



Sample Information

Patient Name: 吳挺琰
Gender: Male
ID No.: P121785190
History No.: 45866908
Age: 60

Ordering Doctor: DOC3109L 邱昭華
Ordering REQ.: 0BBEBWK
Signing in Date: 2021/01/21

Path No.: S110-98097
MP No.: F21006
Assay: Oncomine Focus Assay
Sample Type: FFPE
Block No.: S110-75070C
Percentage of tumor cells: 80%
Note:

Sample Cancer Type: Non-Small Cell Lung Cancer

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Relevant Non-Small Cell Lung Cancer Variants

Gene	Finding	Gene	Finding
ALK	Not detected	NTRK1	Not detected
BRAF	Not detected	NTRK2	Not detected
EGFR	Not detected	NTRK3	Not detected
ERBB2	ERBB2 exon 20 insertion	RET	Not detected
KRAS	Not detected	ROS1	Not detected
MET	Not detected		

Relevant Biomarkers

Tier	Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
IA	ERBB2 exon 20 insertion erb-b2 receptor tyrosine kinase 2 Allele Frequency: 45.19%	ado-trastuzumab emtansine	None	26

Public data sources included in relevant therapies: FDA1, NCCN, EMA2, ESMO

Tier Reference: Li et al. *Standards and Guidelines for the Interpretation and Reporting of Sequence Variants in Cancer: A Joint Consensus Recommendation of the Association for Molecular Pathology, American Society of Clinical Oncology, and College of American Pathologists.* J Mol Diagn. 2017 Jan;19(1):4-23.

Variant Details

DNA Sequence Variants

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect	Coverage
ERBB2	p.(G776delinsVV)	c.2327_2327delGins TTGT	.	chr17:37880998	45.19%	NM_004448.3	nonframeshift Insertion	1963
JAK1	p.(=)	c.2199A>G	.	chr1:65310489	99.75%	NM_002227.3	synonymous	1978
ALK	p.(I1461V)	c.4381A>G	.	chr2:29416572	100.00%	NM_004304.4	missense	1999
ALK	p.(=)	c.3375C>A	.	chr2:29445458	53.94%	NM_004304.4	synonymous	1993
FGFR3	p.(G90del)	c.268_270delGGG	.	chr4:1801137	34.03%	NM_000142.4	nonframeshift Deletion	1919
FGFR3	p.(Q92fs)	c.274delC	.	chr4:1801141	56.64%	NM_000142.4	frameshift Deletion	1919
FGFR3	p.(=)	c.1953G>A	.	chr4:1807894	99.90%	NM_000142.4	synonymous	1993
PDGFRA	p.(=)	c.1701A>G	.	chr4:55141055	99.95%	NM_006206.5	synonymous	1999
FGFR4	p.(P136L)	c.407C>T	.	chr5:176517797	99.40%	NM_213647.2	missense	2000

Biomarker Descriptions

ERBB2 (erb-b2 receptor tyrosine kinase 2)

Background: The ERBB2 gene encodes the erb-b2 receptor tyrosine kinase 2, a member of the human epidermal growth factor receptor (HER) family. Along with ERBB2/HER2, EGFR/ERBB1/HER1, ERBB3/HER3, and ERBB4/HER4 make up the HER protein family¹. All ERBB/HER proteins encode transmembrane receptor tyrosine kinases. However, ERBB2/HER2 is an orphan receptor with no known ligand. ERBB2 preferentially binds other ligand bound ERBB/HER family members to form hetero-dimers resulting in the activation of ERBB2 tyrosine kinase activity and subsequent activation of the PI3K/AKT/MTOR and RAS/RAF/MAPK/ERK signaling pathways which promote cell proliferation, differentiation, and survival². Recurrent focal amplification of the ERBB2 gene leads to increased expression in several cancer types. ERBB2 overexpression in immortalized cell lines is oncogenic and leads to ERBB2 homo-dimerization and activation without ligand binding^{3,4,5}.

Alterations and prevalence: ERBB2 gene amplification occurs in 10-20% of breast, esophageal, and gastric cancers, 5-10% of bladder, cervical, pancreas, and uterine cancers, and 1-5% of colorectal, lung, and ovarian cancers^{6,7,8,9,10,11,12,13}. Recurrent somatic activating mutations in ERBB2/HER2 occur at low frequencies (<1%) in diverse cancer types^{13,14,15}. In breast, bladder, and colorectal cancers, the most common recurrent ERBB2 activating mutations include kinase domain mutations L755S and V777L and the extracellular domain mutation S310F. In lung cancer, the most common recurrent ERBB2 activating mutations include in-frame exon 20 insertions, particularly Y772_A775dup.

Potential relevance: The discovery of ERBB2/HER2 as an important driver of breast cancer in 1987 led to the development of trastuzumab, a humanized monoclonal antibody with specificity to the extracellular domain of HER2^{16,17}. Trastuzumab¹⁸ was FDA approved for the treatment of HER2 positive breast cancer in 1998, and subsequently in HER2 positive metastatic gastric and

Biomarker Descriptions (continued)

gastroesophageal junction adenocarcinoma in 2010. Additional monoclonal antibody therapies have been approved by the FDA for HER2-positive breast cancer including pertuzumab¹⁹ (2012), a humanized monoclonal antibody that inhibits HER2 dimerization, and ado-trastuzumab emtansine²⁰ (2013), a conjugate of trastuzumab and a potent antimicrotubule agent. The combination of pertuzumab, trastuzumab, and a taxane is the preferred front-line regimen for HER2-positive metastatic breast cancer²¹. In addition to monoclonal antibodies, the small molecule inhibitor lapatinib²², with specificity for both EGFR and ERBB2, was FDA approved (2007) for the treatment of patients with advanced HER2-positive breast cancer who have received prior therapy including trastuzumab. In 2017, the FDA approved the use of neratinib²³, an irreversible kinase inhibitor of EGFR, ERBB2/HER2, and ERBB4, for the extended adjuvant treatment of adult patients with early stage HER2-positive breast cancer. In 2020, the FDA approved neratinib²³ in combination with capecitabine for HER2-positive advanced or metastatic patients after two or more prior HER2-directed therapies. Also in 2020, the TKI irbinetinib²⁴ was FDA approved for HER2 overexpressing or amplified breast cancer in combination with trastuzumab and capecitabine. The vaccine, nelinepimut-S²⁵, was granted fast-track designation by the FDA (2016) in patients with low to intermediate HER2 expressing (IHC score 1+ or 2+) breast cancer. Additionally, fast-track designation was granted (2018) to the monoclonal antibody margetuximab²⁶ in patients with ERBB2 positive breast cancer previously treated with an anti-HER2 therapy, the novel bispecific antibody ZW25²⁷ (2019) in combination with standard chemotherapy for patients with HER2-overexpressing gastroesophageal adenocarcinoma (GEA), and BDTX-189²⁸ (2020) for adult patients with solid tumors harboring an allosteric human ERBB2 mutation or exon 20 insertion. The humanized anti-HER2 antibody drug conjugate disitamab vedotin received a breakthrough designation (2020) for adult patients with HER2-positive urothelial cancer after previous platinum-chemotherapy treatment²⁹. Certain activating mutations have been observed to impart sensitivity to neratinib, afatinib, lapatinib, and trastuzumab, or dacomitinib in early and ongoing clinical studies^{30,31,32,33,34}. ERBB2 kinase domain mutations R896G and V659E both showed response to afatinib in two NSCLC case studies^{35,36}. Additionally, acquired HER2 mutations in estrogen receptor-positive (ER+) breast cancer have been shown to confer resistance to hormone therapy³⁷. However, this was shown to be overcome by neratinib in combination with therapies targeting ER³⁷.

Relevant Therapy Summary

☒ In this cancer type
 ☐ In other cancer type
 ☒ In this cancer type and other cancer types
 ☒ No evidence

ERBB2 exon 20 insertion

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
ado-trastuzumab emtansine	×	●	×	×	×
afatinib	×	×	×	×	● (II)
anti-PD-L1 antibody, pyrotinib	×	×	×	×	● (II)
neratinib	×	×	×	×	● (II)
pertuzumab + trastuzumab	×	×	×	×	● (II)
poziotinib	×	×	×	×	● (II)
pyrotinib	×	×	×	×	● (II)
sintilimab	×	×	×	×	● (II)
targeted therapy, chemotherapy	×	×	×	×	● (II)
tarloxotinib	×	×	×	×	● (II)
trastuzumab deruxtecan	×	×	×	×	● (II)
trastuzumab, pertuzumab, chemotherapy	×	×	×	×	● (II)
BDTX-189	×	×	×	×	● (I/II)
CBT-502, anlotinib hydrochloride	×	×	×	×	● (I/II)

* Most advanced phase (IV, III, II/III, II, I/II, I) is shown and multiple clinical trials may be available.

Relevant Therapy Summary (continued)

☒ In this cancer type
 ☐ In other cancer type
 ☒ In this cancer type and other cancer types
 ☒ No evidence

ERBB2 exon 20 insertion (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
DZD-9008	×	×	×	×	● (I/II)
zotatifin	×	×	×	×	● (I/II)
disitamab vedotin	×	×	×	×	● (I)
neratinib, palbociclib, everolimus, trametinib	×	×	×	×	● (I)
pirotinib	×	×	×	×	● (I)
SHR-A1811	×	×	×	×	● (I)
trastuzumab deruxtecan, pembrolizumab	×	×	×	×	● (I)

* Most advanced phase (IV, III, II/III, II, I/II, I) is shown and multiple clinical trials may be available.

Relevant Therapy Details

Current NCCN Information

☒ In this cancer type
 ☐ In other cancer type
 ☒ In this cancer type and other cancer types

NCCN information is current as of 2020-11-02. For the most up-to-date information, search www.nccn.org.
For NCCN International Adaptations & Translations, search www.nccn.org/global/international_adaptations.aspx.

ERBB2 exon 20 insertion

ado-trastuzumab emtansine

Cancer type: Non-Small Cell Lung Cancer

Variant class: ERBB2 mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Non-Small Cell Lung Cancer; Emerging biomarker in metastatic disease (Not specified)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 8.2020]

Clinical Trials Summary

ERBB2 exon 20 insertion

NCT ID	Title	Phase
NCT03066206	A Phase II Study of Poziotinib in EGFR in Exon 20 Mutant Advanced Non Small Cell Lung Cancer (NSCLC)	II
NCT03318939	A Phase II Study of Poziotinib in Patients With Non-Small Cell Lung Cancer (NSCLC), Locally Advanced or Metastatic, With EGFR or HER2 Exon 20 Insertion Mutation (ZENITH20).	II

Clinical Trials Summary (continued)

ERBB2 exon 20 insertion (continued)

NCT ID	Title	Phase
No NCT ID	A Prospective, Single-center, Single-arm Phase II Clinical Study for Advanced Non-small Cell Lung Cancer with EGFR/HER2 gene exon 20 insertion Mutations Treated with Sintilimab	II
NCT03845270	Phase II Trial of Trastuzumab in Combination With Pertuzumab in Pretreated Patients With Non-small Cell Lung Cancer (NSCLC) Harboring a Her2 Mutation and Receiving Docetaxel	II
NCT03974022	A Phase I/II, Open-Label, Multicenter Study to Assess the Safety, Tolerability, Pharmacokinetics and Anti-tumor Efficacy of DZD9008 in Patients With Advanced Non-Small Cell Lung Cancer (NSCLC) With EGFR or HER2 Mutation	I/II
NCT04402008	A Phase I/II Dose Finding Study of Pozitotinib in Japanese Patients With Locally Advanced or Metastatic Non-Small Cell Lung Cancer (NSCLC)	I/II
NCT04144569	The Effectiveness and Safety Study on PD-1 Combined With Pyrotinib for First-line Chemotherapy Failed HER2 Insertion Mutation Advanced Non-small Cell Lung Cancer	II
No NCT ID	A Single-center, Open-label , Non-randomized Control Clinical Trial On Clinical Features and Medical Treatment of Advanced NSCLC With Rare Gene Mutations	II
NCT03805841	Phase II Study - Evaluate the Clinical Activity of Tarloxotinib in Patients With Non-Small Cell Lung Cancer That Harbors an EGFR Exon 20 Insertion or HER2-Activating Mutation and Other Advanced Solid Tumors With NRG1/ERBB Family Gene Fusions.	II
NCT03505710	A Phase II, Multicenter, Open-Label, 2-Cohort Study of Trastuzumab Deruxtecan (DS-8201a), an Anti-HER2 Antibody Drug Conjugate (ADC), for HER2-Over-Expressing or -Mutated, Unresectable and/or Metastatic Non Small Cell Lung Cancer (NSCLC) (DESTINY-Lung01)	II
NCT04311034	A Phase Ib Study to Evaluate the Efficacy and Safety of RC48-ADC for Injection in Subjects With Advanced Non-small Cell Lung Cancer With HER2 Overexpression or HER2 Mutation	I
NCT02183883	Deciphering Afatinib Response and Resistance With INtratumour Heterogeneity	II
NCT02535507	Single Arm Phase II Clinical Trial to Investigate the Efficacy and Safety of Pyrotinib as a Single Agent in HER2 Mutation Advanced Non-small Cell Lung Cancer Patients Who Failed to Previous at Least 2nd Line Treatments	II
NCT03574402	An Open-label, Multi-center, Phase II Umbrella Study to Assess Efficacy of Targeted Therapy or Immunotherapy Directed by Next Generation Sequencing (NGS) in Chinese Patients With Advanced NSCLC (TRUMP)	II
NCT03983928	A Phase Ib, Open-label, Single Center, Non-randomized Study for Safety and Efficacy of TQB2450 Combined With Anlotinib in Subjects With Advanced Mutation Positive Non-Small Cell Lung Cancer	I/II
No NCT ID	Phase I Study of DZD9008 in EGFR or HER2 Mutant NSCLC Chinese Patients	I
NCT04042701	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, In Subjects With Locally Advanced/Metastatic Breast Or Non-Small Cell Lung Cancer (NSCLC).	I
NCT04209465	MasterKey-01: A Phase I/II, Open-label, Two-part, Multicenter Study to Assess the Safety, Tolerability, Pharmacokinetics & Antitumor Activity of BDTX-189, an Inhibitor of Allosteric ErbB Mutations, in Patients w/ Advanced Solid Malignancies	I/II
NCT01953926	An Open-Label, Phase II Basket Study of Neratinib in Patients With Solid Tumors With Somatic Activating HER Mutations	II
NCT04092673	A Phase 1-2 Dose-Escalation and Cohort-Expansion Study of Intravenous Zotatfin (eFT226) in Subjects With Selected Advanced Solid Tumor Malignancies	I/II

Clinical Trials Summary (continued)

ERBB2 exon 20 insertion (continued)

NCT ID	Title	Phase
NCT03810872	An Open Explorative Phase II, Open Label Study of Afatinib in the Treatment of Advanced Cancer Carrying an EGFR, a HER2 or a HER3 Mutation	II
NCT02693535	Targeted Agent and Profiling Utilization Registry (TAPUR) Study	II
NCT03065387	Phase I Study of the Pan-ERBB Inhibitor Neratinib Given in Combination With Everolimus, Palbociclib, or Trametinib in Advanced Cancer Subjects With EGFR Mutation/Amplification, HER2 Mutation/Amplification, or HER3/4 Mutation or KRAS Mutation	I
No NCT ID	Phase I Clinical Study With Advanced Solid Tumors KBP-5209 Treatment	I
NCT04446260	A Phase I Multi-Country, Multi-Center, Open-Label Study to Evaluate the Safety, Tolerability, Pharmacokinetics and Efficacy of SHR-A1811 in HER2 Expressing or Mutated Advanced Malignant Solid Tumor Subjects	I
NCT03297606	Canadian Profiling and Targeted Agent Utilization Trial (CAPTUR): A Phase II Basket Trial	II

Alerts Informed By Public Data Sources

Current NCCN Information

 Contraindicated
  Not recommended
  Resistance

NCCN information is current as of 2020-11-02. For the most up-to-date information, search www.nccn.org.
For NCCN International Adaptations & Translations, search www.nccn.org/global/international_adaptations.aspx.

ERBB2 exon 20 insertion

afatinib

Cancer type: Non-Small Cell Lung Cancer Variant class: ERBB2 mutation

Summary:

NCCN Guidelines® include the following supporting statement(s):

- "The NCCN NSCLC Panel does not recommend single-agent therapy with trastuzumab or afatinib (both for ERBB2 mutations), because response rates are lower and treatment is less effective when these agents are used for patients with ERBB2 mutations."

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 8.2020]

trastuzumab

Cancer type: Non-Small Cell Lung Cancer Variant class: ERBB2 mutation

Summary:

NCCN Guidelines® include the following supporting statement(s):

- "The NCCN NSCLC Panel does not recommend single-agent therapy with trastuzumab or afatinib (both for ERBB2 mutations), because response rates are lower and treatment is less effective when these agents are used for patients with ERBB2 mutations."

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 8.2020]

Signatures

Testing Personnel:

Laboratory Supervisor:

Pathologist:

References

1. King et al. Amplification of a novel v-erbB-related gene in a human mammary carcinoma. *Science*. 1985 Sep 6;229(4717):974-6. PMID: 2992089
2. Gutierrez et al. HER2: biology, detection, and clinical implications. *Arch. Pathol. Lab. Med.* 2011 Jan;135(1):55-62. PMID: 21204711
3. Di et al. erbB-2 is a potent oncogene when overexpressed in NIH/3T3 cells. *Science*. 1987 Jul 10;237(4811):178-82. PMID: 2885917
4. Hudziak et al. Increased expression of the putative growth factor receptor p185HER2 causes transformation and tumorigenesis of NIH 3T3 cells. *Proc. Natl. Acad. Sci. U.S.A.* 1987 Oct;84(20):7159-63. PMID: 2890160
5. Lonardo et al. The normal erbB-2 product is an atypical receptor-like tyrosine kinase with constitutive activity in the absence of ligand. *New Biol.* 1990 Nov;2(11):992-1003. PMID: 1983208
6. Ciriello et al. Comprehensive Molecular Portraits of Invasive Lobular Breast Cancer. *Cell*. 2015 Oct 8;163(2):506-19. PMID: 26451490
7. Cancer Genome Atlas Research Network. Comprehensive molecular characterization of gastric adenocarcinoma. *Nature*. 2014 Sep 11;513(7517):202-9. doi: 10.1038/nature13480. Epub 2014 Jul 23. PMID: 25079317
8. Cancer Genome Atlas Research Network. Comprehensive molecular characterization of urothelial bladder carcinoma. *Nature*. 2014 Mar 20;507(7492):315-22. doi: 10.1038/nature12965. Epub 2014 Jan 29. PMID: 24476821
9. Cancer Genome Atlas Network. Comprehensive molecular characterization of human colon and rectal cancer. *Nature*. 2012 Jul 18;487(7407):330-7. PMID: 22810696
10. Cancer Genome Atlas Research Network. Comprehensive molecular profiling of lung adenocarcinoma. *Nature*. 2014 Jul 31;511(7511):543-50. doi: 10.1038/nature13385. Epub 2014 Jul 9. PMID: 25079552
11. Cancer Genome Atlas Research Network. Integrated genomic analyses of ovarian carcinoma. *Nature*. 2011 Jun 29;474(7353):609-15. PMID: 21720365
12. Weinstein et al. The Cancer Genome Atlas Pan-Cancer analysis project. *Nat. Genet.* 2013 Oct;45(10):1113-20. PMID: 24071849
13. Cerami et al. The cBio cancer genomics portal: an open platform for exploring multidimensional cancer genomics data. *Cancer Discov.* 2012 May;2(5):401-4. PMID: 22588877
14. Petrelli et al. Clinical and pathological characterization of HER2 mutations in human breast cancer: a systematic review of the literature. *Breast Cancer Res. Treat.* 2017 Nov;166(2):339-349. PMID: 28762010
15. Bose et al. Activating HER2 mutations in HER2 gene amplification negative breast cancer. *Cancer Discov.* 2013 Feb;3(2):224-37. doi: 10.1158/2159-8290.CD-12-0349. Epub 2012 Dec 7. PMID: 23220880
16. Hudis. Trastuzumab—mechanism of action and use in clinical practice. *N. Engl. J. Med.* 2007 Jul 5;357(1):39-51. PMID: 17611206
17. Slamon et al. Human breast cancer: correlation of relapse and survival with amplification of the HER-2/neu oncogene. *Science*. 1987 Jan 9;235(4785):177-82. PMID: 3798106
18. https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/103792s5345lbl.pdf
19. https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/125409s124lbl.pdf
20. https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/125427s108lbl.pdf
21. NCCN Guidelines® - NCCN-Breast Cancer [Version 6.2020]
22. https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/022059s024lbl.pdf
23. https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/208051s007lbl.pdf
24. https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/213411s000lbl.pdf
25. <https://www.globenewswire.com/news-release/2016/06/01/845166/0/en/Galena-Biopharma-Receives-Fast-Track-Designation-for-NeuVax-nelipepimut-S-PRESENT-Clinical-Trial.html>
26. <http://ir.macrogenics.com/news-releases/news-release-details/macrogenics-announces-continuation-sophia-study-margetuximab?ReleaseID=1055055>
27. <https://ir.zymeworks.com/News-Releases/news-details/2019/Zymeworks-Lead-Asset-ZW25-Granted-Fast-Track-Designation-from-the-FDA/default.aspx>
28. <https://investors.blackdiamondtherapeutics.com/news-releases/news-release-details/black-diamond-therapeutics-granted-fast-track-designation-fda>
29. <https://remegen.com/remegen-announces-us-fda-has-granted-breakthrough-therapy-designation-for-disitamab-vedotin-rc48-in-urothelial-cancer/>

References (continued)

30. Ma et al. Neratinib Efficacy and Circulating Tumor DNA Detection of HER2 Mutations in HER2 Nonamplified Metastatic Breast Cancer. *Clin. Cancer Res.* 2017 Oct 1;23(19):5687-5695. PMID: 28679771
31. De et al. Clinical activity of afatinib (BIBW 2992) in patients with lung adenocarcinoma with mutations in the kinase domain of HER2/neu. *Lung Cancer.* 2012 Apr;76(1):123-7. PMID: 22325357
32. Kris et al. Targeting HER2 aberrations as actionable drivers in lung cancers: phase II trial of the pan-HER tyrosine kinase inhibitor dacomitinib in patients with HER2-mutant or amplified tumors. *Ann. Oncol.* 2015 Jul;26(7):1421-7. PMID: 25899785
33. Falchook et al. Non-small-cell lung cancer with HER2 exon 20 mutation: regression with dual HER2 inhibition and anti-VEGF combination treatment. *J Thorac Oncol.* 2013 Feb;8(2):e19-20. PMID: 23328556
34. David et al. Neratinib in HER2- or HER3-mutant solid tumors: SUMMIT, a global, multi-histology, open-label, phase 2 'basket' study. AACR 2017. Abstract CT001
35. Lin et al. Response to Afatinib in a Patient with Non-Small Cell Lung Cancer Harboring HER2 R896G Mutation: A Case Report. *Onco Targets Ther.* 2019;12:10897-10902. PMID: 31849493
36. Chang et al. Sustained Partial Response to Afatinib in a Patient With Lung Adenocarcinoma Harboring HER2V659E Mutation. *JCO Precis Oncol.* 2020 Aug; 912-915. DOI: 10.1200/PO.20.00114
37. Nayar et al. Acquired HER2 mutations in ER+ metastatic breast cancer confer resistance to estrogen receptor-directed therapies. *Nat. Genet.* 2019 Feb;51(2):207-216. PMID: 30531871