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DEEP GENOMIC ANALYSIS OF TUMOR

TEST REPORT

Ms. ABC

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DATAR CANCER GENETICS

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Patient Details

Name	:	Ms. ABC
Birth Date	:	07-Feb-1994
Gender	:	Female
Address	:	---
Referring Doctor	:	Dr. XYZ

Specimen Details

Tumor Type	:	Breast carcinoma
Specimen Type	:	FFPE Tumor Block
Collection Date	:	25-Jul-2023
Accession Date	:	25-Jul-2023
Report Date	:	02-Aug-2023

Specimen Analysis Summary

Tissue

FFPE Tumor Specimen	:	90% Neoplastic Cellularity (2131)
511 Genes	:	Tumor DNA- 497 Genes (SNAs | Indels | CNAs | TMB) Tumor RNA-51 Genes (Fusion Transcripts)
MMR IHC	:	MLH1 | MSH2 | MSH6 | PMS2
PD-L1 IHC	:	22C3 | 28-8
213 Clinical Trials	:	Refer to page no. 23 - 63

Report Highlights

Indications	USFDA Approved* / NCCN Recommended*	Off Label Therapy*
TMB - High 12 Mutations/Mb **MMR deficient (dMMR)**	☑ Pembrolizumab ☑ Dostarlimab-gxly	☑ Nivolumab ☑ Atezolizumab ☑ Avelumab ☑ Durvalumab ☑ Cemiplimab-rwlc
PD-L1 - 22C3 CPS - <1	--	--
PD-L1 - 28-8 TPS - <1%	--	--
ERBB2 Amplification (46 copies)	☑ Ado-Trastuzumab emtansine (T-DM1) ☑ Fam-Trastuzumab deruxtecan ☑ Margetuximab cmkb ☑ Trastuzumab ☑ Pertuzumab ☑ Lapatinib ☑ Neratinib ☑ Tucatinib	☑ Afatinib ☑ Dacomitinib
PIK3CA p.E545K (MAF 4.05% at 3897X)	☑ Alpelisib	☐ None
PIK3CA p.E545K (MAF 4.05% at 3897X) **NF1 p.R1968*** (MAF 85.63% at 1322)	☑ Everolimus	☑ Temsirolimus

☑ SOC Drugs with Benefit ☑ Off Label Drugs with Benefit ☒ Drugs without Clinical Benefit / with Potential Resistance

MAF: Mutant Allele Frequency; TMB: Tumor mutation burden; MMR: Mismatch Repair; TPS: Tumor Proportion Score; CPS: Combined Positive Score; SOC: Standard of Care; NCCN: National Comprehensive Cancer Network - Breast cancer.

* The USFDA approval or NCCN recommendation may not be for the detected biomarker or alteration. The association of the detected biomarker or alteration and the drug may be based only on the literature evidence.

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Disease Relevant Findings

Biomarker	Result
PIK3CA p.E545K	Mutation detected
BRCA1/2	No mutations detected
BRAF	No mutations detected
NTRK1/2/3	No fusions detected

Biomarker	Result
HRR genes	No pathogenic/likely pathogenic mutations detected
ESR1	No mutations detected
RET	No fusions detected

Summary of Other Genomic Alterations

Gene	Alteration Type (SNAs / Indels / CNAs/ Fusion)	Variant Classification	Therapeutic / Clinical Significance
TP53	p.R248Q (MAF 84.52% at 1783X)	Pathogenic	Refer to page no. 6
CDKN1B	p.G97Vfs*22 (MAF 61.62% at 895X)	Pathogenic	Refer to page no. 6
KMT2B	p.G275* (MAF 23% at 2655X)	Pathogenic (Novel)	Refer to page no. 6
POLD1	p.R968C (MAF 20.54% at 1919X)	VUS	---
MCL1	p.D72G (MAF 50.62% at 324X)	VUS	---
TP63	p.R226H (MAF 54.58% at 1846X)	VUS	---
MAP3K1	p.Y553H (MAF 6.64% at 301X)	VUS	---
PTPRD	p.R733H (MAF 36.49% at 519X)	VUS	---
NTRK2	p.R691C (MAF 41.6% at 2648X)	VUS	---
ABL1	p.G249G (MAF 45.79% at 6427X)	VUS	---
NOTCH1	p.L1794L (MAF 25.29% at 692X)	VUS	---
B2M	p.L15Ffs*41 (MAF 24.05% at 4830X)	VUS	---
AXIN1	p.R412W (MAF 20.41% at 735X)	VUS	---
ZFHX3	p.E3549Q (MAF 10.56% at 3181X)	VUS	---
NOTCH3	p.P2222L (MAF 45.77% at 1928X)	VUS	---
KMT2B	p.D2640D (MAF 44.39% at 1106X)	VUS	---
ERCC2	p.R487Q (MAF 6.58% at 836X)	VUS	---
FGFR3	c.1645+37_1646-36delCCCTCCTGG (MAF 24.58% at 1017X)	VUS	---
SPOP	Amplification (36 copies)	---	---

SNA: Single Nucleotide Alteration; CNA: Copy Number Alteration; INDELS: Insertion / Deletion; VUS: Variant of unknown/uncertain significance

Tumor Mutation Burden (TMB)

Genomic Findings

Markers	Result	Interpretation	Category
Tumor Mutation Burden (TMB)	12 Mutations/Mb	TMB High	Tier I (Level A)

Patient's tumor mutation burden based on targeted genomic profiling of 511 genes was found to be 12 Mutations/Mb.

Tumor mutation burden (TMB), the total number of somatic coding mutations in a tumor, is a promising predictive biomarker for immunotherapy response in cancer patients (Chan et al., 2018; Fancello et al., 2019). The somatic mutations in tumor DNA can give rise to neoantigens, mutation-derived antigens that are recognized and targeted by the immune system, especially after treatment with agents that activate T cells. Therefore, more somatic mutations a tumor has, the more neoantigens it is likely to form, and TMB can represent a useful estimation of tumor neoantigenic load (Chan et al., 2018; Fancello et al., 2019). Tumor mutation burden (TMB) is, thus, an informative biomarker for predicting response to immune checkpoint inhibitors like Pembrolizumab, Nivolumab, Atezolizumab, Avelumab, Durvalumab and Ipilimumab.

Clinical studies have shown associations between elevated TMB and efficacy of immune checkpoint inhibitors, alone or in combination with other agents, in multiple solid tumors including, lung cancer, urothelial carcinoma, melanoma, colorectal cancer, head and neck squamous cell carcinoma and other cancer types (Johnson et al., 2016; Goodman et al., 2017; Carbone et al., 2017; Hellmann et al., 2018; Eroglu et al., 2018; Miao et al., 2018; Rizvi et al., 2018; Powles et al., 2018; Socinski et al., 2018; Legrand et al., 2018; Chae et al., 2019; Ott et al., 2019).

Analysis of tumor mutation burden (TMB) across more than 100,000 multiple solid cancer specimens suggests that patients with TMB >20 mutations/Mb may derive benefit from immune checkpoint inhibitors (Chalmers et al., 2017).

In various malignancies TMB >10 mutations/Mb have shown benefit from immune checkpoint inhibitors (Johnson et al., 2016; Legrand et al., 2018; Gerber et al., 2018; Georges et al., 2019; Zhu et al., 2019; Rizvi et al., 2020; Gullapalli et al., 2020; Ready, 2020).

Pembrolizumab has been USFDA approved for the treatment of patients with tumor mutation burden-high (TMB-H) [≥10 mutations/megabase (mut/Mb)] solid tumors.

The median tumor mutation burden (TMB) (n=4722) for breast carcinoma is reported to be 3.8 mutations/Mb, while the maximum TMB is 135.1 mutations/Mb (95% Confidence Interval, 2.6 - 3.6) (Chalmers et al., 2017).

High TMB (TMB-H) is indicative of potential benefit from immune checkpoint inhibitors. Tumor mutation burden (TMB) detected in the submitted sample is 12 mutations/Mb. Therefore in this case, the patient may derive benefit from immune checkpoint inhibitor therapy based on high TMB.

Genomic Findings

Single Nucleotide Alterations / Indels / Copy Number Alterations / Fusion

Gene/s (Transcript ID)	Variant	Result	Category
PIK3CA (NM_006218.4)	c.1633G>A, p.E545K; [p.(Glu545Lys)]	Positive	Tier I (Level A)

Interpretation: PIK3CA mutations are present in 30-40% of estrogen receptor positive (ER+), human epidermal growth factor receptor 2 - negative (HER2-) primary as well as metastatic breast cancer patients and result in the activation of PI3K/AKT pathway (Mukohara, 2015; Bhat-Nakshatri et al., 2016; Andre et al., 2019; Sonnenblick et al., 2019). Therefore, activating mutations in PIK3CA gene, are suggestive of potential benefit from the PI3K inhibitor, Alpelisib as well as mTOR inhibitors, Everolimus and Temsirolimus (Andre et al., 2019; Yi et al., 2019).

Alpelisib is a USFDA approved kinase inhibitor indicated in combination with Fulvestrant for the treatment of postmenopausal women and men with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, PIK3CA-mutated, advanced or metastatic breast cancer.

Everolimus is USFDA approved for treatment of multiple tumor types, including hormone receptor positive, HER2 negative breast cancer. Alpelisib and Everolimus are also standard of care drugs for breast cancer as per NCCN guidelines (NCCN guidelines, 2023).

Temsirolimus is USFDA approved for the treatment of patients with advanced renal cell carcinoma.
In a phase II study, Temsirolimus showed objective response rate of 9.2%, median time to progression of 12 weeks and tolerable safety profile in heavily pretreated patients with locally advanced or metastatic breast cancer (n=109) (Chan et al., 2005).
In a phase II randomized 3-arm study, combination of Temsirolimus and Letrozole demonstrated a clinical benefit rate of 82% (Letrozole +10 mg daily Temsirolimus), 83% (Letrozole + 30 mg daily Temsirolimus for 5 days every 2 weeks) and 79% (Letrozole alone) in postmenopausal women with locally advanced or metastatic breast cancer (n=92). Progression free survival at one year was higher for the combination arms (69% and 62%), than for the Letrozole alone arm (48%) (Carpenter et al., 2005).

The USFDA has granted a fast-track designation to Gedatolisib (the PI3K/mTOR inhibitor) for use as a potential therapeutic option in patients with hormone receptor positive, HER2-negative metastatic breast cancer who experienced disease progression on CDK4/6 therapy.
In a phase Ib expansion study of Gedatolisib in combination with Palbociclib and endocrine therapy in women with ER+ advanced breast cancer (n=103), arm A with Gedatolisib plus Palbociclib and Letrozole as first-line treatment (n=31), arm B as CDK inhibitor naive and received Gedatolisib plus Palbociclib/Fulvestrant as second-line treatment (n=13), arm C previously received CDK inhibitors and received Gedatolisib plus Palbociclib/Fulvestrant in the second- or third-line setting on a weekly basis (n=32), and those in arm D had previously received CDK inhibitors and received Gedatolisib plus Palbociclib/Fulvestrant as second- or third-line treatment on a 3-weeks-on and 1-week-off basis (n=27) showed the objective response rate (ORR) of 85%, 77%, 32% and 63% in arms A, B, C, and D respectively. The clinical benefit rates in these arms were 96%, 100%, 79%, and 96% respectively. Moreover, the ORR was found to be superior in arm D relative to arm C, irrespective of prior therapies received (Layman et al., 2021).

Mutations in PIK3CA gene are suggestive of acquired resistance to endocrine therapy in ER-positive breast cancer (Vasan et al., Huang et al., 2019; Zhou et al., 2019; De Mattos-Arruda, 2020; Schwartzberg and Vidal, 2020). However, contradictory evidence exists for the same (Ueno, 2020).

Various studies suggest simultaneous activating PIK3CA mutation leads to lower pathological complete response (pCR) to anti-HER2 therapies Trastuzumab, Lapatinib or their combination in HER2 positive breast cancer (Berns et al., 2007; O'Brien et al., 2010; Jensen et al, 2012; Cizkova et al, 2013; Contreras et al., 2013; Majewski et al., 2015; Loibl et al., 2016; Rasti et al., 2022).

PIK3CA activating mutations are reported to be associated with less responsiveness to EGFR-targeted monoclonal antibodies, Cetuximab, Panitumumab and Necitumumab (Sartore-Bianchi et al., 2009; Sahin and Garrett, 2013; Rochefordiere et al., 2015) as well as anti-EGFR tyrosine kinase inhibitors (TKIs) (Xia et al., 2014; Xu et al., 2017; Wang et al., 2018; Jakobsen et al., 2018; Fang et al., 2019). However, several clinical studies have reported that PIK3CA mutations may not be associated with primary resistance to EGFR therapies (Eng et al., 2015; Wu et al., 2016; Fiala et al., 2016).

It is reported that PIK3CA mutated tumors are associated with worse survival in patients treated with immune checkpoint inhibitors (Collins et al., 2019; Yang et al., 2020). However, contradictory evidence exists for the same (Nusrat et al., 2019; Nusrat et al., 2020; Cheng et al., 2022).

PIK3CA p.E545K is a hotspot mutation that lies within the PIK helical domain of the PIK3CA protein, which results in increased phosphorylation of AKT and MEK1/2; and growth factor-independent cell survival (Karakas et al., 2006; Gymnopoulos et al., 2007). It is reported in tumors of breast, large intestine, urinary tract, upper aerodigestive tract and cervix.

The PIK3CA gene provides instructions for making the p110 alpha protein, which is a subunit of an enzyme called phosphatidylinositol 3-kinase (PI3K). The p110 alpha protein is called the catalytic subunit because it performs the action of PI3K, while the other subunit (produced by a different gene) regulates the enzyme's activity.

Markers (Cytoband)	Result	Category
ERBB2 (17q12)	**Amplification (46 copies)**	**Tier I (Level A)**

Interpretation: Approximately 15-20% of breast cancers have amplification at 17q12 chromosome region (Badache et al. 2006; Jernstrom et al., 2017; Alexander et al., 2017). Amplification of ERBB2 is frequently reported in breast cancer and shown to be associated with poor survival and an adverse prognosis in these patients (Sircoulomb et al., 2010; Marotta et al., 2012; Ellegard et al., 2019). ERBB2 amplification

is suggestive of potential benefit from Ado-Trastuzumab emtansine (T-DM1), Fam-Trastuzumab deruxtecan, Trastuzumab, Pertuzumab, Margetuximab-cmkb, Lapatinib, Neratinib, Tucatinib, Afatinib and Dacomitinib (Kalous et al., 2012; Nahta, 2013; Matsuoka et al., 2015; Zhu et al., 2015; Faber and Burns, 2018; Liu et al., 2018; Sanchez-Vega et al., 2019; Lee et al., 2019).

Ado-Trastuzumab emtansine (T-DM1) is USFDA approved for the treatment of HER2 positive breast cancer patients who have already been treated with Trastuzumab and a taxane. It is also used if the cancer recurs after adjuvant therapy.
Fam-Trastuzumab deruxtecan and Trastuzumab are USFDA approved for the treatment of HER2 positive breast cancer and HER2 overexpressing metastatic gastric or gastroesophageal junction (GEJ) adenocarcinoma.
Pertuzumab, Margetuximab cmkb, Lapatinib and Neratinib are USFDA approved for the treatment of HER2 positive breast cancer.
Tucatinib is USFDA approved for the treatment of HER2 positive breast cancer and colorectal cancer.
Ado-Trastuzumab emtansine (T-DM1), Fam-Trastuzumab deruxtecan, Trastuzumab, Pertuzumab, Margetuximab-cmkb, Lapatinib, Neratinib and Tucatinib are standard of care drugs for treatment of breast cancer as per NCCN guidelines (NCCN guidelines, 2023).

Afatinib is USFDA approved for treatment of non-small cell lung cancer.
In a neoadjuvant, randomized, open-label phase II trial of Afatinib (n=10) versus Trastuzumab (n = 11) versus Lapatinib (n = 8) in patients with locally advanced HER2-positive breast cancer, Afatinib demonstrated clinical activity which compared favorably to Trastuzumab and Lapatinib (stable disease: 37.9% vs 12.5% vs 9%, respectively) (Rimawi et al., 2015).

Dacomitinib is USFDA approved for treatment of patients with metastatic non-small cell lung cancer (NSCLC).
In a pre-clinical study, Dacomitinib inhibited growth and proliferation of HER2-amplified breast cancer cell lines resistant to Trastuzumab and Lapatinib (Kalous et al., 2012).

Several pre-clinical and clinical studies have suggested that HER2-amplified tumors are less likely to respond to EGFR targeted monoclonal antibodies, Panitumumab, Necitumumab and Cetuximab as well as anti-EGFR tyrosine kinase inhibitors (TKIs), Gefitinib, Erlotinib, Osimertinib (Yonesaka et al., 2011; Martin et al., 2013; Zhao et al., 2017; Greally et al., 2018; Liu et al., 2018; Sartore-Bianchi et al., 2019).

Gene/s (Transcript ID)	Variant	Result	Category
NF1 (NM_001042492.3)	c.5902C>T, p.R1968*; [p.(Arg1968Ter)]	Positive	Tier I (Level B)

Interpretation: NF1 mutations are reported in breast cancer and associated with an adverse prognosis (Wallace et al., 2012; Griffith et al., 2018; Pearson et al., 2020). Truncating NF1 mutations are associated with shorter disease free survival and an adverse prognosis in breast cancer patients (Griffith et al., 2018; Pearson et al., 2020). NF1 is involved in negatively regulating the mTOR pathway and functional loss of NF1 gene has been shown to result in elevated mTOR signaling (Giovannini et al., 2014; Sato and Sekido, 2018). Therefore, loss-of-function pathogenic and likely pathogenic mutations in NF1 gene are suggestive of potential benefit from mTOR inhibitors, Everolimus and Temsirolimus (Cheaib et al., 2015).

Kindly refer to USFDA labels/ studies of Everolimus and Temsirolimus mentioned earlier.

In a clinical study, treatment of Everolimus in 39 patients with solid tumors (gastric, renal cell, thyroid, head and neck and sarcomas), demonstrated clinical benefit with partial response in 9 and stable disease in 13 patients with genomic alterations in 10 out of 22 patients (45%), conferring activating effect on mTOR signaling pathway, including NF1 mutations (Lim et al., 2016).

However, efficacy of these drugs in NF1 mutated breast cancers is not well evaluated.

The NF1 gene is a tumor suppressor encoding neurofibromin, a RAS GTPase-activating protein that inhibits RAS activity as well as MAPK pathway activation (Py et al., 2018; Romo et al., 2019; Awada et al., 2020). NF1 p.R1968* does not lies within GAP-related domain (GRD) (Thomas et al., 2012).Therefore, its impact on activation of MAPK pathway is not yet known (Roth et al., 2008).

In silico analysis predicts NF1 p.R1968* to be a loss-of-function mutation. It is reported in tumors of prostate, lung, soft tissue, central nervous system, haematopoietic and lymphoid system.

Germline NF1 p.R1968* is reported in individual(s) with neurofibromatosis type 1 (Lee et al., 2019; Melloni et al., 2019; Riva et al., 2022). In view of high allele frequency (85.63%) of NF1 p.R1968* variant, germline nature cannot be ruled out.

The NF1 gene provides instructions for making a protein called neurofibromin. This gene product appears to function as a negative regulator of the ras signal transduction pathway. Neurofibromin acts as a tumor suppressor protein.

Gene/s (Transcript ID)	Variant	Result	Category
TP53 (NM_000546.5)	c.743G>A, p.R248Q; [p.(Arg248Gln)]	Positive	Tier I (Level B)

Interpretation: Mutations in the tumor suppressor gene TP53 are present in 30% of all breast cancers (Andersson et al., 2005; Bertheau et al., 2013; Cheasley et al., 2020; Shahbandi et al., 2020) and associated with an adverse prognosis (Varna et al., 2011; Walerych et al., 2012; Huszno and Grzybowska. 2018; Meric-Bernstam et al., 2018; Bai et al., 2021).

TP53 p.R248Q lies within the DNA binding domain of TP53 protein (Freed-Pastor and Prives, 2012). It results in a loss of DNA binding and decreased transactivation of TP53 targets and interference with wild-type TP53 transactivation, leads to resistance to apoptosis and failure of G1 arrest (Dearth et al., 2007; Hanel et al., 2013; Boettcher et al., 2019), as well as increased AKT activation, STAT3 dependent migration, enhanced tumor onset and growth (Schulz-Heddergott et al., 2018). It is reported in tumors of large intestine, breast, oesophagus, upper aerodigestive tract, haematopoietic and lymphoid system.

Germline TP53 p.R248Q variant is reported in individual(s) with Li-Fraumeni syndrome (Da Silva et al., 2022; Donato et al., 2022). In view of high allele frequency (84.52%) of TP53 p.R248Q variant, germline nature cannot be ruled out.

The TP53 gene provides instructions for making a protein called tumor protein TP53 (or p53). This protein acts as a tumor suppressor, which means that it regulates cell division by keeping cells from growing and dividing too fast or in an uncontrolled way. Because p53 is essential for regulating cell division and preventing tumor formation, it has been nicknamed the "guardian of the genome".

Gene/s (Transcript ID)	Variant	Result	Category
CDKN1B (NM_004064.4)	c.285delC, p.G97Vfs*22; [p.(Gly97ValfsTer22)]	Positive	Tier III

Interpretation: Mutations in CDKN1B gene are reported in breast cancer (Cusan et al., 2018; Viotto et al., 2021). In silico analysis predicts CDKN1B p.G97Vfs*22 to be a loss-of-function mutation. It is reported in tumors of small intestine, large intestine, prostate, stomach, haematopoietic and lymphoid system. However, the clinical significance of this variant in breast cancer is not yet known.

CDKN1B gene encodes a cyclin-dependent kinase inhibitor, which shares a limited similarity with CDK inhibitor CDKN1A/p21. The encoded protein binds to and prevents the activation of cyclin E-CDK2 or cyclin D-CDK4 complexes, and thus controls the cell cycle progression at G1. The degradation of this protein, which is triggered by its CDK dependent phosphorylation and subsequent ubiquitination by SCF complexes, is required for the cellular transition from quiescence to the proliferative state.

Gene/s (Transcript ID)	Variant	Result	Category
KMT2B (NM_014727.3)	c.823G>T, p.G275*; [p.(Gly275Ter)]	Positive	Tier III

Interpretation: Mutations in KMT2B gene are reported in breast cancer (Ghanbari et al., 2019; Zhu et al., 2022; Simigdala et al., 2023). In silico analysis predicts KMT2D p.G275*, a novel mutation, to be a loss-of-function. However, the literature evidence for the functional characterization of this novel variant is currently insufficient, therefore, the clinical significance of this variant in breast cancer cannot be conclusively determined.

KMT2B gene encodes a protein which contains multiple domains including a CXXC zinc finger, three PHD zinc fingers, two FY-rich domains, and a SET (suppressor of variegation, enhancer of zeste, and trithorax) domain. The SET domain is a conserved C-terminal domain that characterizes proteins of the MLL (mixed-lineage leukemia) family.

BRCA1/2 Mutation Analysis

Genomic Findings

No pathogenic/likely pathogenic mutations detected in BRCA1/BRCA2 genes in the submitted tumor tissue sample as evaluated by Next-Generation Sequencing (NGS).

Gene	Alterations	Drugs without Benefit
BRCA1, BRCA2	Negative	Olaparib, Rucaparib, Niraparib, Talazoparib

Interpretation: Absence of pathogenic/likely pathogenic mutations in BRCA1/2 genes is suggestive of lack of benefit from Olaparib, Talazoparib, Rucaparib and Niraparib.

Olaparib is USFDA approved for treatment of multiple cancers, including germline BRCA-mutated breast cancer.

Talazoparib is USFDA approved for treatment of germline BRCA-mutated breast cancer. It is also USFDA approved for prostate cancer patients with germline or somatic mutations in the genes involved in the HRR pathway.

Rucaparib is USFDA approved for prostate cancer and advanced ovarian epithelial, fallopian tube, or primary peritoneal cancer patients with germline BRCA mutations.

Niraparib is USFDA approved for advanced ovarian cancer patients with BRCA mutations.

Homologous Recombination Repair (HRR) Analysis

HRR

No pathogenic/likely pathogenic mutations were detected in analyzed homologous recombination repair (HRR) genes in the submitted sample.

To cope with DNA damage, cells possess a complex signaling network called the 'DNA damage response', which coordinates cell cycle control with DNA repair. A biochemical pathway which uses homologous recombination to repair DNA double strand breaks is known as homologous recombination repair (HRR) pathway. HRR-deficiency (HRD)/homologous recombination deficiency (HRD) is a phenomenon which results in less efficient and error-prone DNA double strand break (DSB) repair. This causes genomic instability and increases HRD cancer cells susceptibility to Poly-(ADP-Ribose)-polymerase (PARP) inhibitors. PARP inhibitors are a class of drugs indicated for the treatment of HRR-deficient solid tumors like, breast, ovarian, prostate and pancreatic cancers. PARP inhibition in homologous recombination-deficient tumor cells can induce "synthetic lethality", which targets two DNA repair pathways and induces serious cytotoxicity to tumor cells without damaging normal cells (Jiang et al., 2019). BRCA1 and BRCA2 are key components of the BRCA–Fanconi anemia DNA repair pathway that controls DNA repair via homologous recombination. There is emerging evidence of role of other non-BRCA genes such as, ATM, ATR, MRE11, NBN, PALB2, RAD50, etc. in HRR pathway. Germline as well as somatic deficiency or loss-of-function of genes involved in homologous recombination mediated DNA repair mechanism in multiple solid tumors is suggestive of increased sensitivity to PARP inhibitors, Niraparib, Olaparib, Rucaparib and Talazoparib (McCabe et. al. 2006; Sisay et al., 2017; Teply and Antonarakis, 2017; Heeke et al., 2018; Francica and Rottenberg et al., 2018; Hoppe et al., 2018; Handy et al., 2018; Belli et al., 2019; Keung et al., 2019; Gupta et al., 2019; Yap et al., 2019; Jiang et al., 2019).

Mismatch Repair (MMR) Status

Immunohistochemistry

Marker	Staining pattern
MLH1	Intact nuclear expression
PMS2	Intact nuclear expression
MSH2	Loss of nuclear expression
MSH6	Focal nuclear expression

Interpretation: Immunohistochemistry (IHC) for four mismatch repair (MMR) proteins (MLH1, MSH2, MSH6 and PMS2) was performed on formalin-fixed, paraffin-embedded tissue taken from representative sections of the resection specimens. MSH2 showed loss of nuclear expression, MSH6 showed focal nuclear expression while MLH1 and PMS2 showed intact nuclear expression, which indicates deficient mismatch repair (dMMR) proteins.

IHC for MMR proteins is used to identify MMR status: being diffusely positive (intact/retained nuclear staining) or showing loss of nuclear staining (MMR protein deficient) (Kanopiene et al, 2014; McCarthy et al, 2019). Loss of expression of MMR proteins may occur due to germline MMR gene mutations, somatic MMR gene inactivation or epigenetic silencing via promoter hypermethylation.

PD-1/PD-L1 checkpoints have important function in maintaining immune-tolerance and preventing effective antitumor immunity. Various clinical trials have demonstrated that mismatch repair deficiency (dMMR) or microsatellite instability-high (MSI-H) is significantly associated with long-term immunotherapy-related response and better prognosis in various tumors treated with immune checkpoint inhibitors, Nivolumab, Atezolizumab, Avelumab, Durvalumab and Cemiplimab-rwlc (Kim et al., 2020; Rocha et al., 2022). Tumors with dMMR or MSI-H are sensitive to immune checkpoint blockade (ICB), particularly to PD-1 and PD-L1 inhibitors. It is worth emphasizing that dMMR or MSI-H status could identify responders regardless of tumor location and tumor type, that is, they have the ability to guide different tumor immunotherapies in the same manner. Subsequently, USFDA approved Pembrolizumab and Dostarlimab-gxly for all dMMR/MSI-H solid tumors (Lemery et al., 2017; Zhao et al., 2019; Luchini et al., 2019; Andre et al., 2021; Oaknin et al., 2022).

Immunohistochemistry (IHC) Analysis

Immunohistochemistry

Marker	Result
PD-L1 (Antibody clone 22C3)	CPS - <1

Interpretation: PD-L1 (Antibody clone 22C3) showed combined positive score (CPS) <1.

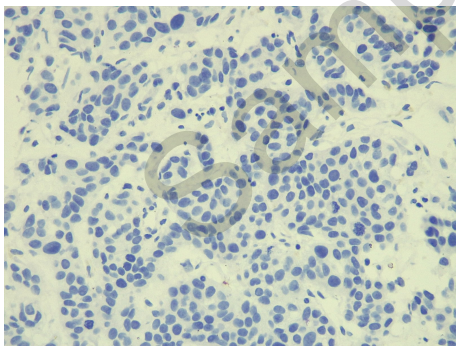
Pembrolizumab is USFDA approved for the treatment of multiple tumor types, including breast cancer.
Pembrolizumab in combination with chemotherapy has been recommended as standard of care therapy (category 1) for PD-L1 expression positive (threshold for positivity combined positivity score ≥10) breast tumors as per NCCN guidelines (NCCN guidelines, 2023).
Pembrolizumab is recommended as a standard of care regimen (category 2A) for the treatment of microsatellite instability high (MSI-H)/ mismatch repair deficient (dMMR)/ tumor mutation burden-high (TMB-H) (≥10 mutations/Mb) breast cancer as per NCCN guidelines (NCCN guidelines, 2023).

Cemiplimab-rwlc is USFDA approved for treatment of cutaneous squamous cell carcinoma, basal cell carcinoma and PD-L1 expression (TPS ≥50%) positive tumors of non-small cell lung cancer.

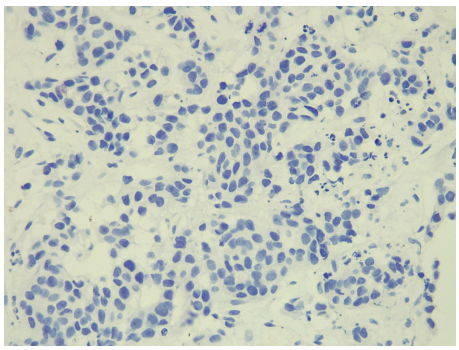
Marker	Result
PD-L1 (Antibody clone 28-8)	TPS - <1%

Interpretation: PD-L1 (Antibody clone 28-8) is immunoreactive in <1% of neoplastic cells.

Nivolumab is USFDA approved for classical Hodgkin lymphoma, colorectal cancer, gastric (stomach) cancer, esophageal cancer, non-small cell lung cancer, gastroesophageal junction adenocarcinoma, renal cell carcinoma, urothelial carcinoma, squamous cell carcinoma of the esophagus, squamous cell carcinoma of the head and neck, melanoma and malignant pleural mesothelioma.



PD-L1 (Antibody clone: 28-8)



PD-L1 (Antibody clone: 22C3)

Tumor Tissue

Variant Allele Fraction and Coverage

Variant (Transcript ID)	Genomic co-ordinates	Allele fraction	Coverage (X)
PIK3CA (NM_006218.4) c.1633G>A, p.E545K	chr3: 178936091G>A	4.05	3897
CDKN1B (NM_004064.4) c.285delC, p.G97Vfs*22	chr12: 12871053delC	61.62	895
TP53 (NM_000546.5) c.743G>A, p.R248Q	chr17: 7577538C>T	84.52	1783
NF1 (NM_001042492.3) c.5902C>T, p.R1968*	chr17: 29661945C>T	85.63	1322
KMT2B (NM_014727.3) c.823G>T, p.G275*	chr19: 36211072G>T	23	2655
POLD1 (NM_001256849.1) c.2902C>T, p.R968C	chr19: 50919734C>T	20.54	1919
MCL1 (NM_021960.5) c.215A>G, p.D72G	chr1: 150551792T>C	50.62	324
TP63 (NM_003722.5) c.677G>A, p.R226H	chr3: 189582118G>A	54.58	1846
MAP3K1 (NM_005921.2) c.1657T>C, p.Y553H	chr5: 56168803T>C	6.64	301
PTPRD (NM_002839.4) c.2198G>A, p.R733H	chr9: 8499771C>T	36.49	519
NTRK2 (NM_006180.5) c.2071C>T, p.R691C	chr9: 87570331C>T	41.6	2648
ABL1 (NM_005157.6) c.747C>T, p.G249G	chr9: 133738347C>T	45.79	6427
NOTCH1 (NM_017617.5) c.5382C>T, p.L1794L	chr9: 139396726G>A	25.29	692
B2M (NM_004048.3) c.43_44delCT, p.L15Ffs*41	chr15: 45003781delCT	24.05	4830
AXIN1 (NM_003502.4) c.1234C>T, p.R412W	chr16: 354324G>A	20.41	735
ZFHX3 (NM_006885.4) c.10645G>C, p.E3549Q	chr16: 72821530C>G	10.56	3181
NOTCH3 (NM_000435.3) c.6665C>T, p.P2222L	chr19: 15271774G>A	45.77	1928
KMT2B (NM_014727.3) c.7920C>T, p.D2640D	chr19: 36229230C>T	44.39	1106
ERCC2 (NM_000400.4) c.1460G>A, p.R487Q	chr19: 45860547C>T	6.58	836

Variant (Transcript ID)	Genomic co-ordinates	Allele fraction	Coverage (X)
FGFR3 (NM_000142.4) c.1645+37_1646-36del CCCTCCTGG	chr4: 1807433delCCCTCCTGG	24.58	1017

In view of high allele frequency of CDKN1B p.G97Vfs*22, TP53 p.R248Q, NF1 p.R1968*, MCL1 p.D72G, TP63 p.R226H, NTRK2 p.R691C, ABL1 p.G249G, NOTCH3 p.P2222L and KMT2B p.D2640D variants, germline nature cannot be ruled out.

Criteria for Classification of Somatic Variants

Analysis Criteria

The criteria/guidance used in this report is in accordance with the guidelines provided by the American College of Medical Genetics and Genomics (ACMG) for the interpretation and reporting of sequence variants in cancer. Somatic sequence variations are categorized into four tiers based on their clinical significance (Li et al., 2017).

- **Tier I:** Variants/biomarkers with strong clinical significance (therapeutic, prognostic and/or diagnostic)
  - **Level A evidence:** FDA approved therapies or standard guidelines for a specific tumor type.
  - **Level B evidence:** Statistically significant studies with consensus for specific tumor type.
- **Tier II:** Biomarkers with potential clinical significance (therapeutic, prognostic and/or diagnostic)
  - **Level C evidence:** FDA approved therapies or standard guidelines for a different tumor type (off-label use of the drug). An inclusion criteria for clinical trials.
  - **Level D evidence:** No consensus among different studies.
- **Tier III:** Biomarker whose association with cancer is not evident from available literature and is not frequently present in general population.
- **Tier IV:** Biomarker whose association with cancer has not been reported till date and is frequently present in general population. This category of variants is not included in this report as per guidelines.

Genes Analyzed

Gene List

SNVs/Indels/CNAs

ABCB1	ABL1	ABL2	ABRAXAS1	ACVR1*	ACVR1B	ACVR2A	ADAMTS12	ADAMTS2	AKT1
AKT2	AKT3	ALK	AMER1	APC	AR	ARAF	ARHGAP35	ARID1A	ARID1B
ARID2	ARID5B	ASXL1	ASXL2	ATM	ATP1A1*	ATR	ATRX	AURKA	AURKC
AXIN1	AXIN2	AXL	B2M	BAP1	BARD1	BCL2	BCL2L12	BCL6	BCOR
BCR*	BLM	BMP5*	BMPR2	BRAF	BRCA1	BRCA2	BRIP1	BTK*	CACNA1D*
CALR*	CARD11	CASP8	CBFB	CBL	CCND1	CCND2	CCND3	CCNE1	CD274
CD276	CD79B*	CDC73	CDH1	CDH10	CDK12	CDK4	CDK6	CDKN1A	CDKN1B
CDKN2A	CDKN2B	CDKN2C	CHD4	CHEK1	CHEK2	CIC	CIITA*	CREBBP	CSF1R*
CSMD3	CTCF	CTLA4	CTNNB1*	CTNND2	CUL1*	CUL3	CUL4A	CUL4B	CYLD
CYP2C9	CYP2D6*	CYSLTR2*	DAXX	DDR1	DDR2	DDX3X	DGCR8*	DICER1	DNMT3A
DOCK3	DPYD	DROSHA*	DSC1	DSC3	E2F1*	EGFR	EIF1AX	ELF3	EMSY
ENO1	EP300	EPAS1*	EPCAM	EPHA2	ERAP1	ERAP2	ERBB2	ERBB3	ERBB4
ERCC2	ERCC4	ERCC5*	ERRFI1	ESR1	ETV6	EZH2	FAM135B	FANCA	FANCC
FANCD2	FANCE	FANCF	FANCG	FANCI	FANCL	FANCM	FAS*	FAT1	FBXW7
FGF19	FGF23	FGF3	FGF4	FGF7*	FGF9	FGFR1	FGFR2	FGFR3	FGFR4
FLT3	FLT4	FOXA1	FOXL2*	FOXO1*	FUBP1	FYN	GATA2	GATA3	GLI1*
GLI3	GNA11*	GNA13	GNAQ*	GNAS	GPS2	H3F3A	H3F3B	HDAC2	HDAC9
HIF1A*	HIST1H2BD*	HIST1H3B*	HLA-A	HLA-B	HNF1A	HRAS*	ID3*	IDH1*	IDH2
IGF1R	IKBKB	IL6ST*	IL7R	INPP4B	IRF4*	IRS4*	JAK1	JAK2	JAK3
KDM5C	KDM6A	KDR	KEAP1	KIT	KLF4*	KLF5	KLHL13*	KMT2A	KMT2B
KMT2C	KMT2D	KNSTRN*	KRAS	LARP4B	LATS1	LATS2	MAGOH	MAP2K1	MAP2K2*
MAP2K4	MAP2K7	MAP3K1	MAP3K4	MAPK1	MAPK8	MAX	MCL1	MDM2	MDM4
MECOM	MED12*	MEF2B	MEN1	MET	MGA	MITF	MLH1	MLH3	MPL
MRE11	MSH2	MSH3	MSH6	MTAP	MTOR	MTUS2*	MUTYH	MYC	MYCL
MYCN	MYD88	MYOD1*	NBN	NCOR1	NF1	NF2	NFE2L2	NOTCH1	NOTCH2
NOTCH3	NOTCH4	NRAS	NSD2*	NT5C2*	NTRK1	NTRK2*	NTRK3	NUP93*	PALB2
PARP1	PARP2	PARP3	PARP4	PAX5*	PBRM1	PCBP1	PDCD1	PDCD1LG2	PDGFRA
PDGFRB	PDIA3	PGD	PHF6	PIK3C2B	PIK3CA	PIK3CB	PIK3CD*	PIK3CG*	PIK3R1
PIK3R2	PIM1	PLCG1	PMS1	PMS2	POLD1	POLE	POT1	PPM1D	PPP2R1A
PPP2R2A	PPP6C	PRDM1	PRDM9	PRKACA	PRKAR1A	PSMB10*	PSMB8*	PSMB9*	PTCH1
PTEN	PTPN11	PTPRD*	PTPRT	PXDNL	RAC1	RAD50	RAD51	RAD51B	RAD51C
RAD51D	RAD52	RAD54L	RAF1	RARA	RASA1	RASA2	RB1	RBM10	RECQL4
RET	RGS7*	RHEB	RHOA*	RICTOR	RIT1	RNASEH2A	RNASEH2B	RNASEH2C*	RNF43
ROS1	RPA1	RPL10*	RPL22*	RPL5*	RPS6KB1	RPTOR	RUNX1	RUNX1T1*	SDHA
SDHB	SDHC*	SDHD	SETBP1	SETD2	SF3B1	SIX1*	SIX2*	SLCO1B3	SLX4
SMAD2	SMAD4	SMARCA4	SMARCB1	SMC1A	SMO	SNCAIP*	SOCS1*	SOS1*	SOX2*
SOX9	SPEN	SPOP	SRC	SRSF2*	STAG2	STAT1*	STAT3	STAT5B*	STAT6
STK11	SUFU	TAF1*	TAP1	TAP2	TBX3	TCF7L2	TERT	TET2	TGFBR1*
TGFBR2	TMEM132D*	TNFAIP3	TNFRSF14	TOP1	TP53	TP63	TPMT	TPP2	TRRAP*
TSC1	TSC2	TSHR*	U2AF1	UGT1A1*	USP8	USP9X	VHL	WAS*	WT1

XPO1	XRCC2	XRCC3	YAP1	YES1	ZBTB20*	ZFHX3	ZMYM3	ZNF217	ZNF429
ZRSR2									

* No CNA

Fusion:

AKT2	ALK	AR	AXL	BRAF	BRCA1	BRCA2	CDKN2A	EGFR	ERBB2	ERBB4
ERG	ESR1	ETV1	ETV4	ETV5	FGFR1	FGFR2	FGFR3	FGR	FLT3	JAK2
KRAS	MDM4	MET	MYB	MYBL1	NF1	NOTCH1	NOTCH4	NRG1	NTRK1	NTRK2
NTRK3	NUTM1	PDGFRA	PDGFRB	PIK3CA	PPARG	PRKACA	PRKACB	PTEN	RAD51B	RAF1
RB1	RELA	RET	ROS1	RSPO2	RSPO3	TERT				

Antibody Details - Immunohistochemistry (IHC) Analysis

Antibody List

Marker	Clone	Vendor	Visualization System
PD-L1	28-8	Dako	Polymer detection system
PD-L1	22C3	Dako	
MLH1	ES05	Dako	
MSH2	FE11	Dako	
MSH6	EP49	Dako	
PMS2	EP51	Dako	

PD-L1

PD-L1 Interpretation

PD-L1 (Clone: 22C3): PD-L1 protein expression is determined by using Tumor Proportion Score (TPS), which is the percentage of viable tumor cells showing partial or complete membrane staining. PD-L1 IHC 22C3 pharmDx is indicated as an aid in identifying NSCLC patients for treatment with KEYTRUDA® (Pembrolizumab). According to PD-L1 IHC 22C3 pharmDx literature, specimen should be considered PD-L1 positive if TPS ≥ 50% of the viable tumor cells exhibit membrane staining at any intensity. However, an open-label, phase 3 KEYNOTE-042 study proved Pembrolizumab to be superior over platinum-based chemotherapy in patients with previously untreated advanced/metastatic NSCLC without sensitizing EGFR or ALK alterations and a PD-L1 TPS ≥ 1%.

Phase 3 trial of Cemiplimab versus platinum-based chemotherapies showed that Cemiplimab is indicated for the first-line treatment of patients with NSCLC whose tumors have high PD-L1 expression [Tumor Proportion Score (TPS) ≥ 50%] as determined by an FDA-approved test, with no EGFR, ALK or ROS1 aberrations (NCT03088540).

In certain tumor types (e.g. Gastric or gastroesophageal carcinoma, urothelial carcinoma, cervical, esophageal carcinoma, and head and neck squamous cell carcinoma (HNSCC), PD-L1 protein expression is determined by using Combined Positive Score (CPS), which is the number of PD-L1 staining cells (tumor cells, lymphocytes, macrophages) divided by the total number of viable tumor cells, multiplied by 100.

PD-L1 (Clone: 28-8): PD-L1 protein expression is defined as the percentage of tumor cells exhibiting positive complete circumferential or partial linear plasma membrane staining at any intensity. Cytoplasmic staining, if present, is not considered positive for scoring purposes. Non-malignant cells and immune cells (e.g. such as infiltrating lymphocytes or macrophages) may also stain with PD-L1; however, these are not included in the scoring for the determination of PD-L1 positivity.

PD-L1 expression cut off for positive test result varies according to the cancer type.

#PD-L1 IHC 28-8 pharmDx is a qualitative immunohistochemical assay using monoclonal Rabbit Anti PD-L1, Clone 28-8 intended for use in the detection of PD-L1 protein in formalin-fixed, paraffin-embedded (FFPE) non-squamous non-small cell lung cancer (NSCLC), squamous cell carcinoma of the head and neck (SCCHN), urothelial carcinoma (UC), and melanoma tissues.

Methods and Limitations

Methods

Tumor tissue was analyzed for mutation, copy number alterations and fusion detection using semiconductor based Next Generation Sequencing technology. High quality FFPE tissue DNA and RNA extracted from the submitted specimen was subjected to target enrichment by multiplex PCR amplification using Oncomine™ Comprehensive Assay Plus panel targeting 511 Oncogenes and Tumor suppressor genes. (see gene list in the 'Genes Analysed' section). Enriched DNA sequences were ligated with platform specific adaptor molecules and were sequenced using semiconductor chip. Sequenced data was aligned with the human genome (hg19), analyzed at 1000x minimum average depth using a customized in-house pipeline DCGL NGS Bioinformatics Pipeline vS15.3 and DCGL NGS Bioinformatics Pipeline vS10.5, designed to accurately detect the somatic variants.

This test does not detect gene variants other than those listed. Alterations in the primer binding regions can affect the testing, and ultimately, the genotyping assessments made. Rare diagnostic errors may occur due to primer site mutations. Tumor panel has limitations in detecting the following types of mutations (this might not be exhaustive): large rearrangements, epigenetic factors, mutations in repetitive or high GC rich regions and mutations in gene with corresponding pseudo genes or other highly homologous sequences. Presence of PCR inhibitors in the sample may prevent DNA amplification for mutation analysis. Rare and novel mutations may be clinically uncharacterized.

A negative test result does not exclude the possibility of mutations being present in the test sample probably due to the representation of reads representing minor allele fraction is below the detectable limit of the assay. The scope of copy number variations analysis includes copy number gain/amplification of the detected gene(s).

IHC analysis:
FFPE tissue was analyzed for immunohistochemistry. The test results relate specifically to the sample received in the lab. The pre-analytical variables like cold ischemia time, fixative and duration of fixation, which are beyond the control of DCGL laboratory, may affect the test results.

Important Information for Patients:
This is a Laboratory developed test, and its performance characteristics were determined by Datar Cancer Genetics UK Private Limited, United Kingdom. It has not been cleared or approved by the U.S. Food and Drug Administration. This Laboratory is registered under the Clinical Laboratory Improvement Amendments (CLIA)-USA to perform high complexity clinical laboratory testing.

The processing of samples for Molecular Genetics and Cell Culture analysis is carried out at our Laboratory - Datar Cancer Genetics UK Private Limited, United Kingdom.

The analysis of the generated data as well as the preparation of Reports is carried out by our partner laboratory - Datar Cancer Genetics Private Limited, Nasik, India.

This facility is certified by the College of American Pathologists (CAP) and under the Clinical Laboratory Improvement Amendments (CLIA)-USA as qualified to perform high complexity clinical laboratory testing. It is accredited under ISO 15189:2012 and ISO 27001:2013 for Information Security Management Systems.

Disclaimer

This report documents the genetic alterations detected in the submitted sample material. Information in this report is provided for information purpose only and should only 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 physicians, taking into consideration all applicable information concerning the patient's condition, such as patients and family history, physician's examination, information from other diagnostic test and patient references, in accordance with the standard of care in a given community. A treating physician's decisions should not be based on a single test or on the information contained in this report.

The information in this report does not constitute a treatment recommendation by Datar Cancer Genetics, either to use or not to use any specific therapeutic agent and should not be interpreted as treatment advice. Decisions on patient care and treatment rest solely within the discretion of the patient's treating physician.

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** End of Report **

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Medical Director

Clinical Trials Relevant to Patient's Genomic Findings

Clinical Trials

ERBB2 amplification

NCT number: NCT05230810
Phase: I/II
Treatment: Alpelisib, Tucatinib, Hormone Therapy
Cancer Type: Breast Cancer

Study Title: This is a Multicenter, Single Arm, Open-label, run-in Phase Ib / Roll-over Phase II Study of Tucatinib in Combination With Alpelisib in Subjects With PIK3CA-mutant HER2-positive Locally Advanced Unresectable or Metastatic Breast Cancer.
Variant Classification: ERBB2 amplification, PIK3CA activating mutation
Locations:
United States
Contacts:
Ash Philpott [518-583-0095; aphilpott@criteriuminc.com]

NCT number: NCT05063786
Phase: III
Treatment: Trastuzumab, Alpelisib, Hormone Therapy, Chemotherapy
Cancer Type: Breast Cancer

Study Title: A Randomized Phase III Trial of Trastuzumab + ALpelisib +/- Fulvestrant Versus Trastuzumab + Chemotherapy in Patients With PIK3CA Mutated Previously Treated HER2+ Advanced BrEasT Cancer. "ALPHABET Study".
Variant Classification: ERBB2 overexpression, PIK3CA mutation
Locations:
Austria, Spain, Switzerland

NCT number: NCT05306041
Phase: II
Treatment: Hormone Therapy, Pertuzumab/trastuzumab/hyaluronidase-zzxf, Inavolisib
Cancer Type: Breast Cancer

Study Title: A Randomized, Open-label, Phase II Trial Comparing Neoadjuvant Endocrine Therapy in Combination With Trastuzumab, Pertuzumab +/- the PI3K Inhibitor Inavolisib in Patients With HER2-positive, HR-positive, PIK3CA Mutant Early Breast Cancer-GeparPiPPa
Variant Classification: ERBB2 overexpression, PIK3CA mutation
Locations:
Germany

NCT number: NCT03273595
Phase: II
Treatment: Lapatinib, Trastuzumab, Chemotherapy
Cancer Type: Breast Cancer

Study Title: A Prospective, Open-label,Multicentre,Real-word Study of Lapatinib Plus Chemotherapy Versus Trastuzumab Plus Chemotherapy as Neoadjuvant Therapy for Women With HER2-positive and p95HER2-positive,PI3K Mutation,or PTEN Loss Breast Cancer
Variant Classification: ERBB2 amplification, PIK3CA mutation
Locations:
China

NCT number: NCT03698383
Phase: II
Treatment: Trastuzumab (Celltrion), Gedatolisib
Cancer Type: Breast Cancer

Study Title: Phase II Study of Trastuzumab Biosimilar (Herzuma) Plus Gedatolisib in Patients With HER-2 Positive Metastatic Breast Cancer Who Progressed After 2 or More HER-2 Directed Chemotherapy
Variant Classification: ERBB2 amplification, PIK3CA mutation
Locations:
Republic of Korea

NCT number: NCT04108858 **Phase: I/II** **Treatment:** Copanlisib, Trastuzumab, Pertuzumab **Cancer Type:** Breast Cancer	**Study Title:** Phase Ib/II Trial of Copanlisib in Combination With Trastuzumab and Pertuzumab After Induction Treatment of HER2 Positive (HER2+) Metastatic Breast Cancer (MBC) With PIK3CA Mutation or PTEN Mutation **Variant Classification:** ERBB2 overexpression, PIK3CA mutation **Locations:** United States **Contacts:** Multiple contacts: See www.clinicaltrials.gov for complete list of contacts.
NCT number: NCT04253561 **Phase: I** **Treatment:** Ipatasertib, Pertuzumab, Trastuzumab **Cancer Type:** Breast Cancer	**Study Title:** A Phase Ib Study of Ipatasertib, an AKT Inhibitor, in Combination With Pertuzumab Plus Trastuzumab in Patients With PI3KCA-mutant, HER2-positive Locally Advanced or Metastatic Breast Cancer **Variant Classification:** ERBB2 overexpression, PIK3CA mutation **Locations:** Spain
NCT number: NCT03006172 **Phase: I** **Treatment:** Inavolisib, Trastuzumab, Pertuzumab **Cancer Type:** Breast Cancer	**Study Title:** A Phase I, Open-Label, Dose-Escalation Study Evaluating the Safety, Tolerability, and Pharmacokinetics of Inavolisib as a Single Agent in Patients With Locally Advanced or Metastatic PIK3CA-Mutant Solid Tumors and in Combination With Endocrine and Targeted Therapies in Patients With Locally Advanced or Metastatic PIK3CA-Mutant Breast Cancer **Variant Classification:** ERBB2 positive, PIK3CA mutation **Locations:** Canada, France, Spain, United Kingdom, United States **Contacts:** Reference Study ID Number: GO39374 [888-662-6728; global-roche-genentech-trials@gene.com]
NCT number: NCT04215003 **Phase: I/II** **Treatment:** Alpelisib + Pertuzumab + Trastuzumab + Chemotherapy **Cancer Type:** Breast Cancer	**Study Title:** This is a Phase Ib/II, Prospective , Open-label, Single Center, Bayesian Adaptive Design, Umbrella Study Evaluating the Efficacy and Safety of Neo-adjuvant Therapy in Patients With Breast Cancer **Variant Classification:** ERBB2 positive, PI3K/AKT/MTOR mutation **Locations:** China
NCT number: NCT05131841 **Phase: IV** **Treatment:** Inetetamab, Chemotherapy **Cancer Type:** Breast Cancer	**Study Title:** A Multi-center, Randomized, Open-label Study on Pharmacokinetics, Safety, Efficacy, and Immunogenicity of Cipterbin Combined With Vinorelbine Injection Every Week or Every Three Weeks in the Treatment of Patients With HER2-positive Metastatic Breast Cancer **Variant Classification:** ERBB2 overexpression **Locations:** China

NCT number:
NCT05167643

Phase: IV

Treatment: Trastuzumab, Piperacillin, Hormone Therapy

Cancer Type: Breast Cancer

Study Title: Exploratory Study of HR-positive HER2-positive MBC Combined Treatment Plan

Variant Classification: ERBB2 overexpression

Locations:
China

NCT number:
NCT05122494

Phase: III

Treatment: Hemay022, Hormone Therapy, Lapatinib, Chemotherapy

Cancer Type: Breast Cancer

Study Title: A Randomized, Multicenter, Parallel,Phase III Open-label Study of the Efficacy and Safety of Hemay022 + AI in Patients With ER+/HER2+ Advanced or Metastatic Breast Cancer Who Have Received Prior Trastuzumab-Based Therapy

Variant Classification: ERBB2 overexpression

Locations:
China

NCT number:
NCT04514419

Phase: III

Treatment: HS627, Pertuzumab, Trastuzumab, Chemotherapy

Cancer Type: Breast Cancer

Study Title: A Phase III Study to Compare HS627 vs. Pertuzumab on the Efficacy, Safety and Immunogenicity in Combination With Trastuzumab and Docetaxel as Neoadjuvant Therapy in Patients With Early-stage or Locally Advanced HER2 Positive Breast Cancer

Variant Classification: ERBB2 overexpression

Locations:
China

NCT number:
NCT05760612

Phase: III

Treatment: Nilotinib, Trastuzumab, Pertuzumab

Cancer Type: Breast Cancer

Study Title: A Prospective, Randomized, Controlled, Phase III Clinical Study on Hormone Receptor Positive HER2 Positive Breast Cancer of RCB1-2 After Neoadjuvant Treatment With Trastuzumab Combined With Parezumab

Variant Classification: ERBB2 overexpression

Locations:
China

NCT number:
NCT05346224

Phase: III

Treatment: Pertuzumab (Shanghai Henlius Biotech), Pertuzumab, Trastuzumab, Chemotherapy

Cancer Type: Breast Cancer

Study Title: A Multicenter, Randomized, Double-Blind, Parallel-Controlled Phase III Clinical Study to Evaluate the Efficacy and Safety of Pertuzumab Biosimilar HLX11 vs. EU-Perjeta in the Neoadjuvant Therapy of HER2-Positive and HR-Negative Early-stage or Locally Advanced Breast Cancer

Variant Classification: ERBB2 overexpression

Locations:
China

NCT number: NCT04646759 **Phase: III** **Treatment:** Pyrotinib, Hormone Therapy, Chemotherapy **Cancer Type:** Breast Cancer	**Study Title:** Fulvestrant or Capecitabine Combined With Pyrotinib in HR-positive and HER2-Positive Metastatic Breast Cancer: A Multicenter, Randomized, Phase III Study **Variant Classification:** ERBB2 overexpression **Locations:** China
NCT number: NCT05424835 **Phase: III** **Treatment:** SHR-A1811, Pyrotinib, Chemotherapy **Cancer Type:** Breast Cancer	**Study Title:** A Phase III, Multicenter, Randomized, Open-Label, Parallel Controlled Study of SHR-A1811 Versus Pyrotinib in Combination With Capecitabine for HER2-Positive, Unresectable and/or Metastatic Breast Cancer Subjects Previously Treated With Trastuzumab and Taxane **Variant Classification:** ERBB2 overexpression **Locations:** China
NCT number: NCT05720026 **Phase: III** **Treatment:** SYSA1901, Pertuzumab, Trastuzumab, Chemotherapy **Cancer Type:** Breast Cancer	**Study Title:** Phase III Comparison Of The Efficacy And Safety Of SYSA1901 Mab Injection/Pertuzumab (Parjet®) Combined With Trastuzumab And Docetaxel In Neoadjuvant Treatment Of Patients With Early Or Locally Advanced HER2-Positive Breast Cancer Clinical Research **Variant Classification:** ERBB2 overexpression **Locations:** China
NCT number: NCT01785420 **Phase: III** **Treatment:** Trastuzumab **Cancer Type:** Breast Cancer	**Study Title:** A Phase III Double Blind Randomized Placebo Controlled Study of Trastuzumab as Short Duration Preoperative Therapy in Patients with HER2-neu Positive Operable Breast Cancer **Variant Classification:** ERBB2 overexpression **Locations:** India
NCT number: NCT04622319 **Phase: III** **Treatment:** Trastuzumab Deruxtecan, Ado-trastuzumab Emtansine **Cancer Type:** Breast Cancer	**Study Title:** A Phase III, Multicenter, Randomized, Open-Label, Active-Controlled Study of Trastuzumab Deruxtecan (T-DXd) Versus Trastuzumab Emtansine (T-DM1) in Participants With High-Risk HER2-Positive Primary Breast Cancer Who Have Residual Invasive Disease in Breast or Axillary Lymph Nodes Following Neoadjuvant Therapy (DESTINY-Breast05) **Variant Classification:** ERBB2 amplification **Locations:** Argentina, Australia, Belgium, Brazil, Canada, Chile, China, Czech Republic, Denmark, France, Germany, Greece, Hong Kong, Ireland, Israel, Italy, Japan, Mexico, Netherlands, Peru, Poland, Portugal, Republic of Korea, Romania, Russian Federation, Singapore, Spain, Taiwan, United Kingdom, United States **Contacts:** Daiichi Sankyo Contact for Clinical Trial Information [908-992-6400; CTRinfo@dsi.com]

NCT number: NCT04784715 **Phase: III** **Treatment:** Trastuzumab Deruxtecan, Pertuzumab, Trastuzumab, Chemotherapy **Cancer Type:** Breast Cancer	**Study Title:** Phase III Study of Trastuzumab Deruxtecan (T-DXd) With or Without Pertuzumab Versus Taxane, Trastuzumab and Pertuzumab in HER2-positive, First-line Metastatic Breast Cancer (DESTINY-Breast09) **Variant Classification:** ERBB2 overexpression **Locations:** Argentina, Belgium, Brazil, Canada, China, Denmark, France, Germany, Hungary, India, Israel, Italy, Japan, Mexico, Peru, Philippines, Republic of Korea, Romania, Saudi Arabia, South Africa, Spain, Sweden, Taiwan, Turkey, United Kingdom, United States **Contacts:** AstraZeneca Clinical Study Information Center [877-240-9479; information.center@astrazeneca.com]
NCT number: NCT05159193 **Phase: III** **Treatment:** Trastuzumab, Pertuzumab, Chemotherapy **Cancer Type:** Breast Cancer	**Study Title:** A Multicentre, Open-label, Randomised Trial of Neoadjuvant Pegylated Liposomal Doxorubicin Plus Cyclophosphamide Sequential Docetaxel Plus Trastuzumab and Pertuzumab Versus Docetaxel Plus Carboplatin Combined With Trastuzumab and Pertuzumab in HER-2 Positive Breast Cancer **Variant Classification:** ERBB2 overexpression **Locations:** China
NCT number: NCT05474690 **Phase: III** **Treatment:** Trastuzumab, Pertuzumab, Chemotherapy **Cancer Type:** Breast Cancer	**Study Title:** A Non-inferior, Randomized Controlled Phase III Clinical Study Comparing the Efficacy of TCbHPand ECHP-THP in Neoadjuvant Treatment of Operable HER2-positive Breast Cancer **Variant Classification:** ERBB2 amplification **Locations:** China
NCT number: NCT05871918 **Phase: III** **Treatment:** Trastuzumab, Pertuzumab, Chemotherapy **Cancer Type:** Breast Cancer	**Study Title:** A Multicenter, Randomized, Open, Phase III Trial of ddEC-THP（Epirubicin，Cyclophosphamide，TAX(Taxol)，Trastuzumab，Pertuzumab）vs Evaluating the Efficacy and Safety of TCHP（CBP(Carboplatin),TXT(Taxotere),Trastuzumab，Pertuzumab）Neoadjuvant Therapy for HER2-positive Breast Cancer **Variant Classification:** ERBB2 overexpression **Locations:** China
NCT number: NCT05429684 **Phase: III** **Treatment:** Trastuzumab, Pertuzumab, Chemotherapy, Pyrotinib, Palbociclib, Ado-trastuzumab Emtansine, Everolimus, Hormone Therapy, Sintilimab **Cancer Type:** Breast Cancer	**Study Title:** Precise Targeted Therapy for Refractory HER2 Positive Advanced Breast Cancer Based on Genome Signature and Drug Sensitivity of PDO Model **Variant Classification:** ERBB2 overexpression **Locations:** China

NCT number: NCT02344472 **Phase: III** **Treatment:** Trastuzumab, Pertuzumab, Ribociclib, Chemotherapy, Hormone Therapy **Cancer Type:** Breast Cancer	**Study Title:** DETECT V / CHEVENDO A Multicenter, Randomized Phase III Study to Compare Chemo- Versus Endocrine Therapy in Combination With Dual HER2-targeted Therapy of Herceptin (Trastuzumab) and Perjeta (Pertuzumab) Plus Kisqali® (Ribociclib) in Patients With HER2 Positive and Hormone-receptor Positive Metastatic Breast Cancer. **Variant Classification:** ERBB2 amplification **Locations:** Germany
NCT number: NCT05346861 **Phase: III** **Treatment:** Trastuzumab, Pyrotinib, Chemotherapy **Cancer Type:** Breast Cancer	**Study Title:** Pyrotinib Rechallenge in Her2-positive Metastatic Breast Cancer Pretreated With Pyrotinib and Trastuzumab **Variant Classification:** ERBB2 overexpression **Locations:** China
NCT number: NCT04457596 **Phase: III** **Treatment:** Tucatinib, Ado-trastuzumab Emtansine **Cancer Type:** Breast Cancer	**Study Title:** The CompassHER2 Trials (Comprehensive Use of Pathologic Response Assessment to Optimize Therapy in HER2-Positive Breast Cancer) CompassHER2 Residual Disease (RD), a Double-Blinded, Phase III Randomized Trial of T-DM1 Compared With T-DM1 and Tucatinib. **Variant Classification:** ERBB2 amplification **Locations:** Canada, Puerto Rico, United States **Contacts:** Ciara C. O'Sullivan [507-293-0526; osullivan.ciara@mayo.edu]
NCT number: NCT05132582 **Phase: III** **Treatment:** Tucatinib, Trastuzumab, Pertuzumab **Cancer Type:** Breast Cancer	**Study Title:** A Randomized, Double-blind, Phase III Study of Tucatinib or Placebo in Combination With Trastuzumab and Pertuzumab as Maintenance Therapy for Metastatic HER2+ Breast Cancer (HER2CLIMB-05). **Variant Classification:** ERBB2 amplification **Locations:** Australia, Austria, Belgium, Brazil, Canada, China, France, Germany, Italy, Japan, Poland, Portugal, Republic of Korea, Spain, Switzerland, Taiwan, United Kingdom, United States **Contacts:** Seagen Trial Information Support [866-333-7436; clinicaltrials@seagen.com]
NCT number: NCT05283837 **Phase: III** **Treatment:** ZRC-3277, Pertuzumab, Trastuzumab, Chemotherapy **Cancer Type:** Breast Cancer	**Study Title:** A Prospective, Randomized, Multicenter, Comparative, Double-blind, Parallel Study to Evaluate the Efficacy and Safety of Test Pertuzumab (ZRC-3277, Cadila Healthcare Ltd.,) With Reference Pertuzumab (Perjeta Genentech Inc.,) in Patients With HER2 Positive Metastatic Breast Cancer **Variant Classification:** ERBB2 overexpression **Locations:** India

NCT number: NCT05426486 **Phase: II/III** **Treatment:** ARX-788, Pyrotinib, Trastuzumab, Pertuzumab, Chemotherapy **Cancer Type:** Breast Cancer	**Study Title:** A Randomized, Open Label, Multi-center Phase II-III Neoadjuvant Study Comparing the Efficacy and Safety of ARX788 Combined With Pyrotinib Maleate Versus TCBHP (Trastuzumab Plus Pertuzumab With Docetaxel and Carboplatin) in Patients With HER2-positive Breast Cancer **Variant Classification:** ERBB2 overexpression **Locations:** China
NCT number: NCT03500380 **Phase: II/III** **Treatment:** Disitamab Vedotinaide, Lapatinib, Chemotherapy **Cancer Type:** Breast Cancer	**Study Title:** A Randomized, Controlled, Multi-center Phase II Clinical Study to Evaluate the Efficacy and Safety of Recombinant Humanized Anti-HER2 Monoclonal Antibody-MMAE Conjugate for Injection in the Treatment of HER2-positive Locally Advanced or Metastatic Breast Cancer and Phase III Clinical Study to Evaluate the Efficacy and Safety of Recombinant Humanized Anti-HER2 Monoclonal Antibody-MMAE Conjugate for Injection in the Treatment of HER2-positive Advanced Breast With Liver Metastases **Variant Classification:** ERBB2 overexpression **Locations:** China
NCT number: NCT05189067 **Phase: II/III** **Treatment:** Trastuzumab, Chemotherapy **Cancer Type:** Breast Cancer	**Study Title:** A Single-center, Prospective, Randomized Study of Adjuvant Paclitaxel and Trastuzumab Versus Docetaxel and Trastuzumab in Stage I HER2 Positive Breast Cancer **Variant Classification:** ERBB2 amplification **Locations:** China
NCT number: NCT04158947 **Phase: II** **Treatment:** Afatinib, Ado-trastuzumab Emtansine **Cancer Type:** Breast Cancer	**Study Title:** A Randomized Study of HER2+ Breast Cancer Patients With Active Refractory Brain Metastases Treated With Afatinib in Combination With T-DM1 vs. T-DM1 Alone **Variant Classification:** ERBB2 overexpression **Locations:** China
NCT number: NCT05180006 **Phase: II** **Treatment:** Atezolizumab, Trastuzumab, Pertuzumab **Cancer Type:** Breast Cancer	**Study Title:** Impact of Neoadjuvant Immunotherapy in Early Stage Breast Cancer Before Standard Therapy **Variant Classification:** ERBB2 amplification **Locations:** France
NCT number: NCT03367676 **Phase: II** **Treatment:** Chemotherapy, Trastuzumab **Cancer Type:** Breast Cancer	**Study Title:** 12 Weeks Adjuvant Docetaxel Plus Trastuzumab in Patients With Tumors < or = 1cm, Node-negative, HER2-positive Breast Cancer (SOBER): A Single-group Arm, Open-label, Prospective, Phase II Study **Variant Classification:** ERBB2 overexpression **Locations:** China

NCT number: NCT04296162 **Phase: II** **Treatment:** Chemotherapy, Trastuzumab **Cancer Type:** Breast Cancer	**Study Title:** A Phase II Study to Assess the Effectiveness and Safety of Oral Vinorelbine or Capecitabine Combined With Trastuzumab as Adjuvant Treatment for Patients With Lymph Node Negative, HER-2 Positive and Small Tumor Size Breast Cancer (ORCHID) **Variant Classification:** ERBB2 amplification **Locations:** China
NCT number: NCT04997798 **Phase: II** **Treatment:** Dalpiciclib, Hormone Therapy, Trastuzumab, Pyrotinib **Cancer Type:** Breast Cancer	**Study Title:** Phase II Open-label, Multicentre, Exploratory Trial of Neoadjuvant Dalpiciclib in Combination With Exemestane and Trastuzumab Plus Pyrotinib in Early Triple Positive Breast Cancer **Variant Classification:** ERBB2 overexpression **Locations:** China
NCT number: NCT04095390 **Phase: II** **Treatment:** Dalpiciclib, Pyrotinib, Hormone Therapy **Cancer Type:** Breast Cancer	**Study Title:** A Phase II Trial Program Exploring The Integration Of Novel HER2-targeted Tyrosine Kinase Inhibitor Pyrotinib and CDK4/6 Inhibitor SHR6390 Into Current Chemotherapy/Endocrine Therapy Regimes For Prior Trastuzumab-treated Advanced HER2-positive Breast Cancer **Variant Classification:** ERBB2 overexpression **Locations:** China
NCT number: NCT05328440 **Phase: II** **Treatment:** Dalpiciclib, Pyrotinib, Hormone Therapy, Inetetamab **Cancer Type:** Breast Cancer	**Study Title:** A single-arm, double-cohort, prospective, open-label, phase II exploratory study evaluating dalpiciclib combined with pyrotinib maleate in first-line treatment of HER2+ advanced breast cancer **Variant Classification:** ERBB2 amplification **Locations:** China
NCT number: NCT05331326 **Phase: II** **Treatment:** Disitamab Vedotinaide **Cancer Type:** Breast Cancer	**Study Title:** A Multicenter, Single Arm Phase II Clinical Study Evaluating the Efficacy and Safety of RC48-ADC for the Treatment of HER2-expression Metastatic Breast Cancer With Abnormal Activation of PAM Pathway **Variant Classification:** ERBB2 overexpression **Locations:** China
NCT number: NCT05334810 **Phase: II** **Treatment:** DP-303c **Cancer Type:** Breast Cancer	**Study Title:** A Multi-center, Open-lable, Single-arm Phase II Study to Evaluate the Efficacy and Safety of DP303c in Patients With HER2-positive Unresectable Locally Advanced, Relapsed, or Metastatic Breast Cancer **Variant Classification:** ERBB2 overexpression **Locations:** China

NCT number: NCT03820141 **Phase: II** **Treatment:** Durvalumab, Trastuzumab, Pertuzumab **Cancer Type:** Breast Cancer	**Study Title:** Multicenter Phase II Trial of Durvalumab (MEDI4736) With Trastuzumab and Pertuzumab Combination in HER2-Enriched and HER2-Amplified Breast Cancer (DTP Trial) **Variant Classification:** ERBB2 amplification **Locations:** United States **Contacts:** Houston Methodist Cancer Center [713-441-0629; ccresearch@houstonmethodist.org]
NCT number: NCT04941885 **Phase: II** **Treatment:** Inetetamab, Chemotherapy, Hormone Therapy **Cancer Type:** Breast Cancer	**Study Title:** A Phase II Single-arm Clinical Trial of the Efficacy and Tolerability of Inetetamab Combined With Cyclophosphamide Metronomic Chemotherapy and Aromatase Inhibitor in Metastatic HER2+/HR+ Breast Cancer **Variant Classification:** ERBB2 amplification **Locations:** China
NCT number: NCT05823623 **Phase: II** **Treatment:** Inetetamab, Pyrotinib, Chemotherapy **Cancer Type:** Breast Cancer	**Study Title:** A Phase II Single-arm Clinical Trial of Inetetamab Combined With Pyrotinib Plus Oral Vinorelbine for the Treatment of Patients With HER2-positive Metastatic Breast Cancer **Variant Classification:** ERBB2 overexpression **Locations:** China
NCT number: NCT04425018 **Phase: II** **Treatment:** Margetuximab, Trastuzumab, Pertuzumab, Chemotherapy **Cancer Type:** Breast Cancer	**Study Title:** Margetuximab or Trastuzumab (MARGOT): A Phase II Study Comparing Neoadjuvant Paclitaxel/Margetuximab/Pertuzumab to Paclitaxel/Trastuzumab/Pertuzumab in Patients With Stage II-III HER2-positive Breast Cancer **Variant Classification:** ERBB2 overexpression **Locations:** United States **Contacts:** Dr. Adrienne Waks [617-632-6973; Adrienne_Waks@DFCI.HARVARD.EDU]
NCT number: NCT04886531 **Phase: II** **Treatment:** Neratinib, Hormone Therapy, Trastuzumab **Cancer Type:** Breast Cancer	**Study Title:** An Open Label, Phase II Trial of Pre-operative Neratinib and Endocrine Therapy With Trastuzumab in Triple Positive Breast Cancers Hoosier Cancer Research Network BRE17-141 **Variant Classification:** ERBB2 overexpression **Locations:** United States **Contacts:** Dr. Ruth O'Regan [608-265-9701; ruth_oregan@urmc.rochester.edu]

NCT number: NCT02448420 **Phase: II** **Treatment:** Palbociclib, Trastuzumab, Hormone Therapy **Cancer Type:** Breast Cancer	**Study Title:** A Phase II Trial of Palbociclib in Combination With Trastuzumab and Endocrine Therapy in Patients With Previously-treated Locally Advanced or Metastatic HER2-positive Breast Cancer (PATRICIA II) **Variant Classification:** ERBB2 amplification **Locations:** Spain
NCT number: NCT04334330 **Phase: II** **Treatment:** Palbociclib, Trastuzumab, Pyrotinib, Hormone Therapy **Cancer Type:** Breast Cancer	**Study Title:** Palbociclib, Trastuzumab, Pyrotinib and Fulvestrant Treatment in Patients With Brain Metastasis From ER/PR Positive, HER-2 Positive Breast Cancer: A Multi-center, Prospective Study in China **Variant Classification:** ERBB2 overexpression **Locations:** China
NCT number: NCT04699630 **Phase: II** **Treatment:** Patritumab Deruxtecan **Cancer Type:** Breast Cancer	**Study Title:** A Phase II Study of U3-1402 in Patients With Metastatic Breast Cancer **Variant Classification:** ERBB2 overexpression **Locations:** United States **Contacts:** Sarah Cannon Development Innovations [844-710-6157; CANN.InnovationsMedical@sarahcannon.com]
NCT number: NCT03765983 **Phase: II** **Treatment:** Paxalisib, Trastuzumab **Cancer Type:** Breast Cancer	**Study Title:** Phase II Trial of GDC-0084 in Combination With Trastuzumab for Patients With HER2-Positive Breast Cancer Brain Metastases **Variant Classification:** ERBB2 amplification **Locations:** United States **Contacts:** Dr. Jose P. Leone [617-632-3800; JoseP_Leone@dfci.harvard.edu]
NCT number: NCT04348747 **Phase: II** **Treatment:** Pembrolizumab, HER2 Dendritic Cell Vaccine **Cancer Type:** Breast Cancer	**Study Title:** A Phase IIa Study of Dendritic Cell Vaccines Against Her2/Her3 and Pembrolizumab in Patients With Asymptomatic Brain Metastasis From Triple Negative Breast Cancer (TNBC) or HER2+ Breast Cancer (HER2+BC) **Variant Classification:** ERBB2 amplification **Locations:** United States **Contacts:** Shipra Gandhi [716-845-1486; Shipra.Gandhi@roswellpark.org]

NCT number: NCT03095352 **Phase: II** **Treatment:** Pembrolizumab, Trastuzumab, Chemotherapy **Cancer Type:** Breast Cancer	**Study Title:** A Randomized Phase II Study of Pembrolizumab, an Anti-Programmed Cell Death (PD)-1 Antibody, in Combination With Carboplatin Compared to Carboplatin Alone in Breast Cancer Patients With Chest Wall Disease **Variant Classification:** ERBB2 overexpression **Locations:** United States **Contacts:** Ivy Wong [415-353-7873; Ivy.Wong@ucsf.edu]
NCT number: NCT04675827 **Phase: II** **Treatment:** Pertuzumab, Chemotherapy, Trastuzumab **Cancer Type:** Breast Cancer	**Study Title:** De-Escalation of Adjuvant Chemotherapy in HER2-positive, Estrogen Receptor-negative, Node-negative Early Breast Cancer Patients Who Achieved Pathological Complete Response After Neoadjuvant Chemotherapy and Dual HER2 Blockade **Variant Classification:** ERBB2 amplification **Locations:** Australia, Belgium, France, Israel, Republic of Korea, Switzerland
NCT number: NCT04266249 **Phase: II** **Treatment:** Pertuzumab, Trastuzumab, Chemotherapy **Cancer Type:** Breast Cancer	**Study Title:** (CompassHER2-pCR): Preoperative THP and Postoperative HP in Patients Who Achieve a Pathologic Complete Response **Variant Classification:** ERBB2 overexpression **Locations:** Puerto Rico, United States **Contacts:** Multiple contacts: See www.clinicaltrials.gov for complete list of contacts.
NCT number: NCT04733118 **Phase: II** **Treatment:** Pertuzumab/trastuzumab/hyaluronidase-zzxf, Ado-trastuzumab Emtansine **Cancer Type:** Breast Cancer	**Study Title:** Chemotherapy-Free pCR-Guided Strategy With Subcutaneous Trastuzumab-Pertuzumab and T-DM1 in HER2-Positive Early Breast Cancer (PHERGAIN-2) **Variant Classification:** ERBB2 overexpression **Locations:** Bulgaria, Germany, Hungary, Italy, Spain
NCT number: NCT04569747 **Phase: II** **Treatment:** Pertuzumab/trastuzumab/hyaluronidase-zzxf, Hormone Therapy **Cancer Type:** Breast Cancer	**Study Title:** A Single Arm Phase II Study of Adjuvant Endocrine Therapy, Pertuzumab, and Trastuzumab for Patients With Anatomic Stage I Hormone Receptor-positive, HER2-positive Breast Cancer (ADEPT) **Variant Classification:** ERBB2 amplification **Locations:** United States **Contacts:** Dr. Adrienne Waks [617-632-3800; awaks@partners.org]
NCT number: NCT05834764 **Phase: II** **Treatment:** Pyrotinib **Cancer Type:** Breast Cancer	**Study Title:** Evaluating the Efficacy and Safety of Pyrotinib After Adjuvant Anti-HRE2 Therapy in Women With High-risk in Early or Locally Advanced Stage Breast Cancer **Variant Classification:** ERBB2 overexpression **Locations:** China

NCT number: NCT04983121 **Phase: II** **Treatment:** Pyrotinib, ARX-788 **Cancer Type:** Breast Cancer	**Study Title:** Efficacy and Safety of Pyrotinib Maleate Combined with ARX788 Neoadjuvant Treatment in Stage II-III HER2-positive Breast Cancer Patients who have Poor Outcomes After Treatment with Trastuzumab and Pertuzumab: Study Protocol for a Prospective, Single-arm, Multi-center, Phase II Clinical Trial **Variant Classification:** ERBB2 amplification **Locations:** China
NCT number: NCT04659499 **Phase: II** **Treatment:** Pyrotinib, Chemotherapy **Cancer Type:** Breast Cancer	**Study Title:** A Multicenter, Open-label, Single-arm, Phase II Clinical Trial of Nab-paclitaxel in Combination With Pyrotinib in Adjuvant Therapy for Lymph Node-negative and Small Tumor HER2-positive Breast Cancer **Variant Classification:** ERBB2 overexpression **Locations:** China
NCT number: NCT04033172 **Phase: II** **Treatment:** Pyrotinib, Hormone Therapy **Cancer Type:** Breast Cancer	**Study Title:** Pyrotinib Plus Fulvestrant in Patients HR+/HER2+ Metastatic Breast Cancer : A Prospective, Single-arm, Single-center Study **Variant Classification:** ERBB2 amplification **Locations:** China
NCT number: NCT04407988 **Phase: II** **Treatment:** Pyrotinib, Hormone Therapy **Cancer Type:** Breast Cancer	**Study Title:** Phase II Study of Pyrotinib in Combination With Letrozole in Patients With HER2-Positive, ER-Positive Metastatic Breast Cancer **Variant Classification:** ERBB2 overexpression **Locations:** China
NCT number: NCT04917900 **Phase: II** **Treatment:** Pyrotinib, Trastuzumab, Chemotherapy **Cancer Type:** Breast Cancer	**Study Title:** Single-arm, Multi-center Clinical Study of Pyrotinib Maleate Tablets Combined With Albumin-bound Paclitaxel and Trastuzumab in Neoadjuvant Treatment of Her2-positive Early or Locally Advanced Breast Cancer **Variant Classification:** ERBB2 amplification **Locations:** China
NCT number: NCT05042791 **Phase: II** **Treatment:** Radiation Therapy, Pyrotinib, Chemotherapy **Cancer Type:** Breast Cancer	**Study Title:** SRT Versus WBRT Combined With Pyrotinib and Capecitabine in the Treatment of HER2-positive Advanced Breast Cancer Patients With Brain Metastases: A Randomized Controlled, Prospective Clinical Study **Variant Classification:** ERBB2 overexpression **Locations:** China

NCT number: NCT04197687 **Phase: II** **Treatment:** TAP-11, Sargramostim, Ado-trastuzumab Emtansine, Trastuzumab, Pertuzumab **Cancer Type:** Breast Cancer	**Study Title:** Phase II Trial to Evaluate Immune-Related Biomarkers for Pathological Response in Stage II-III HER2-Positive Breast Cancer Receiving Neoadjuvant Chemotherapy With Subsequent Randomization to Multi-Epitope HER2 Vaccine vs. Placebo in Patients With Residual Disease Post-Neoadjuvant Chemotherapy **Variant Classification:** ERBB2 overexpression **Locations:** United States **Contacts:** Multiple contacts: See www.clinicaltrials.gov for complete list of contacts.
NCT number: NCT05530057 **Phase: II** **Treatment:** Trastuzumab (Samsung Bioepis), Chemotherapy **Cancer Type:** Breast Cancer	**Study Title:** Randomized, Open Label, Multi-Center, Phase II Trial of Eribulin With or Without SB3 (Trastuzumab-biosimilar) in Patients With HER2-overexpressed Recurrent or Stage IV Breast Cancer Who Have Received at Least 2 Prior HER2-directed Regimens **Variant Classification:** ERBB2 overexpression **Locations:** Republic of Korea
NCT number: NCT04893109 **Phase: II** **Treatment:** Trastuzumab And Hyaluronidase-oysk, Chemotherapy, Ado-trastuzumab Emtansine **Cancer Type:** Breast Cancer	**Study Title:** A Randomized Phase II Trial of Adjuvant Trastuzumab Emtansine (T-DM1) Followed by Subcutaneous Trastuzumab Versus Paclitaxel in Combination With Subcutaneous Trastuzumab for Stage I HER2-positive Breast Cancer (ATEMPT 2.0) **Variant Classification:** ERBB2 overexpression **Locations:** United States **Contacts:** Dr. Sara Tolaney [617-632-2335; sara_tolaney@dfci.harvard.edu]
NCT number: NCT05795101 **Phase: II** **Treatment:** Trastuzumab Deruxtecan, Durvalumab **Cancer Type:** Breast Cancer	**Study Title:** TRUDI: A Phase II Study of Neoadjuvant Trastuzumab Deruxtecan and Durvalumab for Stage III, HER2-expressing Inflammatory Breast Cancer **Variant Classification:** ERBB2 overexpression **Locations:** United States **Contacts:** Dr. Filipa Lynce [617-632-3800; filipa_lynce@dfci.harvard.edu]
NCT number: NCT01042379 **Phase: II** **Treatment:** Trastuzumab, Chemotherapy, Durvalumab, Cemiplimab, ARX-788, VSV-hIFNbeta-NIS, Datopotamab Deruxtecan, Zanidatamab, Hormone Therapy **Cancer Type:** Breast Cancer	**Study Title:** I-SPY 2 Trial (Investigation of Serial Studies to Predict Your Therapeutic Response With Imaging And moLecular Analysis 2) **Variant Classification:** ERBB2 amplification **Locations:** United States **Contacts:** Won Chang [855-866-0505; w.chang@quantumleaphealth.org]

NCT number: NCT04993014 **Phase: II** **Treatment:** Trastuzumab, Pertuzumab **Cancer Type:** Breast Cancer	**Study Title:** Circulating Tumor Cells and Adjuvant Treatment De-escalation After Neoadjuvant Therapy With Trastuzumab and Pertuzumab for HER2 Positive Early Breast Cancer **Variant Classification:** ERBB2 amplification **Locations:** Brazil
NCT number: NCT05656079 **Phase: II** **Treatment:** Trastuzumab, Pertuzumab, Chemotherapy **Cancer Type:** Breast Cancer	**Study Title:** To Evaluate the Cardiac Safety of Pegylated Liposomal Doxorubicin Concurrently Plus Trastuzumab and Pertuzumab in the Adjuvant Setting for Early-stage HER-2-positive Breast Cancer: a Multicenter, Randomized Controlled Clinical Study **Variant Classification:** ERBB2 overexpression **Locations:** China
NCT number: NCT03747120 **Phase: II** **Treatment:** Trastuzumab, Pertuzumab, Pembrolizumab, Chemotherapy **Cancer Type:** Breast Cancer	**Study Title:** Neoadjuvant HER2-Targeted Therapy and Immunotherapy with Pembrolizumab (neoHIP) **Variant Classification:** ERBB2 overexpression **Locations:** United States **Contacts:** Meredith Carter [214-648-7097; meredith.carter@utsouthwestern.edu]
NCT number: NCT04481932 **Phase: II** **Treatment:** Trastuzumab, Pyrotinib, Chemotherapy **Cancer Type:** Breast Cancer	**Study Title:** Trastuzumab Combined With Pyrotinib and Chemotherapy for Locally Advanced, Inflammatory, or Early HER2-positive Mammary glandsCancer: One Arm, Open, Phase II Clinical Study **Variant Classification:** ERBB2 amplification **Locations:** China
NCT number: NCT05076695 **Phase: II** **Treatment:** Trastuzumab, Pyrotinib, Palbociclib, Hormone Therapy **Cancer Type:** Breast Cancer	**Study Title:** Neoadjuvant With Trastuzumab, Pyrotinib Plus Palbociclib and Fulvestrant in HER2-positive, ER-positive Breast Cancer **Variant Classification:** ERBB2 amplification **Locations:** China
NCT number: NCT05292742 **Phase: II** **Treatment:** Trastuzumab, Pyrotinib, Pertuzumab, Chemotherapy **Cancer Type:** Breast Cancer	**Study Title:** A Randomized, Open-label, Multicenter Study Comparing Continuation of Original Targeted Therapy With Trastuzumab Combined With Pyrotinib and Capecitabine as Postoperative Adjuvant Therapy in Non-pCR Patients With HER2 Positive Early Breast Cancer **Variant Classification:** ERBB2 overexpression **Locations:** China

NCT number: NCT05583110
Phase: II
Treatment: Trastuzumab, Tucatinib, Chemotherapy
Cancer Type: Breast Cancer

Study Title: Single Arm Phase II Study of the Efficacy and Safety of the Combination of Trastuzumab Plus TUCAtinib Plus viNorelbine in Patients With HER2-positive Non-resectable Locally Advanced or Metastatic Breast Cancer "TrasTUCAN Study"
Variant Classification: ERBB2 overexpression
Locations:
Spain

NCT number: NCT04789096
Phase: II
Treatment: Tucatinib, Pembrolizumab, Trastuzumab
Cancer Type: Breast Cancer

Study Title: A Phase II, Two-arm, Non-comparative, Multicentre Study of Tucatinib (ONT-380), Pembrolizumab and Trastuzumab in Patients With Pre-treated Advanced HER2-positive Breast Cancer
Variant Classification: ERBB2 amplification
Locations:
Australia

NCT number: NCT05041842
Phase: II
Treatment: Tucatinib, Pertuzumab, Trastuzumab, Hormone Therapy
Cancer Type: Breast Cancer

Study Title: Treatment with Tucatinib in Addition to Pertuzumab and Trastuzumab in Patients with HER2-positive Metastatic Breast Cancer After Local Therapy of Isolated Brain Progression
Variant Classification: ERBB2 overexpression
Locations:
France

NCT number: NCT05458674
Phase: II
Treatment: Tucatinib, Trastuzumab, Chemotherapy
Cancer Type: Breast Cancer

Study Title: A Phase II Study of the Safety, Tolerability and Antitumor Activity of Tucatinib in Combination With Eribulin and Trastuzumab in Patients With Pretreated Unresectable Locally Advanced or Metastatic HER2+ Breast Cancer
Variant Classification: ERBB2 amplification
Locations:
United States
Contacts:
Ruth Stone [518-583-0095; restone@criteriuminc.com]

NCT number: NCT03179904
Phase: II
Treatment: TVB-2640, Trastuzumab, Chemotherapy
Cancer Type: Breast Cancer

Study Title: Phase II Trial to Evaluate the Efficacy of the FASN Inhibitor, TVB-2640, in Combination With Trastuzumab Plus Paclitaxel or Endocrine Therapy in Patients With HER2+ Metastatic Breast Cancer Resistant to Trastuzumab-Based Therapy
Variant Classification: ERBB2 amplification
Locations:
United States
Contacts:
Multiple contacts: See www.clinicaltrials.gov for complete list of contacts.

NCT number: NCT05035836
Phase: II
Treatment: Zanidatamab
Cancer Type: Breast Cancer

Study Title: A Phase II Single-Arm Open-Label Pilot Trial Evaluating Zanidatamab (ZW25) in Patients With Early Stage HER2/Neu Positive (HER2+) Breast Cancer (BC)
Variant Classification: ERBB2 overexpression
Locations:
United States
Contacts:
Vicente Valero [713-563-0751; vvalero@mdanderson.org]

NCT number: NCT04278144
Phase: I/II
Treatment: BDC-1001, Nivolumab
Cancer Type: Breast Cancer

Study Title: Phase I/II Study of BDC-1001 as a Single Agent and in Combination With Nivolumab in Patients With Advanced HER2-Expressing Solid Tumors
Variant Classification: ERBB2 overexpression
Locations: Republic of Korea, Spain, United States
Contacts: Bolt Biotherapeutics [650-665-9295; info@boltbio.com]

NCT number: NCT05555251
Phase: I/II
Treatment: BI-1607, Trastuzumab
Cancer Type: Breast Cancer

Study Title: Phase I/IIa Open-label Clinical Trial of BI-1607, an Fc-Engineered Monoclonal Antibody to CD32b (FcγRIIB), in Combination With Trastuzumab in Subjects With HER2-positive Advanced Solid Tumors
Variant Classification: ERBB2 overexpression
Locations: Spain, United Kingdom

NCT number: NCT04020575
Phase: I/II
Treatment: CART-MUC1 (Minerva)
Cancer Type: Breast Cancer

Study Title: Adoptive Immunotherapy for Advanced MUC1* Positive Breast Cancer With Autologous T Cells Engineered to Express a Chimeric Antigen Receptor, huMNC2-CAR44 Specific for a Cleaved Form of MUC1 (MUC1*)
Variant Classification: ERBB2 amplification
Locations: United States
Contacts: Dr. Yuan Yuan [800-826-4673; Minerva18625@coh.org]

NCT number: NCT04947189
Phase: I/II
Treatment: Hormone Therapy, Steroid, Chemotherapy
Cancer Type: Breast Cancer

Study Title: 4CAST: A Phase Ib Dose Exploration and Dose Expansion, Open-label, Single-centre Study Evaluating the Safety and Efficacy of INO-464 in Combination With Chemotherapy in Patients With metASTatic Breast Cancer
Variant Classification: ERBB2 overexpression
Locations: Australia

NCT number: NCT03368729
Phase: I/II
Treatment: Niraparib, Trastuzumab
Cancer Type: Breast Cancer

Study Title: A Phase Ib/II Study of the PARP Inhibitor Niraparib in Combination With Trastuzumab in Patients With Metastatic HER2+ Breast Cancer
Variant Classification: ERBB2 amplification
Locations: United States
Contacts: Dr. Erica Stringer-Reasor [205-975-2816; strinem@uab.edu]

NCT number: NCT05582499
Phase: I/II
Treatment: Pyrotinib, SHR-A1811, Pertuzumab, Trastuzumab, Chemotherapy
Cancer Type: Breast Cancer

Study Title: Fudan University Shanghai Cancer Center Breast Cancer Precision Platform Series Study- Neoadjuvant Therapy (FASCINATE-N)
Variant Classification: ERBB2 overexpression
Locations: China

NCT number: NCT04588545 **Phase: I/II** **Treatment:** Radiation Therapy, Trastuzumab, Pertuzumab **Cancer Type:** Breast Cancer	**Study Title:** Phase I/II Study of Radiation Therapy Followed by Intrathecal Trastuzumab/Pertuzumab in the Management of HER2+ Breast Leptomeningeal Disease **Variant Classification:** ERBB2 overexpression **Locations:** United States **Contacts:** Dr. Kamran Ahmed [813-745-8424; kamran.ahmed@moffitt.org]
NCT number: NCT05319873 **Phase: I/II** **Treatment:** Ribociclib, Tucatinib, Trastuzumab **Cancer Type:** Breast Cancer	**Study Title:** A Phase IB Trial Evaluating the Safety of Ribociclib, Tucatinib, and Trastuzumab in Patients With Metastatic, HER2+ Breast Cancer and a Multicenter, Randomized, Open-Label, Phase II Study of Preoperative Treatment With Ribociclib,Ttrastuzumab, Tucatinib, and Fulvestrant Versus Docetaxel, Carboplatin,Ttrastuzumab, and Pertuzumab in HR+/HER2+ Breast Cancer and Ribociclib, Trastuzumab, and Tucatinib Versus Docetaxel, Carboplatin, Trastuzumab, and Pertuzumab in Patients With HR-/HER2+ Breast Cancer **Variant Classification:** ERBB2 overexpression **Locations:** United States **Contacts:** Monica Rocha [310-998-4747 ext 20384; mprocha@mednet.ucla.edu]
NCT number: NCT05353361 **Phase: I/II** **Treatment:** SHR-A1811, Pyrotinib, Pertuzumab, Adebrelimab, Chemotherapy **Cancer Type:** Breast Cancer	**Study Title:** A Phase Ib/II Multicenter, Open-Label Clinical Trial of SHR-A1811 Injection in Combination With Pyrotinib or Pertuzumab or SHR-1316 or Paclitaxel for Injection (Albumin Bound) in HER2-Positive Breast Cancer **Variant Classification:** ERBB2 amplification **Locations:** China
NCT number: NCT04727151 **Phase: I/II** **Treatment:** TAC01-HER2 **Cancer Type:** Breast Cancer	**Study Title:** A Phase I/II Study Investigating Safety and Efficacy of Autologous TAC T Cells Targeting HER2 in Relapsed or Refractory Solid Tumors. **Variant Classification:** ERBB2 overexpression **Locations:** Canada, United States **Contacts:** Nathan Ternus [512-646-4516; patient.info@triumvira.com]
NCT number: NCT03994107 **Phase: I/II** **Treatment:** Trastuzumab, Chemotherapy **Cancer Type:** Breast Cancer	**Study Title:** A Single-center, Prospective, Single Arm Study of Neoadjuvant Treatment With Pegylated Liposomal Doxorubicin(PLD)Plus Albumin-Bound Paclitaxel and Trastuzumab in HER-2 Positive Breast Cancer **Variant Classification:** ERBB2 amplification **Locations:** China

NCT number: NCT03913234
Phase: I/II
Treatment: Trastuzumab, Ribociclib, Hormone Therapy
Cancer Type: Breast Cancer

Study Title: Phase IB & II Study of Ribociclib With Trastuzumab Plus Letrozole in Postmenopausal HR+, HER2+ Advanced Breast Cancer Patients
Variant Classification: ERBB2 overexpression
Locations: Republic of Korea

NCT number: NCT05027139
Phase: I/II
Treatment: Zanidatamab, Evorpacept
Cancer Type: Breast Cancer

Study Title: A Phase Ib/II, 2-part Open-label Study to Assess the Safety and Antitumor Activity of Zanidatamab in Combination With ALX148 in Advanced HER2-expressing Cancer
Variant Classification: ERBB2 amplification
Locations: United States
Contacts: Zymeworks Clinical Trial Resource [206-237-1030; medinfo@zymeworks.com]

NCT number: NCT04092673
Phase: I/II
Treatment: Zotatifin, Trastuzumab
Cancer Type: Breast Cancer

Study Title: A Phase 1-2 Dose-Escalation and Cohort-Expansion Study of Intravenous Zotatifin (eFT226) in Subjects With Selected Advanced Solid Tumor Malignancies
Variant Classification: ERBB2 overexpression
Locations: United States
Contacts: Mark Densel [858-925-8215; clinicaltrials@effector.com]

NCT number: NCT03944499
Phase: I
Treatment: Ado-trastuzumab Emtansine (Shanghai Fosun Pharma)
Cancer Type: Breast Cancer

Study Title: A Phase I,Multicenter,Open-label,Single-arm Study:A Dose-escalation Phase Evaluating FS1502 in Patients With HER2 Expressed Advanced Solid Tumors,and a Dose-expanded Phase in Patients With Local Advanced or Metastatic,HER2+ Breast Cancer
Variant Classification: ERBB2 overexpression
Locations: China

NCT number: NCT05414136
Phase: I
Treatment: BAT-1006
Cancer Type: Breast Cancer

Study Title: A Single-Arm, Open, Dose-Escalation Phase I Clinical Study Evaluating The Safety, Tolerability And Pharmacokinetics Of BAT1006 In Patients With HER2-Positive Advanced Solid Tumors
Variant Classification: ERBB2 overexpression
Locations: China

NCT number: NCT05461768
Phase: I
Treatment: BL-M07D1
Cancer Type: Breast Cancer

Study Title: A Phase I Clinical Study to Evaluate the Safety, Tolerability, Pharmacokinetic Characteristics, and Preliminary Efficacy of BL-M07D1injection in Patients With Locally Advanced or Metastatic HER2-positive/Low-expression Breast Cancer and Other Solid Tumors
Variant Classification: ERBB2 overexpression
Locations: China

NCT number: NCT04511871 **Phase: I** **Treatment:** CART **Cancer Type:** Breast Cancer	**Study Title:** A Phase I Trial to Assess Safety, Tolerability and Anti-tumor Activity of Autologous T Cell Modified Chimeric Antigen Receptor (CAR) (CCT303-406) in Patients With Relapsed or Refractory HER2 Positive Solid Tumors **Variant Classification:** ERBB2 overexpression **Locations:** China
NCT number: NCT03696030 **Phase: I** **Treatment:** CART-HER2, Chemotherapy **Cancer Type:** Breast Cancer	**Study Title:** A Phase I Cellular Immunotherapy Study of Intraventricularly Administered Autologous HER2-Targeted Chimeric Antigen Receptor (HER2-CAR) T Cells in Patients With Brain and/or Leptomeningeal Metastases From HER2 Positive Cancers **Variant Classification:** ERBB2 amplification **Locations:** United States **Contacts:** Jana L. Portnow [626-256-4673; jportnow@coh.org]
NCT number: NCT04684459 **Phase: I** **Treatment:** CART-HER2/PD-L1 **Cancer Type:** Breast Cancer	**Study Title:** Phase I Study of Specific CAR-T Dual-targeting HER2 and PD-L1 in Patients With Pleural or Peritoneal Metastasis of HER2 Positive Cancer **Variant Classification:** ERBB2 overexpression **Locations:** China
NCT number: NCT05378464 **Phase: I** **Treatment:** Dendritic Cell Vaccine, Trastuzumab, Pepinemab, T-cell Therapy **Cancer Type:** Breast Cancer	**Study Title:** Phase 1 Study of Adoptive T Cell Therapy Following HER2-Pulsed Dendritic Cell Vaccine and Pepinemab / Trastuzumab in Patients With Metastatic HER2-Positive Breast Cancer **Variant Classification:** ERBB2 amplification **Locations:** United States **Contacts:** Jessica Malka [813-745-8885; Jessica.Malka@moffitt.org]
NCT number: NCT04146610 **Phase: I** **Treatment:** DP-303c **Cancer Type:** Breast Cancer	**Study Title:** A Phase Ia, Multicenter, Open and Dose-increasing Study of DP303c to Evaluate the Safety , Pharmacokinetics, Immunogenicity and Antitumor Activity of Subjects With HER2-Positive Advanced Solid Tumors **Variant Classification:** ERBB2 overexpression **Locations:** China
NCT number: NCT05650879 **Phase: I** **Treatment:** ELVN-002, Ado-trastuzumab Emtansine **Cancer Type:** Breast Cancer	**Study Title:** A Phase Ia/Ib Study of ELVN-002 for the Treatment of Patients With HER2 Mutant Non-Small Cell Lung Cancer **Variant Classification:** ERBB2 overexpression **Locations:** Australia, Republic of Korea, United States **Contacts:** Dr. Helen L. Collins [707-799-3272; helen.collins@enliventherapeutics.com]

NCT number: NCT05564858 **Phase: I** **Treatment:** FDA022-BB05 **Cancer Type:** Breast Cancer	**Study Title:** Phase Ia/Ib clinical study of FDA022-BB05 in patients with advanced solid tumors **Variant Classification:** ERBB2 overexpression **Locations:** China
NCT number: NCT04450732 **Phase: I** **Treatment:** GQ1001 **Cancer Type:** Breast Cancer	**Study Title:** A Phase I, First-In-Human, Multicenter, Open-Label, Study of GQ1001, a HER2 Targeted Antibody-Drug Conjugate, Administered Intravenously, in Adult Patients With HER2-Positive Advanced Solid Tumors **Variant Classification:** ERBB2 overexpression **Locations:** Australia, China
NCT number: NCT03308201 **Phase: I** **Treatment:** Hemay022, Hormone Therapy **Cancer Type:** Breast Cancer	**Study Title:** Study Evaluating Hemay022 in Combination With Endocrine Therapy In Subjects With ER Positive and HER2 Positive Advanced Breast Cancer **Variant Classification:** ERBB2 amplification **Locations:** China
NCT number: NCT05076591 **Phase: I** **Treatment:** IMM2902 **Cancer Type:** Breast Cancer	**Study Title:** A Phase I, Open-Label, Multicenter, Dose Escalation Study Evaluating the Safety, Tolerability, and Preliminary Efficacy of IMM2902 in Patients With HER2-Expressing Advanced Solid Tumors **Variant Classification:** ERBB2 amplification **Locations:** United States **Contacts:** Rachel Qianwen Shao [770-918-0861; qianwen.shao@immuneonco.com]
NCT number: NCT05143970 **Phase: I** **Treatment:** IPH-5301, Trastuzumab, Chemotherapy **Cancer Type:** Breast Cancer	**Study Title:** A Phase I First-In-Human Study of the Anti-CD73 IPH5301 Alone or in Combination With Chemotherapy and Trastuzumab in Patients With Advanced Solid Tumors **Variant Classification:** ERBB2 overexpression **Locations:** France

NCT number: NCT05013554
Phase: I
Treatment: SAR-443216
Cancer Type: Breast Cancer

Study Title: A Phase I/Ib Open-label, First-in-human, Single Agent, Dose Escalation and Expansion Study for the Evaluation of Safety, Pharmacokinetics, Pharmacodynamics, and Anti-tumor Activity of SAR443216 in Participants with Relapsed/Refractory HER2 Expressing Solid Tumors.
Variant Classification: ERBB2 overexpression
Locations: Republic of Korea, Spain, Taiwan, United States
Contacts: email recommended (Toll free number for US & Canada) [800-633-1610 ext Option 6; Contact-US@sanofi.com]

NCT number: NCT04042701
Phase: I
Treatment: Trastuzumab Deruxtecan, Pembrolizumab
Cancer Type: Breast Cancer

Study Title: A Phase Ib, Multicenter, Two-Part, Open-Label Study of Trastuzumab Deruxtecan (DS-8201a), An Anti-Human Epidermal Growth Factor Receptor-2 (HER2)-Antibody Drug Conjugate (ADC), In Combination With Pembrolizumab, An Anti-PD-1 Antibody, For Subjects With Locally Advanced/Metastatic Breast Or Non-Small Cell Lung Cancer (NSCLC).
Variant Classification: ERBB2 overexpression
Locations: France, Spain, United Kingdom, United States
Contacts: Daiichi Sankyo Contact for Clinical Trial Information [908-992-6400; CTRinfo@dsi.com]

NCT number: NCT04487236
Phase: I
Treatment: ZN-A-1041, Chemotherapy, Trastuzumab
Cancer Type: Breast Cancer

Study Title: A Phase I Clinical Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Efficacy of ZN-A-1041 Enteric Capsules as a Single Agent or in Combination in Patients With HER2-Positive Advanced Solid Tumors
Variant Classification: ERBB2 overexpression
Locations: China

NCT number: NCT05036005
Phase: IV
Treatment: Trastuzumab (Samsung Bioepis), Chemotherapy, Pertuzumab
Cancer Type: Breast Cancer

Study Title: Neoadjuvant Treatment of Ontruzant (SB3) in Patients With HER2-positive Early Breast Cancer: An Open-Label, Multicenter, Phase IV Study
Variant Classification: ERBB2 positive
Locations: Germany

NCT number: NCT05755048
Phase: III
Treatment: Ado-trastuzumab Emtansine (Shanghai Fosun Pharma), Ado-trastuzumab Emtansine
Cancer Type: Breast Cancer

Study Title: A Multicenter, Open-label, Randomized Controlled Phase III Clinical Study to Compare the Efficacy and Safety of FS-1502 Versus T-DM1 in Patients With HER2-positive Unresectable Locally Advanced or Metastatic Breast Cancer
Variant Classification: ERBB2 positive
Locations: China

NCT number:
NCT05296798

Phase: III

Treatment: Hormone Therapy, Pertuzumab/trastuzumab/hyaluronidase-zzxf, Chemotherapy

Cancer Type: Breast Cancer

Study Title: A Phase III, Randomized, Open-Label Study Evaluating the Efficacy and Safety of Giredestrant in Combination With Phesgo Versus Phesgo After Induction Therapy With Phesgo + Taxane in Patients With Previously Untreated HER2-Positive, Estrogen Receptor-Positive Locally-Advanced or Metastatic Breast Cancer

Variant Classification: ERBB2 positive

Locations:
Argentina, Belgium, Brazil, China, Colombia, France, Germany, Hungary, Italy, Mexico, Poland, Portugal, Republic of Korea, Spain, Taiwan, Thailand, Turkey, United Kingdom, United States

Contacts:
Reference Study ID Number: WO43571 [888-662-6728; global-roche-genentech-trials@gene.com]

NCT number:
NCT04254263

Phase: III

Treatment: Pyrotinib

Cancer Type: Breast Cancer

Study Title: Adjuvant Trastuzumab Plus Pyrotinib for Residual Invasive HER2-positive Breast Cancer After Neoadjuvant Chemotherapy Plus Anti-HER2 Target Therapy

Variant Classification: ERBB2 positive

Locations:
China

NCT number:
NCT04385563

Phase: III

Treatment: Trastuzumab (Chia Tai Tianqing Pharmaceutical), Chemotherapy, Trastuzumab

Cancer Type: Breast Cancer

Study Title: A Phase III,Randomized,Multicenter,Double-blind Clinical Trail to Evaluate the Efficacy,Safety and Immunogenicity of the Combination of TQ-B211 Plus Docetaxel Versus Herceptin Plus Docetaxel as First-line Treatment in Patients With HER2-positive MBC.

Variant Classification: ERBB2 positive

Locations:
China

NCT number:
NCT03975647

Phase: III

Treatment: Tucatinib, Ado-trastuzumab Emtansine

Cancer Type: Breast Cancer

Study Title: Randomized, Double-blind, Phase III Study of Tucatinib or Placebo in Combination With Ado-trastuzumab Emtansine (T-DM1) for Subjects With Unresectable Locally-advanced or Metastatic HER2+ Breast Cancer (HER2CLIMB-02)

Variant Classification: ERBB2 positive

Locations:
China

NCT number:
NCT00781612

Phase: II

Treatment: Ado-trastuzumab Emtansine, Pertuzumab, Trastuzumab, Chemotherapy, Atezolizumab

Cancer Type: Breast Cancer

Study Title: An Open-Label, Multicenter Extension Study of Trastuzumab Emtansine Administered as a Single Agent or in Combination With Other Anti-Cancer Therapies in Patients Previously Enrolled in a Genentech and/or F. Hoffmann-La Roche Ltd-Sponsored Trastuzumab Emtansine Study

Variant Classification: ERBB2 positive

Locations:
China

NCT number: NCT05018702
Phase: II
Treatment: ARX-788
Cancer Type: Breast Cancer

Study Title: A Prospective, Single-arm, Single-center Phase II Clinical Study of Recombinant Humanized Anti-HER2 Monoclonal Antibody-AS269 Conjugate (ARX788) in the Treatment of HER2-positive Breast Cancer Patients With Brain Metastases
Variant Classification: ERBB2 positive
Locations:
China

NCT number: NCT04759248
Phase: II
Treatment: Atezolizumab, Trastuzumab, Chemotherapy
Cancer Type: Breast Cancer

Study Title: A Phase II With 2 Parallel Cohorts Clinical Trial Targeting Estrogen Receptor Negative or PAM50 Non-luminal Disease With Atezolizumab in Combination With Trastuzumab and Vinorelbine in HER2-positive Advanced/Metastatic Breast Cancer - ATREZZO Study
Variant Classification: ERBB2 positive
Locations:
Spain

NCT number: NCT04034823
Phase: II
Treatment: Envafolimab, Trastuzumab, Chemotherapy
Cancer Type: Breast Cancer

Study Title: KN035, a Single Domain PD-L1 Subcutanuous Injection Antibody, in Combination With Trastuzumab and Docetaxel in HER2-positive Breast Cancer
Variant Classification: ERBB2 positive
Locations:
China

NCT number: NCT04924699
Phase: II
Treatment: MRG-002
Cancer Type: Breast Cancer

Study Title: A Study of MRG002 in the Treatment of Patients With HER2-positive Unresectable Locally Advanced or Metastatic Breast Cancer.
Variant Classification: ERBB2 positive
Locations:
China

NCT number: NCT05263869
Phase: II
Treatment: MRG-002
Cancer Type: Breast Cancer

Study Title: An Open-label, Multi-center, Single-arm Phase II Clinical Study to Evaluate the Efficacy and Safety of MRG002 in Advanced HER-2 Positive Breast Cancer Patients Previously Treated With Trastuzumab and TKIs (Magic-009)
Variant Classification: ERBB2 positive
Locations:
China

NCT number: NCT02436993
Phase: II
Treatment: Pertuzumab, Trastuzumab, Chemotherapy
Cancer Type: Breast Cancer

Study Title: A Phase II Study of Breast Cancer Treatment Using Weekly Carboplatin + Paclitaxel With Pertuzumab + Trastuzumab (HER2+) or Bevacizumab (HER2-) in the Neoadjuvant Setting
Variant Classification: ERBB2 positive
Locations:
United States
Contacts:
UC Irvine Health Chao Family Comprehensive Cancer Center [877-827-8839; UCstudy@uci.edu]

NCT number: NCT05262400
Phase: II
Treatment: PF-07220060, PF-07104091
Cancer Type: Breast Cancer

Study Title: A phase I B/2, open-label, multicenter, dose escalation and dose expansion study to evaluate the safety, tolerability, pharmacokinetics, pharmacodynamics, and antitumor activity of PF-07220060 in combination with PF-07104091 plus endocrine therapy in participants with advanced solid tumors
Variant Classification: ERBB2 positive
Locations:
Czech Republic, Mexico, United States
Contacts:
Pfizer CT.gov Call Center [800-718-1021; ClinicalTrials.gov_Inquiries@pfizer.com]

NCT number: NCT05880927
Phase: II
Treatment: Pyrotinib
Cancer Type: Breast Cancer

Study Title: Pyrotinib After Trastuzumab-based Adjuvant Therapy in Patients With HER2-positive Breast Cancer: an Open-label, Multi-center Trial
Variant Classification: ERBB2 positive
Locations:
China

NCT number: NCT04605575
Phase: II
Treatment: Pyrotinib, Chemotherapy
Cancer Type: Breast Cancer

Study Title: A Single-arm, Multi-center Phase II Clinical Study of Pyrotinib Combined With Vinorelbine in the Treatment of HER2-positive and Treated Metastatic Breast Cancer
Variant Classification: ERBB2 positive
Locations:
China

NCT number: NCT04900311
Phase: II
Treatment: Pyrotinib, Pertuzumab, Chemotherapy, Trastuzumab
Cancer Type: Breast Cancer

Study Title: Pyrotinib Versus Pertuzumab in Combination With Neoadjuvant Trastuzumab and Nab-Paclitaxel in HER2+ Early or Locally Advanced Breast Cancer
Variant Classification: ERBB2 positive
Locations:
China

NCT number: NCT04717531
Phase: II
Treatment: Pyrotinib, Trastuzumab, Chemotherapy
Cancer Type: Breast Cancer

Study Title: Pyrotinib as Neoadjuvant Agent for Non-objective Response Patients of HER2-positive Early Breast Cancer Treated by Trastuzumab, Pertuzumab, and Chemotherapy (PYHOPE-BC-104): a Randomized, Controlled, Phase II Trial
Variant Classification: ERBB2 positive
Locations:
China

NCT number: NCT05429294
Phase: II
Treatment: Pyrotinib, Trastuzumab, Chemotherapy
Cancer Type: Breast Cancer

Study Title: Pyrotinib Combined With Trastuzumab and Albumin Paclitaxel in First-line Treatment of HER2-positive Advanced or Metastatic Breast Cancer, a Prospective, Single-arm, Multicenter, Phase II Study
Variant Classification: ERBB2 positive
Locations:
China

NCT number: NCT05635487 **Phase: II** **Treatment:** SHR-A1811, Pyrotinib **Cancer Type:** Breast Cancer	**Study Title:** A Single-arm, Phase II Study of SHR-A1811 Combined With Pyrotinib Maleate as Neoadjuvant Treatment in HER2-positive Breast Cancer Patients **Variant Classification:** ERBB2 positive **Locations:** China
NCT number: NCT05769010 **Phase: II** **Treatment:** SHR-A1811, Pyrotinib, Bevacizumab **Cancer Type:** Breast Cancer	**Study Title:** A Prospective, Open-label Explorative Study of SHR-A1811 in HER2-expression Advanced Breast Cancer With Brain Metastases **Variant Classification:** ERBB2 positive **Locations:** China
NCT number: NCT04172259 **Phase: II** **Treatment:** Trastuzumab, Chemotherapy **Cancer Type:** Breast Cancer	**Study Title:** A Multi-center Randomized Phase II Study of Doxorubicin Liposome Versus Epirubicin Plus Cyclophosphamide Combined With Trastuzumab, Followed by Docetaxel Plus Trastuzumab as Neoadjuvant Therapy for HER2-positive Early Breast Cancer **Variant Classification:** ERBB2 positive **Locations:** China
NCT number: NCT04094896 **Phase: II** **Treatment:** Trastuzumab, Pertuzumab, Chemotherapy **Cancer Type:** Breast Cancer	**Study Title:** TCHP (Docetaxel/Carboplatin/Trastuzumab/Pertuzumab) Versus EC - THP(Epirubicin/ Cyclophosphamide Followed by Docetaxe/Trastuzumab/Pertuzumab) as Neoadjuvant Treatment for HER2-Positive Breast Cancer **Variant Classification:** ERBB2 positive **Locations:** China
NCT number: NCT05638594 **Phase: II** **Treatment:** Trastuzumab, Pyrotinib, Dalpiciclib, Hormone Therapy, Pertuzumab, Chemotherapy **Cancer Type:** Breast Cancer	**Study Title:** A Randomized Controlled, Open-label, Multicenter Clinical Study of Pyrotinib Maleate Combined With Trastuzumab,Dalpiciclib, and Letrozole Versus Trastuzumab Combined With Pertuzumab, Docetaxel, and Carboplatin as Neoadjuvant Therapy for Stage II-III HR +/HER2 + Breast Cancer **Variant Classification:** ERBB2 positive **Locations:** China
NCT number: NCT04467515 **Phase: I/II** **Treatment:** CAM-H2 **Cancer Type:** Breast Cancer	**Study Title:** A Multi-Center Open Label Dose Escalation and Dose Expansion Study to Evaluate Safety, Tolerability, Dosimetry, and Preliminary Efficacy of the HER2 Directed Radioligand CAM-H2 in Patients With Advanced/Metastatic HER2-Positive Breast, Gastric, and GEJ Cancer **Variant Classification:** ERBB2 positive **Locations:** Canada

NCT number: NCT04802759 **Phase: I/II** **Treatment:** Pertuzumab/trastuzumab/hyaluronidase-zzxf + Hormone Therapy, Abemaciclib + Pertuzumab/trastuzumab/hyaluronidase-zzxf + Hormone Therapy, Palbociclib + Pertuzumab/trastuzumab/hyaluronidase-zzxf + Hormone Therapy **Cancer Type:** Breast Cancer	**Study Title:** A Phase Ib/II, Open-Label, Multicenter, Randomized Umbrella Study Evaluating the Efficacy and Safety of Multiple Treatment Combinations in Patients With Breast Cancer (MORPHEUS- BREAST CANCER) **Variant Classification:** ERBB2 positive **Locations:** Australia, Israel, Republic of Korea, Spain, United States **Contacts:** Reference Study ID Number: CO42867 [888-662-6728; global-roche-genentech-trials@gene.com]
NCT number: NCT04246671 **Phase: I/II** **Treatment:** TAEK-VAC-HerBy, Trastuzumab, Pertuzumab **Cancer Type:** Breast Cancer	**Study Title:** Phase I Trial of Intravenous Administration of TAEK-VAC-HerBy Vaccine Alone and in Combination With HER2 Antibodies in Patients With Advanced Cancer **Variant Classification:** ERBB2 positive **Locations:** United States **Contacts:** Dr. Tatiana Adams [info@bavarian-nordic.com]
NCT number: NCT05523947 **Phase: I/II** **Treatment:** YH32367 **Cancer Type:** Breast Cancer	**Study Title:** A Phase I/II, Non-randomized, Open-label, Multicenter, First-in-Human Study to Evaluate the Safety, Tolerability, Pharmacokinetics and Anti-tumor Activity of YH32367 in Patients With HER2-Positive Locally Advanced or Metastatic Solid Tumors **Variant Classification:** ERBB2 positive **Locations:** Republic of Korea
NCT number: NCT04834778 **Phase: I** **Treatment:** HC-5404-FU **Cancer Type:** Breast Cancer	**Study Title:** A Multicenter, Open-label, Phase 1a Study of HC-5404-FU in Subjects With Selected, Advanced Solid Tumors **Variant Classification:** ERBB2 positive **Locations:** United States **Contacts:** Viviana Cecinato [708-295-1226; Viviana.Cecinato@covance.com]
NCT number: NCT03842085 **Phase: I** **Treatment:** MBS301 **Cancer Type:** Breast Cancer	**Study Title:** Evaluation on Open-Labeled and Dose-Escalation Phase I Clinical Study of Safety and Pharmacokinetics of Recombinant Humanized Bispecific Monoclonal Antibody MBS301 for Injection in Treatment of HER2 Positive Recurrent or Metastatic Malignant Solid Tumor **Variant Classification:** ERBB2 positive **Locations:** China

NCT number: NCT05385705 **Phase: I** **Treatment:** Natural Killer Cell Therapy, Trastuzumab, Pertuzumab, Chemotherapy, Interleukin-2 (Ajinomoto) **Cancer Type:** Breast Cancer	**Study Title:** A Phase Ib Study With a Safety lead-in Cohort and Expansion Phase, of the Safety, Tolerability, Biological Effect, and Efficacy of Allogenic Natural Killer Cells in Combination With Trastuzumab and Pertuzumab in Adult Patients With Refractory Metastatic Her2 Positive Breast Cancer **Variant Classification:** ERBB2 positive **Locations:** Spain
NCT number: NCT02872025 **Phase: I** **Treatment:** Pembrolizumab **Cancer Type:** Breast Cancer	**Study Title:** Testing the Ability of Pembrolizumab to Alter the Tumor Immune MicroEnvironment (TIME) of High Risk DCIS **Variant Classification:** ERBB2 positive **Locations:** United States
NCT number: NCT04557449 **Phase: I** **Treatment:** PF-07220060, Midazolam **Cancer Type:** Breast Cancer	**Study Title:** A Phase I/IIa Study Evaluating The Safety, Tolerability, Pharamcokinetics, Pharmacodynamics, And Anti-Tumor Activity Of PF-07220060 As A Single Agent And as Part of Combination Therapy In Participants With Advanced Solid Tumors **Variant Classification:** ERBB2 positive **Locations:** Argentina, China, Czech Republic, Mexico, Slovakia, United Kingdom, United States **Contacts:** Pfizer CT.gov Call Center [800-718-1021; ClinicalTrials.gov_Inquiries@pfizer.com]
NCT number: NCT05538572 **Phase: I** **Treatment:** PRT-3645 **Cancer Type:** Breast Cancer	**Study Title:** A Phase I Open-Label, Multi-Center, Safety and Efficacy Study of PRT3645 in Participants With Select Advanced or Metastatic Solid Tumors **Variant Classification:** ERBB2 positive **Locations:** United States **Contacts:** Study Contact (Please Do Not Disclose Personal Information) [PRT3645-01study@preludetx.com]
NCT number: NCT05245058 **Phase: I** **Treatment:** SPH5030 **Cancer Type:** Breast Cancer	**Study Title:** A Phase I Study to Evaluate the Safety, Tolerability, and Pharmacokinetic Characteristics of SPH5030 Tablets in Subjects With Advanced Her2-positive Solid Tumors **Variant Classification:** ERBB2 positive **Locations:** China

NCT number: NCT04982926 **Phase: I** **Treatment:** TAS 2940 **Cancer Type:** Breast Cancer	**Study Title:** A Phase I Study of TAS2940 in Patients With Locally Advanced or Metastatic Solid Tumors With EGFR and / or HER2 Aberrations **Variant Classification:** ERBB2 positive **Locations:** France, United States **Contacts:** Dr. Taiho Oncology [609-250-7336; clinicaltrialinfo@taihooncology.com]
NCT number: NCT05722886 **Phase: II/III** **Treatment:** Pertuzumab + Trastuzumab **Cancer Type:** Unspecified Solid Tumor	**Study Title:** DETERMINE (Determining Extended Therapeutic Indications for Existing Drugs in Rare Molecularly Defined Indications Using a National Evaluation Platform Trial): An Umbrella-Basket Platform Trial to Evaluate the Efficacy of Targeted Therapies in Rare Adult, Paediatric and Teenage/Young Adult (TYA) Cancers With Actionable Genomic Alterations, Including Common Cancers With Rare Actionable Alterations **Variant Classification:** ERBB2 amplification **Locations:** United Kingdom
NCT number: NCT04551521 **Phase: II** **Treatment:** Atezolizumab + Pertuzumab + Trastuzumab **Cancer Type:** Unspecified Solid Tumor	**Study Title:** Continuous ReAssessment With Flexible ExTension in Rare Malignancies - CRAFT: The NCT-PMO-1602 Phase II Trial **Variant Classification:** ERBB2 overexpression **Locations:** Germany
NCT number: NCT02693535 **Phase: II** **Treatment:** Pertuzumab + Trastuzumab, Atezolizumab + Pertuzumab/trastuzumab/hyaluronidase-zzxf, Trastuzumab + Tucatinib **Cancer Type:** Unspecified Solid Tumor	**Study Title:** Targeted Agent and Profiling Utilization Registry (TAPUR) Study **Variant Classification:** ERBB2 overexpression **Locations:** United States **Contacts:** Pam Mangat [tapur@asco.org]
NCT number: NCT04423185 **Phase: II** **Treatment:** Pyrotinib **Cancer Type:** Unspecified Solid Tumor	**Study Title:** Platform Study of Genotyping Guided Precision Medicine for Rare Tumors in China **Variant Classification:** ERBB2 amplification **Locations:** China

NCT number: NCT03239015 **Phase: II** **Treatment:** Trastuzumab **Cancer Type:** Unspecified Solid Tumor	**Study Title:** Efficacy and Safety of Precision Therapy in Refractory Tumor (Long March Pathway) **Variant Classification:** ERBB2 amplification **Locations:** China
NCT number: NCT05673928 **Phase: II** **Treatment:** Tucatinib, Ado-trastuzumab Emtansine **Cancer Type:** Unspecified Solid Tumor	**Study Title:** A Phase II Study of Tucatinib and Ado-trastuzumab Emtansine (T-DM1) in Patients With HER2-positive Metastatic Solid Tumors and Metastases to Brain (TUCATEMEB) **Variant Classification:** ERBB2 overexpression **Locations:** United States **Contacts:** Dr. Ecaterina Dumbrava [713-563-1930; eeileana@mdanderson.org]
NCT number: NCT05315700 **Phase: I/II** **Treatment:** ORIC-114 **Cancer Type:** Unspecified Solid Tumor	**Study Title:** A Phase Ib/II, Single agent, Tumor-Agnostic Trial of ORIC-114 in Patients With Advanced Solid Tumors With EGFR or HER2 Exon 20 Alterations or HER2 Amplification And Will allow Patients With CNS Metastases that are Either Treated or Untreated But Asymptomatic. **Variant Classification:** ERBB2 overexpression **Locations:** Australia, Republic of Korea, United States **Contacts:** ORIC Clinical [650-388-5600; clinical@oricpharma.com]
NCT number: NCT05372614 **Phase: I/II** **Treatment:** Trastuzumab Deruxtecan, Neratinib **Cancer Type:** Unspecified Solid Tumor	**Study Title:** Phase I Trial of DS-8201a (Trastuzumab Deruxtecan) in Combination With Neratinib in Solid Tumors With HER2 Alterations **Variant Classification:** ERBB2 overexpression **Locations:** United States
NCT number: NCT04886804 **Phase: I** **Treatment:** BI-1810631 **Cancer Type:** Unspecified Solid Tumor	**Study Title:** An Open Label, Phase I Dose Escalation Trial, With Dose Confirmation and Expansion, of BI 1810631 as Monotherapy in Patients With Advanced or Metastatic Solid Tumors With HER2 Aberrations **Variant Classification:** ERBB2 amplification **Locations:** Australia, China, Germany, Japan, Netherlands, Republic of Korea, Spain, United States **Contacts:** Boehringer Ingelheim [800-243-0127; clintriage.rdg@boehringer-ingelheim.com]

NCT number: NCT05631964 **Phase: I** **Treatment:** BL-M07D1 **Cancer Type:** Unspecified Solid Tumor	**Study Title:** A Phase I Clinical Study to Evaluate the Safety, Tolerability, Pharmacokinetic Characteristics, and Initial Efficacy of BL-M07D1 for Injection in Patients With Locally Advanced or Metastatic Digestive Tract Tumors and Other Solid Tumors **Variant Classification:** ERBB2 overexpression **Locations:** China
NCT number: NCT02442297 **Phase: I** **Treatment:** CART-HER2 **Cancer Type:** Unspecified Solid Tumor	**Study Title:** Phase I Study of Intracranial Injection of T Cells Expressing HER2-specific Chimeric Antigen Receptors (CAR) in Subjects With HER2-Positive Tumors of the Central Nervous System (iCAR) **Variant Classification:** ERBB2 overexpression **Locations:** United States **Contacts:** Dr. Nabil M. Ahmed [832-824-4611; nmahmed@txch.org]
NCT number: NCT04501770 **Phase: I** **Treatment:** M802 **Cancer Type:** Unspecified Solid Tumor	**Study Title:** A Phase I Study to Evaluate the Safety, Tolerability, Pharmacokinetics, Pharmacodynamics and Immunogenicity Profiles of the Recombinant Anti-HER2 and Anti-CD3 Humanized Bispecific Antibody (M802) in HER2-Positive Advanced Solid Tumors **Variant Classification:** ERBB2 overexpression **Locations:** China
NCT number: NCT04585958 **Phase: I** **Treatment:** Trastuzumab Deruxtecan, Olaparib **Cancer Type:** Unspecified Solid Tumor	**Study Title:** A Phase I Study of DS-8201a in Combination With Olaparib in HER2-Expressing Malignancies **Variant Classification:** ERBB2 amplification **Locations:** United States **Contacts:** Multiple contacts: See www.clinicaltrials.gov for complete list of contacts.
NCT number: NCT05593094 **Phase: I** **Treatment:** ZN-A-1041 **Cancer Type:** Unspecified Solid Tumor	**Study Title:** A Phase I Clinical Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Efficacy of ZN-A-1041 Enteric Capsules as a Single Agent or in Combination in Patients With HER2-Positive Advanced Solid Tumors **Variant Classification:** ERBB2 overexpression **Locations:** United States **Contacts:** Dr. Ding Zhou [391-636-0900; ding.zhou@zionpharma.com]
NCT number: NCT05423977 **Phase: I** **Treatment:** ZV-0203 **Cancer Type:** Unspecified Solid Tumor	**Study Title:** An Open-label, Multicenter, Phase I Dose-escalation Study to Assess the Safety, Pharmacokinetic (PK), Immunogenicity and Preliminary Anti-tumor Activity of ZV0203 in Patients With HER2-Positive Advanced Solid Tumors **Variant Classification:** ERBB2 amplification **Locations:** China

High Tumor Mutational Burden

NCT number: NCT03767075
Phase: II
Treatment: Atezolizumab
Cancer Type: Unspecified Solid Tumor

Study Title: Basket of Baskets: A Modular, Open-label, Phase II, Multicentre Study To Evaluate Targeted Agents in Molecularly Selected Populations With Advanced Solid Tumours
Variant Classification: Tumor Mutational Burden
Locations:
France, Germany, Netherlands, Spain, Sweden, United Kingdom

NCT number: NCT04185831
Phase: II
Treatment: Atezolizumab
Cancer Type: Unspecified Solid Tumor

Study Title: MEGALiT - a Multicenter, Basket and Umbrella Explorative Trial on the Efficacy and Safety of Molecular Profile Selected Commercially Available Targeted Anti-cancer Drugs in Patients With Advanced Cancers Progressive on Standard Therapy
Variant Classification: Tumor Mutational Burden
Locations:
Sweden

NCT number: NCT04589845
Phase: II
Treatment: Atezolizumab
Cancer Type: Unspecified Solid Tumor

Study Title: Tumor-Agnostic Precision Immunooncology and Somatic Targeting Rational for You (TAPISTRY) Phase II Platform Trial
Variant Classification: Tumor Mutational Burden
Locations:
Australia, Belgium, Brazil, Canada, China, Denmark, France, Germany, Hong Kong, Israel, Italy, Japan, New Zealand, Poland, Puerto Rico, Republic of Korea, Singapore, Spain, Swaziland, Switzerland, Taiwan, United Kingdom, United States
Contacts:
Reference Study ID Number: BO41932 [888-662-6728; Global-Roche-Genentech-Trials@gene.com]

NCT number: NCT02029001
Phase: II
Treatment: Durvalumab, Tremelimumab
Cancer Type: Unspecified Solid Tumor

Study Title: A Two-period, Multicenter, Randomized, Open-label, Phase II Study Evaluating the Clinical Benefit of a Maintenance Treatment Targeting Tumor Molecular Alterations in Patients with Progressive Locally-advanced or Metastatic Solid Tumors.
Variant Classification: Tumor Mutational Burden
Locations:
France

NCT number: NCT04891198
Phase: II
Treatment: Envafolimab
Cancer Type: Solid Tumor

Study Title: An Open, Single-arm, Multi-center Phase II Clinical Study of ENVAFOLIMAB Single-agent Treatment in Patients With Advanced Solid Tumors
Variant Classification: Tumor Mutational Burden
Locations:
China

NCT number: NCT05199272 **Phase: I/II** **Treatment:** 23ME-00610 **Cancer Type:** Unspecified Solid Tumor	**Study Title:** A First-in-human Phase I/IIa, Multicenter, Open-Label, Dose-Escalation and Expansion Study of Intravenously Administered 23ME-00610 in Patients With Advanced Solid Malignancies **Variant Classification:** Tumor Mutational Burden **Locations:** Canada, United States **Contacts:** Study Inquiry [650-963-8997; studyinquiry@23andme.com]
NCT number: NCT03838042 **Phase: I/II** **Treatment:** Entinostat, Nivolumab **Cancer Type:** Unspecified Solid Tumor	**Study Title:** INFORM2 Exploratory Multinational Phase I/II Combination Study of Nivolumab and Entinostat in Children and Adolescents with Refractory High-risk Malignancies **Variant Classification:** Tumor Mutational Burden **Locations:** Australia, Austria, France, Germany, Netherlands, Sweden, Switzerland
NCT number: NCT03809624 **Phase: I/II** **Treatment:** INBRX-105, Pembrolizumab **Cancer Type:** Unspecified Solid Tumor	**Study Title:** An Open-Label, Multicenter, First-in-Human, Dose-Escalation, Phase I/II Study of INBRX-105 and INBRX-105 in Combination With Pembrolizumab in Patients With Locally Advanced or Metastatic Solid Tumors **Variant Classification:** Tumor Mutational Burden **Locations:** United States **Contacts:** Amanda Sweeney [858-500-7833; clinicaltrials@inhibrx.com]
NCT number: NCT05315167 **Phase: I/II** **Treatment:** PRJ1-3024 **Cancer Type:** Unspecified Solid Tumor	**Study Title:** A Phase I/II, Open-label Study Evaluating the Safety, Tolerability, Pharmacokinetics, Pharmacodynamics, and Prime Efficacy of PRJ1-3024 in Subjects With Advanced Solid Tumors **Variant Classification:** Tumor Mutational Burden **Locations:** China
NCT number: NCT05592626 **Phase: I/II** **Treatment:** STAR-0602 **Cancer Type:** Unspecified Solid Tumor	**Study Title:** A Phase I/II, First-in-Human, Open-Label, Dose Escalation and Expansion Study of STAR0602, a Selective T Cell Receptor (TCR) Targeting, Bifunctional Antibody-fusion Molecule, in Subjects With Unresectable, Locally Advanced, or Metastatic Solid Tumors That Are Antigen-rich (START-001) **Variant Classification:** Tumor Mutational Burden **Locations:** United States **Contacts:** Dr. Ke Liu [617-917-4980; kliu@marengotx.com]

NCT number: NCT04198766 **Phase: I** **Treatment:** INBRX-106, Pembrolizumab **Cancer Type:** Unspecified Solid Tumor	**Study Title:** An Open-Label, Multicenter, First-in-Human, Dose-Escalation, Multicohort, Phase I/II Study of INBRX-106 and INBRX-106 in Combination With Pembrolizumab in Subjects With Locally Advanced or Metastatic Solid Tumors **Variant Classification:** Tumor Mutational Burden **Locations:** United States **Contacts:** Amanda Sweeney [858-500-7833; clinicaltrials@inhibrx.com]

PIK3CA p.(E545K) c.1633G>A

NCT number: NCT04586335 **Phase: I** **Treatment:** HH-CYH33, Olaparib **Cancer Type:** Breast Cancer	**Study Title:** Open Label, Phase Ib Study to Evaluate the Safety, Tolerability, Pharmacokinetics and Clinical Activity of CYH33, an Oral a-specific PI3K Inhibitor in Combination With Olaparib, an Oral PARP Inhibitor in Patients With Advanced Solid Tumors. **Variant Classification:** PIK3CA E545 mutation **Locations:** China
NCT number: NCT05307705 **Phase: I** **Treatment:** LOXO-783, Chemotherapy **Cancer Type:** Breast Cancer	**Study Title:** A Study of LOXO-783 Administered as Monotherapy and in Combination With Anticancer Therapies for Patients With Advanced Breast Cancer and Other Solid Tumors With a PIK3CA H1047R Mutation **Variant Classification:** PIK3CA activating mutation **Locations:** Australia, Canada, Japan, Singapore, United States **Contacts:** Patient Advocacy [855-569-6305; clinicaltrials@loxooncology.com;]
NCT number: NCT05082025 **Phase: II** **Treatment:** Copanlisib, Hormone Therapy **Cancer Type:** Breast Cancer	**Study Title:** Phase II Study of PI3K Inhibitor Copanlisib in Combination With Fulvestrant in Selected ER+ and/or PR+ Cancers With PI3K (PIK3CA, PIK3R1) and/or PTEN Alterations **Variant Classification:** PIK3CA mutation **Locations:** United States **Contacts:** Dr. Timothy Yap [713-563-1784; tyap@mdanderson.org]
NCT number: NCT04317105 **Phase: I/II** **Treatment:** Copanlisib, Nivolumab, Ipilimumab **Cancer Type:** Unspecified Solid Tumor	**Study Title:** A Phase I/II Biomarker Driven Combination Trial of Copanlisib and Immune Checkpoint Inhibitors in Patients With Advanced Solid Tumors **Variant Classification:** PIK3CA E545 mutation **Locations:** Canada, United States **Contacts:** Multiple contacts: See www.clinicaltrials.gov for complete list of contacts.

NCT number: NCT05768139 **Phase: I/II** **Treatment:** STX-478, Hormone Therapy **Cancer Type:** Unspecified Solid Tumor	**Study Title:** First-in-Human Study of STX-478, a Mutant-Selective PI3Kα Inhibitor as Monotherapy and in Combination With Other Antineoplastic Agents in Participants With Advanced Solid Tumor **Variant Classification:** PIK3CA E545 mutation **Locations:** United States **Contacts:** For questions concerning enrollment [clinicaltrials@scorpiontx.com]
NCT number: NCT03842228 **Phase: I** **Treatment:** Copanlisib, Olaparib, Durvalumab **Cancer Type:** Unspecified Solid Tumor	**Study Title:** A Phase Ib Biomarker-Driven Combination Trial of Copanlisib, Olaparib, and Durvalumab (MEDI4736) in Patients With Advanced Solid Tumors **Variant Classification:** PIK3CA E545 mutation **Locations:** United States **Contacts:** Multiple contacts: See www.clinicaltrials.gov for complete list of contacts.
NCT number: NCT05216432 **Phase: I** **Treatment:** RLY-2608 **Cancer Type:** Unspecified Solid Tumor	**Study Title:** A First-in-Human Study of Mutant-selective PI3Ka Inhibitor, RLY-2608, as a Single Agent in Advanced Solid Tumor Patients and in Combination With Fulvestrant in Patients With Advanced Breast Cancer **Variant Classification:** PIK3CA E545 mutation **Locations:** Spain, United States **Contacts:** Relay Therapeutics Inc [617-322-0731; ClinicalTrials@relaytx.com]
NCT number: NCT03673787 **Phase: I/II** **Treatment:** Ipatasertib, Atezolizumab **Cancer Type:** Unspecified Solid Tumor	**Study Title:** Ice-CAP: A Phase I Trial of Ipatasertib in Combination With Atezolizumab in Patients With Advanced Solid Tumours With PI3K Pathway Hyperactivation. **Variant Classification:** PIK3CA activating mutation **Locations:** United Kingdom
NCT number: NCT05300048 **Phase: I** **Treatment:** Serabelisib **Cancer Type:** Unspecified Solid Tumor	**Study Title:** A Phase Ib Study of Serabelisib in Combination With an Insulin Suppressing Diet (Study ISD) and With or Without Nab-paclitaxel in Adult Subjects With Advanced Solid Tumors With PIK3CA Mutations With or Without PTEN Loss **Variant Classification:** PIK3CA activating mutation **Locations:** United States **Contacts:** Study Inquiry [708-406-9282; clinicaltrials@faeththerapeutics.com]

NCT number: NCT04344795 **Phase: I** **Treatment:** TPST-1495, Pembrolizumab **Cancer Type:** Unspecified Solid Tumor	**Study Title:** Phase Ia/Ib Open Label Dose-escalation and Expansion Study of TPST-1495 as a Single Agent and in Combination With Pembrolizumab in Subjects With Solid Tumors **Variant Classification:** PIK3CA activating mutation **Locations:** United States **Contacts:** Tempest Clinical Trial Support [415-798-8589 ext 122; 1495-Inquiries@tempesttx.com]
NCT number: NCT03065062 **Phase: I** **Treatment:** Palbociclib, Gedatolisib **Cancer Type:** Unspecified Solid Tumor	**Study Title:** Phase I Study of the CDK4/6 Inhibitor Palbociclib (PD-0332991) in Combination With the PI3K/mTOR Inhibitor Gedatolisib (PF-05212384) for Patients With Advanced Squamous Cell Lung, Pancreatic, Head & Neck and Other Solid Tumors **Variant Classification:** PIK3CA mutation **Locations:** United States **Contacts:** Dr. Geoffrey Shapiro [617-632-4942; Geoffrey_Shapiro@dfci.harvard.edu]
NCT number: NCT04192981 **Phase: I** **Treatment:** Paxalisib, Radiation Therapy **Cancer Type:** Unspecified Solid Tumor	**Study Title:** A Phase I Study With Expansion Cohort of Concurrent GDC-0084 With Radiation Therapy for Patients With Solid Tumor Brain Metastases or Leptomeningeal Metastases Harboring PI3K Pathway Mutations **Variant Classification:** PIK3CA mutation **Locations:** United States **Contacts:** Dr. Brandon Imber [631-212-6346; imberb@mskcc.org]
NCT number: NCT05759949 **Phase: I** **Treatment:** RLY-5836 **Cancer Type:** Unspecified Solid Tumor	**Study Title:** A First-in-Human Study of PI3Kα Inhibitor, RLY-5836, in Combination With Targeted and Endocrine Therapies in Participants With Advanced Breast Cancer and as a Single Agent in Advanced Solid Tumors **Variant Classification:** PIK3CA mutation **Locations:** United States **Contacts:** Relay Therapeutics Inc. [617-322-0731; ClinicalTrials@relaytx.com]
NCT number: NCT05341570 **Phase: I** **Treatment:** BPI-21668 **Cancer Type:** Unspecified Solid Tumor	**Study Title:** Phase I Clinical Study to evaluate the Safety, Tolerability, Pharmacokinetics and effectiveness of BPI-21668 Tablets in Patients with Advanced Solid Tumors **Variant Classification:** PIK3CA mutation status **Locations:** China

NCT number: NCT03297606 **Phase: II** **Treatment:** Temsirolimus **Cancer Type:** Unspecified Solid Tumor	**Study Title:** Canadian Profiling and Targeted Agent Utilization Trial (CAPTUR): A Phase II Basket Trial **Variant Classification:** PIK3CA aberration **Locations:** Canada
NCT number: NCT03155620 **Phase: II** **Treatment:** Samotolisib **Cancer Type:** Unspecified Solid Tumor	**Study Title:** NCI-COG Pediatric MATCH (Molecular Analysis for Therapy Choice) Screening Protocol **Variant Classification:** PI3K/AKT/MTOR mutation **Locations:** Puerto Rico, United States **Contacts:** Multiple contacts: See www.clinicaltrials.gov for complete list of contacts.

NF1 p.(R1968*) c.5902C>T

NCT number: NCT04045496 **Phase: I** **Treatment:** JAB-3312 **Cancer Type:** Breast Cancer	**Study Title:** A Phase I, Multi-Center, Open-Label Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Preliminary Evidence of Antitumor Activity of JAB-3312 in Adult Patients With Advanced Solid Tumors **Variant Classification:** NF1 mutation **Locations:** United States **Contacts:** Jacobio Pharmaceuticals [clinicaltrials@jacobiopharma.com]
NCT number: NCT04534283 **Phase: II** **Treatment:** Abemaciclib + Temuterkib **Cancer Type:** Unspecified Solid Tumor	**Study Title:** A Phase II Basket Trial of an ERK1/2 Inhibitor (LY3214996) in Combination With Abemaciclib for Patients Whose Tumors Harbor Pathogenic Alterations in BRAF, RAF1, MEK1/2, ERK1/2, and NF1 **Variant Classification:** NF1 mutation **Locations:** United States **Contacts:** Anne Younger [317-274-0951; anefoste@iupui.edu]
NCT number: NCT04116541 **Phase: II** **Treatment:** Trametinib **Cancer Type:** Unspecified Solid Tumor	**Study Title:** MegaMOST - A Multicenter, Open-label, Biology Driven, Phase II Study Evaluating the Activity of Anti-cancer Treatments Targeting Tumor Molecular Alterations /Characteristics in Advanced / Metastatic Tumors. **Variant Classification:** NF1 mutation **Locations:** France

NCT number: NCT05578092 **Phase: I/II** **Treatment:** MRTX0902 **Cancer Type:** Unspecified Solid Tumor	**Study Title:** A Phase 1/2 Multiple Expansion Cohort Trial of the SOS1 Inhibitor MRTX0902 in Patients With Advanced Solid Tumors Harboring Mutations in the KRAS MAPK Pathway **Variant Classification:** NF1 mutation **Locations:** United States **Contacts:** Mirati Therapeutics Study Locator Services [844-893-5530; miratistudylocator@careboxhealth.com]
NCT number: NCT05340621 **Phase: I/II** **Treatment:** OKI-179, Binimetinib **Cancer Type:** Unspecified Solid Tumor	**Study Title:** NAUTILUS: A Phase I b/II Study of OKI-179 Plus Binimetinib in Patients With Advanced Solid Tumors and Activating Mutations in the RAS Pathway (Phase 1b) and in Patients With Advanced NRAS-Mutated Melanoma (Phase 2) **Variant Classification:** NF1 mutation **Locations:** United States **Contacts:** Onkure [720-307-2892; info@onkuretherapeutics.com]
NCT number: NCT05831995 **Phase: I** **Treatment:** ABM-168 **Cancer Type:** Unspecified Solid Tumor	**Study Title:** A Phase I, First-In-Human, Multicenter, Open Label, Dose Escalation and Dose Expansion Study to Evaluate the Safety and Efficacy of ABM-168 Administered Orally in Adult Patients With Advanced Solid Tumors **Variant Classification:** NF1 mutation **Locations:** United States **Contacts:** William Liu [917-436-6817; wliu@abmtx.com]
NCT number: NCT04528836 **Phase: I** **Treatment:** BBP-398 **Cancer Type:** Unspecified Solid Tumor	**Study Title:** A Phase I/IB First-in-Human Study of the SHP2 Inhibitor BBP-398 (Formerly Known as IACS-15509) in Patients With Advanced Solid Tumors **Variant Classification:** NF1 mutation **Locations:** United States **Contacts:** Navire Clinical Operations [650-391-9740; nav1001ct.gov@bridgebio.com]
NCT number: NCT05354843 **Phase: I** **Treatment:** ET0038 **Cancer Type:** Unspecified Solid Tumor	**Study Title:** A Phase I, Open-Label, Multi-Center Dose Finding Study to Investigate the Safety, Pharmacokinetics, and Preliminary Efficacy of SHP2 Inhibitor ET0038 Monotherapy in Patients With Advanced Solid Tumors **Variant Classification:** NF1 mutation **Locations:** China

NCT number: NCT05039801 **Phase: I** **Treatment:** IPN-60090 **Cancer Type:** Unspecified Solid Tumor	**Study Title:** A Phase I Open-Label, Dose-Escalation and Dose-Expansion Study to Investigate the Safety, Pharmacokinetics, and Anti-Tumor Activity of IACS-6274 as Monotherapy and in Combination in Patients With Advanced Solid Tumors **Variant Classification:** NF1 mutation **Locations:** United States **Contacts:** Dr. Timothy Timothy [713-563-1930; tyap@mdanderson.org]
NCT number: NCT04800822 **Phase: I** **Treatment:** PF-07284892, Binimetinib **Cancer Type:** Unspecified Solid Tumor	**Study Title:** A Phase I, Open-label, Multi-center, Dose Escalation and Dose Expansion Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Preliminary Evidence of Anti-tumor Activity of Pf-07284892 (ARRY-558) as a Single Agent and in Combination Therapy in Participants with Advanced Solid Tumors **Variant Classification:** NF1 mutation **Locations:** United States **Contacts:** Pfizer CT.gov Call Center [800-718-1021; ClinicalTrials.gov_Inquiries@pfizer.com]
NCT number: NCT05557045 **Phase: I** **Treatment:** JZP-815 **Cancer Type:** Unspecified Solid Tumor	**Study Title:** Phase I, FIH, Open-label, Nonrandomized, Multicenter Study of JZP815 in Participants With Advanced or Metastatic Solid Tumors Harboring Alterations in the MAPK Pathway **Variant Classification:** RAS/RAF/MEK/ERK mutation **Locations:** United States **Contacts:** Clinical Trial Disclosure & Transparency [215-832-3750; ClinicalTrialDisclosure@JazzPharma.com]
NCT number: NCT03520075 **Phase: I/II** **Treatment:** ASTX029 **Cancer Type:** Unspecified Solid Tumor	**Study Title:** A Phase I/II Study of the Safety, Pharmacokinetics, and Activity of ASTX029 in Subjects With Advanced Solid Tumors **Variant Classification:** RAS/RAF/MEK/ERK pathway **Locations:** France, Spain, United Kingdom, United States **Contacts:** General Inquiries [925-560-0100; clinicaltrials@astx.com]
NCT number: NCT05580770 **Phase: I/II** **Treatment:** Mirdametinib, BGB-3245 **Cancer Type:** Unspecified Solid Tumor	**Study Title:** A Phase I/IIa Open-Label, Dose Escalation and Expansion Study to Investigate the Safety, Pharmacokinetics, Pharmacodynamics and Efficacy of Mirdametinib in Combination With BGB-3245 in Patients With Advanced Solid Tumors **Variant Classification:** RAS/RAF/MEK/ERK pathway **Locations:** Australia, United States **Contacts:** SpringWorks Clinical [919-790-1002; clinical@springworkstx.com]

NCT number: NCT03905148 **Phase: I/II** **Treatment:** Mirdametinib, Lifirafenib **Cancer Type:** Unspecified Solid Tumor	**Study Title:** A Phase Ib, Open-Label, Dose-escalation and Expansion Study to Investigate the Safety, Pharmacokinetics and Antitumor Activities of a RAF Dimer Inhibitor BGB-283 in Combination With MEK Inhibitor PD-0325901 in Patients With Advanced or Refractory Solid Tumors **Variant Classification:** RAS/RAF/MEK/ERK pathway **Locations:** Australia, United States **Contacts:** BeiGene [877-828-5568; clinicaltrials@beigene.com]
NCT number: NCT04305249 **Phase: I** **Treatment:** AZD-0364, Nivolumab **Cancer Type:** Unspecified Solid Tumor	**Study Title:** A Phase I, Open-Label, Multi-Center Dose Finding Study to Investigate the Safety, Pharmacokinetics, and Preliminary Efficacy of ATG-017 Monotherapy or Combination Therapy With Nivolumab in Patients With Advanced Solid Tumors and Hematological Malignancies **Variant Classification:** RAS/RAF/MEK/ERK pathway **Locations:** Australia
NCT number: NCT04418167 **Phase: I** **Treatment:** JSI-1187 **Cancer Type:** Unspecified Solid Tumor	**Study Title:** A Phase I Study of ERK1/2 Inhibitor JSI-1187 Administered as Monotherapy and in Combination with Dabrafenib for the Treatment of Advanced Solid Tumors with MAPK Pathway Mutations **Variant Classification:** RAS/RAF/MEK/ERK pathway **Locations:** United States **Contacts:** Georgine N. Price [301-610-4990; georgineprice@westat.com]
NCT number: NCT05488821 **Phase: I** **Treatment:** QLH11906 **Cancer Type:** Unspecified Solid Tumor	**Study Title:** A Phase I Clinical Study to Evaluate the Safety, Tolerability and Pharmacokinetics of the Oral Pan-RAF Inhibitor QLH11906 in Subjects With Advanced Solid Tumors Harboring MAPK Pathway Alterations. **Variant Classification:** RAS/RAF/MEK/ERK pathway **Locations:** China

TP53 mutation

NCT number: NCT04169841 **Phase: II** **Treatment:** Durvalumab, Tremelimumab, Olaparib **Cancer Type:** Breast Cancer	**Study Title:** Precision Medicine Phase II Study Evaluating the Efficacy of a Double Immunotherapy by Durvalumab and Tremelimumab Combined With Olaparib in Patients With Solid Cancers and Carriers of Homologous Recombination Repair Genes Mutation in Response or Stable After Olaparib Treatment **Variant Classification:** HRR mutation **Locations:** France

NCT number: NCT03344965
Phase: II
Treatment: Olaparib
Cancer Type: Breast Cancer

Study Title: A Phase II Study of Olaparib Monotherapy in Metastatic Breast Cancer Patients With Germline or Somatic Mutations in DNA Repair Genes (Olaparib Expanded)
Variant Classification: DNA repair mutation
Locations: United States
Contacts: Dr. Nadine Tung [617-667-1962; ntung@bidmc.harvard.edu]

NCT number: NCT05631886
Phase: I
Treatment: TP53-EphA-2-CAR-DC, Anti-PD-1, Chemotherapy
Cancer Type: Unspecified Solid Tumor

Study Title: A Pilot Clinical Trial of Autologous EphA-2-Targeting Chimeric Antigen Receptor Dendritic Cell Vaccine Loaded With TP53 Mutant Peptide Plus Anti- PD-1 Antibody for Local Advanced/Metastatic Solid Tumors or Relapsed/Refractory Lymphomas.
Variant Classification: TP53 R248Q mutation
Locations: China

NCT number: NCT05740956
Phase: I
Treatment: HS-10502
Cancer Type: Unspecified Solid Tumor

Study Title: A Phase I Study of HS-10502 tablets Intended for the Treatment of Patients with advanced solid tumor
Variant Classification: HRR mutation
Locations: China

NCT number: NCT04905914
Phase: I/II
Treatment: ATRN-119
Cancer Type: Unspecified Solid Tumor

Study Title: A Phase I/IIa, Open-Label, Safety, Pharmacokinetic, And Preliminary Efficacy Study Of Oral ATRN-119 In Patients With Advanced Solid Tumors
Variant Classification: DNA repair mutation
Locations: United States
Contacts: Crystal Miller [617-463-9385; crystal.miller@aprea.com]

NCT number: NCT04901702
Phase: I/II
Treatment: Talazoparib, Chemotherapy
Cancer Type: Unspecified Solid Tumor

Study Title: A Randomized Phase I/II Study of Talazoparib or Temozolomide in Combination With Onivyde in Children With Recurrent Solid Malignancies and Ewing Sarcoma
Variant Classification: HRR pathway
Locations: Canada, United States
Contacts: Dr. Sara Federico [866-278-5833; referralinfo@stjude.org]

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