Summer Training

at

Prescient Health Organization

Gurgaon

MAY 21st to JULY 21st, 2021

Secondary Research on Treatment of Breast Cancer drugs: launched and marketed by Bio-pharmaceutical companies.
[At Prescient Health Group]

by

Dr Khushboo Tyagi

MBA Hospital and Health Management

2020-2022

Acknowledgement

I am glad for the accomplishment of my summer internship job to the lord Almighty and my family whose support and blessings were with me during every moment of my life.

Ms. Rachna Kamra (Associate Director), Ramandeep Singh (Global Travel Manager), and Marselia Tan (Manager, Primary Research Centre UK) deserve my appreciation for giving me the chance to learn and grow professionally. I am grateful for the ability to share my ideas and the trust that was bestowed upon me. I'd want to express my thanks to the entire Prescient Health Organization team in Gurgaon. I'd like to convey my heartfelt appreciation to my academic mentor, Dr. Neetu Purohit of IIHMR University in Jaipur, Rajasthan, for providing me with invaluable advice in completing my work.

I am grateful to her for giving me with direction at all phases of the project and assisting me in completing it.

For the training and learning, I am grateful to everyone of Prescient Health Organization's executive members and employees.

I'd want to express my gratitude to everyone who assisted me in completing this project, both personally and indirectly.

Last but not least, and most significantly, I am grateful to God, who is the originator and director of all the beginning and ultimate means of arriving at one's destination.

Table of contexts:

Prescient Health Organization

Vision & Mission

Biopharma strategy partner and most respected for its client's expertise and beneficial impact. Product and portfolio strategy partner that focuses in turning the science of molecules into optimal patient outcomes and client significance.

Help biopharmaceutical companies to develop launch and market medicine that enlarge treatment options, optimize patient outcomes and deliver high level of return.

Maximize level of clinical and commercial differentiation.

Proprietary cloud-based decision support platform- InflexionRx

That brings the intelligence and associated insight we develop alive. It allows our clients to quickly evaluate if any changes to the situation analysis impact their functional strategy, run analysis that meets their specific decision-making need, download visually impactful analysis into PowerPoint and share notions and thoughts with their teammates in a highly secure environment.

InflexionRx helps you travel the journey from insight to strategy in a timely, aligned and assured manner.

Observational Learning:

- Second secondary research based on drugs manufactured by biopharmaceutical companies for the cure of Breast Cancer.

- Comparative Benchmarking for Biogen Emerging Mechanisms of Action in Immunology.

- IRx training: Prescient's patented software programme, InflexionRx, is a one-of-a-kind cloud-based decision support platform that allows clients to embed dynamic and integrated planning processes. This dynamic decision support system introduces a new way of interacting with intelligence and insight while employing best practises to help you make better decisions.

- IRx confluence and client meeting request

- Part of Virtual ASCO Conference 2021.

Objective:

To know about different drugs that are launched and marketed by Bio pharmaceutical
companies for the treatment of Breast Cancer.

Methodology:

- It is a review-based study.
- Variety of drugs manufactured by bio-pharmaceutical companies for the treatment of breast cancer: variety of articles, research paper, conferences, available public domain data from organization websites and relevant sources document of last five years was thoroughly reviewed.
- **Keywords:** Breast cancer, Metastatic, HR+/HER2, Triple - Negative Carcinoma (TNBC), Hormone receptor.

Breast cancer

Breast cancer is still one of widespread cancer in females worldwide, and a prominent source of cancer mortality in females. Carcinoma affects males, although at a far lesser incidence than it affects women. Cancer can start in the ducts, lobules (produce milk)

Treatment has progressed dramatically in previous years, aided by research.

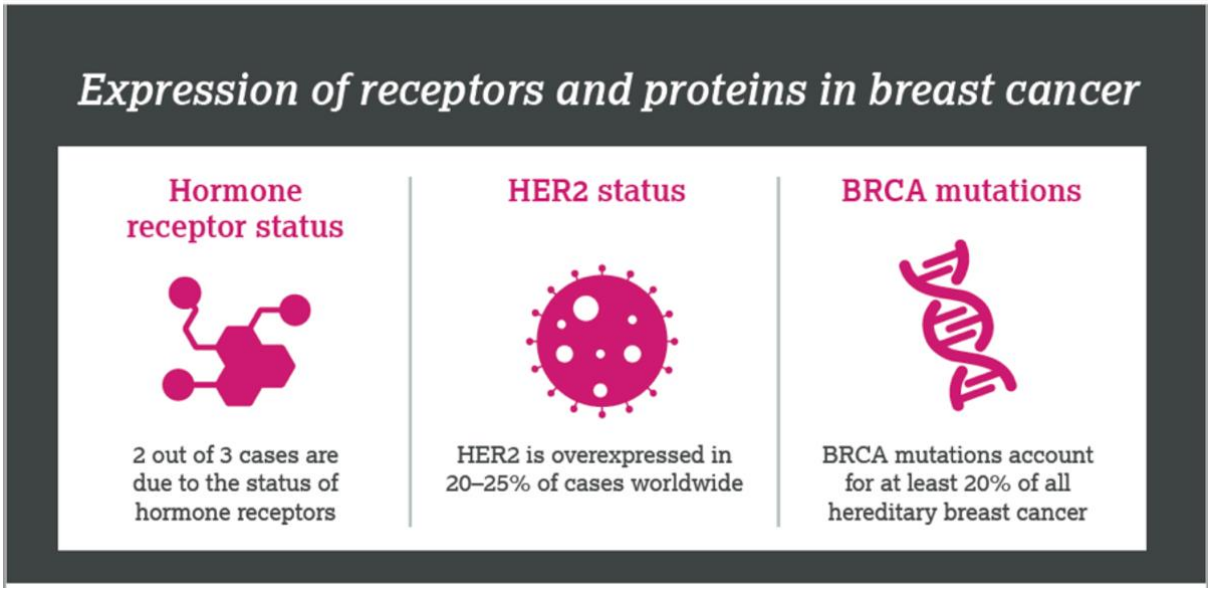
Mastectomy (removal of the whole breast) and chemotherapy, innovations in screening and diagnosis, such as mammography, better understanding of the disease, have considerably enhanced the survival rate of patients including carcinoma.

It is currently recognized as one of the most physiologically varied tumor forms, with a variety of variables contributing to its genesis.

We can categorize and cure breast cancer patients based on hormone receptor or HER2 expression, together with whether or not they have a BRCA mutation. Capacity to design viable treatments for brand spanking new subtypes of patients will improve as our understanding of the numerous variables that drive carcinoma develops.

Classification of Breast Cncer.

This is important to detect key receptors or proteins which will drive tumor growth in order to establish the simplest management method for carcinoma. The way the carcinoma is evaluated is determined by receptors/proteins.



Hormone receptors are used to classify breast cancer.

Hormones are implicated in the formation of malignant tissue in the breasts since they are the driving force behind breast tissue growth. Female breast tissue proliferates and grows during puberty, when hormone stimulation causes cellular differentiation.

The hormones steroid, oestrogen, and progesterone, which behave as "master regulators" of breast growth, have a substantial impact on puberty changes.

By attaching to cellular receptors, the two steroid hormones work together to stimulate growth. Unfortunately, cancer cells that feed themselves with oestrogen and progesterone undermine this precise process.

Oestrogen receptors and progesterone receptors Hormones' role in carcinoma has long been known, and as a result, hormone therapies were among the first drugs created specifically for carcinoma. These drugs function by inhibiting disease causing cells to utilizing estrogen or progesterone in several approaches.

Oestrogen receptors are more common comparatively than progesterone ones, accounting for over 80% of all occurrences of hormone-dependent and estrogen receptor-positive breast cancer. Because oestrogen receptor-negative/progesterone receptor-positive cancers are so rare, medications that target oestrogen-related pathways are often overlooked.

The ER signaling cascade is disturbed when the oestrogen receptor is destroyed, robbing cancer cells of their ability to use oestrogen.

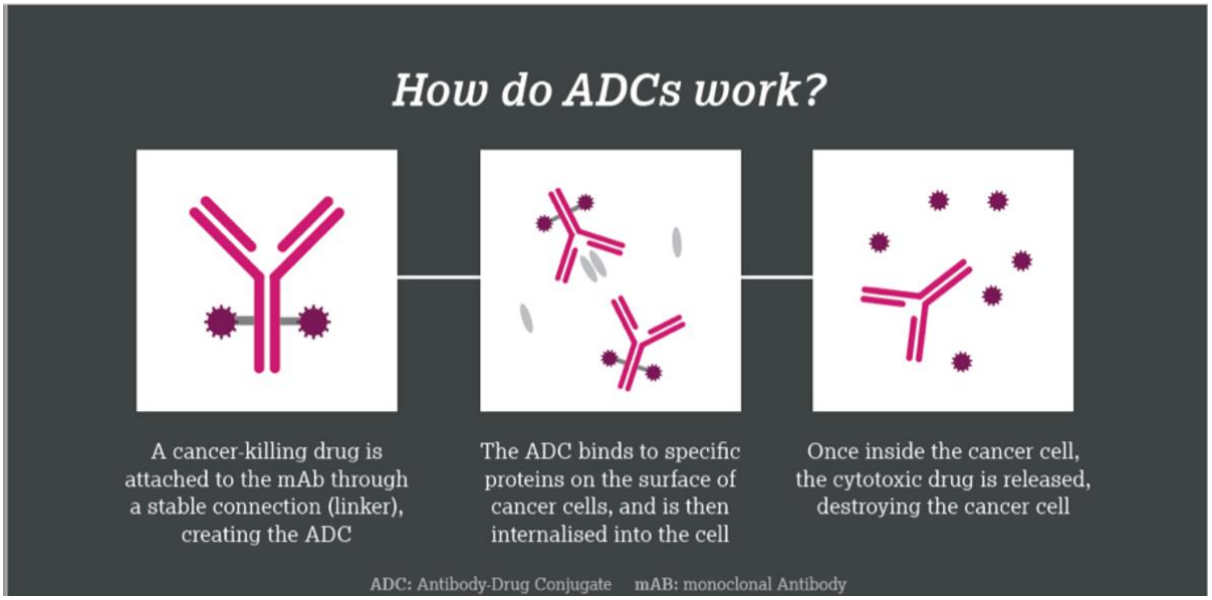
It is often used to treat SERDs when a tumour has grown to different areas of the body, and it is gradually utilised in combination with alternative treatments to surmount endocrine endurance.

The option available drugs for HR+ breast cancer has expanded dramatically in recent years. However, improvement scope is there. Attempting to profoundly alter the life expectancy of girls with HR+ illness.

HER2 receptors are used to classify breast cancer.

When the HER2 gene or protein is overexpressed in carcinoma cells, it promotes excessive neoplastic cell growth and proliferation.

High levels of HER2 protein expression have been linked to severe diseases, a high rate of recurrence, and an increased risk of mortality in roughly 20% of breast cancers.



Although HER2+ carcinoma has traditionally been linked with a poor prognosis, this has changed dramatically.

ADCs are made up of two disease battling drugs: 1 with a cyto-toxic component called as the chemical treatment or payload, and the other with a linker that joins an antibody and a cytotoxic substance (this links to a chosen cancer cell target). This enables for the extremely precise delivery of a known lethal agent with poor cancer cell selectivity into the somatic cell, which might potentially ignite regular cells.

Breast cancer that is triple-negative is known as triple-negative carcinoma (TNBC)

TNBCs are classified as "negative" for all three because they lack oestrogen receptors, progesterone receptors, and significant levels of HER2 overexpression. TNBC is more frequent in women under 40, accounting for 10-15% of all breast cancer cases. This type of carcinoma is recognized as highly

volatile and rapid-increasing, with a high-level threat of metastasis, and it is, sadly, more expected than other types of breast cancer to relapse following treatment.

The role of TNBC in directing therapy alternatives: The quantity of therapy alternatives accessible for TNBC is considerably lesser than for other types of disease due to absence of established biomarker target. like the majority of breast cancer patients

BRCA mutations are used to classify breast cancer.

Thanks to breakthroughs in genomics, further markers for cancer have been discovered, particularly the 2 BRCA genes.

The 2-BRCA genes are regarded as "tumour suppressors" because they restore DNA damage by Damage Response, it's worth noting that DDR contains PARPs (Poly (ADP-Ribose) Polymerases), which are a type of enzyme that aids in damage repair via a different method.

A BRCA gene are mutate, they lose their ability to operate, raising the probability of cancer. A woman who carries the BRCA1 or BRCA2 gene has risk of developing cancer by age of 80.

Steering therapy options is as follows: Defective BRCA genes result in dysfunctional HRR pathways at the cellular level, forcing the cell to rely on alternate routes to survive. Targeted therapy is commonly used to take advantage of this. PARP inhibitors bind to the PARP enzyme and block it from repairing single-stranded DNA breaks. As a result, the number of double-stranded DNA breaks rises, which the HRR pathway cannot fix. The cell must therefore rely on

a less reliable and error-prone backup system, which causes DNA damage to surpass the tolerated limit, leading in neoplastic cell death.

Metastatic carcinoma

Breast cancer spreads to other portions of the body is categorized as MBC, or advanced or stage IV carcinoma.

Cancer can spread to the bones, lungs, liver, and brain, among other places.

A number of factors influence treatment for metastatic carcinoma, including past medication record, menopausal condition, HR and HER2 condition, and the disease's location.

The following are some facts concerning metastatic breast cancer:

• Between 20% and 30% of persons who are detected with initial-stage cancer build metastatic carcinoma.

• Metastatic carcinoma can develop even after preliminary diagnosis of initial cancer, therapy and routine go after appointments with one’s physician.

• Men & women of various ages are frequently diagnosed with metastatic cancer.

• MBC is the first cancer diagnosis in about 6% to 10% of metastatic carcinoma patients. De novo metastatic carcinoma is a word utilized to refer to this kind of cancer.

• There are several types of metastatic carcinoma. HR+, HER2– metastatic carcinoma is the most prevalent subtype, accounting for about 60% of all cases.

Treatment options for HR+& HER2– metastatic carcinoma

When talking with your doctor about treatment options for metastatic carcinoma, keep in mind that you have a lot of options, but the one you choose will be depending on several patient and tumour factors, such as HR or HER2 status.

Options for systemic therapy include:

Systemic treatment is used to treat the majority of metastatic carcinomas. Systemic treatment works by reaching malignant cells all across the body through the circulation. Both malignant and non-cancerous cells benefit from these therapies. Different systemic therapies are sometimes used in conjunction with one another.

The following are examples of systemic treatments:

• Hormonal therapy
• Chemotherapy
• Targeted treatments/chemotherapy, such as Verzonia(drug)

Treatment options available in your area include:

Local treatments, such as surgery or radiation, may be used to help prevent or cure metastatic cancer symptoms.

- **Bio pharmaceutical company and ongoing research about their breast cancer drugs:**

Company Name	Project	Product
Novartis	Breast cancer	Ribociclib (Kisqali), Alpelisib (Piqray)
Eli Lilly & Co.	Breast Cancer	Abemaciclib (Verzenio), LY3484356

Merus	Breast Cancer	Zenocutuzumab (MCLA-128)
Roche	Breast Cancer	Trastuzumab (Kadcycla), Pertuzumab (Perjeta), trastruzumab/pertuzumab FDC (Phesgo
G1 Therapeutics	Breast Cancer	Rintodestrant [BC]
MacroGenics	Breast Cancer	Margetuximab (Margenza) [BC]
Pfizer	Breast Cancer	Palbociclib (Ibrance) [BC]
AstraZeneca	Breast Cancer	Trastuzumab deruxtecan (Enhertu) [BC]
Gilead	Breast Cancer	Sacituzumab govitecan-hziy (Trodelvy) [BC]

NOVARTIS

NOVARTIS ONCOLOGY

Novartis is pushing the boundaries of innovation with bold science, seeking to rework lives, and striving toward cures for patients.

For quite 30 years, Novartis priority has been to deliver targeted therapies to rework lives and extend survival for people living with carcinoma as we work towards a cure.

Novartis bold approach to research has led to unparallel clinical data for women with metastatic carcinoma and precision medicine for patients who face a worst prognosis and poor outcomes.

a) Ribociclib (Kisqali)

Indications:

KISQALI (ribociclib) could even be a kinase inhibitor indicated together :

• As an preliminary endocrine-centered treatment, an aromatase inhibitor for therapy of hormone receptor (HR)-positive, human epidermal protein receptor 2 (HER2)-negative improved or metastatic cancer in pre/perimenopausal or postmenopausal females.

• Fulvestrant, for postmenopausal females with HR-positive, HER2-negative improved or metastatic cancer, an preliminary endocrine-centered treatment or as a follow-up.

In endocrine therapies for premenopausal or postmenopausal women with hormone receptors, the combination of KISQALI (ribocclib) and FEMARA (letrozole) has been reported to be the first therapy for HER2-negative enhanced or metastatic cancer.up to endocrine therapy.

IMPORTANT PROTECTION INFORMATION

Pneumonitis is a kind of interstitial lung disease. Patients using KISQALI and other CDK4/6 inhibitors may develop life-threatening, severe interstitial lung disease and pneumonitis.

Unfavorable Medicine Effects.

• Stevens-Johnson syndrome (SJS)

• Toxic epidermal necrolysis (TEN)

• Drug-induced hypersensitivity syndrome

• Neutropenia (most frequent adverse drug reaction)

Because SCARs have been confirmed, KISQALI will be permanently discontinued.

Toxicity of the hepatobiliary system. Increases in transaminases have been reported in individuals with advanced or metastatic cancer throughout clinical studies. Three and four-grade increases in alanine aminotransferase.

Adverse reactions. In advanced or metastatic carcinoma, Neutropenia > nausea >infection > tiredness > diarrhoea > leuchopenia > diarrhoea > leuchopenia . Among the most common ARs observed in patient clinical trials in the KISQALI therapy groups (potted incidence /20 percent). (21 percent v/s 16 percent). Frequent grade 3/4 ARs (registered at collective frequencies >5%) were neutropenia (59 percent v/s 1), leukopenia (16 percent v/s 3), anomalous LFTs (9 percent v/s 2), and lymphopenia (5 percent v/s 1).

b) Alpelisib (Piqray)

Indication

PIQRAY pills are used to treat hormone receptor (HR)-positive, human epidermal protein receptor 2 (HEPR2)-negative, PIK3CA-mutated advanced or metastatic cancer in postmenopausal women and men who have progressed on or later an endocrine-based regimen.

Vital Protection Warnings

PIQRAY is not recommended for people who have severe Thereto Hypersensitivity.

anaphylaxis, and anaphylaxis, which can arise in PIQRAY-treated patients. Dyspnea, flust, rash, fever, and tachycardia were among the most common hypersensitivity reactions, although they were not the only ones. Hypersensitivity was found to be present in 0.7 percent of students in the third and fourth grades.

ADVERSE DRUG REACTIONS WITH SEVERE ACUTE REACTIONS (SCARs)

- Stevens-Johnson syndrome (SJS)
- Toxic epidermal necrolysis (TEN)
- Drug-induced hypersensitivity syndrome (DIHS) /drug response with eosinophilia and systemic symptoms

SJS (0.4%) and EM (1.1%) were found in total number of participants.SOLAR-1 study. Hyperglycemia affected 65 percent of patients, ketoacidosis affected 0.7 percent, and pneumonitis affected 1.8 percent of PIQRAY patients.

ADR's

Diarrheas (58%), rashes (52%), nausea (45%), tiredness (42%), reduced hunger (30%), stomatite (30%), vomiting (27%), lower weight (27%), and allopia are the most prevalent side events (all grades, occurrence by 20 percent) (20 percent). Rashes (20%), diarrhoea (7%), tiredness (5%), weight losses (3.9%), nausea (2.5%), stomatitis (2.5%) and mucosal inflammation were the most prevalent adverse event of grade ¾ adverse reaction.

2. ELI LILLY & Co.

Lilly Pharma:

Since its inception in 1993, Eli Lilly & Company (India) Private Limited has been dedicated to producing and selling pharmaceutical medicines to treat diabetes, cancer, osteoporosis, atrophic arthritis, men's health, and growth hormone insufficiency in India. Lilly India now has activities in Bangladesh and Sri Lanka, two adjacent nations.

a) Abemaciclib (Verzenio)

Verzonia also mentioned as abemaciclib. Verzenio could even be a prescription wont to treat a kind of carcinoma.

It is a drug you'll take if:

- Your cancer has grown to other portions of your body and is HR+/HER2– (hormone receptor positive/human epidermal protein receptor 2–negative) (metastasized).

- Verzenio is used as an preliminary endocrine-based treatment in postmenopausal females in arrangement with fulvestrant in females whose disease has advanced following hormone treatment or in adults who progress from hormone therapy to prior chemotherapy in other circumstances.

Verzonia has the following side effects:

• Low RBC (Anemia)
• Low WBC (Leukopenia)
• Loss of appetite.
• Nausea
• Nuisance
• Platelet count is lower (Thrombocytopenia)
• Hair thinning or loss (aloepecia)

These are not the only negative effects of Verzonia.

b) LY3484356

The major treatment target for the most frequent carcinoma (BC) subtype impacting patients globally is the oestrogen receptor (ER). New ER degraders and antagonists are

being tested to circumvent both ER-mediated resistance and the bioavailability and dose constraints of fulvestrant (fulv), the only SERD approved.

ER may be overexpressed in about 80% of endometroid endometrial cancers, and endocrine treatment (ET) is the standard of care (SOC) for the illness, while no ER-driven therapy is officially licenced in this circumstance. It could be a completely different SERD with pure antagonistic features that are orally available and result in long-term suppression.

In preclinical studies, LY3484356 monotherapy demonstrated good efficacy and pharmacokinetic features, including anticancer activity in ESR1 mutants, as well as improved antitumor efficacy when coupled with abemaciclib, everolimus, or alpelisib.

In this study, women with ER+ advanced BC and ER+ endometroid endometrial carcinoma receive LY3484356 alone or in combination with existing SOC anticancer treatments.

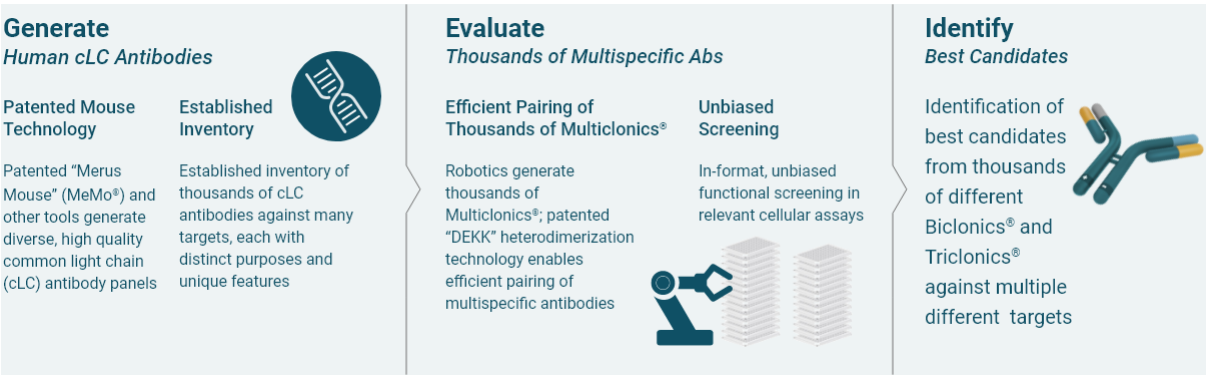
3. Merus

The candidates within the Merus pipeline are supported the Multiclonics format. The employed staretegy attributes of bispecific antibodies and screening technologies to interact and harness the power to differentiate tumour cells.

Zenocutuzomab (Zeno, MCLA-128)

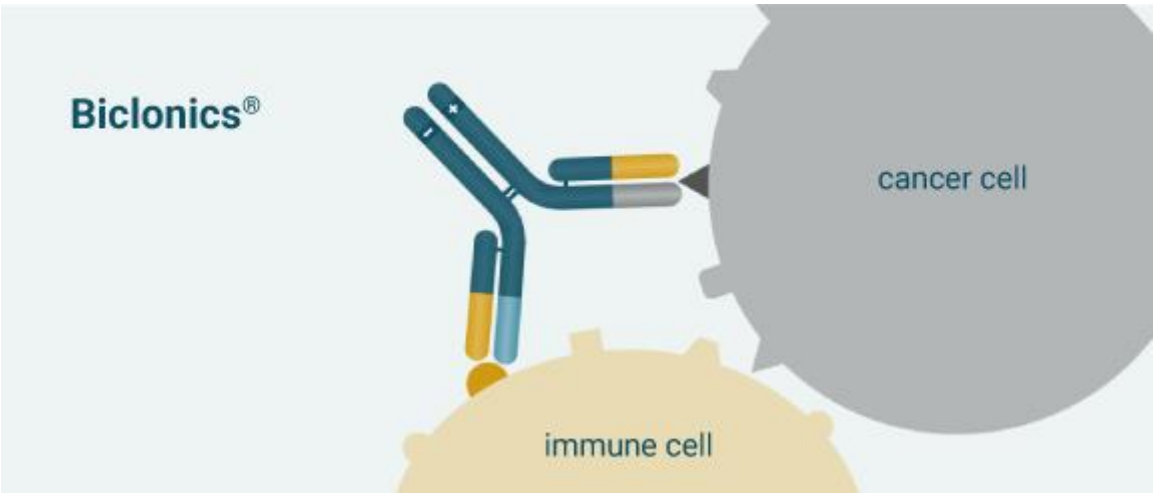
Multiclonics shown to retain qualities of natural human, full-length immunoglobulin antibodies, including stability, long half-life.

Functional screening in molecular and cell-based assays to spot novel, innovative Biclonics and Triclonics antibodies. Lead molecules selected from thousands of candidates generated from the platforms, identifying those molecules that possess the different biology and specific characteristics for therapeutic use.

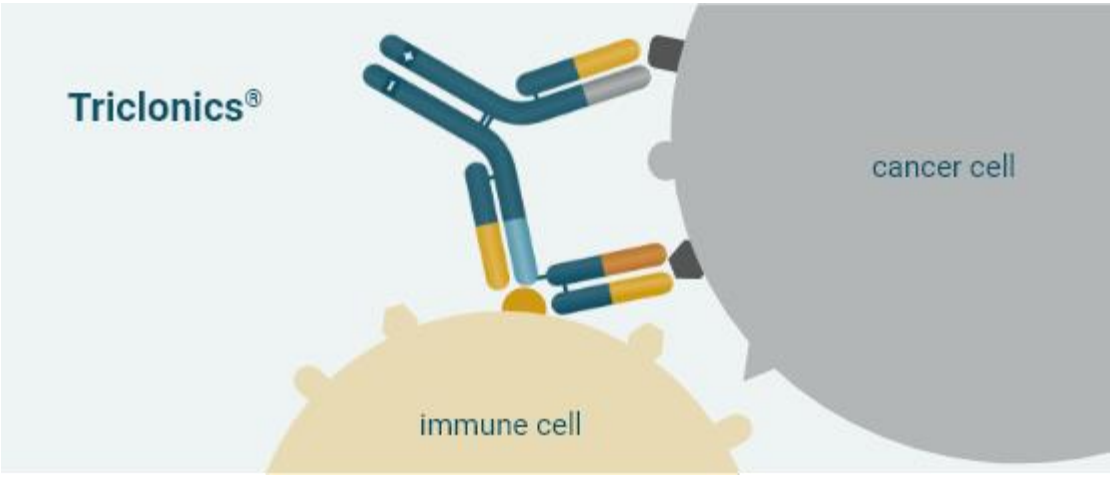


Example of Biclonics platform is zenocutuzomab , It utilizes Dock & Block mechanism to bind to HER2 and disrupt the bond between HER3 and its ligand, NRG1. As with Biclonics, Zeno features full length IgG antibody format for tolerance, simple administration and long half-life for dosing schedules.

Biclonics different from other bispecific antibody formats because they do not require to force correct pairing of heavy and lightweight chains, nor do they require fusion proteins to add functions.



Triclonics have a singular antibody design capable of simultaneously binding three targets directly . Triclonics have the potential to enable tumour cell-killing activity and/or to modulate the system to market more robust and specific anti-tumour immune responses.



Zeno is a Biclonics targeting the HER3 pathway. Zeno docks expressed on tumor cells, and subsequently binds to HER3, blocking stimulated growth of

tumor cells. Zeno is meant to beat tumor cells inherent and purchased resistance to HER2-targeted therapies by both blocking tumor growth, survival pathways and recruiting immune effector cells to assist eliminate tumours.

NRG1 fusions are related to the activation of HER2/HER3 heterodimers and neoplastic cell growth. Merus has observed that Zeno is capable of blocking tumour cell growth harbouring NRG1 fusions.

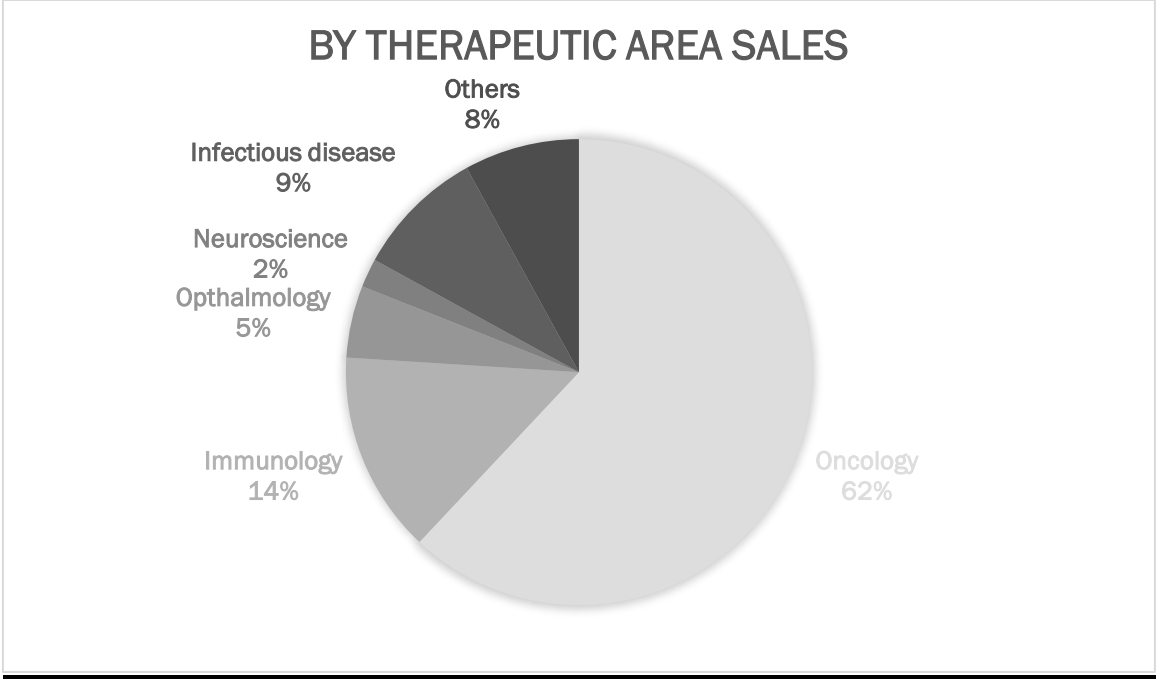
MCLA-128 is the Humanized bispecific antibody ADCC-enhanced targeting HER2 and HER3 and powerfully inhibiting the receptor dimerization produced by HER3 ligands. Upregulation of the Her2:Her3 pathway may be a mechanism of resistance to ET in HR+ carcinoma, implying a function for MCLA-128. In preclinical investigations, the combination of MCLA-128 and ET outperformed single medication treatments in carcinoma xenografts. The current study investigates the use of MCLA-128 to release platelets from ET-resistant MBC that has progressed on a CDK4/6i.

4.ROCHE

Roche is a leader in research-driven healthcare, with expertise in both drugs and diagnostics. Roche is the largest biotechnology corporation in the world, with extremely distinctive treatments in oncology, immunology, infectious disorders, and neurology.

Roche is well-known for its Corporate Governance and Sustainability efforts. Roche is also a market leader in diabetes treatment and a global pioneer in in vitro diagnostics and tissue-based cancer diagnostics.

Roche Pharma, which has a presence in over 150 countries, Genentech, and Chugai, which has the largest stake in Japan, make up the Pharmaceuticals division used in the production of eight of Roche's ten best-selling pharmaceuticals.



a) Kadcyla (trastuzumab emtansine)

It's a strong antibody-drug intended to provide chemotherapy to HER2 Cancer cells while limiting damage near healthy tissues. Two anti-cancer qualities linked together by a stable linker in it, as well as trastuzumab's HER2-targeting properties and hence chemotherapeutic drug DM1.

In over 100 countries, including the U.S and Europe. Kadcyla is approved as a single therapy for breast cancer patients which had earlier had Herceptin and taxane-based chemotherapy, either separately or together.

Kadcyla is also approved for adjuvant (post-surgery) therapy in persons with HER2-positive early cancer with resistance in the United States and the European Union.

b) Pertuzumab and trastuzumab:

Trastuzumab, a HER2-targeted antibody, was first used in clinical trials and completely changed the way HER2-positive cancer patients were treated. Despite this breakthrough, many patients together with HER2-positive Metastatic Cancer continue on the way to advance, underlining need for fresh new medicines.

Pertuzumab is the first in innovative category of medications identified as HER dimerization inhibitors, it was created in response to the growing demand for novel targeted therapies. Pertuzumab is a humanised recombinant antibody that targets the HER2 protein's extracellular domain II, which is required for HER2 to heterodimerize with other HER receptors and activate them.

As a result, signalling pathways downstream are engaged. Pertuzumab with trastuzumab plus docetaxel was authorized for the primary choice treatment of patients with HER2-positive metastatic cancer and has since become the standard of care.

5. G1 Therapeutics:

G1 has 2 new treatments for having cancer patients. Trilaciclib is an experimental treatment that aims to reduce chemotherapy-induced myelosuppression in cancer patients. Rintodestrant is an ER+ breast cancer therapy that is a selective oestrogen receptor degrader (SERD).

Rintodestrant

Rintodestrant may also be a powerful oral selective oestrogen receptor degrader that binds to the oestrogen receptor competitively and inhibits ER signalling in cancers resistant to conventional therapies. In patients with heavily pretreated ER advanced carcinoma (ABC), including those with ESR1 mutations, preliminary results from Part 1 dose escalation showed robust target engagement on F-fluoroestradiol positron emission tomography (FES-PET), a positive safety profile, and inspiring antitumor activity.

Rintodestrant is being developed as a possible best-in-class oral SERD for therapy of oestrogen receptor-positive (ER+) cancer. Rintode has found to be effective in preclinical studies. Preclinical data suggests that rintodestrant is superior to fulvestrant, the only FDA-approved SERD currently on the market. Unlike fulvestrant, which is administered as an injection, rintodestrant has the potential to improve the patient experience dramatically when administered orally.

6.MacroGenics

Macrogenics, a HER2/neu receptor antagonist, has been approved for the medication of adult patients with metastatic HER2-positive cancer who have had twice or additional earlier anti-HER2 regimens in combination with chemotherapy, at minimum one of which was for metastatic disease.

Margetuximab (Margenza) [BC]

Margetuximab is a HER2-directed monoclonal antibody with Fc engineering. Margetuximab-cmkb decreases tumour cell proliferation, diminishes When attached to HER2-expressing tumour cells, the extracellular domain of HER2 sheds and induces antibody-reliant cellular cytotoxicity.

In vitro, the mutated Fc region enhanced triggering Fc receptor FCGR3A binding and decreased inhibitory Fc receptor FCGR2B binding. In vitro, there was a higher increase in antibody-reliant cellular cytoxicity and NK cell stimulation after these alterations. In vitro data does not have any clinical consequences.

Clinical Development and Research

In first-line individual with superior HER2-positive gastric or gastroesophageal junction cancer, margetuximab combined with a checkpoint inhibitor (retifanlimab or tebotelimab) with or without chemotherapy is now being considered.

In HER2+ solid tumours, margetuximab is being tested in combination with tebotelimab (NCT03219268).

Adverse Drug Reactions:

• Fatigue (57 percent)

• Nausea and vomiting (33 percent)

• Constipation (25 percent),

• Nausea and vomiting (21 percent)

• Irritable bowel syndrome (19 percent)

• You have a headache (19 percent)

• Pyrexia is a term that refers to a condition (19 percent)

• Alopecia areata (18 percent)

• Pain in the abdomen (17 percent)

• Peripheral neuropathy is a condition that affects the peripheral nerves (16 percent)

• Myalgia/arthralgia (14 percent)

• A coughing fit (14 percent)

• Loss of appetite (14 percent)

• Dyspnea (shortness of breath) (13 percent)

• Reactions to infusions (13 percent)

• Erythrodysesthesia of the palms and soles (13 percent)

• Severe discomfort (11 percent).

7. Pfizer

One of the world's leading biopharmaceutical businesses produces immunology, cancer, cardiology, endocrinology, and neurology medicines and vaccines.

Pfizer experts have generated important discoveries in the fields of depression, male erectile dysfunction, excessive cholesterol, HIV infection, hypertension, bacterial infections, and systemic fungal infections, to name a few. Pfizer is now concentrating its efforts on a number of the world's most serious diseases, including cancer, arthritis, and osteoporosis.

Palbocicli (Ibrance)

IBRANCE is the first medicine in its class to be authorised by the FDA. IBRANCE is a CDK 4/6 inhibitor, which is a type of targeted therapy. This isn't your typical chemotherapy. IBRANCE, when combined with certain hormone therapy, works to slow down cell proliferation in healthy and malignant cells.

This will in reduction of growth of cancer, but can also have negative side effects & some of them are dangerous:

Neutropenia is a condition in which the body's immune system (Low white blood cell counts)

- Pneumonitis
- Suffer from liver/kidney disease.
- Low red blood corpuscle numbers and low platelet counts
- IBRANCE can harm your unborn child or pregnant women.
- Low platelet counts and red blood corpuscle numbers

- Headaches, dizziness, and shortness of breath

• Easier bruising or bleeding

• bacterial infections

• exhaustion

• a feeling of sickness

• a sore throat

• abnormalities in blood tests for the liver

• diarrhoea diarrhoea diarrhoea di

• baldness or thinning hair

• nausea and vomiting

• hives

• a decrease in appetite

• In males, IBRANCE may cause reproductive issues. These aren't all of IBRANCE's possible negative effects.

IBRANCE stands for hormone positive receptor (HR +), also known as human epidermal growth factor receptor, and it's a drug that's used to treat metastatic breast cancer (MBC).

HR+/HER2-

HR+/HER2-

Hormone receptors are positive. Oestrogen receptor-positive and progesterone receptor-positive groups You're more likely to respond to hormone therapy that limits the effects of hormones, such as an aromatase inhibitor or fulvestrant, if your subtype is ER+ and/or PR+.

Your cancer cells express less HER2 protein if you have the HER2- subtype, and probability of response are slim to anti-HER2 therapy.
The most common subtype of HR+, HER2-metastatic breast cancer is HR+, HER2-metastatic breast cancer.
IBRANCE is the first medicine in its class to be authorised by the FDA. IBRANCE is a CDK 4/6 inhibitor, which is a type of targeted therapy. This isn't your typical chemotherapy. IBRANCE, in combination with other hormone therapy, helps to inhibit the formation of cells in both healthy and malignant cells.

8. AstraZeneca

It is a global biopharmaceutical firm that develops, manufactures, and markets prescription medicines for the treatment of oncology, cardiology, renal and metabolic diseases, and respiratory diseases in three therapeutic categories. AstraZeneca has a presence in over 100 countries, and its pharmaceuticals are used by millions of people around the world.

AstraZeneca's oncology division:

AstraZeneca has a long history in oncology, and it today provides a rapidly developing portfolio of novel pharmaceutical therapies with the ability to renovate patients' life expectancy and, as a result, their futures. AstraZeneca is dedicated to enhancing oncology as a factor, with a focus on lung, ovarian, breast, and blood malignancies.

AstraZeneca's mission is to revolutionise cancer therapy and to wipe out cancer as a reason of fatality in near future.

Trastuzumab deruxtecan (Enhertu)

Enhertu is authorized for adult patients with unresectable or metastatic HER2-positive cancer who have had twice or additional prior anti-HER2 centered treatments in the metastatic positioning.
HER2 is a protein that plays a role in (Human Epidermal Growth Factor 2) HER2, a growth-promoting tyrosine kinase receptor found on the surface of certain cancer cells, has been related to severe disease and a bad prognosis in carcinoma patients. One of two ways for determining whether tumour cancer cells are HER2-positive is immunohistochemistry (IHC) or fluorescence in place hybridisation (FISH) (FISH). An IHC test's results are categorised as 0, IHC 1+, IHC 2+, or IHC 3+. An IHC 3+ and/or FISH amplification result that is positive.

The Phase 2 clinical study's confirmed objective response rate was 60.3 percent, including a 4.3% total response frequency and a 56.0% fractional response frequency.

In a pooled review of data from both the phase II clinical trial DESTINY-Breast01 and previous phase I clinical trial research, 234 patients with metastatic HER2-positive cancer who got at least one dosage of Enhertu, 5.4mg/kg, were assessed.

The most common side effects included nausea, tiredness, vomiting, baldness, and diarrhoea (had by more than or equal to 20 percent of patients).

Pneumonitis struck 9% of the patients. Pneumonitis claimed the lives of six people (2.6%), with two of them dying.

9. Gilead Sciences

For nearly three decades, Gilead Sciences, Inc. has been developing medical breakthroughs with the goal of making the world a healthier place for everyone. Drugs to avert and cure diseases like HIV, hepatitis, and tumor are among the company's top priorities. Gilead operates in 35 countries throughout the globe**.**

Trodelvy.

Gilead Sciences,Inc. has announced the complete approval for Trodelvy by FDA for adult patients receiving two or more prior systemic treatments for metastatic illness with TNAC. The approval is supported by Phase Three ASCENT data in which Trodelvy has shown a 57% decrease in the probability of a disease or death that is statistically significant and clinically significant.

The indication of trodelvy involves therapy of patients who have received two or more previous systemic treatments with unresectable, locally progressed or metastatic TNBC, including at minimum one for metastatic illness.

The ASCENT Research Project

Nearly 500 patients with relapsed/refractory metastatic TNBC who had received twice or additional earlier systemic therapies (including a taxane), at minimum one for metastatic disease, were included in the Phase 3 ASCENT trial, which was an open-label, randomised confirmatory trial. Trodelvy or a chemotherapy regimen suggested by their doctors were given to patients at random.

Important Safety Information:

- Neutropenia & Diarrhea
- Hypersensitivity and Infusion-Related Reactions
- Nausea and Vomiting
- Embryo-Fetal Toxicity

Conclusion:

- Breast cancer is a serious threat, especially in underdeveloped countries like India.

- ELI LILLY & Co. manufacture drug (Verzonia) which is indicated for HR+/HER2-. Roche manufacture drug (Kadcyla) for HR+/HER2- advanced breast cancer who have previously received Herceptin and taxane-based chemotherapy, either separately or together.

- AstraZenca (Enhertu) for the treatment of adult patients with unresectable or metastatic HER2 negative/positive carcinoma who have received two or more prior anti-HER2 based regimens within the metastatic setting.

- Amongst all these biopharmaceutical companies Gilead Sciences (Trodelvy) is the only one indicated for TNAC. Trodelvy by adult patients receiving

two or more prior systemic treatments for metastatic illness with locally advanced or metastatic triple negativity carcinoma (TNAC).

- Main goal is to cure cancer patients or prolong their life considerably, ensuring a good quality of life. To discover, develop and deliver innovative therapeutics for people with life-threatening diseases & to create a healthier world for all people.

- In the fight against breast cancer, screening mammograms are a powerful tool. Mammogram— X-ray pictures of the breast — can help reduce the number of deaths from breast cancer among women ages 40 to 70.

References:

- **ASTRAZENECA - RESEARCH-BASED BIOPHARMACEUTICAL COMPANY**
  - (AstraZeneca - Research-Based BioPharmaceutical Company, 2021)
  - Astrazeneca.com. 2021. *AstraZeneca - Research-Based BioPharmaceutical Company*.
  - [online] Available at: https://www.astrazeneca.com/

- **ANON**
  - Lillyindia.co.in. 2021. [online]
  - Available at: https://www.lillyindia.co.in/

- **CLOSING IN ON CANCER | MERUS**

(Closing in on cancer | Merus, 2021)

Merus. 2021. *Closing in on cancer | Merus*.

[online] Available at: https://merus.nl/

- **DOING NOW WHAT PATIENTS NEED NEXT**
  - (Doing now what patients need next, 2021)
  - Roche.com. 2021. *Doing now what patients need next*.
  - [online] Available at: https://www.roche.com/careers/our-locations/americas/canada/us_ca_doing_now_what_patients_need_next.htm

- **GILEAD SCIENCES, INC.**
  - (Gilead Sciences, Inc., 2021)
  - Gilead.com. 2021. *Gilead Sciences, Inc.*.
  - [online] Available at: https://www.gilead.com/

- **G1 THERAPEUTICS, INC. | TRILACICLIB | LEROCICLIB | G1T48**
  - (G1 Therapeutics, Inc. | trilaciclib | lerociclib | G1T48, 2021)
  - G1therapeutics.com. 2021. *G1 Therapeutics, Inc. | trilaciclib | lerociclib | G1T48*.
  - [online] Available at: https://www.g1therapeutics.com/

- **HOMEPAGE - MACROGENICS**
  - (Homepage - MacroGenics, 2021)

- MacroGenics. 2021. *Homepage - MacroGenics*.
- [online] Available at: https://macrogenics.com/

➢ **NOVARTIS INDIA**

- (Novartis India, 2021)
- Novartis India. 2021. *Novartis India*.
- [online] Available at: https://www.novartis.in/

➢ **PFIZER: ONE OF THE WORLD'S PREMIER BIOPHARMACEUTICAL COMPANIES**

- (Pfizer: One of the world's premier biopharmaceutical companies, 2021)
- Pfizer.com. 2021. *Pfizer: One of the world's premier biopharmaceutical companies*.
- [online] Available at: https://www.pfizer.com/

➢ **PRESCIENT HEALTHCARE GROUP - TURNING SCIENCE INTO VALUE FOR THE BIOPHARMA INDUSTRY**

- (Prescient Healthcare Group - Turning Science into Value for the Biopharma Industry, 2021)
- Prescient Healthcare Group. 2021. *Prescient Healthcare Group - Turning Science into Value for the Biopharma Industry*.
- [online] Available at: https://prescienthg.com/