort of 39 metastatic melanoma patients and PTEN loss has been suggested to contribute to resistance to the Braf inhibitor vemurafenib based on analysis of melanoma cell lines. [82,83]. Low PTEN mRNA expression has been associated with poor response to chemotherapy in a study of 100 osteosarcoma cases. [62].

Relevance of Detected Alterations

Alteration	Role in Disease	Effect on Drug Sensitivity	Effect on Drug Resistance
	with disease progression and decreased time to brain metastasis. [57-59]. Loss of Pten in combination with p53 loss has been reported to result in sarcoma development and progression in mice. [60,61]. Low PTEN mRNA expression has been associated with the presence of metastases in a study of 100 osteosarcoma cases. [62]. Loss of PTEN, together with other drivers of glioma tumorigenesis, including RB1 loss and KRAS activation, may drive progression from lower grade glioma to glioblastoma, as demonstrated in an astrocyte-specific inducible transgenic mouse model. [63].	or in combination with other therapies. [65-69]. The Akt inhibitor capivasertib has been approved by the FDA in combination with fulvestrant for the treatment of adult patients with hormone receptor positive, Her2 negative locally advanced or metastatic breast cancer with PIK3CA /AKT1/PTEN alterations as detected by an FDA-approved test following progression on at least one endocrine-based regimen in the metastatic setting or recurrence on or within 12 months of completing adjuvant therapy. [70]. In addition, preclinical studies have shown that PTEN-deficient tumors may be sensitive to PARP inhibitors, and PARP inhibitors are in clinical trials for patients with PTEN-deficient tumors. [71-78]. Response to mTOR inhibitors in endometrial cancer appears to be independent of molecular markers of PI3K/Akt pathway activation assessed with existing laboratory approaches. [79,80]. A Phase 2 trial of everolimus in 37 chemotherapy-naive patients with castration-resistant prostate cancer reported that loss of PTEN was associated with response and longer progression-free survival. [81].	
CDK12 M1028fs	Cdk12 is involved in transcriptional regulation of DNA damage-response genes, thereby serving a protective role shielding cells from genetic instability. [84].	Loss or inactivation of CDK12 has been reported to sensitize cancer cells to melphalan, cisplatin, and PARP inhibitors. [85,86]. The PARP inhibitor olaparib has been approved by the FDA for use in advanced ovarian cancer, metastatic Her2 negative breast cancer, and pancreatic adenocarcinoma patients with germline BRCA1 or BRCA2 mutations as well as for castration-resistant adult prostate cancer patients with tumors harboring germline or somatic alteration in one or more homologous recombination repair genes, including CDK12; rucaparib has been approved by the FDA for advanced ovarian cancer and castration-resistant prostate cancer patients with either germline or somatic BRCA1 or BRCA2 mutations. [87-95]. In addition, talazoparib in combination with enzalutamide has been FDA-approved for the treatment of metastatic castration-resistant prostate cancer patients with tumors harboring germline or somatic alteration in one or more homologous recombination repair genes, including CDK12. [96-98]. In addition, CDK12 alterations have	

Relevance of Detected Alterations

Alteration	Role in Disease	Effect on Drug Sensitivity	Effect on Drug Resistance
		been associated with tandem duplications across diverse tumor types and the utility of immune checkpoint inhibitors is under clinical investigation in patients with CDK12-altered prostate cancer. [99-107].	
FBXW7 W425*	FBXW7 inactivating mutations have been reported in a large variety of tumors and, combined with the oncogenic potential of several FBXW7 substrates, leads to the conclusion that FBXW7 is a general tumor suppressor. [108].	In preclinical studies, Fbxw7 inactivation stabilizes the mTOR signaling protein and confers sensitivity to rapamycin, an mTOR inhibitor. [109]. However, FBXW7 alterations have been shown to be not predictive of response to everolimus or temsirolimus in clinical studies. [110,111]. Other agents that target mTOR, including dual mTORC1/mTORC2 inhibitors and dual PI3K/mTOR inhibitors, are currently in preclinical and clinical development. [112-114].	Fbxw7 inactivation may result in resistance to several types of chemotherapy, based on results from preclinical studies. [115-121]. In colorectal cancers, concomitant KRAS mutation has been suggested to lead to lack of efficacy of mTOR inhibitors in FBXW7-mutated tumors. [110,123]. In addition, FBXW7 mutations have been associated with regorafenib resistance in a CRC cell model; loss of FBXW7 has been associated with decreased sensitivity of a colon cancer cell line and an intestinal organoid model to 5-Fluorouracil. [120,125]. One study of paclitaxel in combination with 5-Fluorouracil, epirubicin, and cylophosphamide (FEC) in 44 patients with node-negative breast cancer has reported disease progression at 120.6 months in 55.5% and 2.8% of patients with low and high Fbxw7 expression, respectively; of 41 patients treated with FEC alone, disease progression at 113.9 months was reported in 30% and 19% of patients with low and high Fbxw7 expression, respectively. [119].
ARID1A D1850fs	Loss of Arid1a has been associated with mismatch repair deficiency in cancer, including endometrial and colorectal carcinoma. [126-128].	There are no approved targeted therapies to address ARID1A alterations at this time; however, ARID1A alterations may predict sensitivity to Ezh2 inhibitors. [129]. Ezh2 inhibitors, such as tazemetostat, are currently being evaluated in clinical trials in patients with solid tumors or B-cell lymphomas. [130-132]. In addition, ARID1A-deficient preclinical cancer models exhibit sensitivity to Atr, PARP, and BET domain inhibitors and clinical trials are evaluating these agents in patients with loss of Arid1a expression or ARID1A mutations. [72,74,133-142].	
ARID1A G276fs	Loss of Arid1a has been associated with mismatch repair deficiency in cancer, including endometrial and colorectal carcinoma. [126-128].	There are no approved targeted therapies to address ARID1A alterations at this time; however, ARID1A alterations may predict sensitivity to Ezh2 inhibitors. [129]. Ezh2 inhibitors, such as tazemetostat, are currently being evaluated in clinical trials in patients with solid tumors or B-	

Relevance of Detected Alterations

Alteration	Role in Disease	Effect on Drug Sensitivity	Effect on Drug Resistance
		cell lymphomas. [130-132]. In addition, ARID1A-deficient preclinical cancer models exhibit sensitivity to Atr, PARP, and BET domain inhibitors and clinical trials are evaluating these agents in patients with loss of Arid1a expression or ARID1A mutations. [72,74,133-142].	
TP53 K373fs	Loss of tumor suppressor p53, which is encoded by the TP53 gene, is common in aggressive advanced cancers. [143]. 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. [144-146]. 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. [147-151].	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. [152-154]. 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. [155-157]. 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 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. [158-163].	Mutations in TP53 may increase resistance to ionizing radiation therapy. [164,165].

References

1. Lynch H, Lynch P, Lanspa S, Snyder C, Lynch J, Boland C "Review of the Lynch syndrome: history, molecular genetics, screening, differential diagnosis, and medicolegal ramifications." Clinical genetics(2009): 1-18
2. Colas C, Coulet F, Svrcek M, Collura A, Fléjou J, Duval A, Hamelin R "Lynch or not Lynch? Is that always a question?" Advances in cancer research(2012): 121-66
3. Heinimann K "Toward a molecular classification of colorectal cancer: the role of microsatellite instability status." Frontiers in oncology(2013): 272
4. Kim H, Jen J, Vogelstein B, Hamilton S "Clinical and pathological characteristics of sporadic colorectal carcinomas with DNA replication errors in microsatellite sequences." The American journal of pathology(1994): 148-56
5. Alexander J, Watanabe T, Wu T, Rashid A, Li S, Hamilton S "Histopathological identification of colon cancer with microsatellite instability." The American journal of pathology(2001): 527-35
6. Howitt B, Shukla S, Sholl L, Ritterhouse L, Watkins J, Rodig S, Stover E, Strickland K, D'Andrea A, Wu C, Matulonis U, Konstantinopoulos P "Association of Polymerase e-Mutated and Microsatellite-Instable Endometrial Cancers With Neoantigen Load, Number of Tumor-Infiltrating Lymphocytes, and Expression of PD-1 and PD-L1." JAMA oncology(2015): 1319-23
7. Timmermann B, Kerick M, Roehr C, Fischer A, Isau M, Boerno S, Wunderlich A, Barmeyer C, Seemann P, Koenig J, Lappe M, Kuss A, Garshasbi M, Bertram L, Trappe K, Werber M, Herrmann B, Zatloukal K, Lehrach H, Schweiger M "Somatic mutation profiles of MSI and MSS colorectal cancer identified by whole exome next generation sequencing and bioinformatics analysis." PloS one(2010): e15661
8. Llosa N, Cruise M, Tam A, Wicks E, Hechenbleikner E, Taube J, Blosser R, Fan H, Wang H, Luber B, Zhang M, Papadopoulos N, Kinzler K, Vogelstein B, Sears C, Anders R, Pardoll D, Housseau F "The vigorous immune microenvironment of microsatellite instable colon cancer is balanced by multiple counter-inhibitory checkpoints." Cancer discovery(2015): 43-51
9. Le D, Uram J, Wang H, Bartlett B, Kemberling H, Eyring A, Skora A, Luber B, Azad N, Laheru D, Biedrzycki B, Donehower R, Zaheer A, Fisher G, Crocenzi T, Lee J, Duffy S, Goldberg R, de la Chapelle A, Koshiji M, Bhaijee F, Huebner T, Hruban R, Wood L, Cuka N, Pardoll D, Papadopoulos N, Kinzler K, Zhou S, Cornish T, Taube J, Anders R, Eshleman J, Vogelstein B, Diaz L "PD-1 Blockade in Tumors with Mismatch-Repair Deficiency." The New England journal of medicine(2015): 2509-20
10. Migden M, Rischin D, Schmults C, Guminski A, Hauschild A, Lewis K, Chung C, Hernandez-Aya L, Lim A, Chang A, Rabinowits G, Thai A, Dunn L, Hughes B, Khushalani N, Modi B, Schadendorf D, Gao B, Seebach F, Li S, Li J, Mathias M, Booth J, Mohan K, Stankevich E, Babiker H, Brana I, Gil-Martin M, Homsi J, Johnson M, Moreno V, Niu J, Owonikoko T, Papadopoulos K, Yancopoulos G, Lowy I, Fury M "PD-1 Blockade with Cemiplimab in Advanced Cutaneous Squamous-Cell Carcinoma." The New England journal of medicine(2018): 341-351
11. Wang R, Wang H "Immune targets and neoantigens for cancer immunotherapy and precision medicine." Cell research(2017): 11-37
12. Lee V, Le D "Efficacy of PD-1 blockade in tumors with MMR deficiency." Immunotherapy(2016): 1-3
13. Andre T, Shiu K, Kim TW, et al. "Pembrolizumab versus chemotherapy for microsatellite instability-high/mismatch repair deficient metastatic colorectal cancer: The phase 3 KEYNOTE-177 study." J Clin Oncol(2020)
14. Overman M, Lonardi S, Wong K, Lenz H, Gelsomino F, Aglietta M, Morse M, Van Cutsem E, McDermott R, Hill A, Sawyer M, Hendlisz A, Neyns B, Svrcek M, Moss R, Ledeine J, Cao Z, Kamble S, Kopetz S, André T "Durable Clinical Benefit With Nivolumab Plus Ipilimumab in DNA Mismatch Repair-Deficient/Microsatellite Instability-High Metastatic Colorectal Cancer." Journal of clinical oncology : official journal of the American Society of Clinical Oncology(2018): 773-779
15. Overman M, McDermott R, Leach J, Lonardi S, Lenz H, Morse M, Desai J, Hill A, Axelson M, Moss R, Goldberg M, Cao Z, Ledeine J, Maglinte G, Kopetz S, André T "Nivolumab in patients with metastatic DNA mismatch repair-deficient or microsatellite instability-high colorectal cancer (CheckMate 142): an open-label, multicentre, phase 2 study." The Lancet. Oncology(2017): 1182-1191
16. Oaknin A, Tinker A, Gilbert L, Samouëlian V, Mathews C, Brown J, Barretina-Ginesta M, Moreno V, Gravina A, Abdeddaim C, Banerjee S, Guo W, Danaee H, Im E, Sabatier R "Clinical Activity and Safety of the Anti-Programmed Death 1 Monoclonal Antibody Dostarlimab for Patients With Recurrent or Advanced Mismatch Repair-Deficient Endometrial Cancer: A Nonrandomized Phase 1 Clinical Trial." JAMA oncology(2020): 1766-1772
17. Andre T, Berton D, Curigliano G, et al. "Safety and efficacy of anti–PD-1 antibody dostarlimab in patients (pts) with mismatch repair-deficient (dMMR) solid cancers: Results from GARNET study." J Clin Oncol(2021): Abstr 9
18. Mirza M, Chase D, Slomovitz B, dePont Christensen R, Novák Z, Black D, Gilbert L, Sharma S, Valabrega G, Landrum L, Hanker L, Stuckey A, Boere I, Gold M, Auranen A, Pothuri B, Cibula D, McCourt C, Raspagliesi F, Shahin M, Gill S, Monk B, Buscema J, Herzog T, Copeland L, Tian M, He Z, Stevens S, Zografos E, Coleman R, Powell M "Dostarlimab for Primary Advanced or Recurrent Endometrial Cancer." The New England journal of medicine(2023): 2145-2158
19. Makker V, Rasco D, Vogelzang N, Brose M, Cohn A, Mier J, Di Simone C, Hyman D, Stepan D, Dutcus C, Schmidt E, Guo M, Sachdev P, Shumaker R, Aghajanian C, Taylor M "Lenvatinib plus pembrolizumab in patients with advanced endometrial cancer: an interim analysis of a multicentre, open-label, single-arm, phase 2 trial." The Lancet. Oncology(2019): 711-718
20. Davies H, Bignell G, Cox C, Stephens P, Edkins S, Clegg S, Teague J, Woffendin H, Garnett M, Bottomley W, Davis N, Dicks E, Ewing R, Floyd Y, Gray K, Hall S, Hawes R, Hughes J, Kosmidou V, Menzies A, Mould C, Parker A, Stevens C, Watt S, Hooper S, Wilson R, Jayatilake H, Gusterson B, Cooper C, Shipley J, Hargrave D, Pritchard-Jones K, Maitland N, Chenevix-Trench G, Riggins G, Bigner D, Palmieri G, Cossu A, Flanagan A, Nicholson A, Ho J, Leung S, Yuen S, Weber B, Seigler H, Darrow T, Paterson H, Marais R, Marshall C, Wooster R, Stratton M, Futreal P "Mutations of the BRAF gene in human cancer." Nature(2002): 949-54
21. Vultur A, Villanueva J, Herlyn M "Targeting BRAF in advanced melanoma: a first step toward manageable disease." Clinical cancer research : an official journal of the American Association for Cancer Research(2011): 1658-63
22. Solit D, Garraway L, Pratilas C, Sawai A, Getz G, Basso A, Ye Q, Lobo J, She Y, Osman I, Golub T, Sebolt-Leopold J, Sellers W, Rosen N "BRAF mutation predicts sensitivity to MEK inhibition." Nature(2006): 358-62
23. Flaherty K, Puzanov I, Kim K, Ribas A, McArthur G, Sosman J, O'Dwyer P, Lee R, Grippo J, Nolop K, Chapman P "Inhibition of mutated, activated BRAF in metastatic melanoma." The New England journal of medicine(2010): 809-19
24. Flaherty K, Infante J, Daud A, Gonzalez R, Kefford R, Sosman J, Hamid O, Schuchter L, Cebon J, Ibrahim N, Kudchadkar R, Burris H, Falchook G, Algazi A, Lewis K, Long G, Puzanov I, Lebowitz P, Singh A, Little S, Sun P, Allred A, Ouellet D, Kim K, Patel K, Weber J "Combined BRAF and MEK inhibition in melanoma with BRAF V600 mutations." The New England journal of medicine(2012): 1694-703
25. Flaherty K, Robert C, Hersey P, Nathan P, Garbe C, Milhem M, Demidov L, Hassel J, Rutkowski P, Mohr P, Dummer R, Trefzer U, Larkin J, Utikal J, Dreno B, Nyakas M, Middleton M, Becker J, Casey M, Sherman L, Wu F, Ouellet D, Martin A, Patel K, Schadendorf D "Improved survival with MEK inhibition in BRAF-mutated melanoma." The New England journal of medicine(2012): 107-14

References

26. Larkin J, Ascierto P, Dréno B, Atkinson V, Liszkay G, Maio M, Mandalà M, Demidov L, Stroyakovskiy D, Thomas L, de la Cruz-Merino L, Dutriaux C, Garbe C, Sovak M, Chang I, Choong N, Hack S, McArthur G, Ribas A "Combined vemurafenib and cobimetinib in BRAF-mutated melanoma." The New England journal of medicine(2014): 1867-76

27. Dummer R, Ascierto P, Gogas H, Arance A, Mandala M, Liszkay G, Garbe C, Schadendorf D, Krajsova I, Gutzmer R, Chiarion-Sileni V, Dutriaux C, de Groot J, Yamazaki N, Loquai C, Moutouh-de Parseval L, Pickard M, Sandor V, Robert C, Flaherty K "Encorafenib plus binimetinib versus vemurafenib or encorafenib in patients with BRAF-mutant melanoma (COLUMBUS): a multicentre, open-label, randomised phase 3 trial." The Lancet. Oncology(2018): 603-615

28. Diamond E, Subbiah V, Lockhart A, Blay J, Puzanov I, Chau I, Raje N, Wolf J, Erinjeri J, Torrisi J, Lacouture M, Elez E, Martínez-Valle F, Durham B, Arcila M, Ulaner G, Abdel-Wahab O, Pitcher B, Makrutzki M, Riehl T, Baselga J, Hyman D "Vemurafenib for BRAF V600-Mutant Erdheim-Chester Disease and Langerhans Cell Histiocytosis: Analysis of Data From the Histology-Independent, Phase 2, Open-label VE-BASKET Study." JAMA oncology(2018): 384-388

29. "A Multicenter, Randomized, Open-label, 3-Arm Phase 3 Study of Encorafenib + Cetuximab Plus or Minus Binimetinib vs. Irinotecan/Cetuximab or Infusional 5-Fluorouracil (5-FU)/Folinic Acid (FA) /Irinotecan (FOLFIRI)/Cetuximab With a Safety Lead-in of Encorafenib + Binimetinib + Cetuximab in Patients With BRAF V600E-mutant Metastatic Colorectal Cancer" (2019)

30. Kopetz S, Grothey A, Cutsem EV, et al. "Encorafenib plus cetuximab with or without binimetinib for BRAF V600E-mutant metastatic colorectal cancer: Quality-of-life results from a randomized, three-arm, phase III study versus the choice of either irinotecan or FOLFIRI plus cetuximab (BEACON CRC)." J Clin Onc(2020): suppl 8

31. Kopetz S, Grothey A, Yaeger R, Van Cutsem E, Desai J, Yoshino T, Wasan H, Ciardiello F, Loupakis F, Hong Y, Steeghs N, Guren T, Arkenau H, Garcia-Alfonso P, Pfeiffer P, Orlov S, Lonardi S, Elez E, Kim T, Schellens J, Guo C, Krishnan A, Dekervel J, Morris V, Calvo Ferrandiz A, Tarpgaard L, Braun M, Gollerkeri A, Keir C, Maharry K, Pickard M, Christy-Bittel J, Anderson L, Sandor V, Tabernero J "Encorafenib, Binimetinib, and Cetuximab in BRAF V600E-Mutated Colorectal Cancer." The New England journal of medicine(2019): 1632-1643

32. Riely G, Smit E, Ahn M, Felip E, Ramalingam S, Tsao A, Johnson M, Gelsomino F, Esper R, Nadal E, Offin M, Provencio M, Clarke J, Hussain M, Otterson G, Dagogo-Jack I, Goldman J, Morgensztern D, Alcasid A, Usari T, Wissel P, Wilner K, Pathan N, Tonkovyd S, Johnson B "Phase II, Open-Label Study of Encorafenib Plus Binimetinib in Patients With BRAFV600-Mutant Metastatic Non-Small-Cell Lung Cancer." Journal of clinical oncology : official journal of the American Society of Clinical Oncology (2023): 3700-3711

33. Hyman D, Puzanov I, Subbiah V, Faris J, Chau I, Blay J, Wolf J, Raje N, Diamond E, Hollebecque A, Gervais R, Elez-Fernandez M, Italiano A, Hofheinz R, Hidalgo M, Chan E, Schuler M, Lasserre S, Makrutzki M, Sirzen F, Veronese M, Tabernero J, Baselga J "Vemurafenib in Multiple Nonmelanoma Cancers with BRAF V600 Mutations." The New England journal of medicine(2015): 726-36

34. Planchard D, Besse B, Groen H, Souquet P, Quoix E, Baik C, Barlesi F, Kim T, Mazieres J, Novello S, Rigas J, Upalawanna A, D'Amelio A, Zhang P, Mookerjee B, Johnson B "Dabrafenib plus trametinib in patients with previously treated BRAF(V600E)-mutant metastatic non-small cell lung cancer: an open-label, multicentre phase 2 trial." The Lancet. Oncology(2016): 984-993

35. Long G, Stroyakovskiy D, Gogas H, Levchenko E, de Braud F, Larkin J, Garbe C, Jouary T, Hauschild A, Grob J, Chiarion-Sileni V, Lebbe C, Mandalà M, Millward M, Arance A, Bondarenko I, Haanen J, Hansson J, Utikal J, Ferraresi V, Kovalenko N, Mohr P, Probachai V, Schadendorf D, Nathan P, Robert C, Ribas A, DeMarini D, Irani J, Swann S, Legos J, Jin F, Mookerjee B, Flaherty K "Dabrafenib and trametinib versus dabrafenib and placebo for Val600 BRAF-mutant melanoma: a multicentre, double-blind, phase 3 randomised controlled trial." Lancet (London, England)(2015): 444-51

36. Subbiah V, Kreitman R, Wainberg Z, Cho J, Schellens J, Soria J, Wen P, Zielinski C, Cabanillas M, Urbanowitz G, Mookerjee B, Wang D, Rangwala F, Keam B "Dabrafenib and Trametinib Treatment in Patients With Locally Advanced or Metastatic BRAF V600-Mutant Anaplastic Thyroid Cancer." Journal of clinical oncology : official journal of the American Society of Clinical Oncology(2018): 7-13

37. Salama A, Li S, Macrae E, Park J, Mitchell E, Zwiebel J, Chen H, Gray R, McShane L, Rubinstein L, Patton D, Williams P, Hamilton S, Armstrong D, Conley B, Arteaga C, Harris L, O'Dwyer P, Chen A, Flaherty K "Dabrafenib and Trametinib in Patients With Tumors With BRAFV600E Mutations: Results of the NCI-MATCH Trial Subprotocol H." Journal of clinical oncology : official journal of the American Society of Clinical Oncology(2020): 3895-3904

38. Subbiah V, Lassen U, Élez E, Italiano A, Curigliano G, Javle M, de Braud F, Prager G, Greil R, Stein A, Fasolo A, Schellens J, Wen P, Viele K, Boran A, Gasal E, Burgess P, Ilankumaran P, Wainberg Z "Dabrafenib plus trametinib in patients with BRAFV600E-mutated biliary tract cancer (ROAR): a phase 2, open-label, single-arm, multicentre basket trial." The Lancet. Oncology(2020): 1234-1243

39. Bouffet E, Hansford J, Garré ML, et al. "Primary analysis of a phase II trial of dabrafenib plus trametinib (dab + tram) in BRAF V600–mutant pediatric low-grade glioma (pLGG)" J Clin Oncol(2022): Abstract LBA2002

40. McArthur GA, Stroyakovskiy D, Gogas H, et al. "Evaluation of atezolizumab (A), cobimetinib (C), and vemurafenib (V) in previously untreated patients with BRAFV600 mutation-positive advanced melanoma: Primary results from the phase 3 IMspire150 trial" AACR 2020 Online Proceedings(2020): CT012

41. Kilburn L, Khuong-Quang D, Hansford J, Landi D, van der Lugt J, Leary S, Driever P, Bailey S, Perreault S, McCowage G, Waanders A, Ziegler D, Witt O, Baxter P, Kang H, Hassall T, Han J, Hargrave D, Franson A, Yalon Oren M, Toledano H, Larouche V, Kline C, Abdelbaki M, Jabado N, Gottardo N, Gerber N, Whipple N, Segal D, Chi S, Oren L, Tan E, Mueller S, Cornelio I, McLeod L, Zhao X, Walter A, Da Costa D, Manley P, Blackman S, Packer R, Nysom K "The type II RAF inhibitor tovorafenib in relapsed/refractory pediatric low-grade glioma: the phase 2 FIREFLY-1 trial." Nature medicine(2024): 207-217

42. Dienstmann R, Serpico D, Rodon J, Saura C, Macarulla T, Elez E, Alsina M, Capdevila J, Perez-Garcia J, Sánchez-Ollé G, Aura C, Prudkin L, Landolfi S, Hernández-Losa J, Vivancos A, Tabernero J "Molecular profiling of patients with colorectal cancer and matched targeted therapy in phase I clinical trials." Molecular cancer therapeutics (2012): 2062-71

43. Corcoran R, Ebi H, Turke A, Coffee E, Nishino M, Cogdill A, Brown R, Della Pelle P, Dias-Santagata D, Hung K, Flaherty K, Piris A, Wargo J, Settleman J, Mino-Kenudson M, Engelman J "EGFR-mediated re-activation of MAPK signaling contributes to insensitivity of BRAF mutant colorectal cancers to RAF inhibition with vemurafenib." Cancer discovery(2012): 227-35

44. Prahallad A, Sun C, Huang S, Di Nicolantonio F, Salazar R, Zecchin D, Beijersbergen R, Bardelli A, Bernards R "Unresponsiveness of colon cancer to BRAF(V600E) inhibition through feedback activation of EGFR." Nature(2012): 100-3

45. Di Nicolantonio F, Martini M, Molinari F, Sartore-Bianchi A, Arena S, Saletti P, De Dosso S, Mazzucchelli L, Frattini M, Siena S, Bardelli A "Wild-type BRAF is required for response to panitumumab or cetuximab in metastatic colorectal cancer." Journal of clinical oncology : official journal of the American Society of Clinical Oncology(2008): 5705-12

46. Cui D, Cao D, Yang Y, Qiu M, Huang Y, Yi C "Effect of BRAF V600E mutation on tumor response of anti-EGFR monoclonal antibodies for first-line metastatic colorectal cancer treatment: a meta-analysis of randomized studies." Molecular biology reports(2014): 1291-8

47. Bokemeyer C, Van Cutsem E, Rougier P, Ciardiello F, Heeger S, Schlichting M, Celik I, Köhne C "Addition of cetuximab to chemotherapy as first-line treatment for KRAS wild-type metastatic colorectal cancer: pooled analysis of the CRYSTAL and OPUS randomised clinical trials." European journal of cancer (Oxford, England : 1990)(2012): 1466-75

References

48. Tol J, Nagtegaal I, Punt C "BRAF mutation in metastatic colorectal cancer." The New England journal of medicine(2009): 98-9
49. Karapetis C, Jonker D, Daneshmand M, Hanson J, O'Callaghan C, Marginean C, Zalcberg J, Simes J, Moore M, Tebbutt N, Price T, Shapiro J, Pavlakis N, Gibbs P, Van Hazel G, Lee U, Haq R, Virk S, Tu D, Lorimer I "PIK3CA, BRAF, and PTEN status and benefit from cetuximab in the treatment of advanced colorectal cancer--results from NCIC CTG/AGITG CO.17." Clinical cancer research : an official journal of the American Association for Cancer Research(2014): 744-53
50. Pietrantonio F, Petrelli F, Coinu A, Di Bartolomeo M, Borgonovo K, Maggi C, Cabiddu M, Iacovelli R, Bossi I, Lonati V, Ghilardi M, de Braud F, Barni S "Predictive role of BRAF mutations in patients with advanced colorectal cancer receiving cetuximab and panitumumab: a meta-analysis." European journal of cancer (Oxford, England : 1990)(2015): 587-94
51. Staal F, van der Luijt R, Baert M, van Drunen J, van Bakel H, Peters E, de Valk I, van Amstel H, Taphoorn M, Jansen G, van Veelen C, Burgering B, Staal G "A novel germline mutation of PTEN associated with brain tumours of multiple lineages." British journal of cancer(2002): 1586-91
52. Couto S, Cao M, Duarte P, Banach-Petrosky W, Wang S, Romanienko P, Wu H, Cardiff R, Abate-Shen C, Cunha G "Simultaneous haploinsufficiency of Pten and Trp53 tumor suppressor genes accelerates tumorigenesis in a mouse model of prostate cancer." Differentiation; research in biological diversity(2009): 103-11
53. Kwon C, Zhao D, Chen J, Alcantara S, Li Y, Burns D, Mason R, Lee E, Wu H, Parada L "Pten haploinsufficiency accelerates formation of high-grade astrocytomas." Cancer research(2008): 3286-94
54. Kwabi-Addo B, Giri D, Schmidt K, Podsypanina K, Parsons R, Greenberg N, Ittmann M "Haploinsufficiency of the Pten tumor suppressor gene promotes prostate cancer progression." Proceedings of the National Academy of Sciences of the United States of America(2001): 11563-8
55. Velickovic M, Delahunt B, McIver B, Grebe S "Intragenic PTEN/MMAC1 loss of heterozygosity in conventional (clear-cell) renal cell carcinoma is associated with poor patient prognosis." Modern pathology : an official journal of the United States and Canadian Academy of Pathology, Inc(2002): 479-85
56. Hollander M, Blumenthal G, Dennis P "PTEN loss in the continuum of common cancers, rare syndromes and mouse models." Nature reviews. Cancer(2011): 289-301
57. Bucheit A, Chen G, Siroy A, Tetzlaff M, Broaddus R, Milton D, Fox P, Bassett R, Hwu P, Gershenwald J, Lazar A, Davies M "Complete loss of PTEN protein expression correlates with shorter time to brain metastasis and survival in stage IIIB/C melanoma patients with BRAFV600 mutations." Clinical cancer research : an official journal of the American Association for Cancer Research(2014): 5527-36
58. Curtin J, Fridlyand J, Kageshita T, Patel H, Busam K, Kutzner H, Cho K, Aiba S, Bröcker E, LeBoit P, Pinkel D, Bastian B "Distinct sets of genetic alterations in melanoma." The New England journal of medicine(2005): 2135-47
59. Silva J, Bulman C, McMahon M "BRAFV600E cooperates with PI3K signaling, independent of AKT, to regulate melanoma cell proliferation." Molecular cancer research : MCR(2014): 447-63
60. Guijarro M, Dahiya S, Danielson L, Segura M, Vales-Lara F, Menendez S, Popiolek D, Mittal K, Wei J, Zavadil J, Cordon-Cardo C, Pandolfi P, Hernando E "Dual Pten/Tp53 suppression promotes sarcoma progression by activating Notch signaling." The American journal of pathology(2013): 2015-27
61. Puzio-Kuter A, Laddha S, Castillo-Martin M, Sun Y, Cordon-Cardo C, Chan C, Levine A "Involvement of tumor suppressors PTEN and p53 in the formation of multiple subtypes of liposarcoma." Cell death and differentiation(2015): 1785-91
62. Tian Z, Guo B, Yu M, Wang C, Zhang H, Liang Q, Jiang K, Cao L "Upregulation of micro-ribonucleic acid-128 cooperating with downregulation of PTEN confers metastatic potential and unfavorable prognosis in patients with primary osteosarcoma." OncoTargets and therapy(2014): 1601-8
63. Song Y, Zhang Q, Kutlu B, Difilippantonio S, Bash R, Gilbert D, Yin C, O'Sullivan T, Yang C, Kozlov S, Bullitt E, McCarthy K, Kafri T, Louis D, Miller C, Hood L, Van Dyke T "Evolutionary etiology of high-grade astrocytomas." Proceedings of the National Academy of Sciences of the United States of America(2013): 17933-8
64. Wu R, Hu T, Rehemtulla A, Fearon E, Cho K "Preclinical testing of PI3K/AKT/mTOR signaling inhibitors in a mouse model of ovarian endometrioid adenocarcinoma." Clinical cancer research : an official journal of the American Association for Cancer Research(2011): 7359-72
65. Dreyling M, Santoro A, Mollica L, et al. "COPANLISIB IN PATIENTS WITH RELAPSED OR REFRACTORY INDOLENT B-CELL LYMPHOMA (CHRONOS-1)" J Clin Oncol (2017): Abstract 108
66. André F, Ciruelos E, Rubovszky G, Campone M, Loibl S, Rugo H, Iwata H, Conte P, Mayer I, Kaufman B, Yamashita T, Lu Y, Inoue K, Takahashi M, Pápai Z, Longin A, Mills D, Wilke C, Hirawat S, Juric D "Alpelisib for PIK3CA-Mutated, Hormone Receptor-Positive Advanced Breast Cancer." The New England journal of medicine(2019): 1929-1940
67. Massacesi C, di Tomaso E, Fretault N, Hirawat S "Challenges in the clinical development of PI3K inhibitors." Annals of the New York Academy of Sciences(2013): 19-23
68. Janku F, Tsimberidou A, Garrido-Laguna I, Wang X, Luthra R, Hong D, Naing A, Falchook G, Moroney J, Piha-Paul S, Wheler J, Moulder S, Fu S, Kurzrock R "PIK3CA mutations in patients with advanced cancers treated with PI3K/AKT/mTOR axis inhibitors." Molecular cancer therapeutics(2011): 558-65
69. Grunt T, Mariani G "Novel approaches for molecular targeted therapy of breast cancer: interfering with PI3K/AKT/mTOR signaling." Current cancer drug targets(2013): 188-204
70. Turner N, Oliveira M, Howell S, et al. "Capivasertib and fulvestrant for patients with aromatase inhibitor-resistant hormone receptor-positive/human epidermal growth factor receptor 2-negative advanced breast cancer: results from the Phase III CAPItello-291 trial" Cancer Research(2023)
71. "Study of Induction SBRT and Olaparib Followed by Combination Pembrolizumab/Olaparib in Gastric and Gastroesophageal Junction (GEJ) Cancers" (2023)
72. "A Phase II Study of Olaparib in Patients With Advanced Biliary Tract Cancer With Aberrant DNA Repair Gene Mutations" (2023)
73. "Combination of HX008 And Niraparib in GErm-line-mutAted Metastatic Breast Cancer: a muLti-centEr Phase II Study" (2022)
74. "A Phase II Trial of the PARP Inhibitor, Niraparib, in BAP1 and Other DNA Damage Response (DDR) Pathway Deficient Neoplasms (UF-STO-ETI-001)" (2023)
75. "A Phase II Clinical Trial of the PARP Inhibitor Talazoparib in BRCA1 and BRCA2 Wild Type Patients With Advanced Triple Negative Breast Cancer and Homologous Recombination Deficiency or Advanced HER2 Negative Breast Cancer or Other Solid Tumors With a Mutation in Homologous Recombination Pathway Genes" (2023)
76. Mendes-Pereira A, Martin S, Brough R, McCarthy A, Taylor J, Kim J, Waldman T, Lord C, Ashworth A "Synthetic lethal targeting of PTEN mutant cells with PARP inhibitors." EMBO molecular medicine(2009): 315-22
77. Dedes K, Wetterskog D, Mendes-Pereira A, Natrajan R, Lambros M, Geyer F, Vatcheva R, Savage K, Mackay A, Lord C, Ashworth A, Reis-Filho J "PTEN deficiency in endometrioid endometrial adenocarcinomas predicts sensitivity to PARP inhibitors." Science translational medicine(2010): 53ra75

References

78. McEllin B, Camacho C, Mukherjee B, Hahm B, Tomimatsu N, Bachoo R, Burma S "PTEN loss compromises homologous recombination repair in astrocytes: implications for glioblastoma therapy with temozolomide or poly(ADP-ribose) polymerase inhibitors." Cancer research(2010): 5457-64

79. Oza A, Elit L, Tsao M, Kamel-Reid S, Biagi J, Provencher D, Gotlieb W, Hoskins P, Ghatage P, Tonkin K, Mackay H, Mazurka J, Sederias J, Ivy P, Dancey J, Eisenhauer E "Phase II study of temsirolimus in women with recurrent or metastatic endometrial cancer: a trial of the NCIC Clinical Trials Group." Journal of clinical oncology : official journal of the American Society of Clinical Oncology(2011): 3278-85

80. Trédan O, Treilleux I, Wang Q, Gane N, Pissaloux D, Bonnin N, Petit T, Cretin J, Bonichon-Lamichhane N, Priou F, Lavau-Denes S, Mari V, Freyer G, Lebrun D, Alexandre J, Ray-Coquard I "Predicting everolimus treatment efficacy in patients with advanced endometrial carcinoma: a GINECO group study." Targeted oncology(2013): 243-51

81. Templeton A, Dutoit V, Cathomas R, Rothermundt C, Bärtschi D, Dröge C, Gautschi O, Borner M, Fechter E, Stenner F, Winterhalder R, Müller B, Schiess R, Wild P, Rüschoff J, Thalmann G, Dietrich P, Aebersold R, Klingbiel D, Gillessen S "Phase 2 trial of single-agent everolimus in chemotherapy-naive patients with castration-resistant prostate cancer (SAKK 08/08)." European urology(2013): 150-8

82. Peng W, Chen J, Liu C, Malu S, Creasy C, Tetzlaff M, Xu C, McKenzie J, Zhang C, Liang X, Williams L, Deng W, Chen G, Mbofung R, Lazar A, Torres-Cabala C, Cooper Z, Chen P, Tieu T, Spranger S, Yu X, Bernatchez C, Forget M, Haymaker C, Amaria R, McQuade J, Glitza I, Cascone T, Li H, Kwong L, Heffernan T, Hu J, Bassett R, Bosenberg M, Woodman S, Overwijk W, Lizée G, Roszik J, Gajewski T, Wargo J, Gershenwald J, Radvanyi L, Davies M, Hwu P "Loss of PTEN Promotes Resistance to T Cell-Mediated Immunotherapy." Cancer discovery(2016): 202-16

83. Paraiso K, Xiang Y, Rebecca V, Abel E, Chen Y, Munko A, Wood E, Fedorenko I, Sondak V, Anderson A, Ribas A, Palma M, Nathanson K, Koomen J, Messina J, Smalley K "PTEN loss confers BRAF inhibitor resistance to melanoma cells through the suppression of BIM expression." Cancer research(2011): 2750-60

84. Blazek D, Kohoutek J, Bartholomeeusen K, Johansen E, Hulinkova P, Luo Z, Cimermancic P, Ule J, Peterlin B "The Cyclin K/Cdk12 complex maintains genomic stability via regulation of expression of DNA damage response genes." Genes & development(2011): 2158-72

85. Bajrami I, Frankum J, Konde A, Miller R, Rehman F, Brough R, Campbell J, Sims D, Rafiq R, Hooper S, Chen L, Kozarewa I, Assiotis I, Fenwick K, Natrajan R, Lord C, Ashworth A "Genome-wide profiling of genetic synthetic lethality identifies CDK12 as a novel determinant of PARP1/2 inhibitor sensitivity." Cancer research(2014): 287-97

86. Joshi P, Sutor S, Huntoon C, Karnitz L "Ovarian cancer-associated mutations disable catalytic activity of CDK12, a kinase that promotes homologous recombination repair and resistance to cisplatin and poly(ADP-ribose) polymerase inhibitors." The Journal of biological chemistry(2014): 9247-53

87. Ledermann J, Harter P, Gourley C, Friedlander M, Vergote I, Rustin G, Scott C, Meier W, Shapira-Frommer R, Safra T, Matei D, Macpherson E, Watkins C, Carmichael J, Matulonis U "Olaparib maintenance therapy in platinum-sensitive relapsed ovarian cancer." The New England journal of medicine(2012): 1382-92

88. Kim G, Ison G, McKee A, Zhang H, Tang S, Gwise T, Sridhara R, Lee E, Tzou A, Philip R, Chiu H, Ricks T, Palmby T, Russell A, Ladouceur G, Pfuma E, Li H, Zhao L, Liu Q, Venugopal R, Ibrahim A, Pazdur R "FDA Approval Summary: Olaparib Monotherapy in Patients with Deleterious Germline BRCA-Mutated Advanced Ovarian Cancer Treated with Three or More Lines of Chemotherapy." Clinical cancer research : an official journal of the American Association for Cancer Research(2015): 4257-61

89. Swisher E, Lin K, Oza A, Scott C, Giordano H, Sun J, Konecny G, Coleman R, Tinker A, O'Malley D, Kristeleit R, Ma L, Bell-McGuinn K, Brenton J, Cragun J, Oaknin A, Ray-Coquard I, Harrell M, Mann E, Kaufmann S, Floquet A, Leary A, Harding T, Goble S, Maloney L, Isaacson J, Allen A, Rolfe L, Yelensky R, Raponi M, McNeish I "Rucaparib in relapsed, platinum-sensitive high-grade ovarian carcinoma (ARIEL2 Part 1): an international, multicentre, open-label, phase 2 trial." The Lancet. Oncology (2017): 75-87

90. Balasubramaniam S, Beaver J, Horton S, Fernandes L, Tang S, Horne H, Liu J, Liu C, Schrieber S, Yu J, Song P, Pierce W, Robertson K, Palmby T, Chiu H, Lee E, Philip R, Schuck R, Charlab R, Banerjee A, Chen X, Wang X, Goldberg K, Sridhara R, Kim G, Pazdur R "FDA Approval Summary: Rucaparib for the Treatment of Patients with Deleterious BRCA Mutation-Associated Advanced Ovarian Cancer." Clinical cancer research : an official journal of the American Association for Cancer Research(2017): 7165-7170

91. Coleman R, Oza A, Lorusso D, Aghajanian C, Oaknin A, Dean A, Colombo N, Weberpals J, Clamp A, Scambia G, Leary A, Holloway R, Gancedo M, Fong P, Goh J, O'Malley D, Armstrong D, Garcia-Donas J, Swisher E, Floquet A, Konecny G, McNeish I, Scott C, Cameron T, Maloney L, Isaacson J, Goble S, Grace C, Harding T, Raponi M, Sun J, Lin K, Giordano H, Ledermann J "Rucaparib maintenance treatment for recurrent ovarian carcinoma after response to platinum therapy (ARIEL3): a randomised, double-blind, placebo-controlled, phase 3 trial." Lancet (London, England)(2017): 1949-1961

92. Robson M, Im S, Senkus E, Xu B, Domchek S, Masuda N, Delaloge S, Li W, Tung N, Armstrong A, Wu W, Goessl C, Runswick S, Conte P "Olaparib for Metastatic Breast Cancer in Patients with a Germline BRCA Mutation." The New England journal of medicine(2017): 523-533

93. Robson M, Tung N, Conte P, Im S, Senkus E, Xu B, Masuda N, Delaloge S, Li W, Armstrong A, Wu W, Goessl C, Runswick S, Domchek S "OlympiAD final overall survival and tolerability results: Olaparib versus chemotherapy treatment of physician's choice in patients with a germline BRCA mutation and HER2-negative metastatic breast cancer." Annals of oncology : official journal of the European Society for Medical Oncology(2019): 558-566

94. Golan T, Hammel P, Reni M, Van Cutsem E, Macarulla T, Hall M, Park J, Hochhauser D, Arnold D, Oh D, Reinacher-Schick A, Tortora G, Algül H, O'Reilly E, McGuinness D, Cui K, Schlienger K, Locker G, Kindler H "Maintenance Olaparib for Germline BRCA-Mutated Metastatic Pancreatic Cancer." The New England journal of medicine (2019): 317-327

95. Abida W, Patnaik A, Campbell D, Shapiro J, Bryce A, McDermott R, Sautois B, Vogelzang N, Bambury R, Voog E, Zhang J, Piulats J, Ryan C, Merseburger A, Daugaard G, Heidenreich A, Fizazi K, Higano C, Krieger L, Sternberg C, Watkins S, Despain D, Simmons A, Loehr A, Dowson M, Golsorkhi T, Chowdhury S "Rucaparib in Men With Metastatic Castration-Resistant Prostate Cancer Harboring a BRCA1 or BRCA2 Gene Alteration." Journal of clinical oncology : official journal of the American Society of Clinical Oncology(2020): 3763-3772

96. "A PHASE 3, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY OF TALAZOPARIB WITH ENZALUTAMIDE IN METASTATIC CASTRATION-RESISTANT PROSTATE CANCER" (2023)

97. Agarwal N, Azad A, Carles J, et al. "TALAPRO-2: Phase 3 study of talazoparib (TALA) + enzalutamide (ENZA) versus placebo (PBO) + ENZA as first-line (1L) treatment in patients (pts) with metastatic castration-resistant prostate cancer (mCRPC)." J Clin Oncol(2023): LBA17

98. Agarwal N, Azad A, Carles J, Fay A, Matsubara N, Heinrich D, Szczylik C, De Giorgi U, Young Joung J, Fong P, Voog E, Jones R, Shore N, Dunshee C, Zschäbitz S, Oldenburg J, Lin X, Healy C, Di Santo N, Zohren F, Fizazi K "Talazoparib plus enzalutamide in men with first-line metastatic castration-resistant prostate cancer (TALAPRO-2): a randomised, placebo-controlled, phase 3 trial." Lancet (London, England)(2023): 291-303

99. "IMPACT: Immunotherapy in Patients With Metastatic Cancers and CDK12 Mutations" (2020)

100. "A Phase 2 Study of a Checkpoint Inhibitor in Men With Progressive Metastatic Castrate Resistant Prostate Cancer Characterized by a Mismatch Repair Deficiency or Biallelic CDK12 Inactivation" (2020)

101. "Nivolumab as a Non-Castrating Therapy for MMR-deficient and CDK12- Altered Prostate Cancer With PSA Recurrence After Local Therapy" (2021)

102. "A Phase II Multi-Center Trial of Abemaciclib With or Without Atezolizumab in Metastatic Castration Resistant Prostate Cancer" (2021)

References

103. Antonarakis E, Isaacsson Velho P, Fu W, Wang H, Agarwal N, Sacristan Santos V, Maughan B, Pili R, Adra N, Sternberg C, Vlachostergios P, Tagawa S, Bryce A, McNatty A, Reichert Z, Dreicer R, Sartor O, Lotan T, Hussain M "CDK12-Altered Prostate Cancer: Clinical Features and Therapeutic Outcomes to Standard Systemic Therapies, Poly (ADP-Ribose) Polymerase Inhibitors, and PD-1 Inhibitors." JCO precision oncology(2020): 370-381

104. Rescigno P, Gurel B, Pereira R, Crespo M, Rekowski J, Rediti M, Barrero M, Mateo J, Bianchini D, Messina C, Fenor de la Maza M, Chandran K, Carmichael J, Guo C, Paschalis A, Sharp A, Seed G, Figueiredo I, Lambros M, Miranda S, Ferreira A, Bertan C, Riisnaes R, Porta N, Yuan W, Carreira S, de Bono J "Characterizing CDK12-Mutated Prostate Cancers." Clinical cancer research : an official journal of the American Association for Cancer Research(2021): 566-574

105. Schweizer M, Ha G, Gulati R, Brown L, McKay R, Dorff T, Hoge A, Reichel J, Vats P, Kilari D, Patel V, Oh W, Chinnaiyan A, Pritchard C, Armstrong A, Montgomery R, Alva A "CDK12-Mutated Prostate Cancer: Clinical Outcomes With Standard Therapies and Immune Checkpoint Blockade." JCO precision oncology(2020): 382-392

106. Li Y, Zhang H, Li Q, Zou P, Huang X, Wu C, Tan L "CDK12/13 inhibition induces immunogenic cell death and enhances anti-PD-1 anticancer activity in breast cancer." Cancer letters(2020): 12-21

107. Sokol E, Pavlick D, Frampton G, Ross J, Miller V, Ali S, Lotan T, Pardoll D, Chung J, Antonarakis E "Pan-Cancer Analysis of CDK12 Loss-of-Function Alterations and Their Association with the Focal Tandem-Duplicator Phenotype." The oncologist(2019): 1526-1533

108. Akhoondi S, Sun D, von der Lehr N, Apostolidou S, Klotz K, Maljukova A, Cepeda D, Fiegl H, Dafou D, Marth C, Mueller-Holzner E, Corcoran M, Dagnell M, Nejad S, Nayer B, Zali M, Hansson J, Egyhazi S, Petersson F, Sangfelt P, Nordgren H, Grander D, Reed S, Widschwendter M, Sangfelt O, Spruck C "FBXW7/hCDC4 is a general tumor suppressor in human cancer." Cancer research(2007): 9006-12

109. Mao J, Kim I, Wu D, Climent J, Kang H, DelRosario R, Balmain A "FBXW7 targets mTOR for degradation and cooperates with PTEN in tumor suppression." Science (New York, N.Y.)(2008): 1499-502

110. Jardim D, Wheler J, Hess K, Tsimberidou A, Zinner R, Janku F, Subbiah V, Naing A, Piha-Paul S, Westin S, Roy-Chowdhuri S, Meric-Bernstam F, Hong D "FBXW7 mutations in patients with advanced cancers: clinical and molecular characteristics and outcomes with mTOR inhibitors." PloS one(2014): e89388

111. Myers A, Filiaci V, Zhang Y, Pearl M, Behbakht K, Makker V, Hanjani P, Zweizig S, Burke J, Downey G, Leslie K, Van Hummelen P, Birrer M, Fleming G "Tumor mutational analysis of GOG248, a phase II study of temsirolimus or temsirolimus and alternating megestrol acetate and tamoxifen for advanced endometrial cancer (EC): An NRG Oncology/Gynecologic Oncology Group study." Gynecologic oncology(2016): 43-8

112. Wallin J, Edgar K, Guan J, Berry M, Prior W, Lee L, Lesnick J, Lewis C, Nonomiya J, Pang J, Salphati L, Olivero A, Sutherlin D, O'Brien C, Spoerke J, Patel S, Lensun L, Kassees R, Ross L, Lackner M, Sampath D, Belvin M, Friedman L "GDC-0980 is a novel class I PI3K/mTOR kinase inhibitor with robust activity in cancer models driven by the PI3K pathway." Molecular cancer therapeutics(2011): 2426-36

113. Mohan S, Vander Broek R, Shah S, Eytan D, Pierce M, Carlson S, Coupar J, Zhang J, Cheng H, Chen Z, Van Waes C "MEK Inhibitor PD-0325901 Overcomes Resistance to PI3K/mTOR Inhibitor PF-5212384 and Potentiates Antitumor Effects in Human Head and Neck Squamous Cell Carcinoma." Clinical cancer research : an official journal of the American Association for Cancer Research(2015): 3946-56

114. Mortensen D, Fultz K, Xu S, Xu W, Packard G, Khambatta G, Gamez J, Leisten J, Zhao J, Apuy J, Ghoreishi K, Hickman M, Narla R, Bissonette R, Richardson S, Peng S, Perrin-Ninkovic S, Tran T, Shi T, Yang W, Tong Z, Cathers B, Moghaddam M, Canan S, Worland P, Sankar S, Raymon H "CC-223, a Potent and Selective Inhibitor of mTOR Kinase: In Vitro and In Vivo Characterization." Molecular cancer therapeutics(2015): 1295-305

115. Wertz I, Kusam S, Lam C, Okamoto T, Sandoval W, Anderson D, Helgason E, Ernst J, Eby M, Liu J, Belmont L, Kaminker J, O'Rourke K, Pujara K, Kohli P, Johnson A, Chiu M, Lill J, Jackson P, Fairbrother W, Seshagiri S, Ludlam M, Leong K, Dueber E, Maecker H, Huang D, Dixit V "Sensitivity to antitubulin chemotherapeutics is regulated by MCL1 and FBW7." Nature(2011): 110-4

116. Yu H, Wei W, Xia L, Han W, Zhao P, Wu S, Li W, Chen W "FBW7 upregulation enhances cisplatin cytotoxicity in non- small cell lung cancer cells." Asian Pacific journal of cancer prevention : APJCP(2013): 6321-6

117. Yokobori T, Yokoyama Y, Mogi A, Endoh H, Altan B, Kosaka T, Yamaki E, Yajima T, Tomizawa K, Azuma Y, Onozato R, Miyazaki T, Tanaka S, Kuwano H "FBXW7 mediates chemotherapeutic sensitivity and prognosis in NSCLCs." Molecular cancer research : MCR(2014): 32-7

118. Li R, Wu S, Chen X, Xu H, Teng P, Li W "miR-223/FBW7 axis regulates doxorubicin sensitivity through epithelial mesenchymal transition in non-small cell lung cancer." American journal of translational research(2016): 2512-24

119. Gasca J, Flores M, Giráldez S, Ruiz-Borrego M, Tortolero M, Romero F, Japón M, Sáez C "Loss of FBXW7 and accumulation of MCL1 and PLK1 promote paclitaxel resistance in breast cancer." Oncotarget(2016): 52751-52765

120. Lorenzi F, Babaei-Jadidi R, Sheard J, Spencer-Dene B, Nateri A "Fbxw7-associated drug resistance is reversed by induction of terminal differentiation in murine intestinal organoid culture." Molecular therapy. Methods & clinical development(2016): 16024

121. Li N, Lorenzi F, Kalakouti E, Normatova M, Babaei-Jadidi R, Tomlinson I, Nateri A "FBXW7-mutated colorectal cancer cells exhibit aberrant expression of phosphorylated-p53 at Serine-15." Oncotarget(2015): 9240-56

122. Lebwohl D, Anak O, Sahmoud T, Klimovsky J, Elmroth I, Haas T, Posluszny J, Saletan S, Berg W "Development of everolimus, a novel oral mTOR inhibitor, across a spectrum of diseases." Annals of the New York Academy of Sciences(2013): 14-32

123. Bergmann L, Maute L, Guschmann M "Temsirolimus for advanced renal cell carcinoma." Expert review of anticancer therapy(2014): 9-21

124. Nemecek R, Berkovcova J, Radova L, Kazda T, Mlcochova J, Vychytilova-Faltejskova P, Slaby O, Svoboda M "Mutational analysis of primary and metastatic colorectal cancer samples underlying the resistance to cetuximab-based therapy." OncoTargets and therapy(2016): 4695-703

125. Tong J, Tan S, Zou F, Yu J, Zhang L "FBW7 mutations mediate resistance of colorectal cancer to targeted therapies by blocking Mcl-1 degradation." Oncogene(2017): 787-796

126. Shen J, Ju Z, Zhao W, Wang L, Peng Y, Ge Z, Nagel Z, Zou J, Wang C, Kapoor P, Ma X, Ma D, Liang J, Song S, Liu J, Samson L, Ajani J, Li G, Liang H, Shen X, Mills G, Peng G "ARID1A deficiency promotes mutability and potentiates therapeutic antitumor immunity unleashed by immune checkpoint blockade." Nature medicine(2018): 556-562

127. Chou A, Toon C, Clarkson A, Sioson L, Houang M, Watson N, DeSilva K, Gill A "Loss of ARID1A expression in colorectal carcinoma is strongly associated with mismatch repair deficiency." Human pathology(2014): 1697-703

128. Allo G, Bernardini M, Wu R, Shih I, Kalloger S, Pollett A, Gilks C, Clarke B "ARID1A loss correlates with mismatch repair deficiency and intact p53 expression in high-grade endometrial carcinomas." Modern pathology : an official journal of the United States and Canadian Academy of Pathology, Inc(2014): 255-61

129. Bitler B, Aird K, Garipov A, Li H, Amatangelo M, Kossenkov A, Schultz D, Liu Q, Shih I, Conejo-Garcia J, Speicher D, Zhang R "Synthetic lethality by targeting EZH2 methyltransferase activity in ARID1A-mutated cancers." Nature medicine(2015): 231-8

References

130. Kung P, Bingham P, Brooun A, Collins M, Deng Y, Dinh D, Fan C, Gajiwala K, Grantner R, Gukasyan H, Hu W, Huang B, Kania R, Kephart S, Krivacic C, Kumpf R, Khamphavong P, Kraus M, Liu W, Maegley K, Nguyen L, Ren S, Richter D, Rollins R, Sach N, Sharma S, Sherrill J, Spangler J, Stewart A, Sutton S, Uryu S, Verhelle D, Wang H, Wang S, Wythes M, Xin S, Yamazaki S, Zhu H, Zhu J, Zehnder L, Edwards M "Optimization of Orally Bioavailable Enhancer of Zeste Homolog 2 (EZH2) Inhibitors Using Ligand and Property-Based Design Strategies: Identification of Development Candidate (R)-5,8-Dichloro-7-(methoxy(oxetan-3-yl)methyl)-2-((4-methoxy-6-methyl-2-oxo-1,2-dihydropyridin-3-yl)methyl)-3,4-dihydroisoquinolin-1(2H)-one (PF-06821497)." Journal of medicinal chemistry(2018): 650-665

131. Knutson S, Kawano S, Minoshima Y, Warholic N, Huang K, Xiao Y, Kadowaki T, Uesugi M, Kuznetsov G, Kumar N, Wigle T, Klaus C, Allain C, Raimondi A, Waters N, Smith J, Porter-Scott M, Chesworth R, Moyer M, Copeland R, Richon V, Uenaka T, Pollock R, Kuntz K, Yokoi A, Keilhack H "Selective inhibition of EZH2 by EPZ-6438 leads to potent antitumor activity in EZH2-mutant non-Hodgkin lymphoma." Molecular cancer therapeutics(2014): 842-54

132. Copeland R "Molecular pathways: protein methyltransferases in cancer." Clinical cancer research : an official journal of the American Association for Cancer Research (2013): 6344-50

133. Williamson C, Miller R, Pemberton H, Jones S, Campbell J, Konde A, Badham N, Rafiq R, Brough R, Gulati A, Ryan C, Francis J, Vermulen P, Reynolds A, Reaper P, Pollard J, Ashworth A, Lord C "ATR inhibitors as a synthetic lethal therapy for tumours deficient in ARID1A." Nature communications(2016): 13837

134. Shen J, Peng Y, Wei L, Zhang W, Yang L, Lan L, Kapoor P, Ju Z, Mo Q, Shih I, Uray I, Wu X, Brown P, Shen X, Mills G, Peng G "ARID1A Deficiency Impairs the DNA Damage Checkpoint and Sensitizes Cells to PARP Inhibitors." Cancer discovery(2015): 752-67

135. Berns K, Caumanns J, Hijmans E, Gennissen A, Severson T, Evers B, Wisman G, Jan Meersma G, Lieftink C, Beijersbergen R, Itamochi H, van der Zee A, de Jong S, Bernards R "ARID1A mutation sensitizes most ovarian clear cell carcinomas to BET inhibitors." Oncogene(2018): 4611-4625

136. Caumanns J, Wisman G, Berns K, van der Zee A, de Jong S "ARID1A mutant ovarian clear cell carcinoma: A clear target for synthetic lethal strategies." Biochimica et biophysica acta. Reviews on cancer(2018): 176-184

137. "ATARI: ATr Inhibitor in Combination With Olaparib in Gynaecological Cancers With ARId1A Loss" (2019)

138. "A Phase 1b/2a Dose-escalation Study to Assess Safety, Pharmacokinetics, Pharmacodynamics, and Preliminary Efficacy of PLX2853 in Subjects With Advanced Malignancies" (2019)

139. "Phase II Trial of AZD6738 Alone and in Combination With Olaparib in Patients With Selected Solid Tumor Malignancies" (2019)

140. Manuel Avedissian "A Phase II Study of the PARP Inhibitor Olaparib (AZD2281) Alone and in Combination With AZD1775, AZD5363, or AZD6738 in Advanced Solid Tumors" (2022)

141. "A Phase 1b Biomarker-Driven Combination Trial of Copanlisib, Olaparib, and Durvalumab (MEDI4736) in Patients With Advanced Solid Tumors" (2024)

142. "A Phase II Study of M6620 (VX-970) in Selected Solid Tumors" (2019)

143. Brown C, Lain S, Verma C, Fersht A, Lane D "Awakening guardian angels: drugging the p53 pathway." Nature reviews. Cancer(2009): 862-73

144. Malkin D, Li F, Strong L, Fraumeni J, Nelson C, Kim D, Kassel J, Gryka M, Bischoff F, Tainsky M "Germ line p53 mutations in a familial syndrome of breast cancer, sarcomas, and other neoplasms." Science (New York, N.Y.)(1990): 1233-8

145. Srivastava S, Zou Z, Pirollo K, Blattner W, Chang E "Germ-line transmission of a mutated p53 gene in a cancer-prone family with Li-Fraumeni syndrome." Nature(1991): 747-9

146. Santibáñez-Koref M, Birch J, Hartley A, Jones P, Craft A, Eden T, Crowther D, Kelsey A, Harris M "p53 germline mutations in Li-Fraumeni syndrome." Lancet (London, England)(1991): 1490-1

147. Wang Y, Lin R, Tan Y, Chen J, Chen C, Wang Y "Wild-type p53 overexpression and its correlation with MDM2 and p14ARF alterations: an alternative pathway to non-small-cell lung cancer." Journal of clinical oncology : official journal of the American Society of Clinical Oncology(2005): 154-64

148. Koga T, Hashimoto S, Sugio K, Yoshino I, Nakagawa K, Yonemitsu Y, Sugimachi K, Sueishi K "Heterogeneous distribution of P53 immunoreactivity in human lung adenocarcinoma correlates with MDM2 protein expression, rather than with P53 gene mutation." International journal of cancer(2001): 232-9

149. Kato S, Han S, Liu W, Otsuka K, Shibata H, Kanamaru R, Ishioka C "Understanding the function-structure and function-mutation relationships of p53 tumor suppressor protein by high-resolution missense mutation analysis." Proceedings of the National Academy of Sciences of the United States of America(2003): 8424-9

150. Houben R, Hesbacher S, Schmid C, Kauczok C, Flohr U, Haferkamp S, Müller C, Schrama D, Wischhusen J, Becker J "High-level expression of wild-type p53 in melanoma cells is frequently associated with inactivity in p53 reporter gene assays." PloS one(2011): e22096

151. Olivier M, Petitjean A, Marcel V, Pétré A, Mounawar M, Plymoth A, de Fromentel C, Hainaut P "Recent advances in p53 research: an interdisciplinary perspective." Cancer gene therapy(2009): 1-12

152. Schuler P, Harasymczuk M, Visus C, Deleo A, Trivedi S, Lei Y, Argiris A, Gooding W, Butterfield L, Whiteside T, Ferris R "Phase I dendritic cell p53 peptide vaccine for head and neck cancer." Clinical cancer research : an official journal of the American Association for Cancer Research(2014): 2433-44

153. Vermeij R, Leffers N, van der Burg S, Melief C, Daemen T, Nijman H "Immunological and clinical effects of vaccines targeting p53-overexpressing malignancies." Journal of biomedicine & biotechnology(2011): 702146

154. Saito H, Ando S, Morishita N, Lee K, Dator D, Dy D, Shigemura K, Adhim Z, Nibu K, Fujisawa M, Shirakawa T "A combined lymphokine-activated killer (LAK) cell immunotherapy and adenovirus-p53 gene therapy for head and neck squamous cell carcinoma." Anticancer research(2014): 3365-70

155. Ma C, Janetka J, Piwnica-Worms H "Death by releasing the breaks: CHK1 inhibitors as cancer therapeutics." Trends in molecular medicine(2011): 88-96

156. Hirai H, Arai T, Okada M, Nishibata T, Kobayashi M, Sakai N, Imagaki K, Ohtani J, Sakai T, Yoshizumi T, Mizuarai S, Iwasawa Y, Kotani H "MK-1775, a small molecule Wee1 inhibitor, enhances anti-tumor efficacy of various DNA-damaging agents, including 5-fluorouracil." Cancer biology & therapy(2010): 514-22

157. Bridges K, Hirai H, Buser C, Brooks C, Liu H, Buchholz T, Molkentine J, Mason K, Meyn R "MK-1775, a novel Wee1 kinase inhibitor, radiosensitizes p53-defective human tumor cells." Clinical cancer research : an official journal of the American Association for Cancer Research(2011): 5638-48

158. Vilgelm A, Pawlikowski J, Liu Y, Hawkins O, Davis T, Smith J, Weller K, Horton L, McClain C, Ayers G, Turner D, Essaka D, Stewart C, Sosman J, Kelley M, Ecsedy J, Johnston J, Richmond A "Mdm2 and aurora kinase a inhibitors synergize to block melanoma growth by driving apoptosis and immune clearance of tumor cells." Cancer research(2015): 181-93

159. Li Z, Sun Y, Chen X, Squires J, Nowroozizadeh B, Liang C, Huang J "p53 Mutation Directs AURKA Overexpression via miR-25 and FBXW7 in Prostatic Small Cell Neuroendocrine Carcinoma." Molecular cancer research : MCR(2015): 584-91

References

160. Katayama H, Sen S "Functional significance of Aurora kinase A regulatory interactions with p53-ERα complex in human breast cancer cells." Hormones & cancer(2011): 117-24

161. Tentler J, Ionkina A, Tan A, Newton T, Pitts T, Glogowska M, Kabos P, Sartorius C, Sullivan K, Espinosa J, Eckhardt S, Diamond J "p53 Family Members Regulate Phenotypic Response to Aurora Kinase A Inhibition in Triple-Negative Breast Cancer." Molecular cancer therapeutics(2015): 1117-29

162. Gully C, Velazquez-Torres G, Shin J, Fuentes-Mattei E, Wang E, Carlock C, Chen J, Rothenberg D, Adams H, Choi H, Guma S, Phan L, Chou P, Su C, Zhang F, Chen J, Yang T, Yeung S, Lee M "Aurora B kinase phosphorylates and instigates degradation of p53." Proceedings of the National Academy of Sciences of the United States of America(2012): E1513-22

163. Marxer M, Ma H, Man W, Poon R "p53 deficiency enhances mitotic arrest and slippage induced by pharmacological inhibition of Aurora kinases." Oncogene(2014): 3550-60

164. El-Deiry W "The role of p53 in chemosensitivity and radiosensitivity." Oncogene(2003): 7486-95

165. Miyasaka A, Oda K, Ikeda Y, Sone K, Fukuda T, Inaba K, Makii C, Enomoto A, Hosoya N, Tanikawa M, Uehara Y, Arimoto T, Kuramoto H, Wada-Hiraike O, Miyagawa K, Yano T, Kawana K, Osuga Y, Fujii T "PI3K/mTOR pathway inhibition overcomes radioresistance via suppression of the HIF1-α/VEGF pathway in endometrial cancer." Gynecologic oncology(2015): 174-80