Guidance

Central Administration of Pharmaceutical Care
General Administration for Drug Utilization and Pharmacy Practice

Egyptian Guidance for Oncology Pharmacy Practice

Pharmacist's Role in Personalized Medication Management

Part One

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Contents

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List of Abbreviations

ABL	Abelson murine leukemia virus gene
ADC	Antibody Drug Conjugates
AE	Adverse Effect
AI	Aromatase Inhibitor
AKT	Protein Kinase B (N.B. Protein Kinase B is also known as PKB)
ALK	Anaplastic Lymphoma Kinase
ALK-EML4	Echinoderm Microtubule-Associated Protein-Like 4
ALT	Alanine Transaminase
APC	Adenomatous Polyposis Coli
AST	Aspartate Aminotransferase
ATM	Ataxia-Telangiectasia Mutated
ATR	Ataxia Telangiectasia and Rad3-related protein inhibitors
BC	Before Christ
BCR	Breakpoint Cluster Region
BIRP-1	BRCA1 Interacting Protein C-Terminal Helicase 1, BRCA1 Interacting Protein 1
BRAF	Raf Murine Sarcoma Viral Oncogene Homolog B
BRCA	BReast CAncer gene
CADH1	Cadherin-1 or Epithelial cadherin
CBC	Complete Blood Count
CCS	Colon Cancer Subtypes
CD	Cluster of Differentiation
CDK1	Cyclin-Dependent Kinase 1

CEA	Carcinoembryonic antigen
CHEK2	Checkpoint Kinase 2 gene
CHK	Checkpoint Kinase inhibitors
CMP	Comprehensive metabolic panel
CMS	Consensus Molecular Subtypes
COVID-19	Coronavirus disease 2019
CRC	Colorectal Cancer
CT	Computed tomography
CTCAE	Common Terminology Criteria for Adverse Events
ctDNA	Circulating Tumor DNA
CYP2D6	Cytochrome P450 family 2 subfamily D member 6
CYPP450	Cytochrome P450
DCRC	Deleted in Colorectal Cancer
dMMR	Deficient Mismatch Repair
DNA	Deoxyribonucleic Acid
DPYD	Dihydropyrimidine Dehydrogenase
DSB	Double-Strand Break
DTP	Drug Therapy Problem
E_2	Estradiol
EGF	Epidermal Growth Factor
EGFR	Epidermal Growth Factor Receptor
ER	Estrogen Receptor
ERK	Extracellular Signal-Regulated Kinase
FAK	Focal Adhesion Kinase

FDA	Food and Drug Administration
FGFR	Fibroblast Growth Factor Receptor
FISH	Fluorescence in Situ Hybridization
FIT	Fecal immunochemical test
G6PD	Glucose-6-Phosphate Dehydrogenase
GDNF	Glial Cell Line-Derived Neurotrophic Factor
Gfobt	Guaiac-based fecal occult blood test
Grb2	Growth factor receptor-bound protein 2
GSK-3	Glycogen Synthase Kinase
GWAS	Genome-Wide Association
HER2	Human Epidermal Growth Factor Receptor 2
HER2–	Human Epidermal Growth Factor Receptor 2 negative
HER3	Human Epidermal Growth Factor Receptor 3
HFSR	Hand-Foot Skin Reaction
HGP	Human Genome Project
HR	Hormone Receptor
HR+	Hormone Receptor-Positive
HRD	Homologous Recombination Deficiency
IBC	Inflammatory Breast Cancer
IHC	Immunohistochemistry
ICI	Immune Checkpoint Inhibitor
IDC	Invasive (Infiltrating) Ductal Carcinoma
IGF	Insulin-like Growth Factor
ILC	Invasive Lobular Carcinoma

irAE	Immune-related Adverse Effect
JAK	Janus Kinase
KEAP1	Kelch-like ECH-associated protein 1
KRAS	Kirsten Rat Sarcoma Virus
LKB1	Liver Kinase B1
LV	Left Ventricular
mAb	Monoclonal Antibodies
MEK	Mitogen-Activated Protein Kinase
MET	Mesenchymal-Epithelial Transition
MMEJ	Microhomology-Mediated End Joining
MMR/MSI	Mismatch repair/ Microsatellite instability
MRD	Minimal Residual Disease
MRI	Magnetic Resonance Imaging
MTHFR	Methylenetetrahydrofolate Reductase
mTOR	Mammalian Target of Rapamycin
NFE2L2	Nuclear factor, erythroid 2-like 2
NF-Kb	Nuclear Factor Kappa
NGFβ	Nerve Growth Factor Beta
NGS	Next-Generation Sequencing
NHEJ	Non-Homologous End Joining
NRAS	Neuroblastoma RAS viral oncogene homolog
NRG1	Neuregulin
NSCLC	Non-Small Cell Lung Carcinoma
NTRK	Neurotrophic Receptor Tyrosine Kinase

PAH	Pulmonary Arterial Hypertension
PALB-2	Partner And Localizer of BRCA2
PAOD	Peripheral Arterial Occlusive Disease
PARPis	Poly (ADP-ribose) Polymerase Inhibitors
PCR	Polymerase Chain Reaction
PD-1	Programmed Cell Death Protein 1
PDGFR	Platelet-Derived Growth Factor Receptor
PDK1	3- Phosphoinositol-Dependent Protein` Kinase-1
PET	Positron emission tomography
PH	Plekstrin Homology
PI3K	Phosphatidylinositol 3-Kinase
PIK3CA	Phosphatidylinositol 3-Kinase CA
PIP2	Phosphatidylinositol 4,5-bisphosphate
PIP3	Phosphatidylinositol (3,4,5)-trisphosphate
PLK1	Polo-Like Kinase-1
PM	Precision Medicine or Personalized Medicine
POLE	POLymerase Epsilon
PR	Progesterone Receptor
PtdIns	Phosphatidylinositol
PTEN	Phosphatase and TENsin homolog
RAF	Rapidly Accelerated Fibrosarcoma
RAS	Rat Sarcoma
RB1	Retinoblastoma gene
RET	REarranged during Transfection

RNA	Ribonucleic Acid
ROS	Proto-Oncogene Tyrosine-Protein Kinase Receptor
RTK	Receptor Tyrosine Kinase
SCLC	Small Cell Lung Carcinoma
SDOH	Social Determinants of Health
Ser 473	Serine 473
SF	Scatter Factor
Shc	Src homology and collagen
Sos	Son of Sevenless
stage IV	Stage four
STK11	Serine/Threonine Kinase 11
TCR	T cell receptor
TE	Thromboembolism
Thr 308	Threonine 308
TIE	Tyrosine Kinase with Immunoglobulin
TILs	Tumor-infiltrating lymphocytes
TKI	Tyrosine Kinase Inhibitors
TNBC	Triple-Negative Breast Cancer
TP53	Tumor Protein 53 (N.B. Protein 53 is P53)
TTNB	Transthoracic needle biopsy
TYMS	Thymidylate Synthase
UGT1A1	Uridine Diphosphate Glucuronosyltransferase 1A1
UV	Ultraviolet

VATS	Video-assisted thoracoscopic surgery
VEGF	Vascular Endothelial Growth Factor
Wnt	Wingless/Integration

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Aim and Scope

This guide is designed for oncology pharmacists working in hospitals and oncology care centers. Its primary aim is to provide them with essential knowledge and practical insights into precision medicine, empowering them to actively support personalized cancer therapy. By understanding the history, objectives, tools, applications, limitations, and future directions of precision medicine, oncology pharmacists will be better equipped to contribute to multidisciplinary cancer care teams, optimize medication therapy management, and enhance patient outcomes through individualized treatment strategies.

This guide offers a structured overview of the principles, tools, and clinical applications of precision medicine in oncology, as well as the evolving role of pharmacists. By doing so, it aims to empower pharmacists with the knowledge and skills needed to deliver optimal, patient-centered care.

This guide represents Part One and focuses on lung, breast, and colorectal cancers. A subsequent part will address additional cancer types not covered in this guide.

Introduction

Precision medicine, often regarded as synonymous with personalized or individualized medicine, represents a transformative methodology that incorporates genomic, environmental, and lifestyle data to inform clinical decision-making. This approach is fundamentally rooted in understanding the functional implications of genetic (and corresponding proteomic) variations at the cellular level ***(Biesecker, 2025).***

Precision medicine refers to tailoring treatments to a subpopulation who have a common susceptibility to a specific disease or a similar response to a specific drug. Precision medicine is a significant opportunity to make an individualized approach. This differs from the conventional approach of "one size fits all" to diagnostics, drug therapy, and preventive drugs ***(Biesecker, 2025).***

History

During the classical era, when medical practice was divided into specialized categories—with each physician focusing on a single disease or anatomical region—Herodotus documented how traditional Egyptian medicine was tailored to an individual's health condition. This represents the earliest documented instance of personalized medicine, as practitioners recognized that classifying diseases according to bodily systems allowed for a more nuanced understanding of pathology and, consequently, improved therapeutic efficacy. The Greeks were particularly interested in this patient-specific approach, leading to the frequent incorporation of Egyptian medical principles in their writings until the emergence of Hippocratic medicine in the fifth century BCE ***(Visvikis-Siest et al., 2020).***

From Hippocrates, often regarded as the Father of Western Medicine, to contemporary practitioners, the concept of personalized medicine has evolved significantly over the past twenty-five centuries, garnering increasing scholarly and clinical interest. By the mid-20th century, researchers had begun to recognize the necessity of evidence-based medical practices. Modern personalized medicine is fundamentally rooted in the ability to predict pharmacological responses, thereby enhancing patient safety and therapeutic efficacy. Three decades ago, the notion that physicians could tailor treatments based on individual patient characteristics remained largely theoretical, if not fictional, due to limited understanding of the biological mechanisms underlying disease ***(Sykiotis et al., 2005).*** However, advances in biomedical research have since transformed this paradigm, as evidenced by the fact that in 2018, 42% of pharmaceuticals approved by the U.S. Food and Drug Administration (FDA) were associated with specific diagnostic tests or targeted disease subgroups ***(Personalized Medicine Coalition (PMC), 2018).***

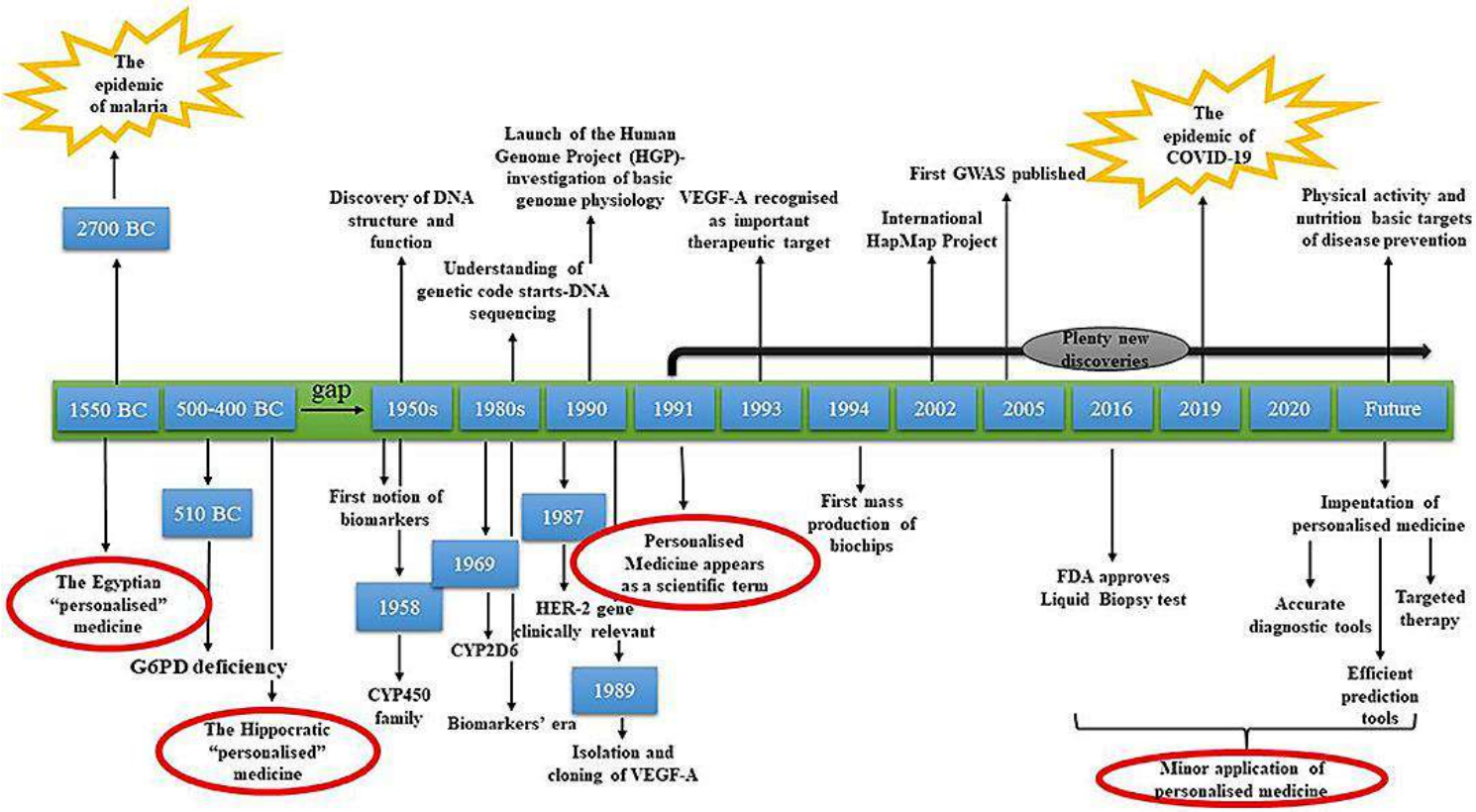


Figure 1: Personalized medicine from ancient times to a promising future (Visvikis-Siest et al., 2020)

BC: Before Christ, COVID-19: Coronavirus disease 2019, CYPP450: Cytochrome P450, CYP2D6: Cytochrome P450 family 2 subfamily D member 6, DNA: Deoxyribonucleic Acid, FDA: Food and Drug Administration in the United States, G6PD: Glucose-6-Phosphate Dehydrogenase, GWAS: Genome-Wide Association, HER-2: Human Epidermal Growth Factor Receptor 2, HGP: Human Genome Project, VEGF: Vascular Endothelial Growth Factor.

Traditional medicine versus precision medicine

Traditional medicine had a "one size fits all" strategy, which meant that all patients with a certain illness were treated with the same medication. This approach has several drawbacks, though, such as the fact that only a small percentage of these people will respond to the particular treatment, a sizable fraction will not respond, and a sizable portion may have negative side effects. Genetic variances, age, gender, addictions, race, ethnicity, concurrent drug use, comorbidities, environmental factors, and more could all contribute to these inter-individual discrepancies. This resulted in drug waste, higher expenses, and lower patient and physician satisfaction ***(Miller et al., 2015).***

The availability of "Big Data" is what really distinguishes precision medicine from conventional treatment. Rapid advancements in molecular biology and genetic testing have made it possible for researchers to gather vast amounts of data. By combining this data with clinical, pharmacological, and socioeconomic data, analysis can be performed using integrated data sets by various computer-based algorithms, allowing for the observation of patterns of effectiveness of specific treatments and titrating treatments to the susceptible populations alone ***(Naithani et al., 2021).***

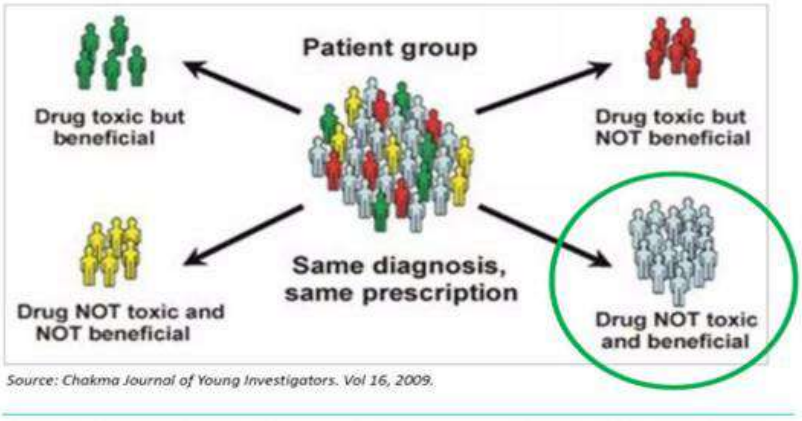


Figure 2: Principle of Personalized/Precision/Targeted Medicine (Khan, 2011)

(A group of people with the same condition may respond differently to the same treatment, as demonstrated)

The Goal of Precision Medicine in Oncology

In the quickly evolving field of oncology, precision medicine (PM) or personalized medicine (PM) requires an interdisciplinary approach of drug therapy specialists. PM is a new method for treating and preventing malignancies that takes into account each cancer patient's lifestyle and morbidities in addition to gene diversity between and within tumors, the tumor (immune) environment, and tumor (immune) environment variability ***(Hoeben et al., 2021).***

PM can target therapy at the oncogenic drivers of the tumor and alter the tumor immunological environment. PM also aims to maximize tumor response while considering each patient's drug adverse effects. In this manner, the tumor response is optimized while maintaining organ function and, consequently, quality of life. Furthermore, doing so ensures better patient care, which is clearly advantageous ***(Hoeben et al., 2021).***

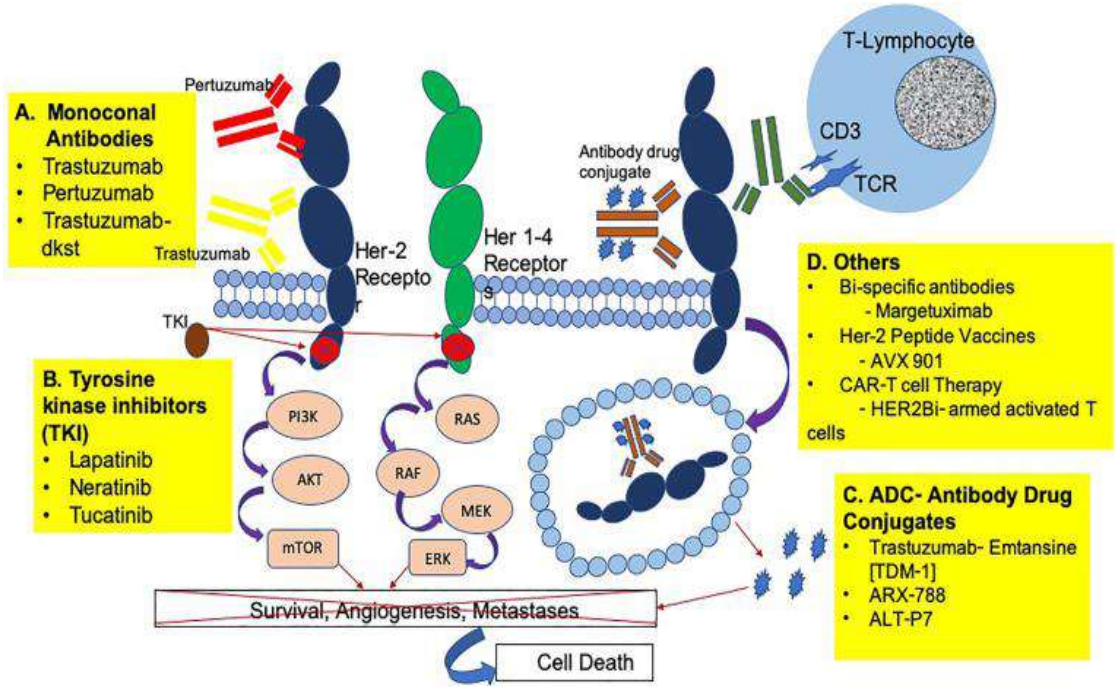


Figure 3: Molecular basis and clinical application of targeted therapy in oncology (Tilak et al., 2023)

ADC: Antibody Drug Conjugates, AKT: Protein Kinase B, CD: Cluster of Differentiation, ERK: Extracellular Signal-Regulated Kinase, HER2: Human Epidermal Growth Factor Receptor 2, MEK: Mitogen-Activated Protein Kinase, mTOR: Mammalian Target of Rapamycin, PI3K: Phosphatidylinositol 3-Kinase, RAF: Raf Murine Sarcoma Viral Oncogene Homolog, RAS: Rat Sarcoma Virus, TCR- T cell receptor, TKI: Tyrosine Kinase Inhibitors,

Tools of Precision Medicine

Precision medicine relies primarily on big data analytics, artificial intelligence, and a range of omics technologies that enable comprehensive analysis of cellular components. Environmental and social determinants of health, along with pharmaco-omics, also play a crucial role. By integrating these elements with population-based medical treatments and preventive strategies, precision medicine supports more personalized and effective healthcare interventions ***(Naithani et al., 2021).*** Omics are a collective study of molecular characterization and quantification of biological molecules from various subdomains of molecular biology using high-throughput technology ***(Naithani et al., 2021).***

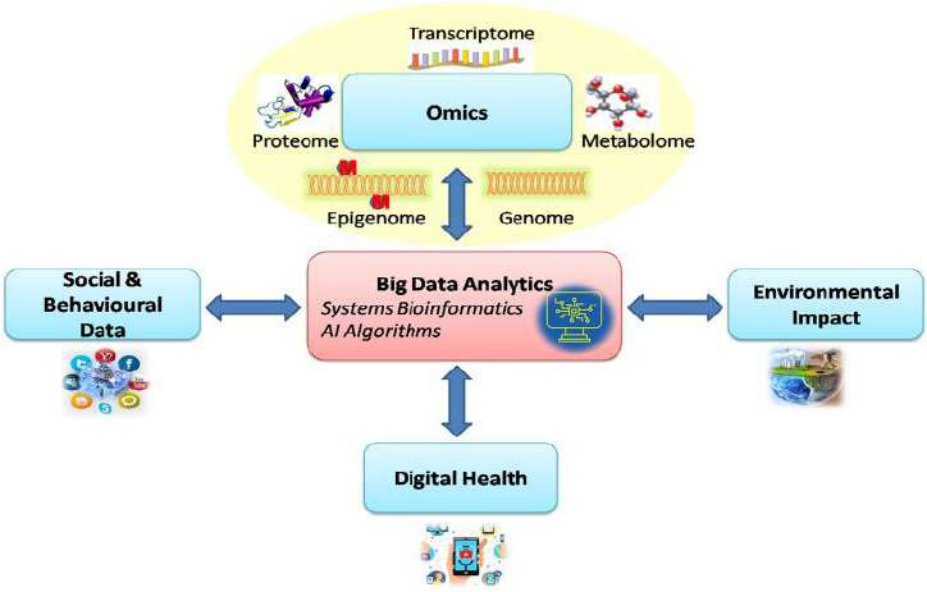


Figure 4: Tools of precision medicine (Naithani et al., 2021)

Precision Medicine in Cancer Care

For some tumors, precision medicine is being utilized to assist in deciding the most effective testing and therapies. Precision medicine could be helpful in

- Identify people who might be at high risk for cancer, and help these people lower their risk,
- Early detection of certain cancers,
- Diagnose a specific type of cancer correctly,
- Choose which cancer treatment options are best,
- Evaluate how well a treatment is working ***(American Cancer Society, Precision or personalized medicine: Precision Medicine for Cancer, 2023).***

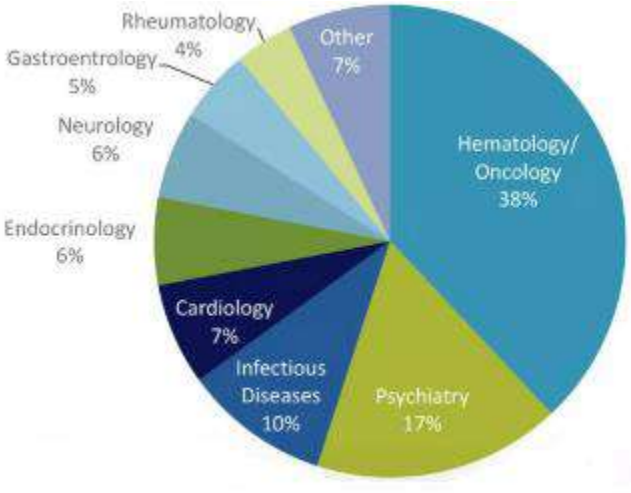


Figure 5: Biomarkers being used across diseases (Passaro et al., 2024)

Types of Cancer Where Precision Medicine is Used

It is crucial to remember that not all forms of cancer are being treated using precision medicine. One day, therapies will be tailored to each patient's specific cancer-related gene and protein changes. This field is the subject of extensive investigation ***(American Cancer Society, Precision or Personalized Medicine: Precision Medicine for Cancer, 2023).***

Precision medicine is being utilized to aid in treatment decisions for several more prevalent cancers, including -

- Lung cancer,
- Breast cancer,
- Colorectal cancer,
- Melanoma,
- Esophageal cancer,
- Stomach cancer,
- Ovarian cancer,
- Thyroid cancer,
- Certain types of leukemia,
- Certain types of lymphoma ***(American Cancer Society, Precision or Personalized Medicine: Precision Medicine for Cancer 2023).***

Common Toxicities with Tyrosine Kinase Inhibitors

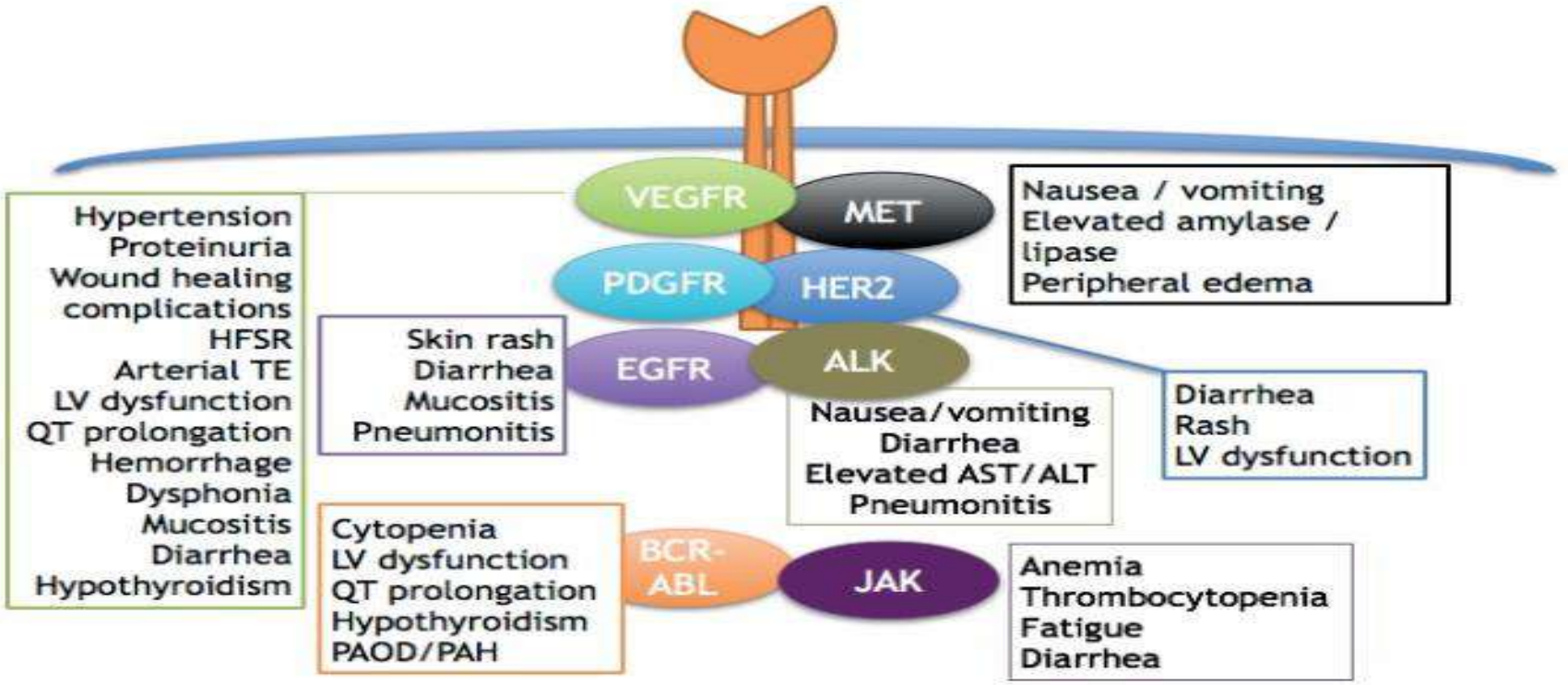


Figure 6: Toxicities associated with different TKIs (Mayor, 2017)

ABL: Abelson murine leukemia virus gene, ALK: Anaplastic Lymphoma Kinase, ALT: Alanine Transferase, AST: Aspartate Aminotransferase, BCR: Breakpoint Cluster Region, EGFR: Epidermal Growth Factor Receptor, HER2: Human Epidermal Growth Factor Receptor 2, HFSR: Hand-Foot Skin Reaction, JAK: Janus Kinase, LV: Left Ventricular, MET: Mesenchymal-Epithelial Transition, PAH: Pulmonary Arterial Hypertension, PAOD: Peripheral Arterial Occlusive Disease, PDGFR: Platelet-Derived Growth Factor Receptor, TE: Thromboembolism, TKI: Tyrosine Kinase Inhibitors, VEGFR: Vascular Endothelial Growth Factor Receptor

Over the past years, numerous tyrosine kinase inhibitors (TKIs) that target certain receptors have been approved for a wide range of cancer types. These substances block kinase enzymes, which function as "on" or "off" switches in a variety of cellular processes, including transcription, metabolism, apoptosis, and proliferation. Certain toxicities are usually linked to different kinds of TKIs that target various receptors ***(Mayor, 2017).***

Common Toxicities with Monoclonal Antibodies

Intravenous administration of monoclonal antibodies involves injecting them into a vein. Since the antibodies are proteins, administering them may occasionally result in an infusion reaction, which is comparable to an allergic reaction. This is more frequent during the initial administration of the medication. Potential signs and symptoms include -

- Fever,
- Chills,
- Weakness,
- Headache,
- Nausea,
- Vomiting,
- Diarrhea,
- Low blood pressure,
- Rashes ***(American Cancer Society, Monoclonal Antibodies and Their Side Effects, 2025c).***

Before administering monoclonal antibodies, it is crucial to inform the patients about potential side effects and what needs to be reported right away. This is because the adverse effects associated with administering monoclonal antibodies vary depending on the intended target of the molecule and its classification. Fever and anaphylaxis are just two examples of the possible side effects. They can also be minor or emergent, happen right away or later. As a result, educating the patient and administering the proper premedication ***(Bayer, 2019).*** Certain monoclonal antibodies may cause adverse reactions associated with the antigens they target ***(Park & Kim, 2024).***

Some Common Side Effects of Monoclonal Antibodies

Table 1: Frequently Reported Side Effects Associated with Monoclonal Antibodies

mAb	Target	Common Side Effects
Trastuzumab	Anti-HER2 (Human Epidermal Growth Factor Receptor 2)	**Cardiotoxicity** • Left ventricular dysfunction • Infusion-related reactions • Increased risk of heart failure ***(Bhardwaj, 2014)***
Pertuzumab		
Zenocutuzumab	Anti- HER2/HER3 dimerization	• Fatigue • Nausea • Diarrhea • Infusion-related reactions • Neutropenia ***(Lexi-Drugs, Zenocutuzuma, 2025)***
Cetuximab	Anti-EGFR (Epidermal Growth Factor Receptor)	**Dermatologic Toxicity** • Papulopustulur rash (acneiform) • Mucositis • Xerosis • Paronychia • Skin fissures ***(Fakih & Vincent, 2010)***
Panitumumab		
Amivantamab		
Bevacizumab	Anti-VEGF (Vascular Endothelial Growth Factor)	• Increased peripheral vascular resistance. • Vascular rarefaction • Hemorrhage • Proteinuria • Gastrointestinal perforation ***(Kamba & McDonald, 2007)***
Ramucirumab		
Dostarlimab-gxly	Anti-PD-1 (Programmed Cell Death Protein 1)	• Diarrhea • Fatigue • Cough • Nausea • Skin rash

Cemiplimab-rwlc		• Poor appetite • Constipation • Muscle and joint pain ***(American Cancer Society, Immune Checkpoint Inhibitors and Their Side Effects, 2024)***
Retifanlimab-dlwr		
Tislelizumab-jsgr		
Toripalimab-tpzi		

Lung Cancer

Lung Cancer

- Lung cancer is the primary cause of cancer-related mortality globally, accounting for the greatest death rates among both genders. Tobacco usage is the main risk factor; about 85% of instances of lung cancer are caused by smoking. Lung cancer is commonly diagnosed at advanced stages, when there are few treatment options and a poor prognosis. This presents a significant management problem. On the other hand, screening high-risk groups for early identification has a substantial chance to enhance survival rates. Primary prevention measures, such as quitting smoking and limiting exposure to environmental carcinogens, are essential for reducing the incidence of lung cancer and averting deaths, in addition to early identification. Non-small cell lung carcinoma (NSCLC) and small cell lung carcinoma (SCLC) are the two primary forms of the disease. While SCLC is less frequent, it is distinguished by rapid growth and aggressive activity, while NSCLC is more common and often advances more slowly ***(WHO, Lung Cancer, 2023).***
- There are two ways that lung cancer-causing gene alterations might occur.
    - Hereditary mutations are known as germline mutations. They are inherited by offspring from their parents,
    - Acquired mutations are known as somatic mutations. They are the most frequent cause of cancer. They arise from exposure to harmful substances like chemicals, tobacco, UV light, and some viruses ***(Watson, 2024).***

Diagnosing Lung Cancer

- **A flexible bronchoscope** consists of fiber optics, a camera, and a light source that enable direct, real-time visualization of the airways. Examining the respiratory system, from the nose or oral cavity to the sub-segmental bronchi, is possible. Advanced bronchoscopic methods, including endobronchial ultrasonography, allow for the ultrasonographic assessment of the lung's periphery and mediastinal structures, including lymph nodes ***(Mahmoud et al., 2023).***
- **Transthoracic needle biopsy (TTNB)** is a thoracic interventional radiology technique that is frequently carried out. It can deliver a precise cytologic or histologic diagnosis safely and effectively ***(Birchard, 2011).***
- **Video-assisted thoracoscopic surgery (VATS)** has become a popular minimally invasive method for many thoracic surgeries, with benefits like less pain after surgery, shorter hospital stays, and faster recovery than open thoracotomy. Surgeons use tiny incisions and a camera-equipped thoracoscope to view and access the thoracic cavity during VATS, enabling precision surgical procedures with the least amount of tissue damage ***(Mehrotra et al, 2024).***
- **Mediastinoscopy** is widely recognized as the gold standard for evaluating mediastinal lymph nodes; nonetheless, it is an intrusive technique carried out under general anesthesia in the operating theater. A suprasternal incision, a mediastinoscopy inserted alongside the trachea, and a biopsy of nearby lymph nodes are necessary ***(Jawad & Chung, 2018).***

Profiling the Most Common Targetable Genetic Mutations in NSCLC

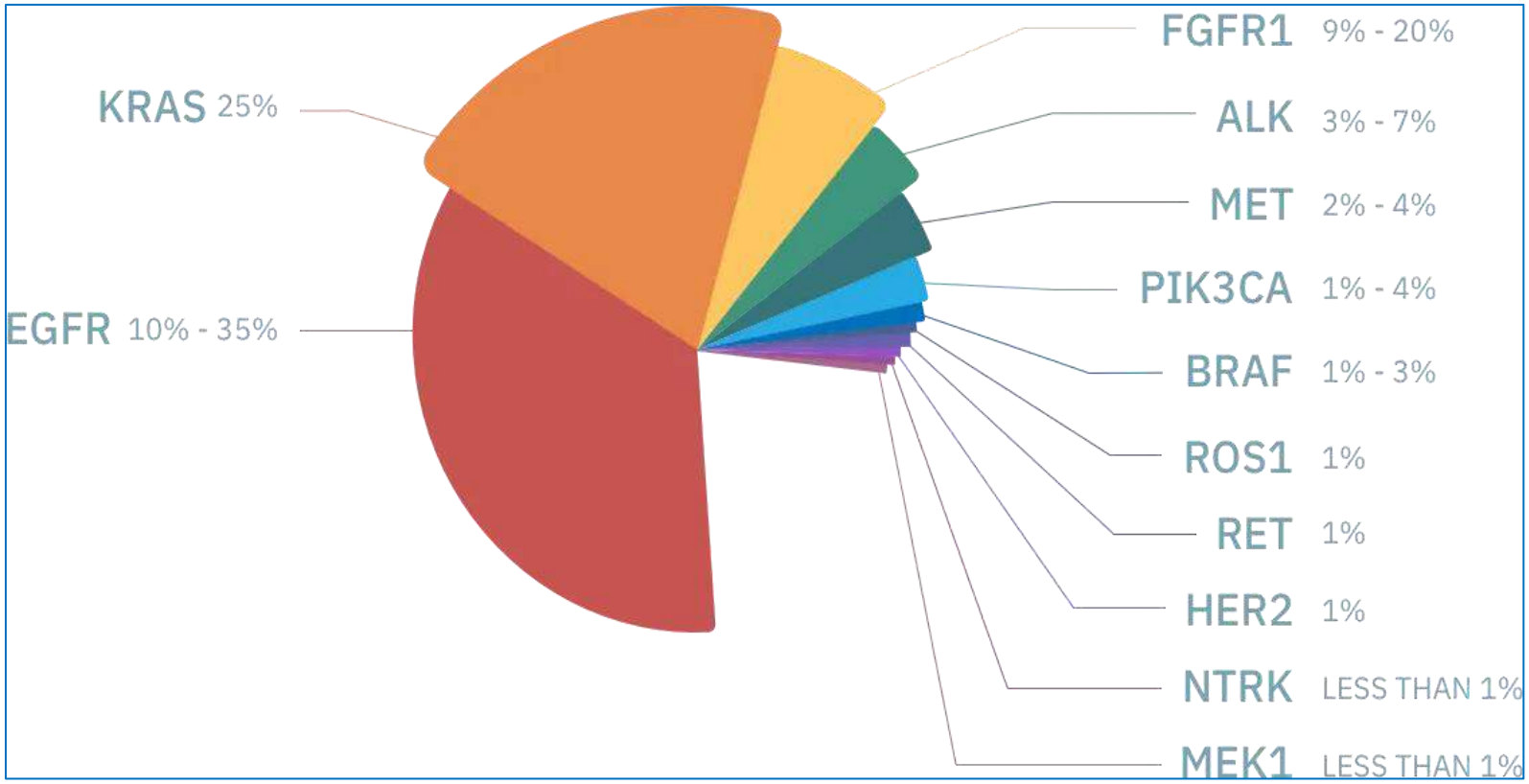


Figure 7: The Most Common Targetable Gene Mutations with NSCLC (Nazario, 2024)

ALK: Anaplastic Lymphoma Kinase, BRAF: Raf Murine Sarcoma Viral Oncogene Homolog B, EGFR: Epidermal Growth Factor Receptor, FGFR: Fibroblast Growth Factor Receptor, HER2: Human Epidermal Growth Factor Receptor 2, KRAS: Kirsten Rat Sarcoma Virus, MEK1: Mitogen-Activated Protein Kinase-1, MET: Mesenchymal-Epithelial Transition, NSCLC: Non-Small Cell Lung Carcinoma, NTRK: Neurotrophic Receptor Tyrosine Kinase, PUK3CA: Phosphatidylinositol 3-Kinase CA, RET: REarranged during Transfection, ROS: Reactive Oxygen Species

Types of Biomarker Tests Used to Detect NSCLC Mutations

NSCLC has evolved from a condition in which medical professionals believed there was little chance of therapy or cure to one marked by therapeutic enthusiasm driven by advances in biomarker research and improvements in survival rates. In NSCLC, EGFR, ALK, and ROS1 are routinely evaluated as biomarkers. Nonetheless, several new biomarkers have entered the field of diagnosis ***(Batra & Nathany, 2025).*** A biomarker is a characteristic that is objectively measured and evaluated as an indicator of normal biologic processes, pathogenic processes, or pharmacologic responses to a therapeutic intervention ***(NIH-NCI, Biomarker Testing for Cancer Treatment, 2021)***

Next-Generation Sequencing (NGS)

The detection of point mutations, insertions, deletions, copy number changes, fusion genes, and microsatellite instability data required to inform the possible use of targeted therapy is enabled by next-generation sequencing (NGS). Its benefits include preserving tissue samples, preventing patient delays, and assisting in matching the patient with the best research trial ***(Batra & Nathany, 2025).***

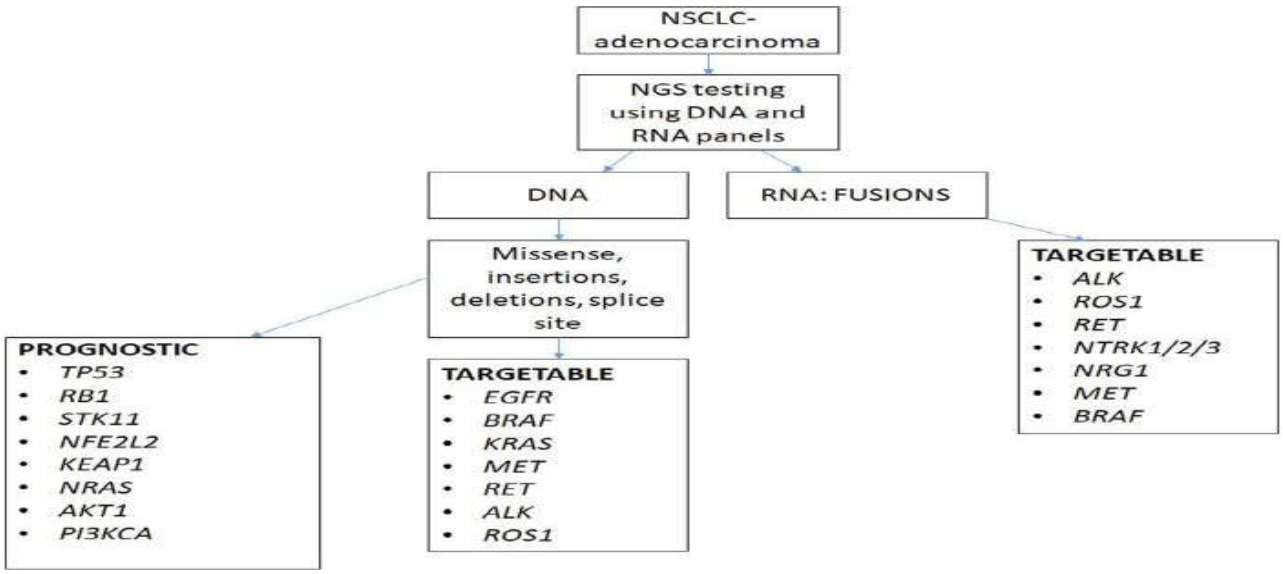


Figure 8: Flow diagram depicting the steps involved in NGS. Step 1: Extraction, Step 2: Library Preparation, Step 3: Bioinformatics, and Step 4: Final Clinical Report (Batra & Nathany, 2025)

ALK: Anaplastic Lymphoma Kinase, AKT1: Protein Kinase B-1, BRAF: Raf Murine Sarcoma Viral Oncogene Homolog B, DNA: Deoxyribonucleic Acid, EGFR: Epidermal Growth Factor Receptor, KEAP1: Kelch-like ECH-associated protein 1, KRAS: Kirsten Rat Sarcoma Virus, MET: Mesenchymal-Epithelial Transition, NFE2L2: Nuclear factor, erythroid 2-like 2, NGS: Next-Generation Sequencing, NRAS: Neuroblastoma RAS viral oncogene homolog, NRG1: Neuregulin, NSCLC: Non-Small Cell Lung Carcinoma, NTRK: Neurotrophic Receptor Tyrosine Kinase, PIK3CA: Phosphatidylinositol 3-Kinase CA, RB1: Retinoblastoma gene, RET: REarranged during Transfection, RNA: Ribonucleic Acid; ROS: Proto-oncogene tyrosine kinase receptor, STK11: Serine/Threonine Kinase 11, TP53: Tumor Protein 53

PCR-Based Tests

To find biomarkers for NSCLC, both traditional direct sequencing techniques, including Sanger sequencing and pyrosequencing, as well as polymerase chain reaction (PCR)-based techniques, are used ***(Batra & Nathany, 2025).***

FISH (Fluorescence in Situ Hybridization)

One common method for routinely diagnosing genetic abnormalities is fluorescence in situ hybridization, or FISH. In situ hybridization screening is helpful for tailored therapy. Fluorescence in situ hybridization (FISH) can be used to assess a variety of known aberrations, including rearrangements brought about by translocations, insertions or inversions, losses (deletions), and gains (such as amplification) ***(Chrzanowska et al., 2020).***

IHC (Immunohistochemistry)

Programmed cell death 1 ligand 1 (PD-L1) immunohistochemistry (IHC) testing is recommended for all stage IV NSCLC cases by the European Society for Medical Oncology to assess whether anti-PD-1 or anti-PD-L1 immune-checkpoint inhibitors are suitable for the patient ***(Zhang et al., 2024).***

The Most Common Targetable Genetic Mutations in NSCLC

Table 2: Key Targetable Genetic Mutations in NSCLC

Mutation	Inhibitors	Common Side Effects
EGFR (Epidermal Growth Factor Receptor) *(Weaver, 2025)*	Erlotinib Dacomitinib Gefitinib Osimertinib Afatinib Amivantamab + Lasartinib	• Follicular acneiform eruption • Stomatitis • Diarrhea • Loss of appetite
ALK (Anaplastic Lymphoma Kinase) *(Costa et al., 2018)*	Brigatinib Lorlatinib Crizotinib Ceritinib Alectinib	• Diarrhea • Nausea • Vomiting • Constipation • Myalgia • Peripheral oedema
KRAS (Kirsten Rat Sarcoma Virus) *(Lexi-Drugs, Sotorasib, 2025)* *(Lexi-Drugs, Adagrasib, 2025)*	Sotorasib Adagrasib	• Edema • Skin rash • Diarrhea • Hepatotoxicity • Musculoskeletal pain • Prolonged QT interval • Kidney impairment
MET (Mesenchymal-Epithelial Transition) *(Lexi-Drugs, Capmatinib, 2025)* *(Lexi-Drugs, Tepotinib, 2025)* *(Lexi-Drugs, Crizotinib, 2025)* *(Lexi-Drugs, Cabozantinib, 2025)* *(Markham, 2021)* *(Reungwetwattana, Liang, Zhu, & Ou, 2017)*	Capmatinib Savolitinib Glesatinib	• Hepatotoxicity • Pulmonary toxicity • Renal toxicity • Pancreatic toxicity • Edema • Lymphocytopenia • Musculoskeletal pain
	Tepotinib	• Pulmonary toxicity • Hepatotoxicity • Peripheral edema • Diarrhea • Fatigue • Renal toxicity
	Crizotinib	• Lymphocytopenia • Hepatotoxicity

		• Neutropenia • Edema • Abdominal pain • Diarrhea
	Cabozantinib	• Endocrinopathy • Diarrhea • Fistula formation and gastrointestinal perforation • Hemorrhage • Hepatotoxicity • Hypertension • Wound healing impairment • Thrombosis • Osteonecrosis of the jaw • Hypocalcemia • Proteinuria
BRAF (Raf Murine Sarcoma Viral Oncogene Homolog B) ***(Lexi-Drugs, Dabrafenib, 2025)*** ***(Lexi-Drugs, Encorafenib, 2025)*** ***(Lexi-Drugs, Vemurafenib, 2025)***	Dabrafenib Encorafenib Vemurafenib	• Cutaneous toxicities • Hyperglycemia • Hyperkeratosis • Headache • Arthralgia • Abdominal pain • Hepatotoxicity • Renal toxicity
MEK (Mitogen-Activated Protein Kinase) ***(Iriarte et al., 2024)*** ***(Stjepanovic et al., 2016)*** ***(Lexi-Drugs, Trametinib, 2025)*** ***(Lexi-Drugs, Binimetinib, 2025)***	Trametinib Binimetinib	• Mucocutaneous toxicities • Ophthalmologic toxicities • Hepatotoxicity • Hypoalbuminemia • Abdominal pain • Anemia • Musculoskeletal pain

ROS1 (proto-oncogene tyrosine-protein kinase, receptor,1) ***(Lexi-Drugs, Entrectinib, 2025)*** ***(Lexi-Drugs, Repotrectinib, 2025)*** ***(Lexi-Drugs, Crizotinib, 2025)*** ***(Lexi-Drugs, Ceritinib, 2025)*** ***(Lexi-Drugs, Lorlatinib, 2025)***	Entrectinib Repotrectinib Crizotinib	• Weight gain • Edema • Constipation • Dysgeusia • Hematologic toxicities • Myalgia • Renal toxicities • Hepatic toxicities • Visual disturbance
	Ceritinib	• Hyperglycemia • Abdominal pain • Diarrhea • Renal toxicities • Hepatic toxicities • Fatigue • Nausea and vomiting
	Lorlatinib	• Edema • Hypercholesterolemia • Hyperglycemia • Diarrhea • Anemia • Renal toxicities • Hepatic toxicities
NTRK (Neurotrophic Receptor Tyrosine Kinase) ***(Lexi-Drugs, Entrectinib, 2025)*** ***(Lexi-Drugs, Larotrectinib, 2025)*** ***(Liu et al., 2020)***	Larotrectinib Entrectinib	• Weight gain • Dizziness • Withdrawal pain • Nausea and vomiting • Abdominal pain
RET (REarranged during Transfection) ***(Nazneen, 2021)***	Selpercatinib Pralsetinib Cabozantinib	• Nausea • Vomiting • Constipation • Diarrhea • Headache

		• Abdominal pain • Tiredness/weakness • Decreased appetite • Dry mouth • Stomatitis • Dysgeusia
HER2 (Human Epidermal Growth Factor Receptor 2) ***(Nazneen, 2022)***	Fam-trastuzumab deruxtecan-nxki Ado-trastuzumab emtansine Zenocutuzumab Mobocertinib Poziotinib Pyrotinib Dacomitinib	• Nausea • Vomiting • Constipation • Diarrhea • Headache • Abdominal pain • Tiredness/weakness • Decreased appetite • Dry mouth • Stomatitis • Dysgeusia

1. Epidermal Growth Factor Receptor (EGFR)

The "epidermal growth factor receptor" protein is regulated by this gene. This protein aids in cell division and growth. Women, nonsmokers, and individuals with the adenocarcinoma form of NSCLC are more likely to have an EGFR mutation ***(El-Telbany & Ma, 2012).***

Examples of EGFR inhibitors

(American Cancer Society, NSCLC Targeted Therapy: Non-small Cell Lung Cancer Medication, 2025d)

Table 3: Commonly Used EGFR Inhibitors in NSCLC

EGFR inhibitors that target cells with either an exon 19 or an exon 21 mutation	**EGFR inhibitors that target cells with S768I, L861Q and/or G719X mutations**	**EGFR inhibitors that target cells with an exon 20 mutation**
Erlotinib **Dacomitinib** **Gefitinib**	**Osimertinib** **Afatinib**	**Amivantamab + Lasartinib** A bispecific monoclonal antibody that targets EGFR and MET, two proteins that aid in the growth of cancer cells. It is referred to as a bispecific antibody since it interacts with two different proteins.

2. Anaplastic Lymphoma Kinase (ALK)

The ALK gene codes for the production of ALK receptor tyrosine kinase, a member of the receptor tyrosine kinases (RTKs) protein family. In this mutation, two genes combine to form a new gene. People with the adenocarcinoma type of non-small cell lung cancer (NSCLC) who have never or infrequently smoked frequently have ALK mutations. Additionally, it is more prevalent in men and younger individuals, such as those in their 50s ***(MedlinePlus, Alk Gene: MedlinePlus Genetics, 2011).***

Examples of ALK inhibitors

(American Cancer Society, NSCLC Targeted Therapy: Non-small Cell Lung Cancer Medication, 2025d)

Table 4: Commonly Used ALK Inhibitors in NSCLC

Crizotinib ***(Costa et al., 2018)***	The first-in-class ALK inhibitor was developed and evaluated in patients with NSCLC harboring ALK rearrangements.
Loratinib ***(Drug Bank, Lorlatinib: Uses, Interactions, Mechanism of Action | drugbank online, 2025e)***	A third-generation ALK tyrosine kinase inhibitor (TKI) for patients with ALK-positive metastatic non-small cell lung cancer.
Brigatinib ***(Drug Bank, Brigatinib: Uses, Interactions, Mechanism of Action | drugbank online, 2025b)***	A reversible dual inhibitor of anaplastic lymphoma kinase (ALK) and epidermal growth factor receptor (EGFR).
Ceritinib ***(Drug Bank, Ceritinib: Uses, Interactions, Mechanism of Action | drugbank online, 2025d)***	An antineoplastic kinase inhibitor used to treat anaplastic lymphoma kinase (ALK)-positive metastatic non-small cell lung cancer (NSCLC) in patients with inadequate clinical response or intolerance to crizotinib.
Alectinib ***(Drug Bank, Alectinib Recruiting Phase 2 Trials for Metastatic Colorectal Cancer (CRC) Treatment | drugbank online, 2025a)***	A second-generation oral drug that selectively inhibits the activity of anaplastic lymphoma kinase (ALK) tyrosine kinase. It is specifically used in the treatment of non-small cell lung cancer (NSCLC) expressing the ALK-EML4 (echinoderm microtubule-associated protein-like 4) fusion protein that causes proliferation of NSCLC cells.

3. Kirsten Rat Sarcoma Viral Oncogene Homolog (KRAS)

KRAS encodes a GTPase that is essential for cell survival, proliferation, and differentiation because it functions as a key modulator of downstream growth factor receptor signaling. Although they are rare in squamous cell carcinoma, KRAS gene mutations can occur in 15% to 25% of lung adenocarcinomas. The mutations are missense mutations primarily in codons 12 and 13 of (exon1) ***(El-Telbany & Ma, 2012).***

Examples of KRAS inhibitors

Table 5: Commonly Used KRAS Inhibitors in NSCLC

Sotorasib	The first, selective KRAS G12C inhibitor to receive approval based on demonstration of significant clinical benefit and tolerable safety profile in previously treated, *KRAS* G12C-mutated NSCLC ***(Santarpia et al., 2023).***
Adagrasib	A highly selective covalent inhibitor of KRAS G12C ***(Santarpia et al., 2023).***

4. Fibroblast Growth Factor Receptor 1 (FGFR1)

This protein is one of four fibroblast growth factor receptors, a family of proteins involved in wound healing, blood vessel creation, cell division, regulation of cell growth and maturation, and embryonic development. Cell growth and dissemination are similarly impacted by a mutation in this gene. The squamous carcinoma type of NSCLC is more likely to experience it. Additionally, smoking increases the likelihood of this mutation ***(MedlinePlus, FGFR1 gene: MedlinePlus Genetics, 2024).***

5. Mesenchymal Epithelial Transition (MET)

Hepatocyte Growth Factor (HGF), also known as scatter factor (SF), is the natural ligand of the receptor tyrosine kinase (RTK) that MET encodes. The MET receptor undergoes a conformational shift as a result of ligand-receptor interaction, which promotes receptor phosphorylation and activation. Tumor growth, survival, branching morphogenesis, motility and migration, cell scattering, invasion, tumor angiogenesis, and metastasis have all been significantly linked to the MET-HGF/SF pathway in the setting of cancer ***(El-Telbany & Ma, 2012).***

Examples of MET inhibitors

(Bazhenova et al., 2021)

Table 6: Commonly Used MET Inhibitors in NSCLC

Capmatinib	Type 1 MET inhibitors The first treatment for metastatic NSCLC with the MET exon 14 skipping mutation.
Tepotinib	
Crizotinib	
Savolitinib	
Cabozantinib	Type 2 MET inhibitors
Glesatinib	

6. Raf Murine Sarcoma Viral Oncogene Homolog B (BRAF)

It contributes to the regulation of the Mitogen-Activated Protein Kinase/Extracellular Signal-Regulated Kinase (MET kinase/ERK) signaling pathway, which influences secretion, differentiation, and cell division. The most common cancer-causing mutation in melanoma is the V600E mutation, which has also been linked to non-Hodgkin lymphoma, colorectal cancer, thyroid cancer, non-small cell lung carcinoma, hairy cell leukemia, and lung adenocarcinoma. This gene is more frequently altered in the NSCLC form known as adenocarcinoma ***(El-Telbany & Ma, 2012).***

Examples of BRAF inhibitors

(American Cancer Society, NSCLC Targeted Therapy: Non-small Cell Lung Cancer Medication, 2025d)

Combination therapy: For advanced non-small cell lung cancer (NSCLC) with the BRAF V600E mutation, a combination of a BRAF inhibitor and a MEK inhibitor is frequently administered as the initial or subsequent treatment. Examples include -

Table 7: Commonly Used BRAF Inhibitors in NSCLC

BRAF inhibitor	Mitogen-activated protein kinase (MEK) inhibitor
Dabrafenib	**Trametinib**
Encorafenib	**Binimetinib**
Vemurafenib A BRAF inhibitor can be taken alone if the patient can't take the combination treatment	

7. Proto-Oncogene Tyrosine-Protein Kinase Receptor -1 (ROS1)

Proto-oncogene is a member of the tyrosine kinase insulin receptor gene subfamily and is highly expressed in a range of tumor cell lines. This gene encodes a type I integral membrane protein that has tyrosine kinase activity. The protein could act as a receptor for growth or differentiation factors. The ALK mutation and this one are comparable. It is more likely to occur in patients who are young, non-smokers, and have an adenocarcinoma type of non-small cell lung cancer. ***(NIH, Ros1 Ros Proto-Oncogene 1, Receptor Tyrosine Kinase [Homo Sapiens (Human)] - Gene – NCBI, 2025).***

Examples of ROS1 inhibitors

(American Cancer Society, NSCLC targeted therapy: Non-small Cell Lung Cancer Medication, 2025d)

Table 8: Commonly Used ROS1 Inhibitors in NSCLC

Entrectinib	Adult patients with metastatic non-small cell lung cancer (NSCLC).
Ceritinib	
Lorlatinib	
Repotrectinib	Adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC).
Crizotinib	Patients with metastatic non-small cell lung cancer (NSCLC) whose tumors are anaplastic lymphoma kinase (ALK) or ROS1-positive.

8. Neurotrophic Receptor Tyrosine Kinase (NTRK)

It plays a role in producing a protein necessary for the growth and survival of nerve cells, or neurons, particularly those that carry information about touch, pain, and temperature (sensory neurons). When another protein known as nerve growth factor beta (NGFβ) binds to the NTRK1 protein and instructs it to phosphorylate itself (autophosphorylation), the NTRK1 protein is activated. Then, to send signals for cell development and survival, the active NTRK1 protein phosphorylates other proteins. The NTRK gene merges with other genes in this mutation. According to research, this can occur in both men and women of all ages and NSCLC kinds. It can also affect nonsmokers and smokers ***(MedlinePlus, NTRK1 gene: MedlinePlus Genetics, 2011).***

Examples of NTRK inhibitors

(Pharmacogenetics, NTRK Inhibitors, A Successful Example of a Tissue-Agnostic Approach in Anticancer Targeted Therapy, 2021)

Table 9: Commonly Used NTRK Inhibitors in NSCLC

Larotrectinib	Pediatric and adult patients with advanced or metastatic solid tumors with neurotrophic receptor tyrosine kinase (NTRK) gene fusion without an acquired resistance mutation ***(Dunn, 2020).***
Entrectinib	

9. Rearranged During Transfection (RET)

A particular kind of proto-oncogene produces a receptor tyrosine kinase for extracellular signaling molecules belonging to the glial cell line-derived neurotrophic factor (GDNF) family. This kind of mutation occurs when NSCLC is of the adenocarcinoma kind. It is more prevalent among nonsmokers ***(MedlinePlus, Ret Gene: MedlinePlus Genetics, 2018).***

Examples of RET inhibitors

(American Cancer Society, NSCLC Targeted Therapy: Non-small Cell Lung Cancer Medication, 2025d)

Table 10: Commonly Used RET Inhibitors in NSCLC

Selpercatinib	The first treatment for metastatic NSCLC
Pralsetinib	
Cabozantinib	Has activity against RET, ROS1, MET, and VEGF

10. Human Epidermal Growth Factor Receptor 2 (HER2)

The HER2 protein is vital in healthy cell division. When this gene is mutated, cancer cells proliferate. This occurs most frequently when a type of NSCLC known as adenocarcinoma is present. Women and those who have never or infrequently smoked are more likely to experience it ***(MedlinePlus, HER2 Tumor Marker Test: MedlinePlus Medical Test, 2023).***

Examples of HER2 inhibitors

(Drugs.com, List of HER2 Inhibitors, 2025e)

Table 11: Commonly Used HER2 Inhibitors in NSCLC

Fam-trastuzumab deruxtecan-nxki	An antibody-drug conjugate (ADC). It's made up of a lab-made antibody that targets the HER2 protein, which is linked to a chemotherapy drug. The antibody acts like a homing signal by attaching to the HER2 protein on cancer cells, bringing the chemo directly to them. It can be used to treat NSCLC with HER2 mutations if you've already had at least one other type of drug treatment.
Ado-trastuzumab emtansine	A HER2-targeted ADC. It can be used to treat HER2-mutated NSCLC in certain situations.
Zenocutuzumab	A bispecific antibody that binds to HER2 and HER3 and prevents a protein called neuregulin 1 (NRG1) from binding to HER3.
Mobocertinib	Tyrosine-kinase inhibitor targeting exon 20 mutations.
Poziotinib	
Pyrotinib	
Dacomitinib	EGFR inhibitors and HER2 inhibitors

Breast Cancer

Breast Cancer

- Breast cancer is the second most common cause of cancer-related deaths among women globally and the most common cancer diagnosed in women, accounting for almost 10% of new cancer diagnoses each year. Risk reduction is essential to lowering the incidence of breast cancer, and the risk factors for the disease are well known. Breast cancer normally develops silently and is found during routine screening. Breast cancer is frequently identified as a palpable breast lump in the absence of screening. Depending on the stage and kind of tumor, breast cancer is treated with a mix of surgery, radiation, chemotherapy, and immunotherapy. Overall survival and patient-reported outcomes have significantly improved as a result of advancements in various therapy approaches ***(Menon, 2024).***
- Breast cancer is a malignant disease marked by the uncontrolled growth of abnormal cells in breast tissue, leading to tumor formation. If not treated promptly, these tumors may spread to distant organs, posing serious and potentially life-threatening outcomes ***(WHO, Breast Cancer, 2024).***

- **There are many types of breast cancer determined by the specific cells in the breast that become cancer** ***(American Cancer Society, 2021b)***
    1. Ductal or lobular carcinoma (intraductal carcinoma)
    2. Invasive Breast Cancer
    a. **Invasive ductal carcinoma (IDC):** A form of breast cancer that begins in the milk ducts and subsequently spreads to the surrounding breast tissue ***(DePolo, 2024a).***
    b. **Invasive lobular carcinoma (ILC):** A form of breast cancer that originates in the milk-producing glands (lobules) of the breast and extends into the surrounding breast tissue ***(Rubio, 2025).***
    c. **Triple-negative breast cancer (TNBC):** Triple-negative breast cancer cells lack HER2 overexpression and do not express estrogen or progesterone receptors ***(American Cancer Society, Triple-Negative Breast Cancer: Details, Diagnosis, and Signs 2025e).***
    d. **Inflammatory breast cancer (IBC):** An aggressive subtype of locally advanced breast cancer, with *de novo* IBC referring to disease present at initial diagnosis. It represents a higher proportion of cases that present at more advanced stages ***(Merajver, 2024).***

- Comprehending DNA damage is essential for managing breast cancer as well as its progression. There is a lot of promise for treating cancer by employing several tactics to target the DNA damage response system in cancer cells. These tactics include blocking DNA repair enzymes or causing DNA damage. Understanding the genetic abnormalities that cause cancer makes it feasible to create customized treatments ***(Qu et al., 2023).***

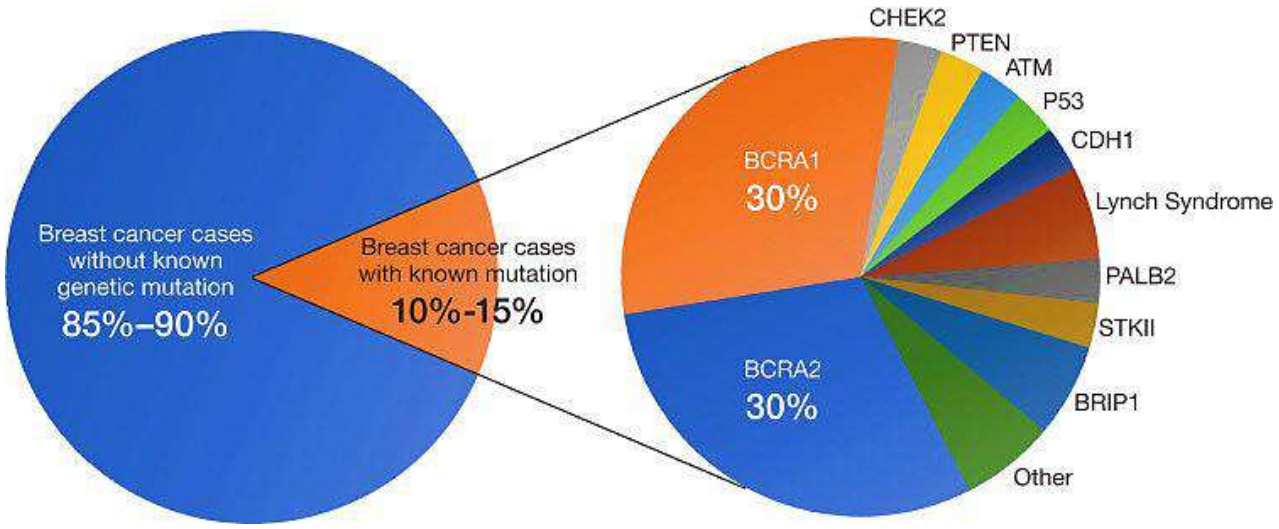


Figure 9: Breast cancer patients with genetic mutations (Hasson et al., 2020)

ATM: Ataxia-Telangiectasia Mutated, BRCA1: BReast CAncer gene -1, BRCA2: BReast CAncer gene -2, BRIP1: BRCA1 Interacting Protein 1, CHEK2: Checkpoint Kinase 2 gene, CDH: Cadherin-1 or Epithelial cadherin, P53: protein 53, PALB2: Partner And Localizer of BRCA2, PTEN: Phosphatase and TENsin homolog, STK11: Serine/Threonine Kinase 11.

About 10–15% of instances of breast cancer are caused by hereditary diseases, and the majority of these cases have a dangerous mutation in either BRCA1 or BRCA2. Cowden (PTEN) and Li-Fraumeni (p53) are two more rare, very penetrant diseases. When BRCA-positive and syndromic genes are removed, other genes experience detrimental alterations ***(Hasson et al., 2020).***

N.B. Penetrance of diseases describes the likelihood that a person with a particular gene mutation (change) that causes a disease would exhibit the disease's symptoms. The illness won't strike everyone with the mutation. For instance, some individuals with a mutation in the BRCA1 or BRCA2 gene may eventually develop cancer, whereas others will not. As of present, it is impossible to predict which individuals with a mutation that causes cancer would get the disease. Complete penetrance means that every person who has the mutation will show signs and symptoms of the disease ***(NCI, NCI Dictionary of Cancer terms 2025).***

Genetic Testing for Breast Cancer

- **Targeted single variant testing:** One particular mutation, or variant, in a single gene is the focus of single variant testing,
- **Panel genetic testing:** Panel genetic testing searches for mutations in multiple genes associated with an illness. Because several gene mutations are associated with an increased risk of breast cancer,
- **Whole genome or exome testing:** These are extensive tests that search the DNA or genetic code for genetic alterations,
- **Polygenic risk score testing:** Single-nucleotide polymorphisms, or genetic mutations, are sought after by polygenic risk score testing ***(DePolo, 2024b).***

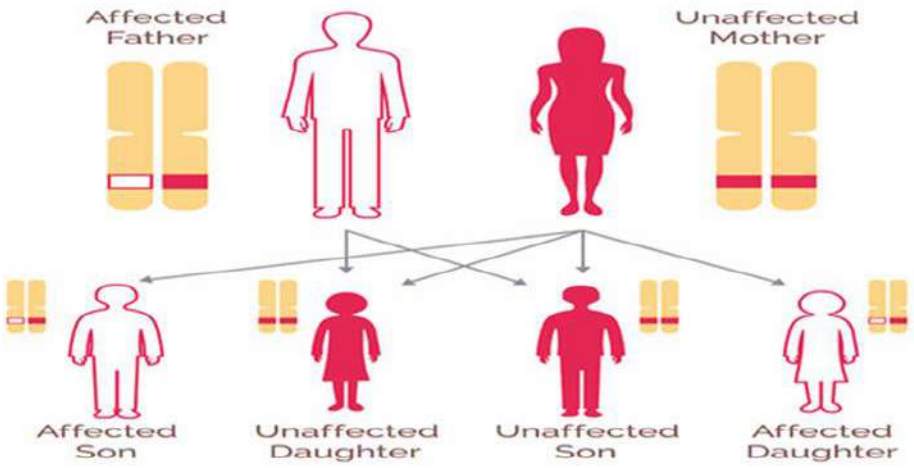


Figure 10: Autosomal dominant mutation in the BRCA gene that is inherited (Knight & Andrade, 2018)

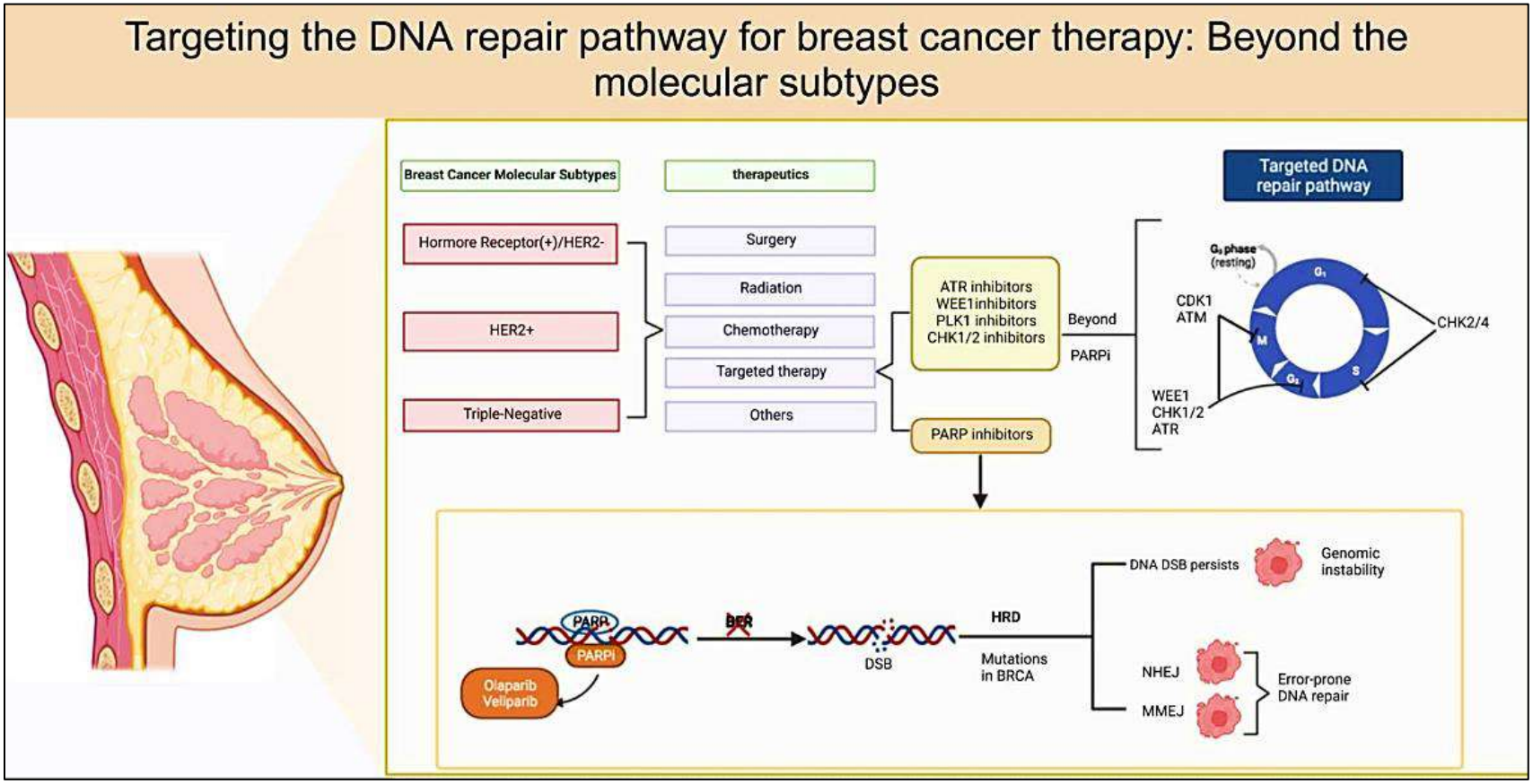


Figure 11a: Targeting the DNA repair pathway for breast cancer therapy (Qu et al., 2023)

ATM: Ataxia-Telangiectasia Mutated, ATR: Ataxia Telangiectasia and Rad3-related protein inhibitors, BRCA: BReast CAncer gene, CDK1: Cyclin-Dependent Kinase 1, CHK: Checkpoint Kinase inhibitors, DNA: Deoxyribonucleic Acid, DSB: DNA Double-Strand Break, HER2: Human Epidermal Growth Factor Receptor 2, HRD: Homologous Recombination Deficiency, MMEJ: Microhomology-Mediated End Joining, NHEJ: Non-Homologous End Joining, PARP: Poly (ADP-ribose) Polymerase, PLK1: Polo-Like Kinase-1

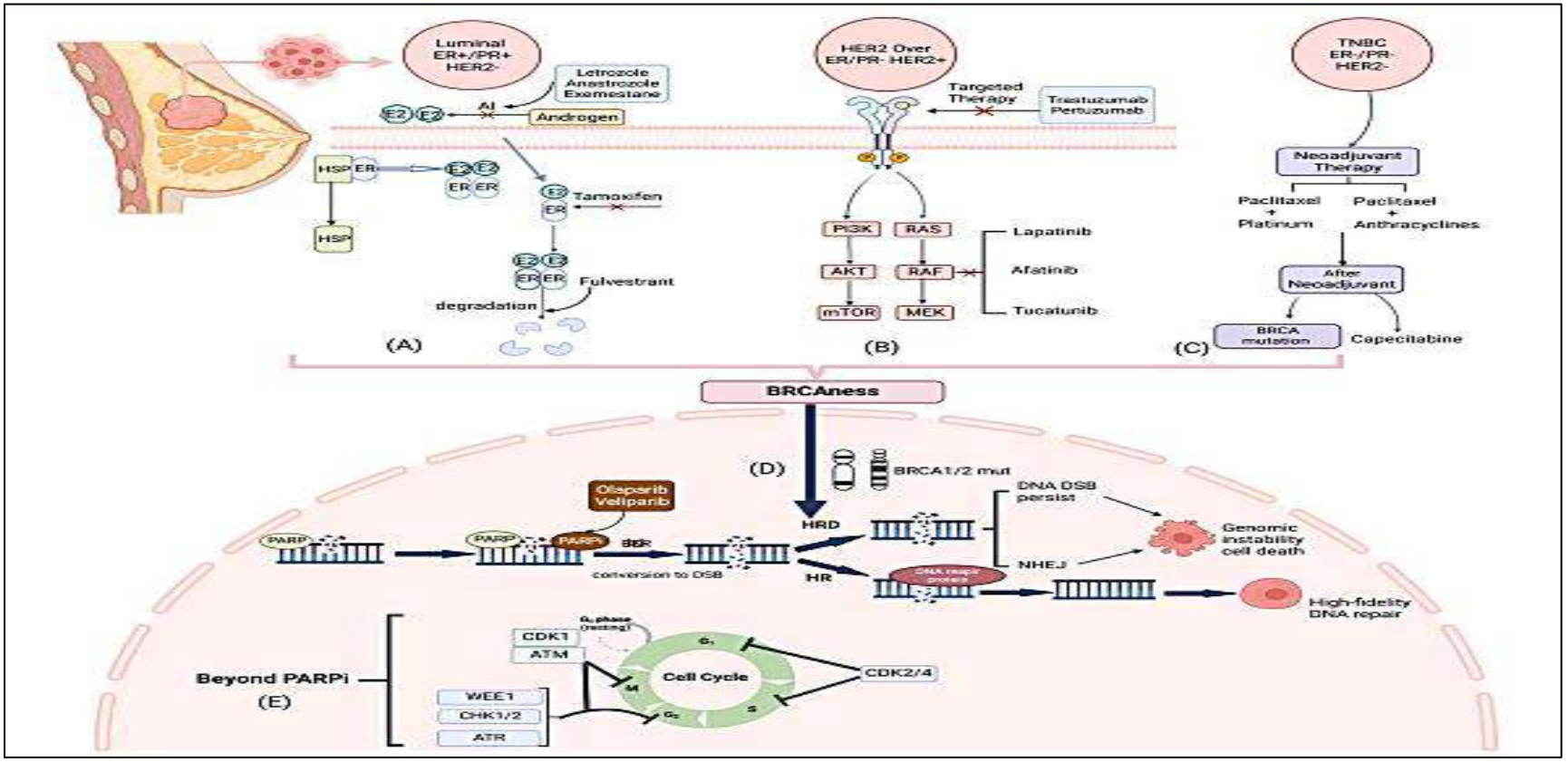


Figure 11b: Targeting the DNA repair pathway for breast cancer therapy (Qu et al., 2023)

AKT: Protein Kinase B, AI: Aromatase Inhibitor, ATM: Ataxia-Telangiectasia Mutated, ATR: Ataxia Telangiectasia and Rad3-related protein inhibitors, BRCA: BReast CAncer gene, CDK: Cyclin-Dependent Kinase, CHK: Checkpoint Kinase inhibitors, DNA: Deoxyribonucleic Acid, DSB: DNA Double-Strand Break, ER: Estrogen Receptor, E_2: Estradiol, HER2: Human Epidermal Growth Factor Receptor 2, HR: Hormone Receptor, HRD: Homologous Recombination Deficiency, HSP: Heat Shock Protein, MEK: Mitogen-Activated Protein Kinase, mTOR: Mammalian Target of Rapamycin, NHEJ: Non-Homologous End Joining, PARP: Poly (ADP-ribose) Polymerase, PR: Progesterone Receptor, PI3K: Phosphatidylinositol 3-Kinase, RAF: Rapidly Accelerated Fibrosarcoma, RAS: Rat Sarcoma, TNBC: Triple-Negative Breast Cancer

The Most Common Targetable Genetic Mutations in Breast Cancer

Table 12: Key Targetable Genetic Alterations in Breast Cancer

Mutations	Inhibitors	Common Side Effects
PARP (Poly (ADP-ribose) Polymerase Inhibitors) ***(Cancer Research UK, PARP inhibitors, 2025)***	Olaparib, Talazoparib	• An increased risk of infection • Thrombocytopenia • Anemia • Tiredness and breathlessness • Diarrhea • Indigestion and taste changes • Headaches and dizziness • Fatigue • Insomnia
HER2 (Human Epidermal Growth Factor Receptor 2) ***(Drugs.com, Enhertu: Uses, Dosage, Side Effects, & Warnings, 2025c)*** ***(Drugs.com, Trastuzumab uses, Side Effects & Warnings, 2025h)*** ***(Lexi-Drugs, Pertuzumab, 2025)*** ***(Lexi-Drugs, Ado-Trastuzumab Emtansine, 2025)*** ***(Pfizer, TUKYSA® (Tucatinib) Tablets Official HCP Site – Safety Info, 2024*** ***(Lexi-Drugs, Lapatinib, 2025)*** ***(Lexi-Drugs, Neratinib, 2025)***	Trastuzumab Pertuzumab Fam-trastuzumab deruxtecan, Hyaluronidase Pertuzumab / trastuzumab Ado-trastuzumab emtansine Tucatinib	• Diarrhea • Alopecia • Nausea and vomiting • Fatigue • Skin rash • Hemorrhage • Headache • Peripheral neuropathy • Musculoskeletal pain • Hepatotoxicity • Cardiotoxicity

	Lapatinib	• Hepatotoxicity • Nail disease (with letrozole) • Palmar-plantar erythrodysesthesia (with capecitabine) • Skin rash (with capecitabine and with letrozole) • Diarrhea
	Neratinib	• Abdominal pain • Diarrhea • Nausea and vomiting • Fatigue
CDK 4/6 (Cyclin-Dependent Kinase 4/6) ***(Pavlovic et al., 2023)***	Abemaciclib Ribociclib Palbociclib	• Diarrhea • Nausea • Vomiting • Fatigue • Alopecia • Neutropenia • QT interval prolongation • Hepatotoxicity • Cardiotoxicity
PI3K (Phosphatidylinositol 3-Kinase) ***(Lexi-Drugs, Alpelisib, 2025)*** ***(Lexi-Drugs, Inavolisib, 2025)*** ***(Lexi-Drugs, Capivasertib, 2025)***	Alpelisib Inavolisib Capivasertib	• Diarrhea • Fatigue • Renal toxicity • Nausea and vomiting • Skin rash • Anemia • Thrombocytopenia

NTRK (Neurotrophic Receptor Tyrosine Kinase) ***(Lexi-Drugs, Larotrectinib, 2025)*** ***(Lexi-Drugs, Entrectinib, 2025)*** ***(Lexi-Drugs, Repotrectinib, 2025)***	Larotrectinib Entrecitinib Repotrectinib	• Skin rash • Abdominal pain • Constipation • Anemia • Nausea and vomiting • Neutropenia • Mood disorder • Musculoskeletal pain • Cough • Fever • Arthralgia • Visual disturbance • Renal toxicity • Hepatotoxicity • Central nervous system dysfunction
RET (REarranged during Transfection) ***(Lexi-Drugs, Selpercatinib, 2025)***	Selpercatinib	• Hemorrhage • Hypersensitivity reactions • Hypertension • Pulmonary toxicity • QT prolongation • Edema • Hypertension • Skin rash • Diarrhea • Fatigue
FGFR (Fibroblast Growth Factor Receptor) ***(Lexi-Drugs, Erdafitinib, 2025)***	Erdafitinib	• Dermatologic disorder • Constipation • Hepatotoxicity • Anemia • Dry eye syndrome • Epistaxis

		• Renal toxicity • Fever
AKT (Protein Kinase B) ***(Lexi-Drugs, Capivasertib, 2025)***	Capivasertib	• Dermatologic disorder • Lymphocytopenia • Neutropenia • Fatigue • Stomatitis
ErbB-2 ***(Pfizer, TUKYSA® (tucatinib) Tablets Official HCP Site – Safety Info, 2024)*** **N.B**. ErbB1s are a type of receptor tyrosine kinase of the EGRF family ***(Tan, 1970).***	Tucatinib	• Diarrhea • Hepatotoxicity • Embryo-fetal toxicity

Breast Cancer (BRCA1) and (BRCA2) Inherited Gene Mutations

The most well-known genes associated with an increased risk of breast cancer are BRCA1 and BRCA2. The BRCA1 and BRCA2 (BRCA1/2) genes are present in all people. Some people are more likely to develop breast cancer due to a hereditary mutation in one or both of these genes ***(Roy et al., 2011).***

In response to DNA damage, BRCA1 and BRCA2 have been identified as regulators of transcription, the cell cycle, and DNA repair. The most frequently altered genes linked to an increased risk of breast cancer are BRCA1 and BRCA2 ***(Lima et al., 2019).***

Treatment response is increased in patients with BRCA gene mutations to poly (ADP-ribose) polymerase inhibitors (PARPis). PARPis can selectively destroy cancer cells by blocking DNA repair in cancer cells and cancer cells with BRCA mutations by focusing on the DNA damage response pathway ***(Qu et al., 2023).***

Poly (ADP-ribose) Polymerase Inhibitors (PARPis) are a post-translational modification in which ADP-ribose units are added to Glu, Asp, and Lys residues of target (or acceptor) proteins by members of the poly (ADP-ribose) polymerase (PARP) family. Seventeen PARP family members have been identified based on homology with PARP1, the founding member of the family ***(Gibson & Kraus, 2012).***

This selective approach improves treatment effectiveness while reducing potential side effects by preventing unnecessary interventions in patients unlikely to benefit from specific therapies ***(Lima et al., 2019).***

In cells, PARP proteins often aid in the repair of damaged DNA. In a slightly different manner, the BRCA genes (BRCA1 and BRCA2) also aid in DNA repair; however, mutations in one of those genes can prevent DNA repair. The PARP proteins are blocked by PARP inhibitors. Blocking the PARP proteins frequently results in the death of tumor cells with a mutant BRCA gene since these cells already struggle to repair damaged DNA. These medications are administered once or twice a day as pills. They can be applied in many ways to treat breast cancer ***(MedlinePlus, Peutz-Jeghers Syndrome: MedlinePlus Genetics, 2013).***

The enzyme PARP is crucial for fixing minor breaks in individual DNA strands. Small breaks in single DNA strands become double-stranded breaks when PARP is inhibited, which can cause cell death if they are not repaired ***(Boekhout, 2023).***

Examples of PARP Inhibitors

Table 13: Commonly Used PARP Inhibitors in Breast Cancer

Olaparib	It can be given to women with a BRCA mutation with early-stage HER2-negative breast cancer after surgery who have been treated with chemotherapy (before or after surgery) and are at high risk of the cancer recurring. It is typically given for one year. When given in this way, it can help some women live longer ***(MedlinePlus, Peutz-Jeghers Syndrome: MedlinePlus Genetics, 2013).***
Talazoparib	Used to treat breast cancer in adults who have deleterious germline BRCA-mutated (gBRCAm) HER2-negative tumors that are locally advanced or have spread to other parts of the body ***(Puckey, 2023).***

Olaparib and talazoparib can be used to treat patients with a BRCA mutation who have already received chemotherapy for advanced or metastatic HER2-negative breast cancer. Women who have already undergone hormone therapy may also benefit from olaparib if the malignancy is hormone receptor-positive ***(MedlinePlus, Peutz-Jeghers Syndrome: MedlinePlus Genetics, 2013).***

Partner and Localizer of BRCA2 (PALB2)

This gene is involved in the repair of homologous recombination. PALB2 heterozygous constitutional (germline) pathogenic mutations are linked to an elevated risk of cancer, primarily breast cancer ***(McVeigh, 2022).*** After BRCA1, this gene is currently the third most common cause of breast cancer ***(Shockney, 2023).*** It repairs damaged DNA in conjunction with the BRCA2 protein. It is thought that the PALB2 protein stabilizes the BRCA2 protein, enabling it to fix damaged DNA ***(Johns Hopkins Medicine, About Familial Pancreatic Cancer, 2025).***

Checkpoint Kinase 2 (CHEK2)

It is a multipurpose enzyme that plays a key role in the induction of apoptosis and cell cycle arrest caused by DNA damage ***(Ahn et al., 2004).*** It is an essential regulator that stops cells with damaged DNA from going into mitosis by blocking the activation of cyclin B-CDK1 complexes in response to DNA damage ***(Genetics Home Reference, 2015).***

Kinase inhibitors represent a broad class of potent and targeted antineoplastic agents that selectively act on protein kinases altered in cancer cells and responsible for their abnormal proliferation. Protein kinases are widely present intracellular and cell-surface proteins that are essential components of cell-signaling pathways regulating metabolism, responses to injury, adaptation, growth, and differentiation. These enzymes function by transferring a phosphate group to specific amino acids on target proteins (phosphorylation), a process that typically activates the protein or enzyme ***(NIH, Protein Kinase Inhibitors, 2025).***

CaDHerin 1 (CDH 1)

A tumor-suppressive gene that promotes cell adhesion to create structured tissues. The risk of developing lobular breast cancer, or cancer that starts in the breast's milk-producing lobules, can be raised by a mutation in the CDH1 gene. A mutation can also make it simpler for individual cancer cells to separate from a breast tumor and metastasize, or spread to other parts of the body, because the gene typically aids in cell adhesion ***(Shockney, 2023).***

Phosphatase and Tensin Homolog Protein (PTEN)

It was shown to be a tumor suppressor gene that is frequently mutated in several types of cancer. This gene encodes a phosphatidylinositol-3,4,5-trisphosphate 3-phosphatase. It has a catalytic domain that resembles the dual specificity protein tyrosine phosphatases and a tensin-like domain ***(NIH, PTEN Phosphatase and Tensin Homolog [Homo Sapiens (Human)] – Gene – NCBI, 2025).***

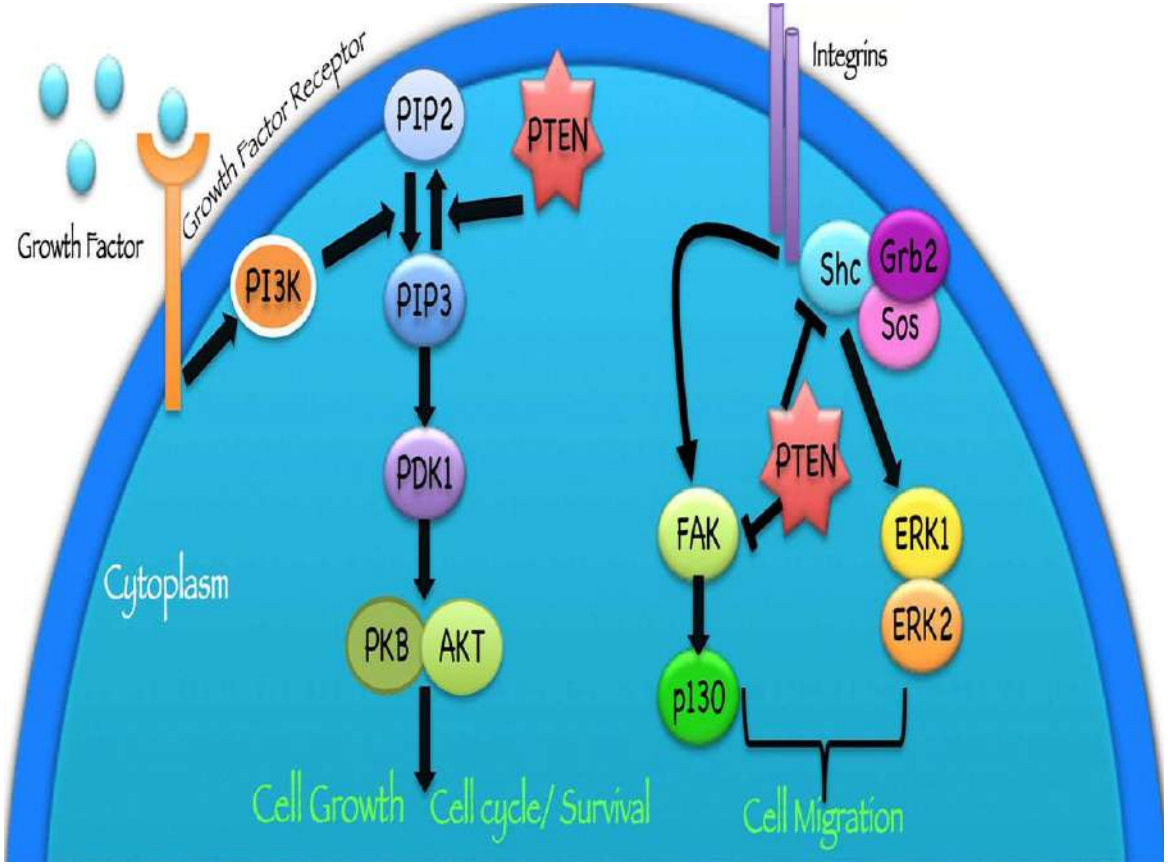


Figure 12: The PTEN protein works in different ways to suppress the formation and spread of tumors (NCI Staff, Turning on the PTEN Tumor Suppressor Protein, 2019)

AKT: Protein Kinase B, ERK: Extracellular Signal-Regulated Kinase, FAK: Focal Adhesion Kinase, Grb2: Growth factor receptor-bound protein 2, PDK1: 3- Phosphoinositol-Dependent protein Kinase-1, PI3K: Phosphatidylinositol 3-Kinase, PIP2: Phosphatidylinositol 4,5-bisphosphate, PIP3: Phosphatidylinositol (3,4,5)-trisphosphate, PKD: Protein Kinase B, PTEN: Phosphatase and TENsin homolog, Shc: Src homology and collagen, Sos: Son of Sevenless.

Serine/Threonine Kinase 11 (STK 11)

The liver kinase B1 (LKB1) protein, an intracellular serine-threonine kinase with significant functions in cellular metabolism, cell polarity, apoptosis regulation, and the DNA damage response, is encoded by the serine/threonine kinase 11 (STK11) gene ***(Holmes, 2022).*** It results in the formation of non-cancerous growths in the gastrointestinal tract known as hamartomatous polyps, a condition known as Peutz-Jeghers syndrome ***(MedlinePlus, Peutz-Jeghers Syndrome: MedlinePlus Genetics, 2013).***

Tumor Protein p53 (TP53)

It is among the most common alterations observed in human cancers, and germline mutations are responsible for Li-Fraumeni syndrome, a condition that increases susceptibility to a broad range of early-onset malignancies. The majority of mutations are single-base substitutions scattered across the coding region. The wide variability in their types and locations can provide insight into the mutagenic mechanisms underlying cancer development ***(Olivier et al., 2009).***

Human Epidermal Growth Factor Receptor (HER2)

Human epidermal growth factor receptors are transmembrane receptors with three components: intracellular tyrosine kinase, transmembrane, and extracellular binding. HER2 is overexpressed in some breast tumors, which causes the cancer cells to proliferate and spread more quickly. This gene mutation promotes the development of cancer cells ***(Drugs.com, List of HER2 inhibitors, 2025e).***

Examples of HER2 Inhibitors

(Drugs.com, List of 89 Breast Cancer Medications Compared, 2025d)

Table 14: Commonly Used HER2 Inhibitors in Breast Cancer

Trastuzumab
Pertuzumab
Fam-trastuzumab deruxtecan
Hyaluronidase, pertuzumab, and trastuzumab
Ado-trastuzumab emtansine
Lapatinib
Neratinib

Cyclin-Dependent Kinase 4/6 (CDK 4/6)

A class of medications known as CDK4/6 inhibitors targets the enzymes CDK4 and CDK6. Cell division depends on the enzyme cyclin-dependent kinase. CDK4/6 inhibitors block signals that promote the growth of cancerous (malignant) cells ***(Braal et al., 2020).***

By controlling the G1-S checkpoint, the cyclin D-cyclin-dependent kinase (CDK) 4/6-inhibitor of CDK4 (INK4)-retinoblastoma (Rb) pathway regulates the progression of the cell cycle. Increased proliferation is the outcome of dysregulation of the cyclin D-CDK4/6-INK4-Rb pathway, which is commonly seen in many cancer types ***(Beggs & Yang, 2019).***

Examples of CDK 4/6 Inhibitors

Table 15: Examples of CDK 4/6 Inhibitors in Breast Cancer

Abemaciclib	Used to treat HR+, HER2– early and metastatic breast cancer in women and men. It blocks proteins involved in cell division called cyclin-dependent kinases (CDK), specifically CDK 4 and 6. Blocking these prevents cancer cells from dividing and multiplying uncontrollably because HR+ breast cancer cells rely heavily on CDK 4/6 for growth used to treat various types of hormone receptor-positive (HR+), human epidermal growth factor receptor 2 negative (HER2–) breast cancer ***(Drugs.com, Abemaciclib for Breast Cancer: Uses, Dosage, Side Effects, & Warnings, 2025a).***
Ribociclib	A targeted treatment used to treat breast cancer that is hormone receptor-positive, HER2-negative breast cancer and has spread (metastasized) or cannot be removed by surgery. It is used in combination with an aromatase inhibitor for stage II and III early breast cancer with a high risk of coming back ***(Drugs.com, Ribociclib: Uses, Dosage, Side Effects, & Warnings, 2024).***
Palbociclib	Used to treat adults with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative breast cancer that has spread to other parts of the body (metastatic) in combination with an aromatase inhibitor as the first hormonal-based therapy, in those with breast cancer progression following hormonal therapy ***(Drugs.com, Palbociclib: Uses, Dosage, Side Effects, & Warnings, 2025f).***

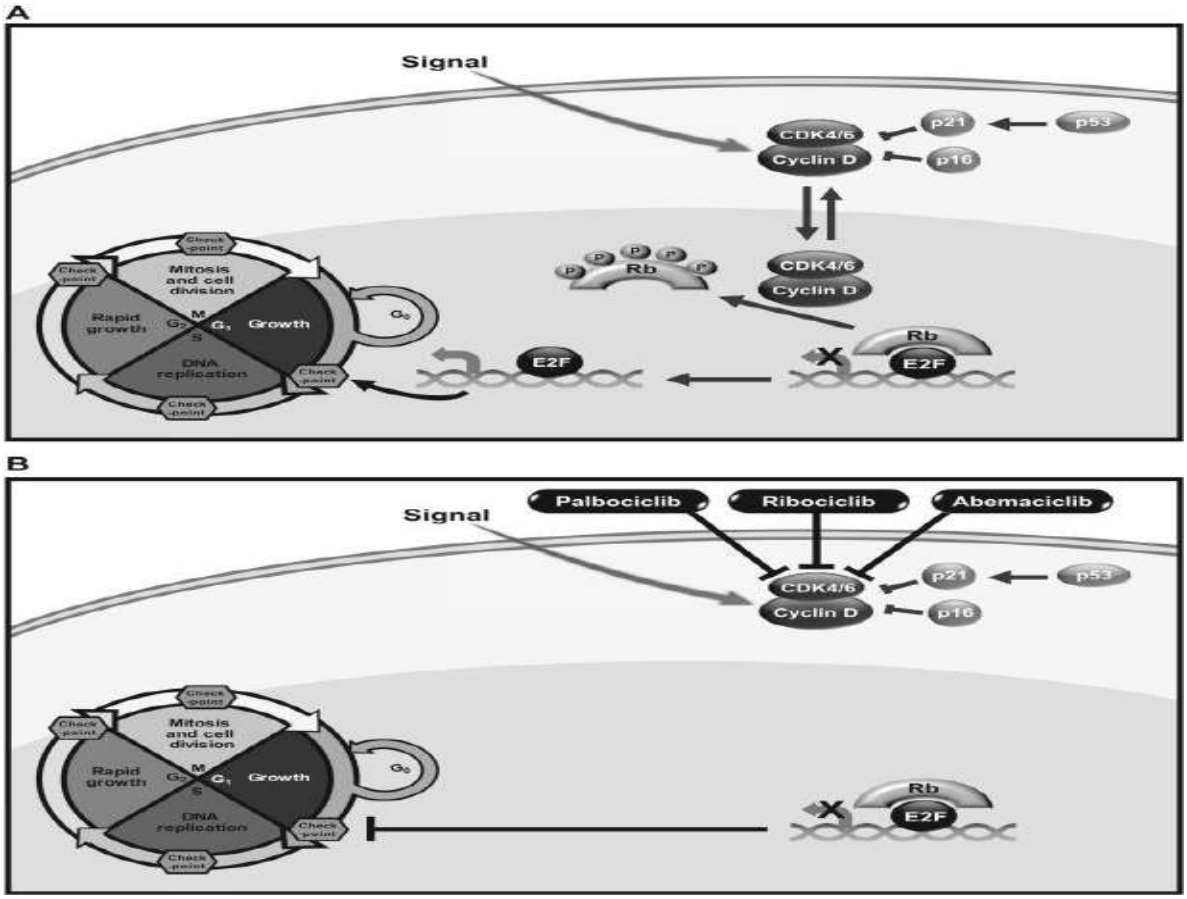


Figure 13: (A) Overview of the cyclin D-CDK4/6-INK4-Rb pathway. (B) CDK4/6 inhibition results in decreased levels of phosphorylated Rb, promoting the formation of Rb-E2F complexes and preventing E2F transcription factor activity (Hamilton & Infante, 2016)

CDK: Cyclin-Dependent Kinase; E2F: E2 transcription factor; Rb: Retinoblastoma Protein.

Phosphoinositide 3-Kinase Inhibitors (PI3K)

Numerous oncogenes and growth factor receptors stimulate phosphoinositide 3-kinase (PI3K) activity, and enhanced PI3K signaling is considered a defining feature of cancer ***(Fruman et al., 2017).***

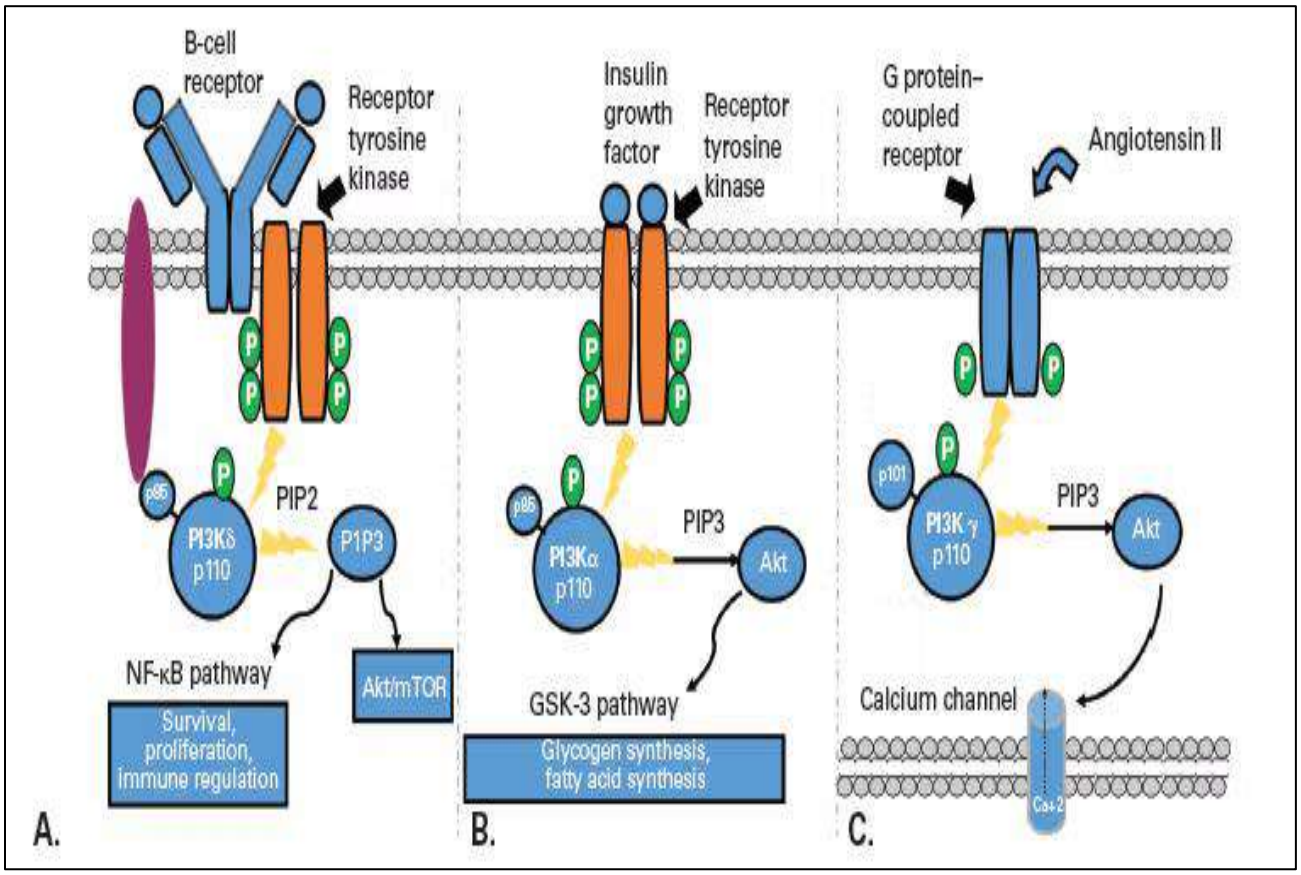


Figure 14: The PI3K/Akt Signaling Pathway is Downstream of Many Important Receptor Tyrosine Kinases, as Well as G-Protein-Coupled Receptors-functions of this cascade include survival, growth, and metabolism. Various organs and tissues can function abnormally when the PI3K pathway is altered. (A) shows the B-cell receptor signaling pathway with the PI3K& axis promoting tumor survival through the NF-Kb pathway. (B) shows the PI3Ka pathway that is involved in glucose metabolism via insulin receptor signaling. (C) shows PI3Ky signaling in cardiac smooth muscles, with a downstream effect on calcium channels (Greenwell & Ip, 2017)

GSK-3 = glycogen synthase kinase 3; mTOR = mammalian target of rapamycin; NF-Kb = nuclear factor kappa B; PI3K = phosphatidylinositol 3-kinase; PIP2 = phosphatidylinositol 4,5-bisphosphate; PIP3 = phosphatidylinositol (3,4,5)-trisphosphate.

Examples of PI3K Inhibitors

(Drug Bank, Phosphatidylinositol-3-kinase (PI3K) inhibitors | Drugbank Online, 2025f)

Table 16: Examples of PI3K Inhibitors in Breast Cancer

Alpelisib	Used in combination with fulvestrant to treat postmenopausal women and men with advanced or metastatic breast cancer that is HR-positive, HER2-negative.
Inavolisib	PIK3CA inhibitor used as part of a three-drug regimen for PIK3CA-mutated, HR-positive, HER2-negative advanced breast cancers.

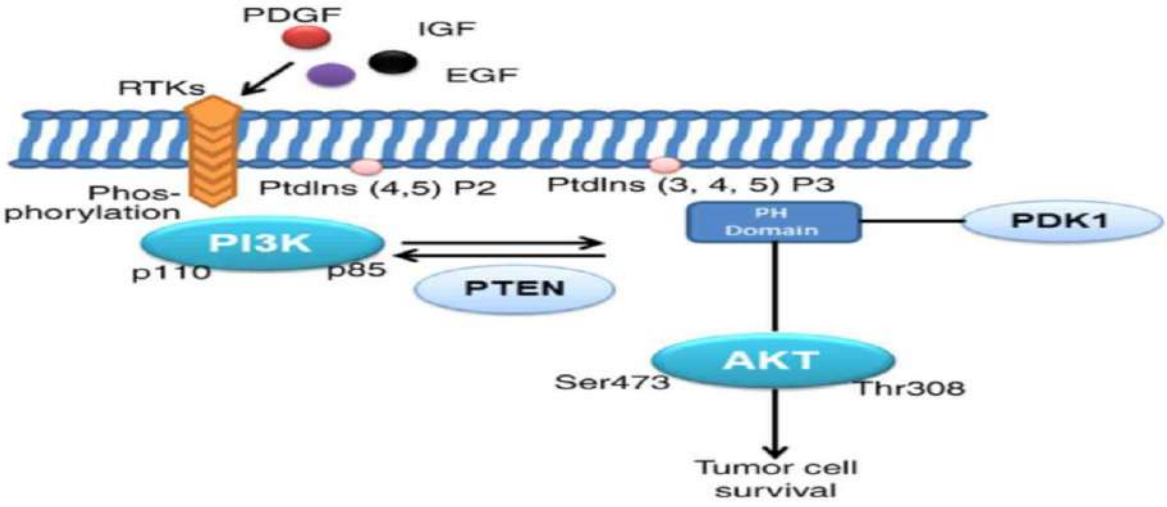


Figure 15: Schematic of the PI3K/Akt signaling pathway (Shi et al., 2019)

AKT: Protein Kinase B, EGF: Epidermal Growth Factor, IGF: Insulin-like Growth Factor; PDGF: Platelet-Derived Growth Factor; PDK1: 3-phosphoinositol-dependent protein kinase-1; PH: Plekstrin Homology; PI3K: Phosphatidylinositol 3-kinase; PtdIns, Phosphatidylinositol; PTEN: Phosphatase and Tensin Homolog; RTK: Receptor Tyrosine Kinase, Ser 473: Serine 473, Thr 308: Threonine 308. (p85 is the regulatory subunit of phosphatidylinositol 3-kinase (PI3K), p110 is the catalytic subunit of the class I phosphoinositide 3-kinase (PI3K) enzyme).

RTK recruits PI3K following activation and phosphorylation, and phosphorylates PtdIns (4,5) P2 to PtdIns (3–5) P3, which activates AKT by recruiting PDK1 to the PH domain of AKT, thereby activating the entire pathway and regulating cell growth ***(Shi et al., 2019).***

Neurotrophic Tyrosine Receptor Kinase (NTRK)

Examples of NTRK Inhibitors

(NCCN, Breast Cancer, Clinical Practice Guidelines in Oncology, 2025)

Table 17: Examples of NTRK inhibitors in Breast Cancer

Larotrectinib	Approved for pediatric and adult patients with advanced or metastatic solid tumors with neurotrophic receptor tyrosine kinase (NTRK) gene fusion without an acquired resistance mutation (***Dunn, 2020).***
Entrecitinib	
Repotrectinib	A next-generation tyrosine kinase inhibitor (TKI) specifically designed to address resistance in the treatment of non-small cell lung cancer (NSCLC), specifically due to mutations in the ROS1 gene ***(Drug Bank, Repotrectinib: Uses, Interactions, Mechanism of Action | Drugbank Online, 2025g).***

Protein kinase B (AKT)

A serine/threonine kinase that, in mammals, consists of three closely related isoforms: PKBα (Akt1), PKBβ (Akt2), and PKBγ (Akt3). PKB/Akt becomes activated in response to a wide range of stimuli, including hormones, growth factors, and components of the extracellular matrix ***(Nicholson & Anderson, 2002).***

Examples of AKT Inhibitors

Table 18: Examples of AKT Inhibitors in Breast Cancer

Capivasertib	A serine/threonine kinase inhibitor used to treat hormone receptor-positive, HER2-negative, locally advanced or metastatic breast cancer ***(Drug Bank, Capivasertib: Uses, Interactions, Mechanism of Action | Drugbank Online, 2025c).***

Receptor tyrosine-protein kinase (erbB-2)

Examples of ErbB-2 Inhibitors

Table 19: Examples of ErbB-2 Inhibitors in Breast Cancer

Tucatinib	Tyrosine kinase inhibitor that targets the human epidermal growth factor receptor 2 (HER2) and is used in combination with other antineoplastic agents in the treatment of refractory, advanced, or metastatic HER2-positive breast and colorectal cancer ***(Bethesda, 2023).***

Colon Cancer

Colon cancer

Colon cancer is the fourth most lethal cancer in the world. Although it can appear at any age, it primarily affects elderly persons. It usually starts with tiny cellular growths on the colon's inner lining called polyps. Although the majority of polyps are benign, some may eventually turn malignant and cause colon cancer ***(Dekker et al., 2019).***

The most prevalent kind of gastrointestinal cancer is colon cancer. The pathogenesis of this complex disease process includes hereditary variables, environmental exposures (including nutrition), and inflammatory states of the digestive tract ***(Dragovich, 2025).***

After lung cancer, breast cancer in women, and prostate cancer in males, colorectal cancers are the most common type of cancer ***(Menon & Cagir, 2024).***

Medical Conditions That Increase Colon Cancer Risk

- Inflammatory bowel disease,
- Inherited conditions: Certain conditions, like Lynch syndrome and familial adenomatous polyposis,
- A family history of colon and other kinds of cancer,
- Many polyps ***(American Cancer Society, Colorectal Cancer Risk Factors: Hereditary Colorectal Risk Factors, 2025a).***

Tests and Procedures Used for Colon Cancer Diagnosis Include

- Using a scope to examine the inside of the colon,
- Removing a sample of tissue for testing,
- Blood tests ***(NIH, Screening Tests to Detect Colorectal Cancer and Polyps, 2024).***

Diagnosis and Tests

- Complete blood count (CBC),
- Proctoscopy, which is a diagnostic medical technique that uses a short, rigid tube called a proctoscope to look within the rectum and the bottom portion of the sigmoid colon ***(NCCN, NCI Dictionary of Cancer Terms, 2025)***
- Comprehensive metabolic panel (CMP),
- Carcinoembryonic antigen (CEA) assay,
- X-rays,
- Computed tomography (CT) scan,
- Magnetic resonance imaging (MRI) scan,
- Positron emission tomography (PET) scan,
- Ultrasound,
- Biopsy ***(American Cancer Society, testing for colorectal cancer: How is colorectal cancer diagnosed? 2024).***

Common Colon Cancer Screening Tests

- Colonoscopy,
- Fecal immunochemical test (FIT),
- Guaiac-based fecal occult blood test (Gfobt),
- Fecal DNA test,
- Flexible sigmoidoscopy,
- Virtual colonoscopy ***(The Johns Hopkins University, Colon Cancer Diagnosis, 2024).***

Inherited Colorectal Cancer

Colorectal cancers arise from the accumulation of several gene mutations in intestinal lining cells. This often begins with a single abnormal cell that proliferates and develops into an early (small) polyp, a late (big) polyp, and ultimately a cancer due to the growing number of cell mutations. In most individuals, this typically occurs sporadically; however, a small proportion inherit an abnormal gene from one parent, placing them further along the pathway toward cancer development. While it is not inevitable that these individuals will develop colorectal cancer, their risk is higher than that of the general population, and they benefit from close monitoring and, in some cases, preventive surgical interventions ***(Tunbridge Wells Colorectal Surgery, Inherited Colorectal Cancer 2025).***

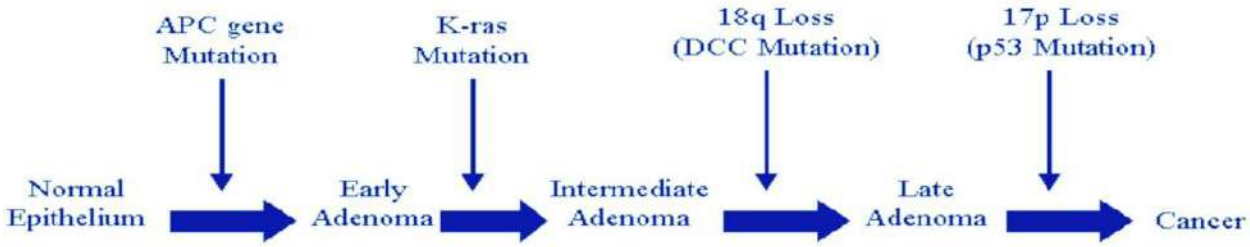


Figure 16: The accumulation of genetic mutations leads to the transition from normal tissue to a polyp or adenoma and finally to a cancer (Vogelstein et al) (Tunbridge Wells Colorectal Surgery, Inherited Colorectal Cancer 2025)

APC: Adenomatous Polyposis Coli, DCC: Deleted in Colorectal Cancer, KRAS: Kirsten Rat Sarcoma Virus, P53: Protein 53

The Predominant Mutations Associated with Colorectal Cancer

The TP53, APC, RAS, and KRAS genes have the most frequent mutations in colon cancer, also known as colorectal cancer (CRC) ***(Armaghany et al, 2012).***

Tumor Protein (TP53) (60-70%)

This tumor suppressor gene typically undergoes mutations that impair its ability to control cell proliferation and death ***(Armaghany et al, 2012).***

Adenomatous Polyposis Coli (APC) (40-60%)

Mutations in the APC gene, another tumor suppressor, interfere with the Wnt (Wingless/Integration) signaling pathway, a critical regulator of cell growth and development ***(Armaghany et al, 2012).***

Reticular Activating System (RAS) Family (30-40%)

Activating mutations in the RAS pathway are responsible for a wide variety of human cancers ***(Kundu et al., 2021).*** Mutations in the RAS gene, which are located at loci in exons 2, 3, and 4, often result in constitutive activation of RAS proteins and persistent downstream signaling. Mutations in KRAS exon 2 (codon 12/13) have been widely used in clinical practice to identify patients with metastatic colorectal cancer (mCRC) who are unlikely to benefit from cetuximab and panitumumab, two anti-EGFR monoclonal antibodies ***(Hechet et al., 2015).***

Other Significant Genes

Prognosis is also greatly impacted by mutations in genes such as BRAF, NTRK, HER2, and RET ***(Armaghany et al, 2012).***

Types of Biomarker Tests Used to Detect Colorectal Cancer Mutations

Identifying prognostic and predictive biomarkers is crucial for enhancing and tailoring cancer therapies ***(Patel et al., 2019).***

Predictive Biomarkers

- Epidermal Growth Factor Receptor (EGFR),
- Consensus Molecular Subtypes (CMS),
- Colon Cancer Subtypes (CCS1 and CCS2),
- v-RAF murine sarcoma viral oncogene homolog B (BRAF),
- Adenomatous Polyposis Coli (APC),
- Deficient Mismatch Repair (dMMR),
- Human Epidermal Growth Factor Receptor 2 (HER2),
- Tumor Protein 53 (TP53) ***(Patel et al., 2019).***

Prognostic Biomarkers

These comprise consensus molecular subtypes (CMS) and colon cancer subtypes (CCS). Right-sided cancers are more likely to exhibit CMS1 (MSI immune) and CMS3 (metabolic), which are linked to BRAF mutations and have poorer prognoses. While CMS2 (canonical) cancers are more frequently seen on the left side, they resemble CCS1 class tumors, which are frequently found on the left side and have TP53/KRAS mutations, overactivation of the wingless integrated signaling pathway (WNT), and noticeable chromosomal instability ***(Patel et al., 2019).***

Somatic Mutations and Immunoprofiling

- Rat Sarcoma Viral Oncogene Homolog (RAS),
- v-RAF murine sarcoma viral oncogene homolog B (BRAF),
- Mitogen-activated protein kinase (MEK),
- Human Epidermal Growth Factor Receptor 2 (HER2),
- Mismatch repair/ Microsatellite instability (MMR/MSI),
- Tumor-infiltrating lymphocytes (TILs),
- POLE Mutations (biomarker that has been investigated is the presence of exonuclease domain mutations in the polymerase epsilon, catalytic subunit) ***(Patel et al., 2019).***

Germline Pharmacogenomics

- Dihydropyrimidine Dehydrogenase (DPYD),
- Uridine Diphosphate Glucuronosyltransferase 1A1 (UGT1A1),
- Thymidylate Synthase (TYMS),
- Methylenetetrahydrofolate Reductase (MTHFR),
- Vascular Endothelial Growth Factor (VEGF) ***(Patel et al., 2019).***

N.B. Pharmacogenomics are studies about how all or multiple genes can influence responses to drugs ***(CDC, Pharmacogenomics, 2024).***

Liquid Biopsy (Circulating Tumor DNA – ctDNA)

The development of highly sensitive liquid biopsy assays has made it possible to identify and describe minimal residual disease (MRD), which is the presence of tumor cells that have spread from the primary lesion to distant organs in patients who do not exhibit any radiological or clinical signs of metastasis or residual tumor cells that remain after local therapy and eventually cause a local recurrence ***(Pantel & Alix-Panabieres, 2019).*** Disease-free survival is influenced by minimal residual disease, which was linked to ctDNA from liquid biopsies ***(Stahler & Stintzing, 2025).***

The Most Common Targetable Genetic Mutations in Colon Cancer

(NCCN, Colon Cancer, Clinical Practice Guidelines in Oncology, 2025)

Table 20: Key Targetable Genetic Mutations in Colon Cancer

Targets	Inhibitors	Common Side Effects
BRAF (Raf Murine Sarcoma Viral Oncogene Homolog B) ***(Lexi-Drugs, Encorafenib, 2025)***	Encorafenib	• Visual impairment • Edema • Dermatologic toxicity • Alopecia • Diarrhea • Abdominal pain • Arthralgia • Myopathy • Hepatic toxicity • Renal toxicity
NTRK (Neurotrophic Receptor Tyrosine Kinase) ***(Lexi-Drugs, Larotrectinib, 2025)*** ***(Lexi-Drugs, Entrectinib, 2025)*** ***(Lexi-Drugs, Repotrectinib, 2025***	Entrectinib Larotrectinib Repotrectinib	• Skin rash • Abdominal pain • Constipation • Anemia • Nausea and vomiting • Neutropenia • Mood disorder • Musculoskeletal pain • Cough • Fever • Arthralgia • Visual disturbance • Renal toxicity • Hepatotoxicity • Central nervous system dysfunction

HER2 (Human Epidermal Growth Factor Receptor 2) ***(Drugs.com, Trastuzumab uses, Side Effects & Warnings, 2025g)*** ***(Lexi-Drugs, Pertuzumab, 2025)*** ***(Pfizer, TUKYSA® (tucatinib) tablets official HCP Site – safety info, 2024)*** ***(Lexi-Drugs, Lapatinib, 2025)***	Trastuzumab Pertuzumab Tucatinib	• Diarrhea • Alopecia • Nausea and vomiting • Fatigue • Skin rash • Hemorrhage • Headache • Peripheral neuropathy • Musculoskeletal pain • Hepatotoxicity • Cardiotoxicity
	Lapatinib	• Hepatotoxicity • Nail disease (with letrozole) • Palmar-plantar erythrodysesthesia (with capecitabine) • Skin rash (with capecitabine and with letrozole) • Diarrhea
HER2/HER3 ***(Lexi-Drugs, Zenocutuzumab, 2025)***	Zenocutuzumab	• Diarrhea • Hematologic toxicity • Infusion-related reaction • Fatigue • Hepatotoxicity • Musculoskeletal pain • Cough • Dyspnea
KRAS (Kirsten Rat Sarcoma Virus) ***(FDA, Sotorasib, 2023)***	Sotorasib, Adagrasib, Cetuximab, Panitumumab	• Hepatotoxicity • Interstitial lung disease (ILD)/pneumonitis • Diarrhea • Musculoskeletal pain

		• Nausea • Fatigue • Cough
RET (REarranged during Transfection) ***(Lexi-Drugs, Selpercatinib, 2025)***	Selpercatinb	• Hemorrhage • Hepatotoxicity • Hypersensitivity reactions • Hypertension • QT prolongation • Pulmonary toxicity • Edema • Abdominal pain • Fatigue • Pan cytopenia
VEGF (Vascular Endothelial Growth Factor)	Ramucirumab ***(Lexi-Drugs, Ramucirumab, 2025)***	• Hypertension • Peripheral edema • Abdominal pain • Fatigue • Thrombocytopenia
	Bevacizumab ***(Lexi-Drugs, Bevacizumab, 2025)***	• Fistula formation and GI perforation • Heart failure • Hemorrhage • Hypertension • Osteonecrosis • Proteinuria and kidney impairment • Reversible posterior leukoencephalopathy syndrome • Thromboembolism • Wound healing impairment
CHK2 (Checkpoint Kinase 2 gene)	Nivolumab	• Cardiovascular toxicity • Dermatologic toxicity

	(Lexi-Drugs, Nivolumab, 2025) Ipilimumab ***(Lexi-Drugs, Ipilimumab, 2025)***	• Endocrine toxicity • GI toxicity • Hematologic toxicity • Hepatotoxicity • Nephrotoxicity • Neurologic toxicity • Ophthalmic toxicity • Pulmonary toxicity
VEGFRs (1-3), TIE2 (Tyrosine Kinase with Immunoglobulin), PDGFR (Platelet-Derived Growth Factor Receptor) ***(Lexi-Drugs, Regorafenib, 2025)***	Regorafenib	• Hepatotoxicity • Palmar-plantar erythrodysesthesia • Diarrhea • Gastrointestinal pain • Asthenia • Fatigue • Hypertension
VEGFRs (1-3) ***(Lexi-Drugs, Fruquintinib, 2025)***	Fruquintinib	• Hypertension • Palmar-plantar erythrodysesthesia • Abdominal pain • Diarrhea • Musculoskeletal pain
PD-1 (Programmed Cell Death Protein 1) ***(American Cancer Society, Immune Checkpoint Inhibitors and Their Side Effects, 2025b)***	Dostarlimab-gxly, Cemiplimab-rwlc, Retifanlimab-dlwr, Tislelizumab-jsgr, Toripalimab-tpzi	• Diarrhea • Fatigue • Cough • Nausea and vomiting • Skin rash • Poor appetite • Constipation • Muscle and joint pain

Pharmacist-Led Intervention in Cancer

Pharmacists contribute significantly to the delivery of high-quality cancer care in a number of ways. Pharmacists are in charge of safely preparing, supplying, and dispensing cancer therapies from a dispensing perspective. To ensure the safe, sensible, and economical use of cancer therapies and supportive medications, pharmacists are also essential in the selection of medications and formulary management ***(Cancer FIP practice transformation programme on NCDS Cancer Care 2022).***

In oncology care settings, clinical pharmacists play a crucial role by supporting a team-based strategy to improve patient outcomes. They can create, carry out, oversee, and adjust pharmacotherapy regimens for cancer patients thanks to their specific expertise. The five main components of the Pharmacists' Patient Care Process are gathering patient data, evaluating drug-related problems, creating a care plan, carrying out interventions, and doing follow-ups. Drug therapy problems (DTPs) are identified and resolved at the center of this process, and then the care plan is continuously assessed and improved. The patient's current drug schedule, recognized DTPs, therapy goals, monitoring metrics, and follow-up techniques are all crucial elements of a well-structured care plan ***(Ali et al., 2025).***

An oncology clinical pharmacist contributes to personalized medication management by implementing the following practices -

- **Check for Biomarker Tests**
  Specific tests for cancer type to ensure that the patient is taking the right medication.
  - For lung cancer, refer to the types of biomarker tests used to detect NSCLC mutations, pages 28 and 29.
  - For breast cancer, refer to genetic testing for breast cancer, page 44.
  - For colon cancer, refer to the types of biomarker tests used to detect colorectal cancer mutations, pages 66 and 67.
- **Patient Education and Counseling**
  A key component of oncology pharmacy practice is educating patients and caregivers about anticancer therapy. Oncology pharmacists require a standardized framework that guarantees critical information is conveyed and tailored to each patient as anticancer regimens become more complex ***(Zacholski et al., 2025).***

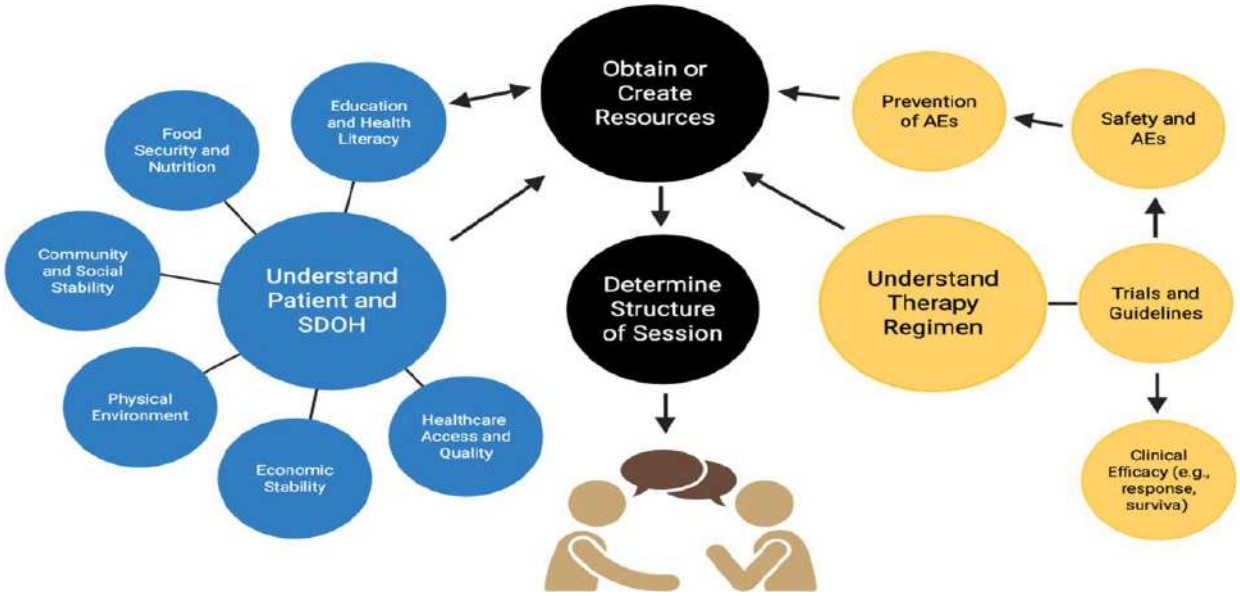


Figure 17: Areas to take into account before chemotherapy education workshops for assessment and preparedness. SDOH, or social determinants of health; AEs, or adverse effects (Zacholski et al., 2025)

- **Multidisciplinary Collaboration**

  As key members of the healthcare team, pharmacists collaborate with multidisciplinary professionals to support high-quality cancer care and work closely with pharmacy assistants and technical staff to ensure proper handling, preparation, and dispensing of anticancer medicines ***(Cancer FIP practice transformation programme on NCDS Cancer Care 2022).***

- **Monitoring Treatment-Related Toxicities**

  With the expanding clinical use of immune checkpoint inhibitor (ICI) therapies, there is a growing need for healthcare practitioners, including pharmacists, to be well-informed about the immune-related adverse effect (irAE) profiles associated with these treatments. Early identification and appropriate management of irAEs are essential to minimize morbidity and support the continuation of ICI therapy ***(Medina et al., 2020).***

Helpful Online Resources on the Side Effects of Personalized Medicine and Their Management

- Common Terminology Criteria for Adverse Events (CTCAE) v6.0 (MedDRA 28.0) by Cancer Therapy Evaluation Program Division of Cancer Therapy and Diagnosis National Cancer Institute National Institutes of Health U.S. Department of Health and Human Services – published on 22 July, 2025. https://dctd.cancer.gov/research/ctep-trials/for-sites/adverse-events/ctcae-v6.pdf
- National Comprehensive Cancer Network (NCCN) Guidelines. Treatment by Cancer Type. https://www.nccn.org/guidelines/category_1
- National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology. Management of Immune Checkpoint Inhibitor- Related Toxicities version 1.2026- October 23, 2025. https://www.nccn.org/professionals/physician_gls/pdf/ici_tox.pdf
- Drugs.com. https://www.drugs.com/
- The ROS1 ders. Coping with ROS1 TKI side effects. https://www.theros1ders.org/coping-with-side-effects
- Target Ovarian Cancer. PARP inhibitors side effects. https://targetovariancancer.org.uk/parp-inhibitors-side-effects
- Chemo care. https://chemocare.com/
- BC Cancer. https://www.bccancer.bc.ca/health-professionals

Limitations to Precision Medicine in Cancer

Access to the newest, precise treatments may be limited in some places. Regarding the use of precision medicine in cancer treatment, there is still a lot to learn. Researchers are attempting to close those gaps in both laboratory studies and clinical trials ***(American Cancer Society, Precision or Personalized Medicine: Precision Medicine for Cancer, 2023).***

Many clinical trials focus on patients with specific cancer types, but eligibility for precision medicine trials depends on the presence of particular genetic or protein alterations in a patient's tumor that can be targeted by the study treatment. Moreover, such trials are frequently limited to large cancer centers, which can restrict participation opportunities for some patients ***(American Cancer Society, Precision or Personalized Medicine: Precision Medicine for Cancer, 2023).***

Precision medicine may not always be utilized to its full potential, even when it is already accessible outside of clinical trials, for example

- A person's family history of cancer may not be effectively recognized or assessed when learning about cancer risk. Alternatively, genetic testing may not have been performed, the results may not be sufficient, or the results may not be utilized to make optimal health-related decisions,
- When it comes to cancer treatment, even if a person is diagnosed with a type of cancer for which testing is available to look for gene or protein changes that can affect treatment options, the cancer may not be examined for these changes,
- Concerns can occasionally arise over the expenses of biomarker testing and the medications that may be suggested as a result of testing ***(American Cancer Society, Precision or Personalized Medicine: Precision Medicine for Cancer, 2023).***

The Future of Personalized Cancer Medicine

Personalized cancer medicine has the potential to improve treatment effectiveness while reducing side effects; however, several challenges remain. These include -

- Not all cancer types and subtypes are eligible for individualized treatment,
- Certain customized therapies are only accessible through clinical trials,
- The cost of genetic testing can be high. It's not always covered by insurance plans. It also takes time to test your DNA and the genes in your tumor. The patient may have to wait longer to receive the customized care as a result,
- Targeted treatments are one type of tailored treatment that might be costly ***(American Cancer Society, Targeted Drug Therapy for Cancer, 2021a).***

Educational Materials

هيئة الدواء المصرية

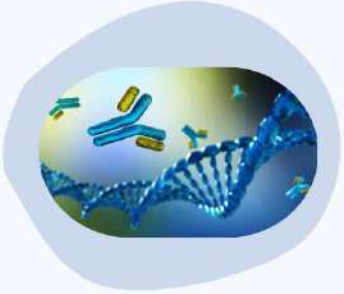
EGYPTIAN DRUG AUTHORITY

العلاج الموجه

معرفة دوائك.. طريقك للأمان

ماهو العلاج بالاجسام المضادة الاحادية MABS

هي بروتينات تُصنع في المختبر لتعمل مثل الأجسام المضادّة الطبيعية الموجودة في جسم الإنسان لتعزيز الاستجابة المناعية ضد الخلايا السرطانية بالارتباط بها واعطاء علامة للجهاز المناعي لتدميرها ولها آثار جانبية أقل خطورة مقارنة بالعلاج الكيماوي



قد تختلف الاثار الجانبيه من دواء لاخر ولكن في حالة حدوث الاتي <u>يجب الاتصال بالطبيب فورًا:</u>

- صعوبة في التنفس أو ضيق في الصدر
- تورم في الوجه أو الشفتين أو اللسان
- طفح جلدي شديد أو حكة قوية
- ارتفاع في درجة الحرارة لا يزول أو قشعريرة شديدة
- ألم أو احمرار شديد في مكان الحقن أو التسريب
- أي علامات عدوى (مثل التهاب الحلق، سعال شديد، حرقة أثناء التبول)

<u>خلال فترة العلاج</u> يجب مراعاة الاتي:

- راقب الاعراض الجانبية المحتملة
- لا تحصل على أي لقاحات أثناء العلاج دون استشارة طبيبك أولاً
- الالتزام بالفحوصات الدورية المطلوبة بواسطة الطبيب المعالج
- ضرورة ابلاغ الطبيب بالادوية الاخري التي تتناولها لتجنب التفاعلات الدوائية المحتملة

يمكن ان يؤدي اعطاء هذه الادوية الي حدوث رد فعل تحسسي وخصوصا عند اعطاؤها لاول مرة مثل: ارتفاع في درجة الحرارة- رعشة-ضعف عام- صداع -غثيان- قيء- اسهال -انخفاض في ضغط الدم- طفح جلدي

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يعني ايه TKIs؟؟

هي اختصار لكلمة مثبطات التايروسين كاينازز، ودي أدوية بتشتغل على حاجة معينة جوا الخلايا السرطانية اسمها التايروسين كاينازز، وبتمنعها من إنها تخلي السرطان يكبر أو ينتشر. يعني باختصار، بتوقف نمو السرطان.

خطواتك مع علاج الـTKIs

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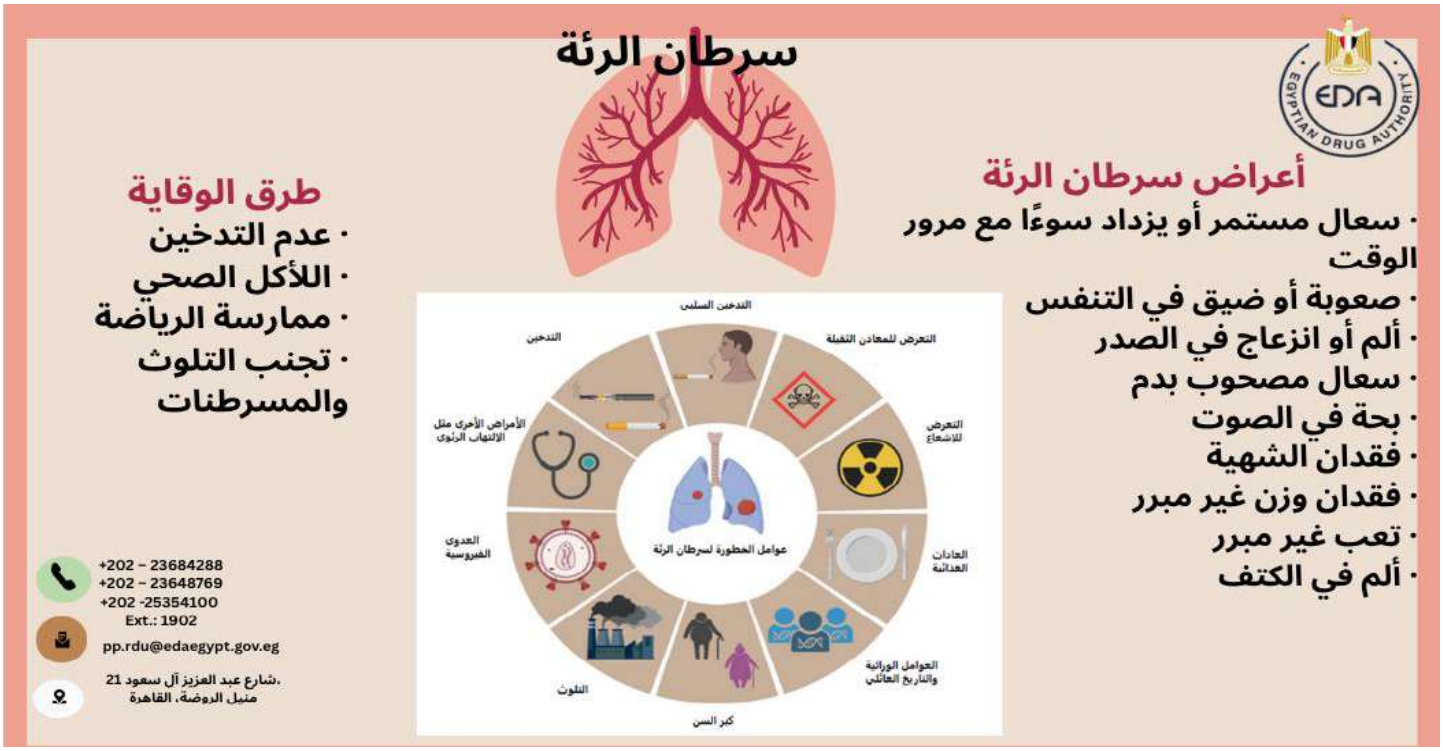
منيل الروضة، القاهرة

إيه الممكن تحسّ بيه؟ وإزاي تتعامل؟

- **طفح جلدى/بشرة ناشفة/حكة**
  - إزاي تتصرف: حط كريم مرطّب على جسمك كذا مرة في اليوم.واستخدم زيت الاستحمام بدل الصابون. وابعد عن الشمس على قد ما تقدر. ولو اتعرضت للشمس ابقى حط واقي شمس.
  - امتى تكلم الدكتور: لو فيه تورّم في الوش، وسخونية، أو صعوبة في التنفّس.
- **تعب ونقص شهية/نقص وزن**
  - إزاي تتصرف: حاول تاكل وجبات منتظمة، ولو وزنك بدأ يقلّ استشير أخصائي تغذية.
- **غثيان/قئ**
  - إزاي تتصرف: اشرب سوايل كتير طول اليوم.كُل واشرب كميات صغيرة وكذا مرة في اليوم وممكن الدكتور يكتبلك دواء ضد الغثيان تاخده في البيت
  - امتى تكلم الدكتور: لو الغثيان أو القيء مستمر أو الدوا مش مأثر.
- **إسهال**
  - إزاي تتصرف: اشرب سوايل كتير طول اليوم. وكُل واشرب بس بكميات صغيرة وعلى فترات. وابعد عن الأكل اللي فيه ألياف كتير.
  - امتى تكلم الدكتور: لو الإسهال استمر اكتر من 24 ساعة.
- **تغيّرات فى الأظافر (ألم/تورم)**
  - إزاي تتصرف: تجنب جرح ضوافرك أو أطراف الأصابع، وتجنب الصابون والمنظفات ومنتجات العناية بالضوافر القاسية، وحافظ على نظافة وجفاف إيديك.
- **تقرحات أو ألم فى الفم**
  - إزاي تتصرف: نظّف سنانك برفق بعد الأكل وقبل النوم باستخدام فرشة أسنان ناعمة جدًا. و اعمل غرغرة بمزج ربع ملعقة صغيرة بيكربونات صوديوم ورُبع ملعقة صغيرة ملح في كباية ميّه دافية، واستخدمها كذا مرة في اليوم.



"This material does not specifically address precision medicine or targeted therapy; however, it has been included in this guide as it may be used to distribute informational flyers to patients' families to support community awareness."

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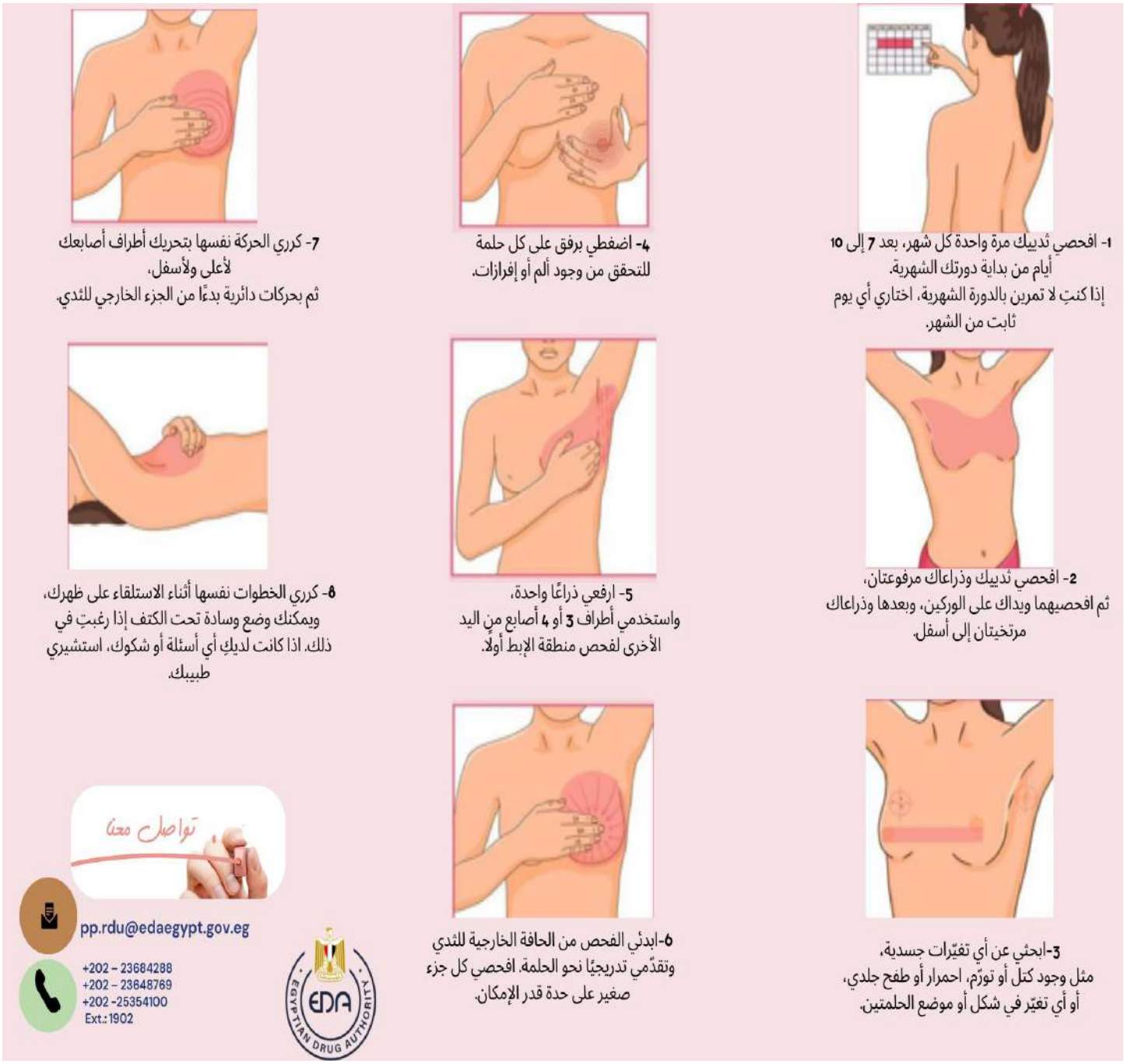

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