ABOUT THE TEST FoundationOne®CDx is a next-generation sequencing (NGS) based assay that identifies genomic findings within hundreds of cancer-related genes.

PATIENT

DISEASE Prostate acinar adenocarcinoma
NAME
DATE OF BIRTH
SEX
MEDICAL RECORD #

PHYSICIAN

ORDERING PHYSICIAN
MEDICAL FACILITY
ADDITIONAL RECIPIENT
MEDICAL FACILITY ID
PATHOLOGIST

SPECIMEN

SPECIMEN SITE
SPECIMEN ID
SPECIMEN TYPE
DATE OF COLLECTION
SPECIMEN RECEIVED

Genomic Signatures

Microsatellite status - MS-Stable
Tumor Mutational Burden - 1 Muts/Mb

Gene Alterations

For a complete list of the genes assayed, please refer to the Appendix.

AR amplification
BRCA2 rearrangement intron 14
RET amplification
TMPRSS2 TMPRSS2-ERG fusion
MLH1 rearrangement intron 16
RAD21 amplification - equivocal†
TP53 L130R

† See About the Test in appendix for details.

12 Therapies approved in the EU
0 Therapies with Lack of Response
26 Clinical Trials

GENOMIC SIGNATURES	ACTIONABILITY
Microsatellite status - MS-Stable	**No therapies or clinical trials.** see Genomic Signatures section
Tumor Mutational Burden - 1 Muts/Mb	**No therapies or clinical trials.** see Genomic Signatures section

Electronically signed by Douglas Lin, M.D. | Julia Elvin, M.D., Ph.D., Laboratory Director Foundation Medicine, Inc. | Roche Customer Care: +49 7624 14 2098 or europe.foundationmedicine@roche.com

Sample Preparation: FMI Germany GmbH, Nonnenwald 2, 82377 Penzberg, Germany
Sample Analysis: FMI Germany GmbH, Nonnenwald 2, 82377 Penzberg, Germany

GENE ALTERATIONS	THERAPIES APPROVED IN THE EU (IN PATIENT'S TUMOR TYPE)	THERAPIES APPROVED IN THE EU (IN OTHER TUMOR TYPE)
AR **-** amplification	Abiraterone	none
	Bicalutamide	
	Cyproterone	
	Degarelix	
	Flutamide	
	Goserelin	
	Leuprorelin	
10 Trials *see p. 12*	Triptorelin	
BRCA2 **-** rearrangement intron 14	none	Niraparib
		Olaparib
		Rucaparib
10 Trials *see p. 15*		Talazoparib
RET **-** amplification	none	none
3 Trials *see p. 19*		
TMPRSS2 **-** TMPRSS2-ERG fusion	none	none
10 Trials *see p. 20*		

GENE ALTERATIONS WITH NO REPORTABLE THERAPEUTIC OR CLINICAL TRIALS OPTIONS

For more information regarding biological and clinical significance, including prognostic, diagnostic, germline, and potential chemosensitivity implications, see the Genomic Alterations section.

NOTE Genomic alterations detected may be associated with activity of certain approved therapies; however, the agents listed in this report may have varied clinical evidence in the patient's tumor type. Therapies and the clinical trials listed in this report may not be complete and exhaustive. Neither the therapeutic agents nor the trials identified are ranked in order of potential or predicted efficacy for this patient, nor are they ranked in order of level of evidence for this patient's tumor type. This report should be regarded and used as a supplementary source of information and not as the single basis for the making of a therapy decision. All treatment decisions remain the full and final responsibility of the treating physician and physicians should refer to approved prescribing information for all therapies.

Therapies contained in this report may have been approved through a centralized EU procedure or a national procedure in an EU Member State. Therapies, including but not limited to the following, have been approved nationally and may not be available in all EU Member States: Tretinoin, Anastrozole, Bicalutamide, Cyproterone, Exemestane, Flutamide, Goserelin, Letrozole, Leuprorelin, Triptorelin.

GENOMIC SIGNATURE

Microsatellite status

RESULT
MS-Stable

POTENTIAL TREATMENT STRATEGIES

On the basis of clinical evidence, MSS tumors are significantly less likely than MSI-H tumors to respond to anti-PD-1 immune checkpoint inhibitors[1-3], including approved therapies nivolumab and pembrolizumab[4]. In a retrospective analysis of 361 patients with solid tumors treated with pembrolizumab, 3% were MSI-H and experienced a significantly higher ORR compared with non-MSI-H cases (70% vs. 12%, p=0.001)[5].

FREQUENCY & PROGNOSIS

MSI has been reported in 3.1-14.6% of prostate cancer samples[6-10]. A study of prostate cancer in hereditary nonpolyposis colorectal cancer (HNPCC) families reported MSI-H in 4-50% of cases[11-13]. The prognostic significance of MSI in prostate cancer has not been extensively studied (PubMed, May 2019).

FINDING SUMMARY

Microsatellite instability (MSI) is a condition of genetic hypermutability that generates excessive amounts of short insertion/deletion mutations in the genome; it generally occurs at microsatellite DNA sequences and is caused by a deficiency in DNA mismatch repair (MMR) in the tumor[14]. Defective MMR and consequent MSI occur as a result of genetic or epigenetic inactivation of one of the MMR pathway proteins, primarily MLH1, MSH2, MSH6, or PMS2[14-16]. This sample is microsatellite-stable (MSS), equivalent to the clinical definition of an MSS tumor: one with mutations in none of the tested microsatellite markers[17-19]. MSS status indicates MMR proficiency and typically correlates with intact expression of all MMR family proteins[14,16,18-19].

GENOMIC SIGNATURE

Tumor Mutational Burden

RESULT
1 Muts/Mb

POTENTIAL TREATMENT STRATEGIES

On the basis of strong clinical evidence, elevated TMB may be associated with greater sensitivity to immunotherapeutic agents, including anti-CTLA-4, anti-PD-L1, and anti-PD-1 immune checkpoint inhibitors; approved agents include ipilimumab, atezolizumab, avelumab, durvalumab, cemiplimab-rwlc, pembrolizumab, and nivolumab. Clinical studies have reported associations between elevated TMB and efficacy of PD-1- or PD-L1-targeting therapies, alone or in combination with other agents, in multiple types of solid tumors, including small cell[20-21] and non-small cell[22-34] lung cancer, urothelial carcinoma[29,35-38], melanoma[25,29-30,39-43], colorectal cancer[29,44], HNSCC[29,45], and other cancer types[25,43,46-48]. For patients with melanoma, increased TMB has also been reported to be associated with clinical benefit from the CTLA-4 inhibitor ipilimumab[32,49-51].

FREQUENCY & PROGNOSIS

Prostate acinar adenocarcinoma harbors a median TMB of 2.7 mutations per megabase (muts/Mb), and 3.4% of cases have high TMB (>20 muts/Mb)[52]. Prostate cancer has been reported to harbor a relatively low TMB among solid tumors[53-54], with approximately 0.5-1.5 (muts/Mb) in localized tumor samples[55-57], and a higher but still low TMB of 2-5 muts/Mb in metastatic, castration-resistant prostate cancer (mCRPC) samples[58-60]. One study reported that 4 of 150 (2.7%) mCRPC cases harbored high TMB (nearly 50 muts/Mb), which was due to defects in mismatch repair genes MLH1 and MSH2 in 3 of the 4 cases[60]. The effects of hypermutation on prognosis and clinical features in prostate cancer have not been extensively investigated (PubMed, Jul 2019).

FINDING SUMMARY

Tumor mutational burden (TMB, also known as mutation load) is a measure of the number of somatic protein-coding base substitution and insertion/deletion mutations occurring in a tumor specimen. TMB is affected by a variety of causes, including exposure to mutagens such as ultraviolet light in melanoma[61-62] and cigarette smoke in lung cancer[63-64], mutations in the proofreading domains of DNA polymerases encoded by the POLE and POLD1 genes[65-69], and microsatellite instability (MSI)[65,68-69]. This sample harbors a low TMB. Compared to patients with tumors harboring higher TMB levels, patients with tumors harboring low TMB levels have experienced lower rates of clinical benefit from treatment with immune checkpoint inhibitors, including anti-CTLA-4 therapy in melanoma[49], anti-PD-L1 therapy in urothelial carcinoma[35], and anti-PD-1 therapy in non-small cell lung cancer and colorectal cancer[4,64].

GENE
AR

ALTERATION
amplification

POTENTIAL TREATMENT STRATEGIES

Several approved drugs are available that target AR and/or the AR pathway in prostate cancer, including the antiandrogens apalutamide, bicalutamide, cyproterone, darolutamide, enzalutamide, flutamide, and nilutamide; the luteinizing hormone-releasing hormone (LHRH) agonists goserelin, leuprolide and triptorelin; the LHRH antagonist degarelix; and the CYP17A1 inhibitor abiraterone[70-77]. Resistance to androgen deprivation therapy (ADT) commonly occurs in prostate cancer through mechanisms such as increased AR expression, AR activation by tyrosine kinase-dependent signaling, alterations in AR co-activators, expression of alternatively spliced isoforms of AR mRNAs (AR-Vs), and extragonadal synthesis of androgenic compounds[78-82]. AR signaling may promote radioresistance in prostate cancer by transcriptionally upregulating DNA repair genes[83]. There is preclinical evidence that development of resistance to anti-AR therapies, such as abiraterone and enzalutamide, may engender cross-resistance to the taxanes docetaxel and cabazitaxel[84]; however, certain AR-Vs may remain sensitive to taxanes[85-86]. Approaches currently in clinical and preclinical development for prostate cancer include therapies that target AR nuclear translocation and degradation pathways[87-93], combination approaches to suppress androgen biosynthesis[94], and the use of bromodomain and extraterminal (BET) inhibitors that disrupt the interaction between AR and BRD4[95-97]; the latter approach has potential to target AR-Vs[96-98]. The BET inhibitor mivebresib led to an SD rate of 60% (6/10) for patients with genomically unselected prostate cancer who had progressed on multiple standard of care therapies[99]. Galeterone, a multifunctional AR inhibitor, has been evaluated in a number of Phase 1 and 2 studies and has been found to reduce prostate-specific antigen levels in 49-73% of patients, although clinical trials of this reagent are not recruiting patients[100].

FREQUENCY & PROGNOSIS

Aberrant activation of AR, through mutation and amplification of AR, has been shown to be fundamental to prostate cancer progression; studies have reported AR gene amplification in 13-44% of patients with castration-resistant prostate cancer (CRPC)[58,101-107]. AR amplification in prostate cancer appears to occur in response to androgen-deprivation therapy, as studies reported that 28-30% of patients with CRPC had AR amplification after, but not before, receiving androgen-deprivation therapy[102-103]. AR gene amplification is associated with advanced, hormone-refractory disease, and thus with poor prognosis. However, a study of prostate tumors that recurred during hormone therapy found no difference in patients with or without AR amplification in histological grade, Gleason score, or tumor stage[108].

FINDING SUMMARY

AR encodes the androgen receptor, a nuclear receptor that binds to testosterone and dihydroxytestosterone. AR is frequently amplified and overexpressed in castration-resistant prostate cancer (CRPC), also called hormone-refractory prostate cancer[109].

GENE
BRCA2

ALTERATION
rearrangement intron 14

POTENTIAL TREATMENT STRATEGIES

Extensive clinical evidence in solid tumors indicates that inactivation of BRCA2 may confer sensitivity to PARP inhibitors, such as olaparib, rucaparib, or niraparib[110-126]. Clinical response to PARP inhibitors has been reported for patients with either germline or somatic BRCA2 mutations[111,116,119,126] and for patients who were platinum-resistant or refractory[110,115,122,125]. Patients with BRCA-mutated platinum-resistant ovarian cancer have also responded to niraparib in combination with pembrolizumab; a Phase 1/2 study reported an ORR and a DCR of 45% (5/11) and 73% (8/11), respectively[127]. In a Phase 2 trial of WEE1 inhibitor adavosertib in 31 patients with BRCA-mutated solid tumors, 1 patient with serous Fallopian tube cancer experienced a PR, and 4 patients (3 with ovarian cancer and 1 with solitary fibrous tumor) experienced SDs of greater than 6 months; patients with ovarian cancers had been previously treated with PARP inhibitors[128]. Inactivation of BRCA2 may also predict sensitivity to DNA-damaging drugs such as the platinum chemotherapies cisplatin and carboplatin[129-131].

FREQUENCY & PROGNOSIS

BRCA2 mutations have been identified in 3–6% of primary and 6–7% of metastatic prostate cancer specimens[57,60,132], with deleterious germline BRCA2 mutations present in 5% of men with metastatic prostate cancer[133]. The positive predictive value of prostate specific antigen (PSA) levels was found to be higher in patients with BRCA1/2 mutations than in the general population[134]. BRCA2 germline mutations have been associated with attributes of aggressive prostate cancer at diagnosis, including high Gleason score, nodal involvement, advanced tumor stage, and metastatic spread[135]. Germline BRCA2 mutation carriers had a significantly shorter cause-specific survival (CSS, 8.6 vs. 15.7 years) than noncarriers[135]. Following radical conventional treatment for localized prostate cancer, patients with germline BRCA1/2 mutations experienced significantly shorter metastasis-free survival (HR=2.36) and CSS (HR=2.17) than noncarriers[136]. For patients with metastatic castration-resistant prostate cancer (mCRPC), germline BRCA2 mutations were an independent marker of poor prognosis (CSS 17.4 vs. 33.2 months, HR=2.11) in 1 study[137]. Germline BRCA2 mutations in mCRPC were associated with relative benefit from first-line abiraterone or enzalutamide compared with taxanes (CSS 24.0 vs. 17.0 months, PFS on the second systemic therapy 18.9 vs. 8.6 months) in a large prospective cohort study[137]. Three patients with non-neuroendocrine prostate cancer harboring BRCA2 mutations derived clinical benefit from treatment with platinum-based chemotherapy[138-139].

FINDING SUMMARY

The BRCA2 tumor suppressor gene encodes a protein that regulates the response to DNA damage[140]. Inactivating mutations in BRCA2 can lead to the inability to repair DNA damage and loss of cell cycle checkpoints, which can lead to tumorigenesis[141]. BRCA2 alterations that disrupt PALB2 binding (aa 21-39)[142], the BRC repeats (aa 1002-2085), the DNA binding domain (aa 2479-3192), and/or the C-terminal RAD51 binding domain, as observed here, are predicted to be inactivating[140,143-158]. Germline mutations in BRCA1 or BRCA2 are associated with breast-ovarian cancer familial susceptibility (BROVCA), also known as hereditary breast-ovarian cancer (HBOC)[159-160]. The lifetime risk of breast and ovarian cancer in BRCA1/2 mutation carriers has been estimated to be as high as 87% and 44%, respectively[161], and elevated risk of other cancers, including gastric, pancreatic, prostate, and colorectal tumors, has been identified at frequencies of 20-60%[162-169]. The estimated prevalence of deleterious germline BRCA1/2 mutations in the general population is between 1:400 and 1:800, with an approximately 10-fold higher prevalence in the Ashkenazi Jewish population[161,163,170-174]. In the appropriate clinical context, germline testing of BRCA2 is recommended.

GENE
RET

ALTERATION
amplification

POTENTIAL TREATMENT STRATEGIES

On the basis of clinical evidence, RET activating alterations may predict response to the multikinase inhibitors alectinib[175], cabozantinib[176-183], lenvatinib[184], sorafenib[185], sunitinib[185-186], and vandetanib[187-193]. Case reports describe clinical benefit lasting 17 months with sunitinib for a patient with RET-amplified germ cell tumor[194] and stable disease from sunitinib and subsequent sorafenib for a patient with RET-amplified tongue adenocarcinoma[185].

FREQUENCY & PROGNOSIS

RET amplification and mutation have been reported in <1% of prostate carcinoma cases (cBioPortal, COSMIC, Oct 2019). Published data investigating the prognostic implications of RET alterations in prostate carcinoma are limited (PubMed, Dec 2018), although RET protein overexpression has been reported in both high-grade prostate intraepithelial neoplasia (PIN) and in prostate carcinomas as compared to normal prostate tissue[195].

FINDING SUMMARY

RET (Rearranged during transfection) encodes a receptor tyrosine kinase primarily expressed in cells of the nervous system. It has been identified as a proto-oncogene that results in transformation of cells upon recombination with a partner gene[196]. RET amplification has been reported to be amplified in cancer[197], and has been associated with responses to therapies that target RET[185,194].

GENE
TMPRSS2

ALTERATION
TMPRSS2-ERG fusion

POTENTIAL TREATMENT STRATEGIES

There are no therapies to target rearrangement of TMPRSS2. Although direct targeting of ETS-family transcription factors is not possible, preclinical studies in prostate cancer with TMPRSS2-ETS family fusions have suggested sensitivity to agents targeting HDAC and PARP[198-200]. Emerging clinical data indicate that 7 patients with ERG-rearranged prostate cancers achieved stable disease upon treatment with the PARP inhibitors niraparib or veliparib[115,201]. Studies in prostate cancer have also reported that TMPRSS2-ETS family fusions may often co-occur with PTEN loss or PI3K pathway activation[202-203]. HDAC and PARP inhibitors are in clinical trials in solid tumors. Limited preclinical data also suggest that bromodomain and extraterminal (BET) inhibitors suppress AR-BRD4 recruitment to the TMPRSS2 promoter, ERG expression, and AR-driven tumor growth in a preclinical castrate-resistant prostate cancer model[95].

FREQUENCY & PROGNOSIS

Fusions of TMPRSS2 with ETS family transcription factors are common in prostate carcinomas, reported in about 50-90% of cases[204-207]. TMPRSS2-ERG fusion is the most commonly observed fusion, reported in 50-59% of prostate cancers, but not in other tumor types examined[204,208-213]. In addition, the TMPRSS2-ERG fusion has been identified in prostatic intraepithelial neoplasia but not in atypical adenomatous hyperplasia[214-215]. In general, a definitive relationship between TMPRSS2-ETS fusions and patient prognosis has been difficult to establish and is an area of ongoing study[216]. TMPRSS2-ERG has been associated with lower prostatic-specific antigen progression-free survival (PSA-PFS) in metastatic resistant prostate cancer patients treated with docetaxel or cabazitaxel[217].

FINDING SUMMARY

TMPRSS2 encodes an androgen-responsive serine protease that is most abundant in prostate tissue and normally expressed in other tissues such as colon, salivary gland, and stomach[218]. It has been found to be downregulated in androgen-independent prostate cancer[219]. The rearrangement seen here results in a fusion between TMPRSS2 and ERG, an ETS family transcription factor. TMPRSS2-ERG has been identified as a recurrent fusion in prostate cancer, in which the androgen-responsive promoter element of TMPRSS2 drives overexpression of ERG[206]. Different TMPRSS2-ERG fusions display varying degrees of oncogenicity[220].

GENE
MLH1

ALTERATION
rearrangement intron 16

POTENTIAL TREATMENT STRATEGIES

MLH1 inactivation leads to MMR defects, high MSI, and increased mutational burden[19,68,221-222], which may predict response to the FDA-approved anti-PD-1 immunotherapies pembrolizumab and nivolumab[4,64,223]. In a Phase 2 study of pembrolizumab in MSI-high colorectal cancer (CRC), three patients with MLH1 (germline) mutations experienced one partial response and two stable diseases[4]. Pembrolizumab demonstrated a significantly higher objective response rate in MSI-high CRC compared with microsatellite stable CRC (40% vs. 0%)[4] and its efficacy correlated with high mutational burden in non-small cell lung cancer[64]. Nivolumab achieved a complete response in a patient with MSI-high CRC[223]. Furthermore, MSI status correlates with higher PD-1 and PD-L1 expression[1], potential biomarkers of response to anti-PD-1 immunotherapies. These therapies are in clinical trials for various tumor types and may be appropriate, particularly for hypermutant tumors.

FREQUENCY & PROGNOSIS

MLH1 mutation has been reported in 0-1.6% of prostate carcinoma cases[55-56,58,60,107]. Approximately 12% (7/60) of prostate cancers were found to be hypermutated, with two of the hypermutated cases having MLH1 mutations[8]. MLH1 expression was shown to be reduced in approximately 50% of 39 prostate tumors analyzed in one study[224]. In another analysis, MLH1 nuclear expression was detected in 85% (6220/7275) prostate cancers; strong expression of MLH1 was observed in 55.2% of TMPRSS2-ERG-positive cases, but only in 32.9% of TMPRSS2-ERG-negative cases[225]. MLH1 expression was significantly associated with early biochemical recurrence in univariate analyses in one study[225].

FINDING SUMMARY

MLH1 encodes the protein MutL homolog 1, colon cancer, nonpolyposis type 2, which binds PMS2 to form MutLalpha, a complex involved in DNA mismatch repair (MMR)[226]. Defective MMR occurring as a result of mutation(s) in the MMR family (MLH1, MSH2, MSH6, or PMS2) can result in microsatellite instability (MSI), common in colon, endometrium, and stomach cancers[15]. MLH1 alterations that result in disruption or loss of the N-terminal ATPase-containing domain (amino acids 25-336)[227-229], the exonuclease 1 (EXO1) interacting region or the C-terminal region necessary for PMS2 binding and formation of the MutL-alpha complex[230], such as observed here, are predicted to be inactivating. Germline mutations in MLH1 are associated with a condition known as Lynch syndrome, which is characterized by increased risk of a number of cancers[231]. Approximately 50% of Lynch syndrome-associated mutations have been attributed to alterations in MLH1[232]. Lynch syndrome (also known as hereditary nonpolyposis colorectal cancer or HNPCC) accounts for 1-7% of all colorectal cancers and has an estimated prevalence in the general population between 1:600 and 1:2000[233-235]. In the appropriate clinical context, germline testing of MLH1 is recommended.

GENE
RAD21

ALTERATION
amplification - equivocal

POTENTIAL TREATMENT STRATEGIES
There are no therapies to target alterations in this gene.

FREQUENCY & PROGNOSIS
RAD21 amplifications, point mutations, and truncating mutations have been reported in various cancers[236]. In the context of breast cancer, increased RAD21 expression has been correlated with poor prognosis in multiple subtypes[237-238], including sporadic Grade 3 but not Grade 1 cancers[237], as well as hereditary BRCA2-mutant and hereditary BRCA-wild-type but not hereditary BRCA1-mutant cancers[237]. Furthermore, SNPs in or near RAD21 have been linked with risk of breast cancer development[239-240]. RAD21 overexpression has also been correlated with poor prognosis in endometrial cancer[241] and in colorectal cancer (CRC), especially in KRAS-mutant CRC[242]. Heterogeneity of RAD21 expression also correlated with aggressive tumor behavior and shorter survival in endometrial cancer[243]. RAD21 amplification has been more frequently reported in hormone-refractory than in treatment-naïve prostate cancer, but RAD21 amplification did not correlate with expression[244]. In the context of ovarian cancer, both RAD21 overexpression and downregulation have been observed, but RAD21 expression was not prognostic[245]. Downregulation of RAD21 expression resulted in sensitization of cultured breast[238,246] and CRC[242] cells to chemotherapy, thereby suggesting that RAD21 overexpression confers resistance to chemotherapy.

FINDING SUMMARY
RAD21 encodes a protein involved in DNA double-strand break repair and sister chromatid cohesion as a part of the cohesin complex[247-250]. In preclinical studies, downregulation of RAD21 or other cohesin components leads to loss of expression from amplified genes, as well as amplifications themselves upon cell passaging[251], but also leads to an increase in deletions, insertions, and other rearrangements[252]. High RAD21 expression has also been associated with increased genomic instability[237]. Cohesin complex also organizes chromatin domains and regulates gene expression[253-254]. Both overexpression and reduction of expression of RAD21 has been reported to alter gene expression[255]. RAD21 amplification has been correlated with increased expression in breast[237-238,256] and endometrial[241] cancers. Other RAD21 alterations, including truncating and point mutations, have been reported in the context of cancer, but the majority have not been characterized.

GENE
TP53

ALTERATION
L130R

TRANSCRIPT NUMBER
NM_000546

CODING SEQUENCE EFFECT
389T>G

POTENTIAL TREATMENT STRATEGIES
There are no approved therapies to address TP53 mutation or loss. However, tumors with TP53 loss of function alterations may be sensitive to the WEE1 inhibitor adavosertib[257-260], or p53 gene therapy and immunotherapeutics such as SGT-53[261-265] and ALT-801[266]. Missense mutations leading to TP53 inactivation may also be sensitive to therapies that reactivate mutant p53 such as APR-246[267-269]. In a Phase 1b trial in patients with p53-positive high-grade serous ovarian cancer, APR-246 combined with carboplatin and pegylated liposomal doxorubicin achieved a 52% (11/21) response rate and 100% DCR[270]. In a Phase 1 study, adavosertib in combination with gemcitabine, cisplatin, or carboplatin elicited PRs in 10% (17/176) and SDs in 53% (94/176) of patients with solid tumors; the response rate was 21% (4/19) in patients with TP53 mutations versus 12% (4/33) in patients who were TP53 wild-type[271]. A Phase 2 trial of adavosertib in combination with chemotherapy (gemcitabine, carboplatin, paclitaxel, or doxorubicin) reported a 32% (30/94, 3 CR) ORR and a 73% (69/94) DCR in patients with platinum refractory TP53-mutated ovarian, Fallopian tube, or peritoneal cancer[272]. A smaller Phase 2 trial of adavosertib in combination with carboplatin achieved a 43% (9/21, 1 CR) ORR and a 76% (16/21) DCR in patients with platinum-refractory TP53-mutated ovarian cancer[273]. The combination of adavosertib with paclitaxel and carboplatin in patients with TP53-mutated ovarian cancer also significantly increased PFS compared with paclitaxel and carboplatin alone[274]. A Phase 1 trial of neoadjuvant adavosertib in combination with cisplatin and docetaxel for head and neck squamous cell carcinoma (HNSCC) elicited a 71% (5/7) response rate in patients with TP53 alterations[275]. In a Phase 1b clinical trial of SGT-53 in combination with docetaxel in patients with solid tumors, 75% (9/12) of evaluable patients experienced clinical benefit, including 2 confirmed and 1 unconfirmed PRs and 2 instances of SD with significant tumor shrinkage[265]. Additionally, the combination of a CHK1 inhibitor and irinotecan reportedly reduced tumor growth and prolonged survival in a TP53-mutant, but not TP53-wild-type, breast cancer xenotransplant mouse model[276].

FREQUENCY & PROGNOSIS
TP53 mutations have been reported in 18-40% of prostate cancers[277-278]. Overexpression of p53, which is indicative of TP53 dysregulation, has been reported to be significantly more common in late-stage and hormone-refractory prostate cancers and has been found to be associated with prostate-specific antigen (PSA) recurrence in low- and intermediate-grade prostate cancer[279]. TP53 loss has been found to be associated with prostate cancer-specific mortality in univariate analysis[280].

FINDING SUMMARY
Functional loss of the tumor suppressor p53, which is encoded by the TP53 gene, is common in aggressive advanced cancers[281]. Any alteration that results in the disruption or partial or complete loss of the region encoding the TP53 DNA-binding domain (DBD, aa 100-292) or the tetramerization domain (aa 325-356), such as observed here, is thought to dysregulate the transactivation of p53-dependent genes and is predicted to promote tumorigenesis[282-284]. Germline mutations in TP53 are associated with the very rare disorder Li-Fraumeni syndrome and the early onset of many cancers[285-287], including sarcomas[288-290]. Estimates for the prevalence of germline TP53 mutations in the general population range from 1:5,000[291] to 1:20,000[290]. In the appropriate clinical context, germline testing of TP53 is recommended.

Abiraterone

Assay findings association

AR
amplification

AREAS OF THERAPEUTIC USE

Abiraterone is an orally available CYP17 inhibitor. It is available in the EU in combination with prednisone or prednisolone to treat metastatic castration-resistant prostate cancer after progression on docetaxel-based chemotherapy, or after androgen blockade when chemotherapy is not indicated. It is also available in combination with prednisone or prednisolone and androgen deprivation therapy to treat newly diagnosed high-risk metastatic hormone-sensitive prostate cancer.

GENE ASSOCIATION

AR activation or amplification may predict sensitivity to abiraterone.

SUPPORTING DATA

The Phase 3 LATITUDE study in patients with previously untreated high-risk metastatic castration-naive prostate cancer demonstrated that abiraterone plus prednisone and androgen deprivation therapy (ADT) significantly improved median OS (53.3 vs. 36.5 months, HR=0.66) and radiographic PFS (33.0 vs. 14.8 months, HR=0.47) compared to ADT plus placebo[292-293] . Phase 3 studies have shown that abiraterone plus prednisone compared with placebo plus prednisone significantly improved median OS in patients with metastatic castration-resistant prostate cancer (mCRPC) who were either chemotherapy-naive[294] or had previously received chemotherapy[295]. For patients with non-metastatic CRPC, abiraterone plus prednisone also showed clinical efficacy in a Phase 2 study, with a median time to prostate-specific antigen (PSA) progression of 28.7 months and a median time to radiographic progressive disease of 41.4 months[296]. Abiraterone has also been evaluated to treat mCRPC in combination with other agents. A Phase 1b study evaluating abiraterone combined with docetaxel in chemotherapy-naive mCRPC patients showed 86% (18/21) and 67% (14/21) of patients had ≥ 50% and ≥ 90% PSA decline from baseline, respectively[297]. In a Phase 1/2 study, abiraterone plus cabazitaxel showed further clinical efficacy (46% [12/26] PSA response rate and 21% [3/14] PR rate) in the post-docetaxel, post-abiraterone setting[298]. Treatment with cabazitaxel was more effective than abiraterone in patients with mCRPC that previously progressed on docetaxel and then enzalutamide (8.2 vs. 3.4 months, HR=0.44)[299].

Bicalutamide

Assay findings association

AR
amplification

AREAS OF THERAPEUTIC USE

Bicalutamide is an orally available AR inhibitor that is available in the EU to treat advanced prostate cancer.

GENE ASSOCIATION

Clinical studies have demonstrated that AR activation or gene amplification may predict sensitivity to bicalutamide[300-301] .

SUPPORTING DATA

A long-term follow-up to a Phase 3 clinical trial of bicalutamide/LHRH analog combination therapy in prostate carcinoma reported significant improvement in overall survival compared with LHRH analog monotherapy[301].

Cyproterone

Assay findings association

AR
amplification

AREAS OF THERAPEUTIC USE

Cyproterone is an orally available androgen receptor inhibitor that is available in the EU for the management of patients with prostate cancer.

GENE ASSOCIATION

AR activation or amplification may predict sensitivity to cyproterone.

SUPPORTING DATA

A Phase 2 study of cyproterone in combination with leuprolide for 36 weeks reported a five year survival rate of 80% in patients with prostate adenocarcinoma[302]. A Phase 3 trial of 1045 patients with prostate cancer reported similar overall survival rates in patients treated with intermittent hormonal therapy, as compared to patients treated with cyproterone acetate[303].

Degarelix

Assay findings association

AR
amplification

AREAS OF THERAPEUTIC USE

Degarelix is a gonadotrophin releasing hormone (GnRH) antagonist that is available in the EU to treat advanced hormone-dependent prostate cancer.

GENE ASSOCIATION

AR activation or amplification may predict sensitivity to degarelix.

SUPPORTING DATA

A Phase 3 extension trial in patients with prostate cancer reported that degarelix was associated with significantly improved progression-free survival as compared with leuprolide[304].

Flutamide

Assay findings association

AR
amplification

AREAS OF THERAPEUTIC USE

Flutamide is an orally available anti-androgen that is available in the EU to treat patients with advanced prostate cancer.

GENE ASSOCIATION

AR activation or amplification may predict sensitivity to flutamide.

SUPPORTING DATA

A Phase 2 clinical trial of the combination of suramin, leuprolide, and flutamide in previously untreated patients with metastatic prostate cancer reported an overall response rate of 67%, include three complete responses and 30 partial responses[305]. A ten-year follow-up to a Phase 3 clinical trial in prostate carcinoma reported that long-term androgen-deprivation therapy (flutamide/goserelin) with radiation conferred significant benefit compared with short-term androgen-deprivation therapy with radiation[306].

Goserelin

Assay findings association

AR
amplification

AREAS OF THERAPEUTIC USE

Goserelin is a luteinizing hormone-releasing hormone analog that is available in the EU to treat men with advanced prostate cancer and to treat premenopausal and perimenopausal women with hormone receptor-positive breast cancer.

GENE ASSOCIATION

AR activation or amplification may predict sensitivity to goserelin.

SUPPORTING DATA

A ten-year follow-up to a Phase 3 clinical trial in prostate carcinoma reported that long-term androgen-deprivation therapy (flutamide/goserelin) with radiation conferred significant benefit compared with short-term androgen-deprivation therapy with radiation[306].

Leuprorelin

Assay findings association

AR
amplification

AREAS OF THERAPEUTIC USE

Leuprorelin is an injectable luteinizing hormone-releasing hormone analog that is available in the EU to treat advanced hormone-dependent prostate cancer.

GENE ASSOCIATION

AR activation or amplification may predict sensitivity to leuprolide.

SUPPORTING DATA

A Phase 3 clinical trial reported that leuprolide administration was effective at lowering testosterone concentration to castrate levels in patients with prostate cancer[307]. A Phase 2 clinical trial of the combination of suramin, leuprolide, and flutamide in previously untreated patients with metastatic prostate cancer reported an overall response rate of 67%, include three complete responses and 30 partial responses[305].

Triptorelin

Assay findings association

AR
amplification

AREAS OF THERAPEUTIC USE

Triptorelin is an injectable luteinizing hormone-releasing hormone analog that is available in the EU to treat advanced hormone-dependent prostate carcinoma.

GENE ASSOCIATION

AR activation or amplification may predict sensitivity to triptorelin.

SUPPORTING DATA

A Phase 3 clinical trial reported that triptorelin administration was effective at lowering testosterone concentration to castration levels in patients with prostate cancer[308].

Niraparib

Assay findings association

BRCA2
rearrangement intron 14

AREAS OF THERAPEUTIC USE

The PARP inhibitor niraparib is available in the EU for the maintenance treatment of patients with relapsed high grade serous epithelial ovarian, Fallopian tube, or primary peritoneal cancer who are in complete or partial response to platinum-based chemotherapy.

GENE ASSOCIATION

On the basis of clinical evidence in ovarian and breast cancers[114-115,127] , loss or inactivation of either BRCA1 or BRCA2 may confer sensitivity to PARP inhibitors such as niraparib.

SUPPORTING DATA

In a Phase 2 study of niraparib in metastatic castration-resistant prostate cancer (CRPC) that had progressed on at least 1 line of AR-targeted therapy in addition to at least 1 line of taxane chemotherapy, patients with biallelic BRCA1/2 mutation achieved a 62% (18/29) composite response rate, defined as ORR (38%, 6/16), circulating tumor cell (CTC) conversion (41%, 12/29), or a 50% decline in prostate-specific antigen level (PSA50) (52%, 15/29). Patients with non-BRCA biallelic DNA repair defects exhibited a 24% (5/21) composite RR, including a 13% (2/15) ORR, 19% (4/21) CTC conversion, and a 5% (1/21) PSA50[309]. In a Phase 1 study of niraparib treatment for patients with solid tumors, 43% (9/21) of patients with CRPC achieved SD, and 10 patients exhibited >30% decrease in CTCs[115].

Olaparib

Assay findings association

BRCA2
rearrangement intron 14

AREAS OF THERAPEUTIC USE

The PARP inhibitor olaparib is available in the EU as maintenance therapy for patients with platinum-sensitive relapsed high-grade serous epithelial ovarian, Fallopian tube, or primary peritoneal cancer who are in complete or partial response to platinum-based chemotherapy, or as first-line maintenance for patients with these cancers who have a germline or somatic BRCA mutation and are in CR or PR after platinum-based chemotherapy. Olaparib is also approved to treat patients with HER2-negative advanced breast cancer and germline BRCA mutations who have been previously treated with chemotherapy; patients with hormone receptor-positive breast cancer should have been previously treated with, or considered not appropriate for, endocrine therapy.

GENE ASSOCIATION

Based on extensive clinical evidence in ovarian cancer[120-124] as well as strong clinical evidence in multiple other cancer types[110-112,120,123,310] , loss or inactivation of either BRCA1 or BRCA2 may confer sensitivity to olaparib.

SUPPORTING DATA

In pretreated patients with castrate-resistant prostate cancer (CRPC), a Phase 2 trial of olaparib reported PRs for 50% (4/8) and SDs for 25% (2/8) of heavily pretreated patients, with 88% (7/8) of these patients carrying germline BRCA1/2 mutation[110]. The TOPARP-B Phase 2 trial of olaparib reported a 46% (43/92) ORR and PFS of 5.4 months for pretreated patients with metastatic CRPC, and an 83% (25/30) ORR and PFS of 8.1 months for patients with CRPC and BRCA1/2 alterations[311]. Similarly, another Phase 2 study of olaparib for biochemically recurrent prostate cancer observed a greater median prostate-specific antigen (PSA) PFS in men with BRCA2/ATM mutations (9 vs. 4 months without mutation)[312]. In another study, 33% (16/49) of patients with CRPC, including 88% (14/16) of patients with a mutation in 1 or more genes affecting homologous recombination benefited (PR, SD, and/or decline in PSA levels) from olaparib treatment[111]. In a Phase 2 trial of olaparib combined with abiraterone in genomically unselected patients with CRPC, combination treatment improved median radiographic PFS (rPFS) compared to abiraterone and placebo (13.8 vs. 8.2 months, HR = 0.65); however, an increase in adverse events was noted in the combination group versus placebo[313]. A Phase 1/2 trial combining olaparib with the immunotherapy durvalumab for patients with CRPC who were previously treated with abiraterone and/or enzalutamide reported a PSA decrease from a baseline of greater than or equal to 50% for 53% (9/17) of patients, including 4 RECIST PRs, and a median rPFS of 16.1 months; 3 responders harbored germline inactivating BRCA2 mutations with concurrent BRCA2 deletions of the second allele, while 2 responders displayed homozygous somatic BRCA2 inactivating alterations[314]. A Phase 1 trial combined olaparib with the immunotherapy pembrolizumab for docetaxel-pretreated patients with metastatic CRPC and observed an ORR of 7% (2/28 PRs) and a PSA response rate of 14% (4/28 with 50% PSA decrease) in RECIST-evaluable patients, as well as a median rPFS of 4.7 months and median OS of 13.5 months in the overall population[315]. Of note, homologous recombination deficiency was not detected in any of the patients[315].

Rucaparib

Assay findings association

BRCA2
rearrangement intron 14

AREAS OF THERAPEUTIC USE

The PARP inhibitor rucaparib is available in the EU to treat patients with platinum-sensitive relapsed or progressive BRCA mutated (germline and/or somatic) high-grade epithelial ovarian, fallopian tube, or primary peritoneal cancer who have been treated with 2 or more prior lines of platinum-based chemotherapy and who are unable to tolerate further platinum-based chemotherapy. Rucaparib is also available for the maintenance treatment of patients with platinum sensitive relapsed high-grade epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in complete or partial response to platinum-based chemotherapy.

GENE ASSOCIATION

On the basis of strong clinical evidence in ovarian cancer[116-117,272] , as well as clinical data in other cancer types[117,316-317] , loss or inactivation of either BRCA1 or BRCA2 may confer sensitivity to rucaparib.

SUPPORTING DATA

In the TRITON2 Phase 2 study for patients with metastatic castration-resistant prostate cancer (mCRPC) who previously progressed on androgen receptor–directed therapy and chemotherapy, rucaparib elicited an ORR of 28% (13/46) in an HRR-deficient population[318]. Specifically, 44% (11/25) of patients with BRCA1/2 mutations, 1 patient with a FANCA mutation and 1 patient with a BRIP1 mutation experienced a confirmed RECIST response[318].

Talazoparib

Assay findings association

BRCA2
rearrangement intron 14

AREAS OF THERAPEUTIC USE

The PARP inhibitor talazoparib is available in the EU as monotherapy to treat patients with HER2-negative locally advanced or metastatic breast cancer with germline BRCA mutations, who have been previously treated with, or are not considered candidates for, available therapies.

GENE ASSOCIATION

On the basis of strong clinical data in breast cancer[319-321] and additional clinical evidence in ovarian, pancreatic, and prostate cancer[322-324] , loss or inactivation of either BRCA1 or BRCA2 may confer sensitivity to talazoparib.

SUPPORTING DATA

A study of talazoparib monotherapy reported 2 PRs in patients with BRCA-mutant prostate cancer patients[322]. A case series in metastatic castration-resistant prostate cancer reported a decrease in the prostate-specific antigen (PSA) levels in one patient with a BRCA2 mutation after talazoparib treatment[324].

NOTE Genomic alterations detected may be associated with activity of certain approved therapies; however, the agents listed in this report may have varied clinical evidence in the patient's tumor type. Therapies listed in this report may not be complete and exhaustive and the therapeutic agents are not ranked in order of potential or predicted efficacy for this patient or in order of level of evidence for this patient's tumor type.

CLINICAL TRIALS

IMPORTANT Clinical trials are ordered by gene and prioritized in the following descending order: Pediatric trial qualification → Geographical proximity → Trial phase → Trial verification within last 2 months. While every effort is made to ensure the accuracy of the information contained below, the information available in the public domain is continually updated and should be investigated by the physician or research staff. The clinical trials listed in this report may not be complete and exhaustive or may include trials for which the patient does not meet the clinical trial enrollment criteria. For additional information about listed clinical trials or to conduct a search for additional trials, please see clinicaltrials.gov or local registries in your region.

GENE
AR

ALTERATION
amplification

RATIONALE
Tumors with AR amplification or activation may be responsive to therapies that inhibit the androgen receptor.

NCT03748641

PHASE 3

A Study of Niraparib in Combination With Abiraterone Acetate and Prednisone Versus Abiraterone Acetate and Prednisone for Treatment of Participants With Metastatic Prostate Cancer

TARGETS
CYP17, PARP

LOCATIONS: Calgary (Canada), Arizona, Vancouver (Canada), Victoria (Canada), California, Colorado, Connecticut, Florida, Kentucky, Maryland, Massachusetts, Nebraska, Nevada, New Jersey, New York, Hamilton (Canada), Kingston (Canada), Toronto (Canada), Pennsylvania, Montreal (Canada), South Carolina, Texas, Utah, Virginia, Washington, Buenos Aires (Argentina), Capital Federal (Argentina), Ciudad Automoma Buenos Aires (Argentina), Ciudad Autonoma Buenos Aires (Argentina), Cordoba (Argentina), Mar del Plata (Argentina), Pergamino (Argentina), Rosario (Argentina), San Salvador de Jujuy (Argentina), Adelaide (Australia), Benowa (Australia), Birtinya (Australia), Brisbane (Australia), Darlinghurst (Australia), Hobart (Australia), Macquarie University (Australia), Malvern (Australia), Melbourne (Australia), Murdoch (Australia), Nedlands (Australia), Randwick (Australia), Wahroonga (Australia), Wollongong (Australia), Aalst (Belgium), Antwerpen (Belgium), Charleroi (Belgium), Gent (Belgium), Liege (Belgium), Merksem (Belgium), Natal (Brazil), Rio de Janeiro (Brazil), Sao Paulo (Brazil), Sorocaba (Brazil), São Paulo (Brazil), Pleven (Bulgaria), Plovdiv (Bulgaria), Sofia (Bulgaria), Vratsa (Bulgaria), Hradec Králove (Czechia), Liberec (Czechia), Olomouc (Czechia), Pardubice (Czechia), Plzen (Czechia), Praha 2 (Czechia), Praha 4 (Czechia), Besancon (France), Bordeaux (France), Clermont Ferrand (France), Lyon (France), Nancy (France), Nice Cedex 2 (France), Saint Herblain (France), Saint Mande (France), Strasbourg (France), Braunschweig (Germany), Duisburg (Germany), Magdeburg (Germany), Muenster (Germany), Nuertingen (Germany), Budapest (Hungary), Debrecen (Hungary), Gyula (Hungary), Nyiregyhaza (Hungary), Szeged (Hungary), Beer Yaakov (Israel), Haifa (Israel), Petah Tikva (Israel), Ramat Gan (Israel), Faenza (Italy), Milano (Italy), Napoli (Italy), Padova (Italy), Parma (Italy), Perugia (Italy), Pisa (Italy), Roma (Italy), Terni (Italy), Torino (Italy), Trento (Italy), Busan (Korea, Republic of), Daegu (Korea, Republic of), Daejeon (Korea, Republic of), Goyang-Si (Korea, Republic of), Gwangju (Korea, Republic of), Seongnam-si (Korea, Republic of), Seoul (Korea, Republic of), Suwon (Korea, Republic of), George Town (Malaysia), Johor Bahru (Malaysia), Kota Kinabalu (Malaysia), Kuala Lumpur (Malaysia), Kuching (Malaysia), Aguascalientes (Mexico), Durango (Mexico), Monterrey (Mexico), Zapopan (Mexico), Amsterdam (Netherlands), Groningen (Netherlands), Leidschendam (Netherlands), Nieuwegein (Netherlands), Nijmegen (Netherlands), Rotterdam (Netherlands), Sittard-Geleen (Netherlands), Bydgoszcz (Poland), Gdańsk (Poland), Gdynia (Poland), Lodz (Poland), Siedlce (Poland), Szczecin (Poland), Warszawa (Poland), Wrocław (Poland), Barnaul (Russian Federation), Ivanovo (Russian Federation), Kursk (Russian Federation), Moscow (Russian Federation), Nizhny Novgorod (Russian Federation), Omsk (Russian Federation), Pyatigorsk (Russian Federation), Saint Petersburg (Russian Federation), Saint-Petersburg (Russian Federation), Saransk (Russian Federation), Sochi (Russian Federation), Tambov (Russian Federation), Tomsk (Russian Federation), Tyumen (Russian Federation), Vologda (Russian Federation), Johannesburg (South Africa), Pretoria (South Africa), Barcelona (Spain), Coruña (Spain), Jerez de la Frontera (Spain), Madrid (Spain), Málaga (Spain), Pozuelo de Alarcon (Spain), Sabadell (Spain), Santander (Spain), Valencia (Spain), Stockholm (Sweden), Uppsala (Sweden), Kaohsiung (Taiwan), Taichung (Taiwan), Tainan (Taiwan), Taipei (Taiwan), Taoyuan (Taiwan), Adana (Turkey), Ankara (Turkey), Antalya (Turkey), Edirne (Turkey), Istanbul (Turkey), Izmir (Turkey), Kocaeli (Turkey), Cherkasy (Ukraine), Dnipo (Ukraine), Dnipro (Ukraine), Ivano-Frankivsk (Ukraine), Khakhiv (Ukraine), Kharkiv (Ukraine), Kyiv (Ukraine), Lviv (Ukraine), Poltava (Ukraine), Uzhgorod (Ukraine), Blackburn (United Kingdom), Lancaster (United Kingdom), London (United Kingdom), Torquay (United Kingdom), Truro (United Kingdom), Wolverhampton (United Kingdom)

NCT03732820

PHASE 3

Study on Olaparib Plus Abiraterone as First-line Therapy in Men With Metastatic Castration-resistant Prostate Cancer

TARGETS
PARP, CYP17

LOCATIONS: Alabama, Alaska, Calgary (Canada), Edmonton (Canada), Arizona, Kelowna (Canada), California, Colorado, Connecticut, Illinois, Indiana, Louisiana, Michigan, Missouri, Montana, Nebraska, New Jersey, New York, North Carolina, Halifax (Canada), London (Canada), Toronto (Canada), Pennsylvania, Greenfield Park (Canada), Montreal (Canada), South Carolina, Texas, Wisconsin, Box Hill (Australia), Darlinghurst (Australia), Greenslopes (Australia), Herston (Australia), Kingswood (Australia), Kurralta Park (Australia), St Albans (Australia), Waratah (Australia), Gent (Belgium), Belo Horizonte (Brazil), Curitiba (Brazil), Fortaleza (Brazil), Porto Alegre (Brazil), Rio de Janeiro (Brazil), Sao Paulo (Brazil), São José do Rio Preto (Brazil), Santiago (Chile), Temuco (Chile), Viña del Mar (Chile), Brno (Czechia), Praha (Czechia), Praha 5 (Czechia), Angers Cedex 01 (France), BESANCON Cedex (France), Caen Cedex 05 (France), Marseille (France), Pierre Benite (France), Quimper Cedex (France), Toulouse Cedex 3 (France), Vandoeuvre les Nancy (France), Bergisch Gladbach (Germany), Bremen (Germany), Duisburg (Germany), Freiburg im Breisgau (Germany), Heinsberg (Germany), Köln (Germany), Mettmann (Germany), Nürnberg (Germany), Nürtingen (Germany), Ulm (Germany), Milano (Italy), Napoli (Italy), Orbassano (Italy), Pavia (Italy), Bunkyo-ku (Japan), Hirakata-shi (Japan), Kanazawa-shi (Japan), Kashihara-shi (Japan), Kawagoe-shi (Japan), Kita-gun (Japan), Kyoto-shi (Japan), Maebashi-shi (Japan), Miyazaki-city (Japan), Nagoya-shi (Japan), Osaka-shi (Japan), Osakasayama-shi (Japan), Sagamihara-shi (Japan), Sakura-shi (Japan), Shinjuku-ku (Japan), Toon-shi (Japan), Yokohama-shi (Japan), Daegu (Korea, Republic of), Goyang-si (Korea, Republic of), Seoul (Korea, Republic of), Hilversum (Netherlands), Nijmegen (Netherlands), Tilburg (Netherlands), Bratislava (Slovakia), Presov (Slovakia), Sala (Slovakia), Trencin (Slovakia), Barcelona (Spain), Gerona (Spain), Madrid (Spain), Malaga (Spain), Sevilla (Spain), Adana (Turkey), Ankara (Turkey), Istanbul (Turkey), Izmir (Turkey), Karsiyaka (Turkey), Guildford (United Kingdom), Manchester (United Kingdom), Sheffield (United Kingdom), Southampton (United Kingdom), Swansea (United Kingdom)

NCT03706365

PHASE 2

A Study of Abiraterone Acetate Plus Prednisone With or Without Abemaciclib (LY2835219) in Participants With Prostate Cancer

TARGETS
CYP17, CDK4, CDK6

LOCATIONS: Malaga (Spain), Arizona, Arkansas, Nürtingen (Germany), L'Hospitalet de Llobregat (Spain), California, Colorado, Connecticut, Plymouth (United Kingdom), Craiova (Romania), Florida, Nijmegen (Netherlands), Georgia, London (United Kingdom), Otopeni (Romania), Indiana, Kentucky, Seoul (Korea, Republic of), Chelsea (United Kingdom), Maryland, Massachusetts, Minnesota, Missouri, Nevada, Camperdown (Australia), Kogarah (Australia), Macquarie Park (Australia), Randwick (Australia), New York, Münster (Germany), North Carolina, Oklahoma, Oregon, Rotterdam (Netherlands), Tennessee, Texas, Utah, Vermont, Fitzroy (Australia), Copenhagen (Denmark), Næstved (Denmark), Tübingen (Germany), Utrecht (Netherlands), Bayamon (Puerto Rico), Bucuresti (Romania), Constanta (Romania), Barcelona (Spain), Madrid (Spain), Northampton (United Kingdom)

NCT00268476

PHASE 2/3

STAMPEDE: Systemic Therapy in Advancing or Metastatic Prostate Cancer: Evaluation of Drug Efficacy: A Multi-Stage Multi-Arm Randomised Controlled Trial

TARGETS
CYP17, AR

LOCATIONS: Reading (United Kingdom), Farnworth (United Kingdom), High Wycombe (United Kingdom), Cambridge (United Kingdom), Broomfield (United Kingdom), Chester (United Kingdom), Middlesbrough (United Kingdom), Carlisle (United Kingdom), Barnstaple (United Kingdom), Exeter (United Kingdom), Bournemouth (United Kingdom), Dorchester (United Kingdom), Poole (United Kingdom), Cottingham (United Kingdom), Eastbourne (United Kingdom), Saint Leonards-on-Sea (United Kingdom), Ashford (United Kingdom), Aylesbury (United Kingdom), Basingstoke (United Kingdom), Birmingham (United Kingdom), Brighton (United Kingdom), Burnley (United Kingdom), Burton-upon-Trent (United Kingdom), Bury St. Edmunds (United Kingdom), Crewe (United Kingdom), Darlington (United Kingdom), Derby (United Kingdom), Doncaster (United Kingdom), Dudley (United Kingdom), Gloucester (United Kingdom), Hereford (United Kingdom), Kidderminster (United Kingdom), Leeds (United Kingdom), Leicester (United Kingdom), Liverpool (United Kingdom), London (United Kingdom), Manchester (United Kingdom), Shrewsbury (United Kingdom), Stockport (United Kingdom), Sunderland (United Kingdom), Torquay (United Kingdom), Warrington (United Kingdom), Whitehaven (United Kingdom), Wigan (United Kingdom), Worcester (United Kingdom), Worthing (United Kingdom), Harlow (United Kingdom), Romford (United Kingdom), Westcliff-On-Sea (United Kingdom), Swansea (United Kingdom), Cheltenham (United Kingdom), Chur (Switzerland), Oldham (United Kingdom), Southampton (United Kingdom), Stevenage (United Kingdom), Inverness (United Kingdom), Newport (United Kingdom), Steeton (United Kingdom), Canterbury (United Kingdom), Maidstone (United Kingdom), Margate (United Kingdom), Glasgow (United Kingdom), Preston (United Kingdom), Southport (United Kingdom), Northwood (United Kingdom), Edinburgh (United Kingdom), Newcastle (United Kingdom), Scarborough (United Kingdom), Belfast (United Kingdom), Nottingham (United Kingdom), Sutton-in-Ashfield (United Kingdom), Oxford (United Kingdom), Cosham (United Kingdom), Ayr (United Kingdom), Bath (United Kingdom), Bristol (United Kingdom), Taunton (United Kingdom), Weston Super Mare (United Kingdom), Yeovil (United Kingdom), Sheffield (United Kingdom), Stoke-on-Trent (United Kingdom), Ipswich (United Kingdom), Guildford (United Kingdom), Sutton (United Kingdom), Newcastle-Upon-Tyne (United Kingdom), South Shields (United Kingdom), Lausanne (Switzerland), Aberystwyth (United Kingdom), Cardiff (United Kingdom), Sutton Coldfield (United Kingdom), Bradford (United Kingdom), Huddersfield (United Kingdom), Swindon (United Kingdom), Bebington (United Kingdom), Winterthur (Switzerland), Aarau (Switzerland), Basel (Switzerland), Berne (Switzerland), Liestal (Switzerland), St. Gallen (Switzerland), Zurich (Switzerland), Barnet (United Kingdom), Colchester (United Kingdom), Larbert (United Kingdom), Lincoln (United Kingdom), Stockton-on-Tees (United Kingdom), Wolverhampton (United Kingdom)

NCT02799706

PHASE 3

Trial Comparing Irradiation Plus Long Term Adjuvant Androgen Deprivation With GnRH Antagonist Versus GnRH Agonist Plus Flare Protection in Patients With Very High Risk Localized or Locally Advanced Prostate Cancer

TARGETS
LHRH

LOCATIONS: Brussel (Belgium), Brussels (Belgium), Haine-Saint-Paul (Belgium), Kortrijk (Belgium), Namur (Belgium), Wilrijk (Belgium), Copenhagen (Denmark), Amiens (France), Arras (France), Bayonne (France), Beuvry (France), Grenoble (France), Lyon (France), Nantes (France), Paris (France), Saint-Gregoire (France), Toulouse (France), Berlin (Germany), Freiburg (Germany), Magdeburg (Germany), Firenze (Italy), Meldola (Italy), Alcorcón (Spain), Barcelona (Spain), Bilbao (Spain), Cartagena (Spain), Córdoba (Spain), Las Palmas De Gran Canaria (Spain), Pamplona (Spain), Sabadell (Spain), Salamanca (Spain), Terrassa (Spain), Vigo (Spain), Bellinzona (Switzerland), Bern (Switzerland), Geneve (Switzerland), Nottingham (United Kingdom)

NCT03568656

PHASE 1/2

Study to Evaluate CCS1477 in Advanced Tumours

TARGETS
CYP17, CBP, p300, AR

LOCATIONS: Belfast (United Kingdom), Leicester (United Kingdom), Newcastle (United Kingdom), Sutton (United Kingdom)

NCT03070886

PHASE 2/3

Antiandrogen Therapy and Radiation Therapy With or Without Docetaxel in Treating Patients With Prostate Cancer That Has Been Removed by Surgery

TARGETS
LHRH, AR

LOCATIONS: Alabama, Alaska, Arizona, Arkansas, California, Colorado, Delaware, Florida, Georgia, Idaho, Illinois, Indiana, Iowa, Kansas, Louisiana, Maryland, Massachusetts, Michigan, Minnesota, Mississippi, Missouri, Montana, Nebraska, New Hampshire, New Jersey, New York, North Carolina, North Dakota, Ohio, Oklahoma, Pennsylvania, South Carolina, South Dakota, Texas, Utah, Vermont, Virginia, Washington, West Virginia, Wisconsin, San Juan (Puerto Rico)

NCT03009981

PHASE 3

A Study of Androgen Annihilation in High-Risk Biochemically Relapsed Prostate Cancer

TARGETS
LHRH, AR, CYP17

LOCATIONS: Arizona, California, District of Columbia, Hawaii, Illinois, Kansas, Maine, Massachusetts, Minnesota, Missouri, Nebraska, Nevada, New Hampshire, New Jersey, New Mexico, New York, North Carolina, Ohio, Oklahoma, Oregon, Pennsylvania, South Carolina, Texas, Wisconsin

NCT03414034

PHASE 2

Onvansertib in Combination With Abiraterone and Prednisone in Adult Patients With Metastatic Castration-Resistant Prostate Cancer

TARGETS
PLK1, CYP17

LOCATIONS: Massachusetts

NCT03436654

PHASE 2

Multi-arm Multi-modality Therapy for Very High Risk Localized and Low Volume Metastatic Prostatic Adenocarcinoma

TARGETS
AR, CYP17

LOCATIONS: Illinois, Massachusetts, New York, Ohio

GENE
BRCA2

RATIONALE
BRCA2 loss or inactivating alterations may predict sensitivity to PARP inhibitors.

ALTERATION
rearrangement intron 14

NCT03395197

PHASE 3

Talazoparib + Enzalutamide vs. Enzalutamide Monotherapy in mCRPC (TALAPRO-2)

TARGETS
PARP

LOCATIONS: Santiago de Compostela (Spain), Nagoya (Japan), Alaska, Hirosaki (Japan), Arizona, Tauranga (New Zealand), L'Hospitalet de Llobregat (Spain), Sabadell (Spain), Pergamino (Argentina), Cremona (Italy), California, Christchurch (New Zealand), Kashiwa (Japan), Colorado, Port Elizabeth (South Africa), Meldola (Italy), Goyang-si (Korea, Republic of), Sapporo (Japan), Indiana, Kanazawa (Japan), Yokohama (Japan), Yokosuka (Japan), Kentucky, Nebraska, New Jersey, New Mexico, Camperdown (Australia), Darlinghurst (Australia), Port Macquarie (Australia), New York, Ohio, Osaka-shi (Japan), Osakasayama (Japan), Suita (Japan), Pennsylvania, Auchenflower (Australia), Brisbane (Australia), Chermside (Australia), South Brisbane (Australia), Southport (Australia), Rosario (Argentina), Hamamatsu (Japan), South Carolina, Terni (Italy), Orbassano (Italy), Tennessee, Texas, Meguro-ku (Japan), Shinjuku-ku (Japan), Utah, Vina del Mar (Chile), Melbourne (Australia), North Melbourne (Australia), Hamilton (New Zealand), Washington, Cape Town (South Africa), George (South Africa), Kraaifontein, Cape Town (South Africa), Wisconsin, Cordoba (Argentina), Gent (Belgium), Kortrijk (Belgium), Yvoir (Belgium), Ostrava-Poruba (Czechia), Helsinki (Finland), Kempele (Finland), Kuopio (Finland), Oulu (Finland), Tampere (Finland), Turku (Finland), Suresnes (France), Suresnes Cedex (France), VILLEJUIF cedex (France), Kirchheim (Germany), Muenster (Germany), Nuertingen (Germany), Ravensburg (Germany), Reutlingen (Germany), Budapest (Hungary), Debrecen (Hungary), Pecs (Hungary), Tel Aviv (Israel), Napoli (Italy), Chiba (Japan), Fukuoka (Japan), Kagoshima (Japan), Kumamoto (Japan), Tokushima (Japan), Yamagata (Japan), Busan (Korea, Republic of), Daegu (Korea, Republic of), Seoul (Korea, Republic of), Auckland (New Zealand), Lorenskog (Norway), Norbyhagen (Norway), Oslo (Norway), Trondheim (Norway), Arequipa (Peru), Lima (Peru), Gdynia (Poland), Otwock (Poland), Warszawa (Poland), Barcelona (Spain), Solna (Sweden), Stockholm (Sweden), Umeå (Sweden), Cornwall (United Kingdom), Cronwall (United Kingdom), Glasgow (United Kingdom), London (United Kingdom)

NCT03748641

PHASE 3

A Study of Niraparib in Combination With Abiraterone Acetate and Prednisone Versus Abiraterone Acetate and Prednisone for Treatment of Participants With Metastatic Prostate Cancer

TARGETS
CYP17, PARP

LOCATIONS: Calgary (Canada), Arizona, Vancouver (Canada), Victoria (Canada), California, Colorado, Connecticut, Florida, Kentucky, Maryland, Massachusetts, Nebraska, Nevada, New Jersey, New York, Hamilton (Canada), Kingston (Canada), Toronto (Canada), Pennsylvania, Montreal (Canada), South Carolina, Texas, Utah, Virginia, Washington, Buenos Aires (Argentina), Capital Federal (Argentina), Ciudad Automoma Buenos Aires (Argentina), Ciudad Autonoma Buenos Aires (Argentina), Cordoba (Argentina), Mar del Plata (Argentina), Pergamino (Argentina), Rosario (Argentina), San Salvador de Jujuy (Argentina), Adelaide (Australia), Benowa (Australia), Birtinya (Australia), Brisbane (Australia), Darlinghurst (Australia), Hobart (Australia), Macquarie University (Australia), Malvern (Australia), Melbourne (Australia), Murdoch (Australia), Nedlands (Australia), Randwick (Australia), Wahroonga (Australia), Wollongong (Australia), Aalst (Belgium), Antwerpen (Belgium), Charleroi (Belgium), Gent (Belgium), Liege (Belgium), Merksem (Belgium), Natal (Brazil), Rio de Janeiro (Brazil), Sao Paulo (Brazil), Sorocaba (Brazil), São Paulo (Brazil), Pleven (Bulgaria), Plovdiv (Bulgaria), Sofia (Bulgaria), Vratsa (Bulgaria), Hradec Králove (Czechia), Liberec (Czechia), Olomouc (Czechia), Pardubice (Czechia), Plzen (Czechia), Praha 2 (Czechia), Praha 4 (Czechia), Besancon (France), Bordeaux (France), Clermont Ferrand (France), Lyon (France), Nancy (France), Nice Cedex 2 (France), Saint Herblain (France), Saint Mande (France), Strasbourg (France), Braunschweig (Germany), Duisburg (Germany), Magdeburg (Germany), Muenster (Germany), Nuertingen (Germany), Budapest (Hungary), Debrecen (Hungary), Gyula (Hungary), Nyiregyhaza (Hungary), Szeged (Hungary), Beer Yaakov (Israel), Haifa (Israel), Petah Tikva (Israel), Ramat Gan (Israel), Faenza (Italy), Milano (Italy), Napoli (Italy), Padova (Italy), Parma (Italy), Perugia (Italy), Pisa (Italy), Roma (Italy), Terni (Italy), Torino (Italy), Trento (Italy), Busan (Korea, Republic of), Daegu (Korea, Republic of), Daejeon (Korea, Republic of), Goyang-Si (Korea, Republic of), Gwangju (Korea, Republic of), Seongnam-si (Korea, Republic of), Seoul (Korea, Republic of), Suwon (Korea, Republic of), George Town (Malaysia), Johor Bahru (Malaysia), Kota Kinabalu (Malaysia), Kuala Lumpur (Malaysia), Kuching (Malaysia), Aguascalientes (Mexico), Durango (Mexico), Monterrey (Mexico), Zapopan (Mexico), Amsterdam (Netherlands), Groningen (Netherlands), Leidschendam (Netherlands), Nieuwegein (Netherlands), Nijmegen (Netherlands), Rotterdam (Netherlands), Sittard-Geleen (Netherlands), Bydgoszcz (Poland), Gdańsk (Poland), Gdynia (Poland), Lodz (Poland), Siedlce (Poland), Szczecin (Poland), Warszawa (Poland), Wrocław (Poland), Barnaul (Russian Federation), Ivanovo (Russian Federation), Kursk (Russian Federation), Moscow (Russian Federation), Nizhny Novgorod (Russian Federation), Omsk (Russian Federation), Pyatigorsk (Russian Federation), Saint Petersburg (Russian Federation), Saint-Petersburg (Russian Federation), Saransk (Russian Federation), Sochi (Russian Federation), Tambov (Russian Federation), Tomsk (Russian Federation), Tyumen (Russian Federation), Vologda (Russian Federation), Johannesburg (South Africa), Pretoria (South Africa), Barcelona (Spain), Coruña (Spain), Jerez de la Frontera (Spain), Madrid (Spain), Málaga (Spain), Pozuelo de Alarcon (Spain), Sabadell (Spain), Santander (Spain), Valencia (Spain), Stockholm (Sweden), Uppsala (Sweden), Kaohsiung (Taiwan), Taichung (Taiwan), Tainan (Taiwan), Taipei (Taiwan), Taoyuan (Taiwan), Adana (Turkey), Ankara (Turkey), Antalya (Turkey), Edirne (Turkey), Istanbul (Turkey), Izmir (Turkey), Kocaeli (Turkey), Cherkasy (Ukraine), Dnipo (Ukraine), Dnipro (Ukraine), Ivano-Frankivsk (Ukraine), Khakhiv (Ukraine), Kharkiv (Ukraine), Kyiv (Ukraine), Lviv (Ukraine), Poltava (Ukraine), Uzhgorod (Ukraine), Blackburn (United Kingdom), Lancaster (United Kingdom), London (United Kingdom), Torquay (United Kingdom), Truro (United Kingdom), Wolverhampton (United Kingdom)

NCT02975934

PHASE 3

A Study of Rucaparib Verses Physician's Choice of Therapy in Patients With Metastatic Castration-resistant Prostate Cancer and Homologous Recombination Gene Deficiency

TARGETS
CYP17, PARP, AR

LOCATIONS: Alabama, Calgary (Canada), Arizona, California, Colorado, Connecticut, Delaware, London (United Kingdom), Oxford (United Kingdom), Preston (United Kingdom), Slough (United Kingdom), Florida, Hawaii, Louisiana, Winnipeg (Canada), Maryland, Massachusetts, Michigan, Minnesota, Nebraska, Nevada, Moncton (Canada), Miranda (Australia), Orange (Australia), Saint Leonards (Australia), New York, North Carolina, Ohio, London (Canada), Ottawa (Canada), Toronto (Canada), Oregon, Tennessee, Texas, Virginia, Washington, Subiaco (Australia), Frankston (Australia), Geelong (Australia), Hobart (Australia), Wagga Wagga (Australia), Antwerp (Belgium), Kortrijk (Belgium), Liège (Belgium), Namur (Belgium), Oshawa (Canada), Copenhagen (Denmark), Herlev (Denmark), Vejle (Denmark), Dijon (France), Le Mans (France), Lille (France), Lyon (France), Nancy (France), Paris (France), Plérin (France), Rennes (France), Villejuif (France), Augsburg (Germany), Berlin (Germany), Braunschweig (Germany), Dresden (Germany), Dusseldorf (Germany), Emmendingen (Germany), Jena (Germany), Köln (Germany), Lubeck (Germany), Mannheim (Germany), Nurtingen (Germany), Tuebingen (Germany), Wuppertal (Germany), Cork (Ireland), Dublin (Ireland), Haifa (Israel), Jerusalem (Israel), Kfar Saba (Israel), Petach Tikva (Israel), Tel Aviv (Israel), Tel Hashomer (Israel), Arezzo (Italy), Faenza (Italy), Meldola (Italy), Milano (Italy), Modena (Italy), Roma (Italy), Terni (Italy), Trento (Italy), Barcelona (Spain), Córdoba (Spain), Guadalajara (Spain), Lugo (Spain), Madrid (Spain), Málaga (Spain), Oviedo (Spain), Sabadell (Spain), Santander (Spain), Sevilla (Spain), Valencia (Spain), Cardiff (United Kingdom), Taunton (United Kingdom), Wirral (United Kingdom)

NCT03732820

PHASE 3

Study on Olaparib Plus Abiraterone as First-line Therapy in Men With Metastatic Castration-resistant Prostate Cancer

TARGETS
PARP, CYP17

LOCATIONS: Alabama, Alaska, Calgary (Canada), Edmonton (Canada), Arizona, Kelowna (Canada), California, Colorado, Connecticut, Illinois, Indiana, Louisiana, Michigan, Missouri, Montana, Nebraska, New Jersey, New York, North Carolina, Halifax (Canada), London (Canada), Toronto (Canada), Pennsylvania, Greenfield Park (Canada), Montreal (Canada), South Carolina, Texas, Wisconsin, Box Hill (Australia), Darlinghurst (Australia), Greenslopes (Australia), Herston (Australia), Kingswood (Australia), Kurralta Park (Australia), St Albans (Australia), Waratah (Australia), Gent (Belgium), Belo Horizonte (Brazil), Curitiba (Brazil), Fortaleza (Brazil), Porto Alegre (Brazil), Rio de Janeiro (Brazil), Sao Paulo (Brazil), São José do Rio Preto (Brazil), Santiago (Chile), Temuco (Chile), Viña del Mar (Chile), Brno (Czechia), Praha (Czechia), Praha 5 (Czechia), Angers Cedex 01 (France), BESANCON Cedex (France), Caen Cedex 05 (France), Marseille (France), Pierre Benite (France), Quimper Cedex (France), Toulouse Cedex 3 (France), Vandoeuvre les Nancy (France), Bergisch Gladbach (Germany), Bremen (Germany), Duisburg (Germany), Freiburg im Breisgau (Germany), Heinsberg (Germany), Köln (Germany), Mettmann (Germany), Nürnberg (Germany), Nürtingen (Germany), Ulm (Germany), Milano (Italy), Napoli (Italy), Orbassano (Italy), Pavia (Italy), Bunkyo-ku (Japan), Hirakata-shi (Japan), Kanazawa-shi (Japan), Kashihara-shi (Japan), Kawagoe-shi (Japan), Kita-gun (Japan), Kyoto-shi (Japan), Maebashi-shi (Japan), Miyazaki-city (Japan), Nagoya-shi (Japan), Osaka-shi (Japan), Osakasayama-shi (Japan), Sagamihara-shi (Japan), Sakura-shi (Japan), Shinjuku-ku (Japan), Toon-shi (Japan), Yokohama-shi (Japan), Daegu (Korea, Republic of), Goyang-si (Korea, Republic of), Seoul (Korea, Republic of), Hilversum (Netherlands), Nijmegen (Netherlands), Tilburg (Netherlands), Bratislava (Slovakia), Presov (Slovakia), Sala (Slovakia), Trencin (Slovakia), Barcelona (Spain), Gerona (Spain), Madrid (Spain), Malaga (Spain), Sevilla (Spain), Adana (Turkey), Ankara (Turkey), Istanbul (Turkey), Izmir (Turkey), Karsiyaka (Turkey), Guildford (United Kingdom), Manchester (United Kingdom), Sheffield (United Kingdom), Southampton (United Kingdom), Swansea (United Kingdom)

NCT02952534

PHASE 2

A Study of Rucaparib in Patients With Metastatic Castration-resistant Prostate Cancer and Homologous Recombination Gene Deficiency

TARGETS
PARP

LOCATIONS: Alabama, Arizona, Slough (United Kingdom), California, Colorado, Connecticut, Delaware, District of Columbia, Northwood (United Kingdom), Florida, Georgia, Illinois, Louisiana, Maryland, Massachusetts, Michigan, Minnesota, Missouri, Nebraska, Nevada, New Jersey, Saint Leonards (Australia), New York, North Carolina, Ohio, Hamilton (Canada), London (Canada), Ottawa (Canada), Oregon, Pennsylvania, Sutton (United Kingdom), Hobart (Australia), Tennessee, Texas, Frankston (Australia), Geelong (Australia), Malvern (Australia), Virginia, Washington, Miranda (Australia), Orange (Australia), Subiaco (Australia), Wagga Wagga (Australia), Antwerp (Belgium), Gent (Belgium), Kortrijk (Belgium), Liège (Belgium), Roeselare (Belgium), Toronto (Canada), Copenhagen (Denmark), Herlev (Denmark), Vejle (Denmark), Caen (France), Dijon (France), Le Mans (France), Lille (France), Nancy (France), Paris (France), Plérin (France), Rennes (France), Augsburg (Germany), Berlin (Germany), Dresden (Germany), Dusseldorf (Germany), Emmendingen (Germany), Hamburg (Germany), Heidelberg (Germany), Jena (Germany), Köln (Germany), Lübeck (Germany), Mannheim (Germany), Nürtingen (Germany), Tuebingen (Germany), Wuppertal (Germany), Cork (Ireland), Dublin (Ireland), Haifa (Israel), Jerusalem (Israel), Kfar Saba (Israel), Petach Tikva (Israel), Ramat Gan (Israel), Tel Aviv (Israel), Arezzo (Italy), Faenza (Italy), Milano (Italy), Modena (Italy), Rome (Italy), Terni (Italy), Trento (Italy), Badalona (Spain), Barcelona (Spain), Guadalajara (Spain), Lugo (Spain), Madrid (Spain), Oviedo (Spain), Sabadell (Spain), Santander (Spain), Sevilla (Spain), Valencia (Spain), Headington (United Kingdom), Liverpool (United Kingdom), London (United Kingdom), Southampton (United Kingdom), Taunton (United Kingdom), Wirral (United Kingdom)

NCT03330405

PHASE 2

Javelin Parp Medley: Avelumab Plus Talazoparib In Locally Advanced Or Metastatic Solid Tumors

TARGETS
PD-L1, PARP

LOCATIONS: Edmonton (Canada), Arkansas, California, District of Columbia, Obninsk (Russian Federation), Massachusetts, Minnesota, Sydney (Australia), New York, Ohio, Toronto (Canada), Brisbane (Australia), Texas, Murdoch (Australia), Brussels (Belgium), Bruxelles (Belgium), Charleroi (Belgium), Copenhagen (Denmark), Herlev (Denmark), Budapest (Hungary), Miskolc (Hungary), Pecs (Hungary), Incheon (Korea, Republic of), Seoul (Korea, Republic of), Chelyabinsk (Russian Federation), Moscow (Russian Federation), Omsk (Russian Federation), Yaroslavl (Russian Federation), Leicester (United Kingdom), London (United Kingdom), Newcastle Upon Tyne (United Kingdom)

NCT03742895

PHASE 2

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)

TARGETS
PARP

LOCATIONS: Nagoya (Japan), Medellin (Colombia), Arizona, Oradea (Romania), Berazategui (Argentina), Ciudad de Buenos Aires (Argentina), California, Chelyabinsk (Russian Federation), Kashiwa (Japan), Comuna Floresti (Romania), Bogota (Colombia), Craiova (Romania), Georgia, Seongnam-si (Korea, Republic of), Guadalajara (Mexico), Istanbul (Turkey), Kentucky, Trujillo (Peru), Pozuelo de Alarcon (Spain), Maryland, Massachusetts, Michigan, Nebraska, New Jersey, Port Macquarie (Australia), New York, Monterrey (Mexico), Oklahoma, Suita (Japan), Pennsylvania, Montreal (Canada), South Dakota, Darlinghurst (Australia), Madero (Mexico), Utah, Washington, Nedlands (Australia), Buenos Aires (Argentina), Quebec (Canada), Barranquilla (Colombia), Cali (Colombia), Monteria (Colombia), Valledupar (Colombia), Copenhagen (Denmark), Herlev (Denmark), Odense (Denmark), Bordeaux (France), Dijon (France), Nice (France), Poitiers (France), Strasbourg (France), Villejuif (France), Guatemala (Guatemala), Quetzaltenango (Guatemala), Cork (Ireland), Dublin (Ireland), Haifa (Israel), Jerusalem (Israel), Ramat Gan (Israel), Tel Aviv (Israel), Napoli (Italy), Rozzano (Italy), Siena (Italy), Kyoto (Japan), Tokyo (Japan), Seoul (Korea, Republic of), Chihuahua (Mexico), Mexico City (Mexico), Oaxaca (Mexico), Santiago De Quetaro (Mexico), Lima (Peru), Brasov (Romania), Bucuresti (Romania), Cluj Napoca (Romania), Arkhangelsk (Russian Federation), Kazan (Russian Federation), Moscow (Russian Federation), Ryazan (Russian Federation), Saint Petersburg (Russian Federation), Saint-Petersburg (Russian Federation), Samara (Russian Federation), St.Petersburg (Russian Federation), Barcelona (Spain), Bellinzona (Switzerland), Geneva (Switzerland), Zuerich (Switzerland), Adana (Turkey), Ankara (Turkey), Antalya (Turkey), Edirne (Turkey), Izmir (Turkey), Konya (Turkey), Manchester (United Kingdom), Newcastle-upon-Tyne (United Kingdom), Oxford (United Kingdom), Sheffield (United Kingdom)

NCT03565991

PHASE 2

Javelin BRCA/ATM: Avelumab Plus Talazoparib in Patients With BRCA or ATM Mutant Solid Tumors

TARGETS
PD-L1, PARP

LOCATIONS: Torette Di Ancona (Italy), California, Kashiwa (Japan), Meldola (Italy), Georgia, Louisiana, Monza (Italy), Milano (Italy), Massachusetts, Missouri, Pamplona (Spain), New Jersey, New York, Amsterdam (Netherlands), Ohio, Oklahoma, Pennsylvania, Tennessee, Texas, Chuo-ku (Japan), Rotterdam (Netherlands), Brussel (Belgium), Brussels (Belgium), Edegem (Belgium), Copenhagen (Denmark), Odense C (Denmark), Clermont Ferrand (France), La Rochelle (France), Montpellier Cedex 5 (France), Napoli (Italy), Roma (Italy), Barcelona (Spain), Madrid (Spain), Sevilla (Spain), London (United Kingdom)

NCT02854436

PHASE 2

An Efficacy and Safety Study of Niraparib in Men With Metastatic Castration-Resistant Prostate Cancer and DNA-Repair Anomalies

TARGETS
PARP

LOCATIONS: Arizona, Vancouver (Canada), California, Colorado, Illinois, Kentucky, Louisiana, Massachusetts, Michigan, New York, North Carolina, Toronto (Canada), Pennsylvania, Montreal (Canada), South Carolina, Texas, Virginia, Washington, Wisconsin, Camperdown (Australia), Darlinghurst (Australia), East Albury (Australia), Kurralta Park (Australia), Melbourne (Australia), Murdoch (Australia), North Ryde (Australia), Port Macquarie (Australia), Randwick (Australia), Wahroonga (Australia), Aalst (Belgium), Brussel (Belgium), Charleroi (Belgium), Gent (Belgium), Haine-Saint-Paul, La Louviere (Belgium), Hasselt (Belgium), Kortrijk (Belgium), Liège (Belgium), Namur (Belgium), Ottignies (Belgium), Wilrijk (Belgium), Barretos (Brazil), Belo Horizonte (Brazil), Curitiba (Brazil), Fortaleza (Brazil), Ijuí (Brazil), Itajai (Brazil), Joinville (Brazil), Natal (Brazil), Salvador (Brazil), Sao Paulo (Brazil), Quebec (Canada), Avignon Cedex 9 (France), Besancon (France), Caen (France), Lyon (France), Nice Cedex 2 (France), Paris (France), Reims (France), Strasbourg (France), Villejuif Cedex (France), Beer-Sheva (Israel), Haifa (Israel), Kfar Saba (Israel), Ramat Gan (Israel), Zrifin (Israel), Seoul (Korea, Republic of), Amsterdam (Netherlands), Groningen (Netherlands), Maastricht (Netherlands), Rotterdam (Netherlands), Moscow (Russian Federation), Omsk (Russian Federation), Tomsk (Russian Federation), Barcelona (Spain), Córdoba (Spain), Madrid (Spain), Málaga (Spain), Pozuelo de Alarcon (Spain), Santander (Spain), Santiago de Compostela (Spain), Sevilla (Spain), Valencia (Spain), Lund (Sweden), Stockholm (Sweden), Umeå (Sweden), Kaohsiung (Taiwan), Taichung (Taiwan), Tainan (Taiwan), Taipei (Taiwan), Taoyuan County (Taiwan), Blackburn (United Kingdom), Bristol (United Kingdom), Cardiff (United Kingdom), Exeter (United Kingdom), London (United Kingdom), Preston (United Kingdom)

NCT03521037

PHASE 1

Rucaparib Hepatic Impairment Study in Patients With a Solid Tumor

TARGETS
PARP

LOCATIONS: Biała Podlaska (Poland), Poznań (Poland), Szczecin (Poland), Warszawa (Poland), Bratislava (Slovakia), Newcastle Upon Tyne (United Kingdom)

GENE
RET

ALTERATION
amplification

RATIONALE
RET amplification, activating mutations, or activating fusions may confer sensitivity to kinase inhibitors targeting RET.

NCT02029001

PHASE 2

Adapting Treatment to the Tumor Molecular Alterations for Patients With Advanced Solid Tumors: My Own Specific Treatment

TARGETS
mTOR, FLT3, KIT, PDGFRs, RAFs, RET, VEGFRs, ERBB2, EGFR, FGFR1, FGFR2, FGFR3, PARP, PD-L1, CTLA-4

LOCATIONS: Bordeaux (France), Lyon (France), Marseille (France), Paris (France), Pierre-Bénite (France), Toulouse (France)

NCT03297606

PHASE 2

Canadian Profiling and Targeted Agent Utilization Trial (CAPTUR)

TARGETS
VEGFRs, ABL, SRC, ALK, AXL, MET, ROS1, TRKA, TRKC, DDR2, KIT, PDGFRs, EGFR, PD-1, CTLA-4, PARP, CDK4, CDK6, CSF1R, FLT3, RET, mTOR, ERBB2, ERBB3, BRAF, MEK, SMO

LOCATIONS: Vancouver (Canada), Kingston (Canada), London (Canada), Ottawa (Canada), Toronto (Canada), Montreal (Canada), Regina (Canada), Saskatoon (Canada)

NCT02616185

PHASE 1

A Phase 1 Study To Evaluate Escalating Doses Of A Vaccine-Based Immunotherapy Regimen For Prostate Cancer (PrCa VBIR)

TARGETS
CSF1R, FLT3, KIT, PDGFRs, RET, VEGFRs, CTLA-4, PD-1

LOCATIONS: Arizona, Connecticut, Nebraska, New Jersey, New York, North Carolina, Pennsylvania, Washington

GENE
TMPRSS2

ALTERATION
TMPRSS2-ERG fusion

RATIONALE
Fusion of TMPRSS2 with ETS family transcription factors may indicate sensitivity to inhibitors of HDAC. TMPRSS2-ERG fusions may also indicate sensitivity to PARP inhibitors.

NCT03395197

PHASE 3

Talazoparib + Enzalutamide vs. Enzalutamide Monotherapy in mCRPC (TALAPRO-2)

TARGETS
PARP

LOCATIONS: Santiago de Compostela (Spain), Nagoya (Japan), Alaska, Hirosaki (Japan), Arizona, Tauranga (New Zealand), L'Hospitalet de Llobregat (Spain), Sabadell (Spain), Pergamino (Argentina), Cremona (Italy), California, Christchurch (New Zealand), Kashiwa (Japan), Colorado, Port Elizabeth (South Africa), Meldola (Italy), Goyang-si (Korea, Republic of), Sapporo (Japan), Indiana, Kanazawa (Japan), Yokohama (Japan), Yokosuka (Japan), Kentucky, Nebraska, New Jersey, New Mexico, Camperdown (Australia), Darlinghurst (Australia), Port Macquarie (Australia), New York, Ohio, Osaka-shi (Japan), Osakasayama (Japan), Suita (Japan), Pennsylvania, Auchenflower (Australia), Brisbane (Australia), Chermside (Australia), South Brisbane (Australia), Southport (Australia), Rosario (Argentina), Hamamatsu (Japan), South Carolina, Terni (Italy), Orbassano (Italy), Tennessee, Texas, Meguro-ku (Japan), Shinjuku-ku (Japan), Utah, Vina del Mar (Chile), Melbourne (Australia), North Melbourne (Australia), Hamilton (New Zealand), Washington, Cape Town (South Africa), George (South Africa), Kraaifontein, Cape Town (South Africa), Wisconsin, Cordoba (Argentina), Gent (Belgium), Kortrijk (Belgium), Yvoir (Belgium), Ostrava-Poruba (Czechia), Helsinki (Finland), Kempele (Finland), Kuopio (Finland), Oulu (Finland), Tampere (Finland), Turku (Finland), Suresnes (France), Suresnes Cedex (France), VILLEJUIF cedex (France), Kirchheim (Germany), Muenster (Germany), Nuertingen (Germany), Ravensburg (Germany), Reutlingen (Germany), Budapest (Hungary), Debrecen (Hungary), Pecs (Hungary), Tel Aviv (Israel), Napoli (Italy), Chiba (Japan), Fukuoka (Japan), Kagoshima (Japan), Kumamoto (Japan), Tokushima (Japan), Yamagata (Japan), Busan (Korea, Republic of), Daegu (Korea, Republic of), Seoul (Korea, Republic of), Auckland (New Zealand), Lorenskog (Norway), Norbyhagen (Norway), Oslo (Norway), Trondheim (Norway), Arequipa (Peru), Lima (Peru), Gdynia (Poland), Otwock (Poland), Warszawa (Poland), Barcelona (Spain), Solna (Sweden), Stockholm (Sweden), Umeå (Sweden), Cornwall (United Kingdom), Cronwall (United Kingdom), Glasgow (United Kingdom), London (United Kingdom)

NCT03748641

PHASE 3

A Study of Niraparib in Combination With Abiraterone Acetate and Prednisone Versus Abiraterone Acetate and Prednisone for Treatment of Participants With Metastatic Prostate Cancer

TARGETS
CYP17, PARP

LOCATIONS: Calgary (Canada), Arizona, Vancouver (Canada), Victoria (Canada), California, Colorado, Connecticut, Florida, Kentucky, Maryland, Massachusetts, Nebraska, Nevada, New Jersey, New York, Hamilton (Canada), Kingston (Canada), Toronto (Canada), Pennsylvania, Montreal (Canada), South Carolina, Texas, Utah, Virginia, Washington, Buenos Aires (Argentina), Capital Federal (Argentina), Ciudad Automoma Buenos Aires (Argentina), Ciudad Autonoma Buenos Aires (Argentina), Cordoba (Argentina), Mar del Plata (Argentina), Pergamino (Argentina), Rosario (Argentina), San Salvador de Jujuy (Argentina), Adelaide (Australia), Benowa (Australia), Birtinya (Australia), Brisbane (Australia), Darlinghurst (Australia), Hobart (Australia), Macquarie University (Australia), Malvern (Australia), Melbourne (Australia), Murdoch (Australia), Nedlands (Australia), Randwick (Australia), Wahroonga (Australia), Wollongong (Australia), Aalst (Belgium), Antwerpen (Belgium), Charleroi (Belgium), Gent (Belgium), Liege (Belgium), Merksem (Belgium), Natal (Brazil), Rio de Janeiro (Brazil), Sao Paulo (Brazil), Sorocaba (Brazil), São Paulo (Brazil), Pleven (Bulgaria), Plovdiv (Bulgaria), Sofia (Bulgaria), Vratsa (Bulgaria), Hradec Králove (Czechia), Liberec (Czechia), Olomouc (Czechia), Pardubice (Czechia), Plzen (Czechia), Praha 2 (Czechia), Praha 4 (Czechia), Besancon (France), Bordeaux (France), Clermont Ferrand (France), Lyon (France), Nancy (France), Nice Cedex 2 (France), Saint Herblain (France), Saint Mande (France), Strasbourg (France), Braunschweig (Germany), Duisburg (Germany), Magdeburg (Germany), Muenster (Germany), Nuertingen (Germany), Budapest (Hungary), Debrecen (Hungary), Gyula (Hungary), Nyiregyhaza (Hungary), Szeged (Hungary), Beer Yaakov (Israel), Haifa (Israel), Petah Tikva (Israel), Ramat Gan (Israel), Faenza (Italy), Milano (Italy), Napoli (Italy), Padova (Italy), Parma (Italy), Perugia (Italy), Pisa (Italy), Roma (Italy), Terni (Italy), Torino (Italy), Trento (Italy), Busan (Korea, Republic of), Daegu (Korea, Republic of), Daejeon (Korea, Republic of), Goyang-Si (Korea, Republic of), Gwangju (Korea, Republic of), Seongnam-si (Korea, Republic of), Seoul (Korea, Republic of), Suwon (Korea, Republic of), George Town (Malaysia), Johor Bahru (Malaysia), Kota Kinabalu (Malaysia), Kuala Lumpur (Malaysia), Kuching (Malaysia), Aguascalientes (Mexico), Durango (Mexico), Monterrey (Mexico), Zapopan (Mexico), Amsterdam (Netherlands), Groningen (Netherlands), Leidschendam (Netherlands), Nieuwegein (Netherlands), Nijmegen (Netherlands), Rotterdam (Netherlands), Sittard-Geleen (Netherlands), Bydgoszcz (Poland), Gdańsk (Poland), Gdynia (Poland), Lodz (Poland), Siedlce (Poland), Szczecin (Poland), Warszawa (Poland), Wrocław (Poland), Barnaul (Russian Federation), Ivanovo (Russian Federation), Kursk (Russian Federation), Moscow (Russian Federation), Nizhny Novgorod (Russian Federation), Omsk (Russian Federation), Pyatigorsk (Russian Federation), Saint Petersburg (Russian Federation), Saint-Petersburg (Russian Federation), Saransk (Russian Federation), Sochi (Russian Federation), Tambov (Russian Federation), Tomsk (Russian Federation), Tyumen (Russian Federation), Vologda (Russian Federation), Johannesburg (South Africa), Pretoria (South Africa), Barcelona (Spain), Coruña (Spain), Jerez de la Frontera (Spain), Madrid (Spain), Málaga (Spain), Pozuelo de Alarcon (Spain), Sabadell (Spain), Santander (Spain), Valencia (Spain), Stockholm (Sweden), Uppsala (Sweden), Kaohsiung (Taiwan), Taichung (Taiwan), Tainan (Taiwan), Taipei (Taiwan), Taoyuan (Taiwan), Adana (Turkey), Ankara (Turkey), Antalya (Turkey), Edirne (Turkey), Istanbul (Turkey), Izmir (Turkey), Kocaeli (Turkey), Cherkasy (Ukraine), Dnipo (Ukraine), Dnipro (Ukraine), Ivano-Frankivsk (Ukraine), Khakhiv (Ukraine), Kharkiv (Ukraine), Kyiv (Ukraine), Lviv (Ukraine), Poltava (Ukraine), Uzhgorod (Ukraine), Blackburn (United Kingdom), Lancaster (United Kingdom), London (United Kingdom), Torquay (United Kingdom), Truro (United Kingdom), Wolverhampton (United Kingdom)

NCT03732820

PHASE 3

Study on Olaparib Plus Abiraterone as First-line Therapy in Men With Metastatic Castration-resistant Prostate Cancer

TARGETS
PARP, CYP17

LOCATIONS: Alabama, Alaska, Calgary (Canada), Edmonton (Canada), Arizona, Kelowna (Canada), California, Colorado, Connecticut, Illinois, Indiana, Louisiana, Michigan, Missouri, Montana, Nebraska, New Jersey, New York, North Carolina, Halifax (Canada), London (Canada), Toronto (Canada), Pennsylvania, Greenfield Park (Canada), Montreal (Canada), South Carolina, Texas, Wisconsin, Box Hill (Australia), Darlinghurst (Australia), Greenslopes (Australia), Herston (Australia), Kingswood (Australia), Kurralta Park (Australia), St Albans (Australia), Waratah (Australia), Gent (Belgium), Belo Horizonte (Brazil), Curitiba (Brazil), Fortaleza (Brazil), Porto Alegre (Brazil), Rio de Janeiro (Brazil), Sao Paulo (Brazil), São José do Rio Preto (Brazil), Santiago (Chile), Temuco (Chile), Viña del Mar (Chile), Brno (Czechia), Praha (Czechia), Praha 5 (Czechia), Angers Cedex 01 (France), BESANCON Cedex (France), Caen Cedex 05 (France), Marseille (France), Pierre Benite (France), Quimper Cedex (France), Toulouse Cedex 3 (France), Vandoeuvre les Nancy (France), Bergisch Gladbach (Germany), Bremen (Germany), Duisburg (Germany), Freiburg im Breisgau (Germany), Heinsberg (Germany), Köln (Germany), Mettmann (Germany), Nürnberg (Germany), Nürtingen (Germany), Ulm (Germany), Milano (Italy), Napoli (Italy), Orbassano (Italy), Pavia (Italy), Bunkyo-ku (Japan), Hirakata-shi (Japan), Kanazawa-shi (Japan), Kashihara-shi (Japan), Kawagoe-shi (Japan), Kita-gun (Japan), Kyoto-shi (Japan), Maebashi-shi (Japan), Miyazaki-city (Japan), Nagoya-shi (Japan), Osaka-shi (Japan), Osakasayama-shi (Japan), Sagamihara-shi (Japan), Sakura-shi (Japan), Shinjuku-ku (Japan), Toon-shi (Japan), Yokohama-shi (Japan), Daegu (Korea, Republic of), Goyang-si (Korea, Republic of), Seoul (Korea, Republic of), Hilversum (Netherlands), Nijmegen (Netherlands), Tilburg (Netherlands), Bratislava (Slovakia), Presov (Slovakia), Sala (Slovakia), Trencin (Slovakia), Barcelona (Spain), Gerona (Spain), Madrid (Spain), Malaga (Spain), Sevilla (Spain), Adana (Turkey), Ankara (Turkey), Istanbul (Turkey), Izmir (Turkey), Karsiyaka (Turkey), Guildford (United Kingdom), Manchester (United Kingdom), Sheffield (United Kingdom), Southampton (United Kingdom), Swansea (United Kingdom)

NCT03330405

PHASE 2

Javelin Parp Medley: Avelumab Plus Talazoparib In Locally Advanced Or Metastatic Solid Tumors

TARGETS
PD-L1, PARP

LOCATIONS: Edmonton (Canada), Arkansas, California, District of Columbia, Obninsk (Russian Federation), Massachusetts, Minnesota, Sydney (Australia), New York, Ohio, Toronto (Canada), Brisbane (Australia), Texas, Murdoch (Australia), Brussels (Belgium), Bruxelles (Belgium), Charleroi (Belgium), Copenhagen (Denmark), Herlev (Denmark), Budapest (Hungary), Miskolc (Hungary), Pecs (Hungary), Incheon (Korea, Republic of), Seoul (Korea, Republic of), Chelyabinsk (Russian Federation), Moscow (Russian Federation), Omsk (Russian Federation), Yaroslavl (Russian Federation), Leicester (United Kingdom), London (United Kingdom), Newcastle Upon Tyne (United Kingdom)

NCT03521037

PHASE 1

Rucaparib Hepatic Impairment Study in Patients With a Solid Tumor

TARGETS
PARP

LOCATIONS: Biała Podlaska (Poland), Poznań (Poland), Szczecin (Poland), Warszawa (Poland), Bratislava (Slovakia), Newcastle Upon Tyne (United Kingdom)

NCT03834519

PHASE 3

Study of Pembrolizumab (MK-3475) Plus Olaparib Versus Abiraterone Acetate or Enzalutamide in Metastatic Castration-resistant Prostate Cancer (mCRPC) (MK-7339-010/KEYLYNK-010)

TARGETS
PD-1, CYP17, PARP, AR

LOCATIONS: Edmonton (Canada), L Hospitalet De Llobregat (Spain), Kelowna (Canada), Vancouver (Canada), Berazategui (Argentina), Buenos Aires (Argentina), California, Cambridge (United Kingdom), Avignon (France), Kashiwa (Japan), Sakura (Japan), Matsuyama (Japan), Caceres (Spain), Georgia, Illinois, Kanazawa (Japan), Hwasun Gun (Korea, Republic of), Sagamihara (Japan), Yokohama (Japan), Louisiana, Pozuelo de Alarcon (Spain), Maryland, Massachusetts, Michigan, Rozzano (Italy), Montana, Kashihara (Japan), Nebraska, Nevada, New Mexico, Darlinghurst (Australia), Macquarie University (Australia), Port Macquarie (Australia), Waratah (Australia), Wollongong (Australia), North Carolina, Halifax (Canada), Ohio, Hamilton (Canada), Toronto (Canada), Osakasayama (Japan), Suita (Japan), Rimouski (Canada), Sherbrooke (Canada), Herston (Australia), Tugun (Australia), Ijui (Brazil), Sao Paulo (Brazil), Hidaka (Japan), Koshigaya (Japan), Itajai (Brazil), Rosario (Argentina), Sao Jose do Rio Preto (Brazil), Hamamatsu (Japan), South Carolina, Utah, Box Hill (Australia), Melbourne (Australia), Virginia, Murdoch (Australia), Wisconsin, Ube (Japan), Caba (Argentina), Cordoba (Argentina), Graz (Austria), Linz (Austria), Salzburg (Austria), Wien (Austria), Quebec (Canada), Santiago (Chile), Temuco (Chile), Amiens (France), Besancon (France), Bordeaux (France), Brest (France), Clermont-Ferrand (France), Lyon (France), Marseille (France), Montpellier (France), Nancy (France), Orleans (France), Paris (France), Pierre Benite (France), Saint Quentin (France), Suresnes (France), Toulouse (France), Villejuif (France), Berlin (Germany), Duesseldorf (Germany), Erlangen (Germany), Muenchen (Germany), Nuernberg (Germany), Nuertingen (Germany), Trier (Germany), Tuebingen (Germany), Dublin (Ireland), Limerick (Ireland), Be'er- Ya'akov (Israel), Haifa (Israel), Jerusalem (Israel), Kfar Saba (Israel), Petach-Tikwa (Israel), Ramat Gan (Israel), Tel-Aviv (Israel), Bologna (Italy), Catania (Italy), Roma (Italy), Terni (Italy), Trento (Italy), Chiba (Japan), Fukuoka (Japan), Miyazaki (Japan), Nagasaki (Japan), Tokyo (Japan), Goyang-si (Korea, Republic of), Seoul (Korea, Republic of), Almelo (Netherlands), Amsterdam (Netherlands), Hoofddorp (Netherlands), Leeuwarden (Netherlands), Leidschendam (Netherlands), Nijmegen (Netherlands), Rotterdam (Netherlands), Auckland (New Zealand), Chelyabinsk (Russian Federation), Krasnoyarsk (Russian Federation), Moscow (Russian Federation), Omsk (Russian Federation), Saint Petersburg (Russian Federation), Samara (Russian Federation), Tomsk (Russian Federation), Barcelona (Spain), Girona (Spain), Malaga (Spain), Sabadell (Spain), Taichung (Taiwan), Tainen (Taiwan), Taipei (Taiwan), Bristol (United Kingdom), Sutton (United Kingdom)

NCT03148795

PHASE 2

A Study of Talazoparib in Men With DNA Repair Defects and Metastatic Castration-Resistant Prostate Cancer

TARGETS
PARP

LOCATIONS: Arizona, California, Suresnes (France), Besancon Cedex (France), Meldola (Italy), Georgia, Seongnam-si (Korea, Republic of), Pozuelo de Alarcon (Spain), Northwood (United Kingdom), Missouri, Pamplona (Spain), Darlinghurst (Australia), Northmead (Australia), Westmead (Australia), North Carolina, Auchenflower (Australia), Cairns (Australia), Chermside (Australia), South Brisbane (Australia), Southport (Australia), Ijui (Brazil), Porto Alegre (Brazil), Roma (Italy), Barretos (Brazil), Jau (Brazil), South Carolina, Sutton (United Kingdom), Nijmegen (Netherlands), Texas, Orbassano (Italy), Linz (Austria), Mestre (Italy), Box Hill (Australia), Clayton (Australia), Frankston (Australia), Heidelberg (Australia), Virginia, Washington, Wisconsin, Salzburg (Austria), Vienna (Austria), Bruxelles (Belgium), Gent (Belgium), Leuven (Belgium), Angers Cedex 02 (France), Angers Cedex 2 (France), Angers cedex 02 (France), Bordeaux cedex (France), La Roche sur Yon (France), Le Mans Cedex 02 (France), Strasbourg (France), Strasbourg Cedex (France), Villejuif Cedex (France), Villejuif cedex (France), Mannheim (Germany), Nuertingen (Germany), Tubingen (Germany), Wuerzburg (Germany), Budapest (Hungary), Debrecen (Hungary), Nyiregyhaza (Hungary), Cremona (Italy), Naples (Italy), Padova (Italy), Parma (Italy), Torino (Italy), Busan (Korea, Republic of), Daegu (Korea, Republic of), Seoul (Korea, Republic of), Brzozow (Poland), Kielce (Poland), Barcelona (Spain), Malaga (Spain), Valencia (Spain), Cambridge (United Kingdom)

NCT03431350

PHASE 1/2

A Study of Niraparib Combination Therapies for the Treatment of Metastatic Castration-Resistant Prostate Cancer

TARGETS
PARP, PD-1, CYP17

LOCATIONS: Calgary (Canada), Arizona, Vancouver (Canada), Colorado, Indiana, Maryland, Michigan, New York, Toronto (Canada), Pennsylvania, Montreal (Canada), South Carolina, Tennessee, Texas, Utah, Virginia, Wisconsin, Aalst (Belgium), Antwerpen (Belgium), Brussels (Belgium), Gent (Belgium), Kortrijk (Belgium), Liege (Belgium), Beer Yaakov (Israel), Beer-Sheva (Israel), Haifa (Israel), Petach Tikva (Israel), Ramat Gan (Israel), Firenze (Italy), Lecce (Italy), Macerata (Italy), Milano (Italy), Napoli (Italy), Barcelona (Spain), Madrid (Spain), Malaga (Spain), Bath (United Kingdom), London (United Kingdom), Southampton (United Kingdom), Sutton (United Kingdom), Truro (United Kingdom)

NCT02264678

PHASE 1/2

Ascending Doses of AZD6738 in Combination With Chemotherapy and/or Novel Anti Cancer Agents

TARGETS
ATR, PARP, PD-L1

LOCATIONS: California, New York, Saint Herblain (France), Villejuif (France), Seongnam-si (Korea, Republic of), Seoul (Korea, Republic of), Cambridge (United Kingdom), London (United Kingdom), Sutton (United Kingdom), Withington (United Kingdom)

NCT03338790

PHASE 2

An Investigational Immunotherapy Study of Nivolumab in Combination With Rucaparib, Docetaxel, or Enzalutamide in Metastatic Castration-resistant Prostate Cancer

TARGETS
PD-1, PARP, AR

LOCATIONS: Kelowna (Canada), Caba (Argentina), Capital Federal (Argentina), Ciudad Autonoma de Buenos Aires (Argentina), Monteria (Colombia), Leon (Mexico), Guadalajara (Mexico), Santiago de Chile (Chile), Moncton (Canada), Camperdown (Australia), Westmead (Australia), Hamilton (Canada), South Brisbane (Australia), Porto Alegre (Brazil), Culiacan (Mexico), Elizabeth Vale (Australia), Vina Del Mar (Chile), Clayton (Australia), Heidelberg (Australia), Cordoba (Argentina), Montreal (Canada), Quebec (Canada), Medellin (Colombia), Besancon (France), Clermont-ferrand (France), Lyon (France), Marseille (France), Villejuif (France)

NOTE One or more variants of unknown significance (VUS) were detected in this patient's tumor. These variants may not have been adequately characterized in the scientific literature at the time this report was issued, and/or the genomic context of these alterations makes their significance unclear. We choose to include them here in the event that they become clinically meaningful in the future.

BRCA2
N863S and amplification

IKBKE
N700S

KDR
A1065T

MAF
G145S

NBN
amplification

PALB2
V78I

Electronically signed by Douglas Lin, M.D. | Julia Elvin, M.D., Ph.D., Laboratory Director Foundation Medicine, Inc. | Roche Customer Care: +49 7624 14 2098 or europe.foundationmedicine@roche.com

Sample Preparation: FMI Germany GmbH, Nonnenwald 2, 82377 Penzberg, Germany
Sample Analysis: FMI Germany GmbH, Nonnenwald 2, 82377 Penzberg, Germany

FoundationOne CDx is designed to include genes known to be somatically altered in human solid tumors that are validated targets for therapy, either approved or in clinical trials, and/or that are unambiguous drivers of oncogenesis based on current knowledge. The current assay interrogates 324 genes as well as introns of 36 genes involved in rearrangements. The assay will be updated periodically to reflect new knowledge about cancer biology.

DNA GENE LIST: ENTIRE CODING SEQUENCE FOR THE DETECTION OF BASE SUBSTITUTIONS, INSERTION/DELETIONS, AND COPY NUMBER ALTERATIONS

ABL1	*ACVR1B*	*AKT1*	*AKT2*	*AKT3*	*ALK*	*ALOX12B*	*AMER1 (FAM123B)*	*APC*
AR	*ARAF*	*ARFRP1*	*ARID1A*	*ASXL1*	*ATM*	*ATR*	*ATRX*	*AURKA*
AURKB	*AXIN1*	*AXL*	*BAP1*	*BARD1*	*BCL2*	*BCL2L1*	*BCL2L2*	*BCL6*
BCOR	*BCORL1*	*BRAF*	*BRCA1*	*BRCA2*	*BRD4*	*BRIP1*	*BTG1*	*BTG2*
BTK	*C11orf30 (EMSY)*	*C17orf39 (GID4)*	*CALR*	*CARD11*	*CASP8*	*CBFB*	*CBL*	*CCND1*
CCND2	*CCND3*	*CCNE1*	*CD22*	*CD274 (PD-L1)*	*CD70*	*CD79A*	*CD79B*	*CDC73*
CDH1	*CDK12*	*CDK4*	*CDK6*	*CDK8*	*CDKN1A*	*CDKN1B*	*CDKN2A*	*CDKN2B*
CDKN2C	*CEBPA*	*CHEK1*	*CHEK2*	*CIC*	*CREBBP*	*CRKL*	*CSF1R*	*CSF3R*
CTCF	*CTNNA1*	*CTNNB1*	*CUL3*	*CUL4A*	*CXCR4*	*CYP17A1*	*DAXX*	*DDR1*
DDR2	*DIS3*	*DNMT3A*	*DOT1L*	*EED*	*EGFR*	*EP300*	*EPHA3*	*EPHB1*
EPHB4	*ERBB2*	*ERBB3*	*ERBB4*	*ERCC4*	*ERG*	*ERRFI1*	*ESR1*	*EZH2*
FAM46C	*FANCA*	*FANCC*	*FANCG*	*FANCL*	*FAS*	*FBXW7*	*FGF10*	*FGF12*
FGF14	*FGF19*	*FGF23*	*FGF3*	*FGF4*	*FGF6*	*FGFR1*	*FGFR2*	*FGFR3*
FGFR4	*FH*	*FLCN*	*FLT1*	*FLT3*	*FOXL2*	*FUBP1*	*GABRA6*	*GATA3*
GATA4	*GATA6*	*GNA11*	*GNA13*	*GNAQ*	*GNAS*	*GRM3*	*GSK3B*	*H3F3A*
HDAC1	*HGF*	*HNF1A*	*HRAS*	*HSD3B1*	*ID3*	*IDH1*	*IDH2*	*IGF1R*
IKBKE	*IKZF1*	*INPP4B*	*IRF2*	*IRF4*	*IRS2*	*JAK1*	*JAK2*	*JAK3*
JUN	*KDM5A*	*KDM5C*	*KDM6A*	*KDR*	*KEAP1*	*KEL*	*KIT*	*KLHL6*
KMT2A (MLL)	*KMT2D (MLL2)*	*KRAS*	*LTK*	*LYN*	*MAF*	*MAP2K1 (MEK1)*	*MAP2K2 (MEK2)*	*MAP2K4*
MAP3K1	*MAP3K13*	*MAPK1*	*MCL1*	*MDM2*	*MDM4*	*MED12*	*MEF2B*	*MEN1*
MERTK	*MET*	*MITF*	*MKNK1*	*MLH1*	*MPL*	*MRE11A*	*MSH2*	*MSH3*
MSH6	*MST1R*	*MTAP*	*MTOR*	*MUTYH*	*MYC*	*MYCL (MYCL1)*	*MYCN*	*MYD88*
NBN	*NF1*	*NF2*	*NFE2L2*	*NFKBIA*	*NKX2-1*	*NOTCH1*	*NOTCH2*	*NOTCH3*
NPM1	*NRAS*	*NSD3 (WHSC1L1)*	*NT5C2*	*NTRK1*	*NTRK2*	*NTRK3*	*P2RY8*	*PALB2*
PARK2	*PARP1*	*PARP2*	*PARP3*	*PAX5*	*PBRM1*	*PDCD1 (PD-1)*	*PDCD1LG2 (PD-L2)*	*PDGFRA*
PDGFRB	*PDK1*	*PIK3C2B*	*PIK3C2G*	*PIK3CA*	*PIK3CB*	*PIK3R1*	*PIM1*	*PMS2*
POLD1	*POLE*	*PPARG*	*PPP2R1A*	*PPP2R2A*	*PRDM1*	*PRKAR1A*	*PRKCI*	*PTCH1*
PTEN	*PTPN11*	*PTPRO*	*QKI*	*RAC1*	*RAD21*	*RAD51*	*RAD51B*	*RAD51C*
RAD51D	*RAD52*	*RAD54L*	*RAF1*	*RARA*	*RB1*	*RBM10*	*REL*	*RET*
RICTOR	*RNF43*	*ROS1*	*RPTOR*	*SDHA*	*SDHB*	*SDHC*	*SDHD*	*SETD2*
SF3B1	*SGK1*	*SMAD2*	*SMAD4*	*SMARCA4*	*SMARCB1*	*SMO*	*SNCAIP*	*SOCS1*
SOX2	*SOX9*	*SPEN*	*SPOP*	*SRC*	*STAG2*	*STAT3*	*STK11*	*SUFU*
SYK	*TBX3*	*TEK*	*TET2*	*TGFBR2*	*TIPARP*	*TNFAIP3*	*TNFRSF14*	*TP53*
TSC1	*TSC2*	*TYRO3*	*U2AF1*	*VEGFA*	*VHL*	*WHSC1*	*WT1*	*XPO1*
XRCC2	*ZNF217*	*ZNF703*						

DNA GENE LIST: FOR THE DETECTION OF SELECT REARRANGEMENTS

ALK	*BCL2*	*BCR*	*BRAF*	*BRCA1*	*BRCA2*	*CD74*	*EGFR*	*ETV4*
ETV5	*ETV6*	*EWSR1*	*EZR*	*FGFR1*	*FGFR2*	*FGFR3*	*KIT*	*KMT2A (MLL)*
MSH2	*MYB*	*MYC*	*NOTCH2*	*NTRK1*	*NTRK2*	*NUTM1*	*PDGFRA*	*RAF1*
RARA	*RET*	*ROS1*	*RSPO2*	*SDC4*	*SLC34A2*	*TERC**	*TERT***	*TMPRSS2*

*TERC is an NCRNA

**Promoter region of TERT is interrogated

ADDITIONAL ASSAYS: FOR THE DETECTION OF SELECT CANCER GENOMIC SIGNATURES

Loss of Heterozygosity (LOH) score
Microsatellite (MS) status
Tumor Mutational Burden (TMB)

FoundationOne CDx fulfills the requirements of the European Directive 98/79 EC for in vitro diagnostic medical devices and is registered as a CE-IVD product by Foundation Medicine's EU Authorized Representative, Qarad b.v.b.a, Cipalstraat 3, 2440 Geel, Belgium. CE

ABOUT FOUNDATIONONE CDX

FoundationOne CDx was developed and its performance characteristics determined by Foundation Medicine, Inc. (Foundation Medicine). FoundationOne CDx may be used for clinical purposes and should not be regarded as purely investigational or for research only. Foundation Medicine's clinical reference laboratories are qualified to perform high-complexity clinical testing.

Please refer to technical information for performance specification details: www.rochefoundationmedicine.com/f1cdxtech.

INTENDED USE

FoundationOne®CDx (F1CDx) is a next generation sequencing based in vitro diagnostic device for detection of substitutions, insertion and deletion alterations (indels), and copy number alterations (CNAs) in 324 genes and select gene rearrangements, as well as genomic signatures including microsatellite instability (MSI), tumor mutational burden (TMB), and for selected forms of ovarian cancer, loss of heterozygosity (LOH) score, using DNA isolated from formalin-fixed, paraffin-embedded (FFPE) tumor tissue specimens. The test is intended as a companion diagnostic to identify patients who may benefit from treatment with therapies in accordance with approved therapeutic product labeling. Additionally, F1CDx is intended to provide tumor mutation profiling to be used by qualified health care professionals in accordance with professional guidelines in oncology for patients with solid malignant neoplasms.

TEST PRINCIPLES

FoundationOne CDx will be performed exclusively as a laboratory service using DNA extracted from formalin-fixed, paraffin-embedded (FFPE) tumor samples. The proposed assay will employ a single DNA extraction method from routine FFPE biopsy or surgical resection specimens, 50-1000 ng of which will undergo whole-genome shotgun library construction and hybridization-based capture of all coding exons from 309 cancer-related genes, one promoter region, one non-coding (ncRNA), and select intronic regions from 34 commonly rearranged genes, 21 of which also include the coding exons. The assay therefore includes detection of alterations in a total of 324 genes. Using an Illumina® HiSeq platform, hybrid capture–selected libraries will be sequenced to high uniform depth (targeting >500X median coverage with >99% of exons at coverage >100X). Sequence data will be processed using a customized analysis pipeline designed to accurately detect all classes of genomic alterations, including base substitutions, indels, focal copy number amplifications, homozygous gene deletions, and selected genomic rearrangements (e.g.,gene fusions). Additionally, genomic signatures including loss of heterozygosity (LOH), microsatellite instability (MSI) and tumor mutational burden (TMB) will be reported.

THE REPORT

Incorporates analyses of peer-reviewed studies and other publicly available information identified by Foundation Medicine; these analyses and information may include associations between a molecular alteration (or lack of alteration) and one or more drugs with potential clinical benefit (or potential lack of clinical benefit), including drug candidates that are being studied in clinical research. The F1CDx report may be used as an aid to inform molecular eligibility for clinical trials. Note: The association of a therapy with a genomic alteration or signature does not necessarily indicate pharmacologic effectiveness (or lack thereof); no association of a therapy with a genomic alteration or signature does not necessarily indicate lack of pharmacologic effectiveness (or effectiveness).

Diagnostic Significance

FoundationOne CDx identifies alterations to select cancer-associated genes or portions of genes (biomarkers). In some cases, the Report also highlights selected negative test results regarding biomarkers of clinical significance.

Qualified Alteration Calls (Equivocal and Subclonal)

An alteration denoted as "amplification – equivocal" implies that the FoundationOne CDx assay data provide some, but not unambiguous, evidence that the copy number of a gene exceeds the threshold for identifying copy number amplification. The threshold used in FoundationOne CDx for identifying a copy number amplification is four (4) for ERBB2 and six (6) for all other genes. Conversely, an alteration denoted as "loss – equivocal" implies that the FoundationOne CDx assay data provide some, but not unambiguous, evidence for homozygous deletion of the gene in question. An alteration denoted as "subclonal" is one that the FoundationOne CDx analytical methodology has identified as being present in <10% of the assayed tumor DNA.

Ranking of Alterations and Therapies

Genomic Signatures and Gene Alterations

Therapies are ranked based on the following criteria: Therapies approved in the EU in patient's tumor type (ranked alphabetically within each NCCN category) followed by therapies approved in the EU in another tumor type (ranked alphabetically within each NCCN category).

Clinical Trials

Pediatric trial qualification → Geographical proximity → Later trial phase.

NCCN Categorization

Genomic signatures and gene alterations detected may be associated with certain National Comprehensive Cancer Network (NCCN) Compendium drugs or biologics (www.nccn.org). The NCCN categories indicated reflect the highest possible category for a given therapy in association with each genomic signature or gene alteration. Please note, however, that the accuracy and applicability of these NCCN categories within a report may be impacted by the patient's clinical history, additional biomarker information, age, and/or co-occurring alterations. For additional information on the NCCN categories please refer to the NCCN Compendium.

Limitations

1. The MSI-H/MSS designation by FMI F1CDx test is based on genome wide analysis of 95 microsatellite loci and not based on the 5 or 7 MSI loci described in current clinical practice guidelines. The threshold for MSI-H/MSS was determined by analytical concordance to comparator assays (IHC and PCR) using uterine, cecum and colorectal cancer FFPE tissue. The clinical validity of the qualitative MSI designation has not been established. For Microsatellite Instability (MSI) results, confirmatory testing using a validated orthogonal method should be considered.
2. TMB by F1CDx is defined based on counting the total number of all synonymous and nonsynonymous variants present at 5% allele frequency or greater (after filtering) and reported as mutations per megabase (mut/Mb) unit rounded to the nearest integer. The clinical validity of TMB defined by this panel has not been established.
3. The LOH score is determined by analyzing SNPs spaced at 1Mb intervals across the genome on the FoundationOne CDx test and extrapolating an LOH profile, excluding arm- and chromosome-wide LOH segments. Detection of LOH has been verified only for ovarian cancer patients, and the LOH score result may be reported for epithelial ovarian, peritoneal, or Fallopian tube carcinomas. The LOH score will be reported as "Cannot Be Determined" if the sample is not of sufficient quality to confidently determine LOH.

Performance of the LOH classification has not been established for samples below 35% tumor content. There may be potential interference of ethanol with LOH detection. The interfering effects of xylene, hemoglobin, and triglycerides on the LOH score have not been demonstrated.

LEVEL OF EVIDENCE NOT PROVIDED

Drugs with potential clinical benefit (or potential lack of clinical benefit) are not evaluated for source or level of published evidence.

NO GUARANTEE OF CLINICAL BENEFIT

This Report makes no promises or guarantees that a particular drug will be effective in the treatment of disease in any patient. This Report also makes no promises or guarantees that a drug with potential lack of clinical benefit will in fact provide no clinical benefit.

NO GUARANTEE OF REIMBURSEMENT

Foundation Medicine makes no promises or guarantees that a healthcare provider, insurer or other third party payor, whether private or governmental, will reimburse a patient for the cost of FoundationOne CDx.

TREATMENT DECISIONS ARE RESPONSIBILITY OF PHYSICIAN

Drugs referenced in this Report may not be suitable for a particular patient. The selection of any, all or none of the drugs associated with potential clinical benefit (or potential lack of clinical benefit) resides entirely within the discretion of the treating physician. Indeed, the information in this Report must be considered in conjunction with all other relevant information regarding a particular patient, before the patient's treating physician recommends a course of treatment. Decisions on patient care and treatment must be based on the independent medical judgment of the treating physician, taking into consideration all applicable information concerning the patient's condition, such as patient and family history, physical examinations, information from other diagnostic tests, and patient preferences, in accordance with the standard of care in a given community. A treating physician's decisions should not be based on a single test, such as this Test, or the information contained in this Report. Certain sample or variant characteristics may result in reduced sensitivity. FoundationOne CDx is performed using DNA derived from tumor, and as such germline events may not be reported.

SELECT ABBREVIATIONS

ABBREVIATION	DEFINITION
CR	Complete response
DCR	Disease control rate
DNMT	DNA methyltransferase
HR	Hazard ratio
ITD	Internal tandem duplication
MMR	Mismatch repair
muts/Mb	Mutations per megabase
NOS	Not otherwise specified
ORR	Objective response rate
OS	Overall survival
PD	Progressive disease
PFS	Progression-free survival
PR	Partial response
SD	Stable disease
TKI	Tyrosine kinase inhibitor

PDF Service version: 2.6.0

The median exon coverage for this sample is 1,003x

Electronically signed by Douglas Lin, M.D. | Julia Elvin, M.D., Ph.D., Laboratory Director Foundation Medicine, Inc. | Roche Customer Care: +49 7624 14 2098 or europe.foundationmedicine@roche.com

Sample Preparation: FMI Germany GmbH, Nonnenwald 2, 82377 Penzberg, Germany
Sample Analysis: FMI Germany GmbH, Nonnenwald 2, 82377 Penzberg, Germany

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