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A COMPRESSIVE REVIEW OF NEW MEDICINE: ON THE FRONTLINE OF CANCER TREATMENTS

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❖ ABSTRACT

Cancer is one of the most prevalent diseases globally and is the major cause of death. An abstract on cancer therapy usually encapsulates the salient features of oncology research, breakthroughs, or therapeutic approaches. It summarizes the goals, approaches, findings, and recommendations of research or reviews pertaining to cancer care. Topics include immunotherapy, radiation therapy, chemotherapy, targeted therapy, and new treatments may be included in the abstract. It functions as a succinct synopsis that offers insights into current developments, obstacles, and trends targeted at enhancing patient outcomes in the fight against cancer. The treatment of brain tumors including glioblastoma multiformes (GBM's) remains a challenge. The main option is still surgery to remove the bulk of tumor and adjuvant treatments for the infiltrating parts. The blood brain barrier (BBB), however, restricts the access of chemotherapeutic agents to the tumor.

❖ **KEYWORDS:** Cancer therapy, Chemotherapy, Targeted therapy, glioblastoma multiformes.

❖ INTRODUCTION

Cancer is a group of diseases involving abnormal cell growth with the potential to invade or spread to other parts of the body. The disease was first called cancer by Greek. Physician Hippocrates (460-370 BC). He is considered the "Father of Medicine." Hippocrates used the terms carcinos and carcinoma to describe non-ulcer forming and ulcer-forming tumors. In Greek this means a crab. The description was names after the crab because the finger-like spreading projections from a cancer called to mind the shape of a crab.

Cancer is an important health problem in developed countries where is the second cause of death mainly associated with ageing of the population and lifestylecause of death mainly associated with ageing of the population and lifestyle.

❖ Objectives

The objectives of cancer therapy are as follows

- **Cure:** Total destruction of cancer cells in order to bring about a permanent remission or a less full recovery.
- **Control:** Taking steps to stop cancer from spreading, symptoms, and preserve a high standard of living.
- **Palliation:** Providing patients with advanced cancer or those for whom a cure is unattainable with better comfort and symptom relief.
- **Prevention:** Preventing the development of cancer by focusing on precancerous diseases or high-risk individuals.
- **Adjuvant therapy:** It aims to lower the chance of cancer recurrence by improving the efficacy of initial treatments (Such as chemotherapy or surgery).
- **Personalized therapy:** It is the process of designing a course of action based on a patient's preferences, genetic makeup, and tumor features in order to maximize results.
- **Minimal side effects:** Reducing complications and side effects associated with treatment in order to enhance patients' general health.

❖ Types of cancers

Carcinoma – this cancer begins in the skin or in tissues that line or cover internal organs. There are different subtypes, including adenocarcinoma, basal cell carcinoma, squamous cell carcinoma and transitional cell carcinoma.

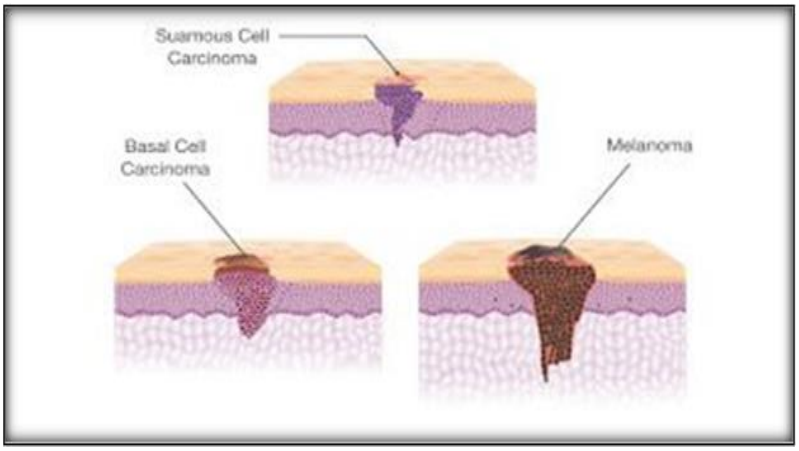

Fig. 1: Carcinoma cancer.

Sarcoma – This cancer begins in the connective or supportive tissues such as bone, cartilage, fat, muscle or blood vessels.

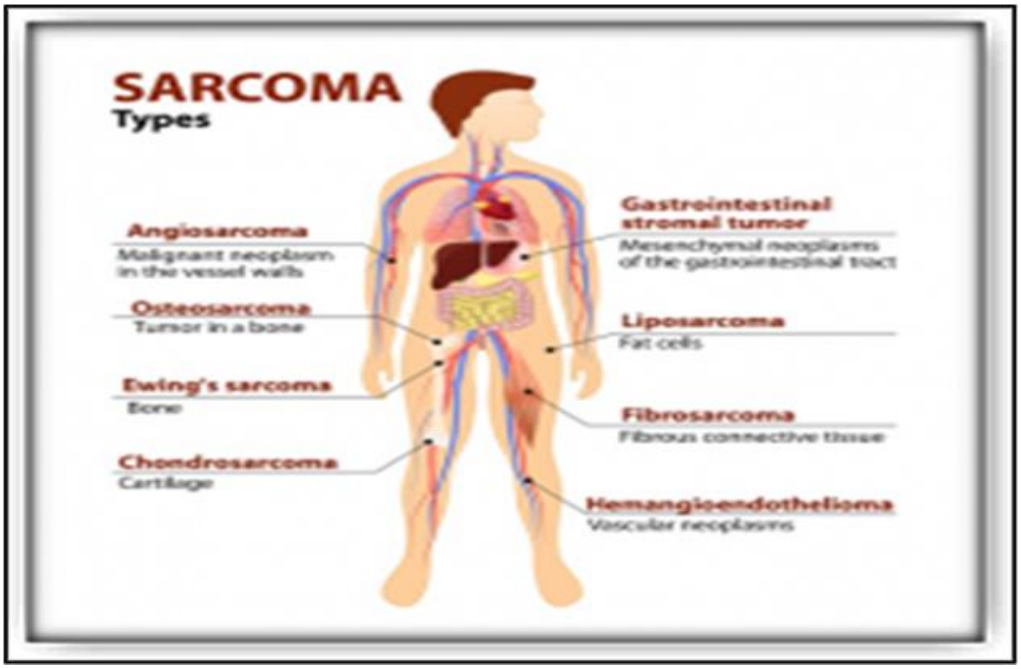

Fig. 2: Sarcoma cancer.

Leukaemia – this is cancer of the white blood cells. It starts in the tissues that make blood cells such as the bone marrow.

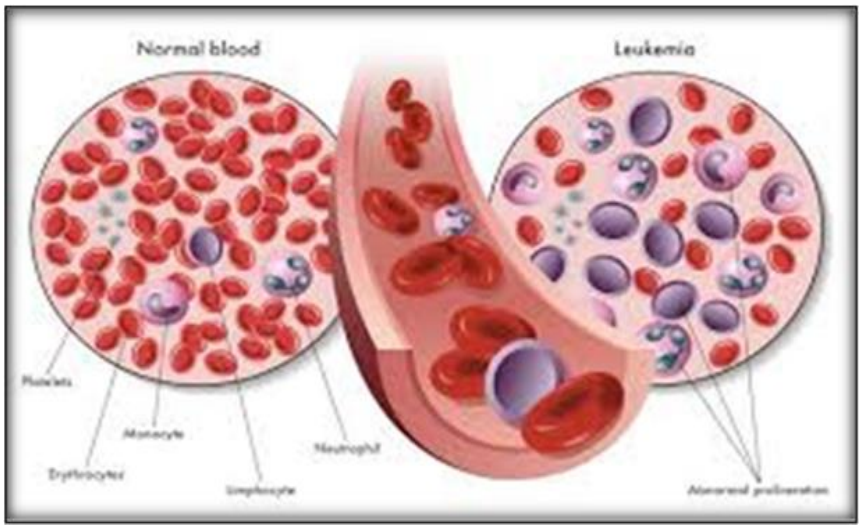

Fig. 3: Leukaemia cancer.

Lymphoma and Myeloma –Lymphomas develop from the cells (Lymphocytes) that makes up the immune system. Myeloma occurs in the cells in the bone marrow, which are responsible for making antibodies.

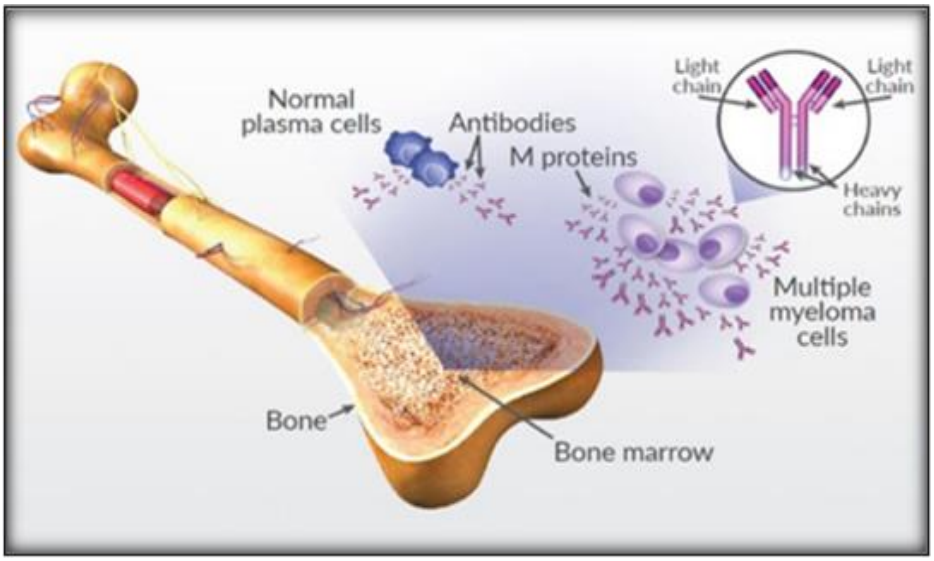

Fig. 4: Lymphoma and Myeloma cancer.

Brain and Spinal cord cancers – It is also known as central nervous system (CNS) Tumors, can be caused by abnormal cells forming in the brain or spinal cord. These cancer can be benign (Non cancerous) or malignant (Cancerous).

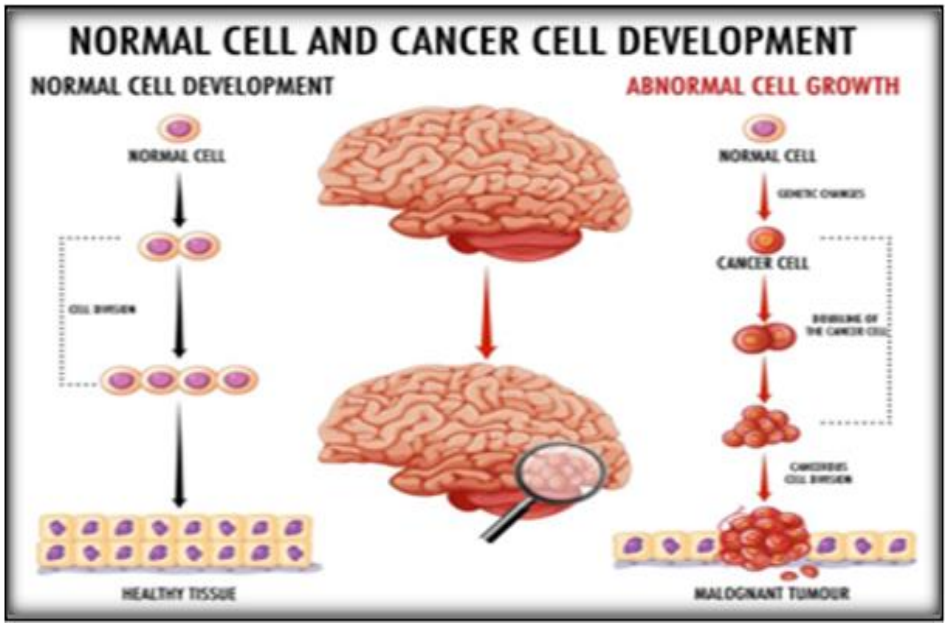

Fig. 5: Brain and Spinal cord cancer.

❖ **Symptoms**

- Fatigue or extreme tiredness that doesn't get better with rest.
- Weight loss or gain of 10 pounds or more for no known reason.
- Eating problems such as not feeling hungry, trouble swallowing, belly pain,or nausea and vomiting

- Swelling or lumps anywhere in the body
- Thickening or lump in the breast or other part of the body
- Pain, especially new or with no known reason, that doesn't go away or gets worse
- Skin changes such as a lump that bleeds or turns scaly, a new mole or a change in a mole, a sore that does not heal, or a yellowish color to the skin or eyes (jaundice).
- Cough or hoarseness that does not go away
- Unusual bleeding or bruising for no known reason
- Change in bowel habits, such as constipation or diarrhea, that doesn't go away or a change in how your stools look
- Bladder changes such as pain when passing urine, blood in the urine or needing to pass urine more or less often
- Fever or nights sweats
- Headaches
- Vision or hearing problems
- Mouth changes such as sores, bleeding, pain, or numbness.

❖ **Treating cancer**

The kind, stage, and location of cancer, in addition to the patient's general condition, all influence the course of cancer treatment.

Typical methods include of

1. **Surgery:** Excising the tumor and relevant tissue.
2. **Radiation therapy:** Targeting and eliminating cancer cells with high-energy radiation.
3. **Chemotherapy:** Drugs used to either eradicate or stop the spread of cancer cell.
4. **Hormone therapy:** Inhibiting or eliminating the hormones that some malignancies use as fuel.
5. **Immunotherapy:** Boosting immunity to combat cancer.
6. **Targeted therapy:** Medications that target cancer cells exclusively while causing the least amount of harm to healthy cells.
7. **Stem cell or bone marrow transplant:** Using healthy cells to replace damaged bone marrow. Customized treatment regimens may incorporate a mix of these technique.

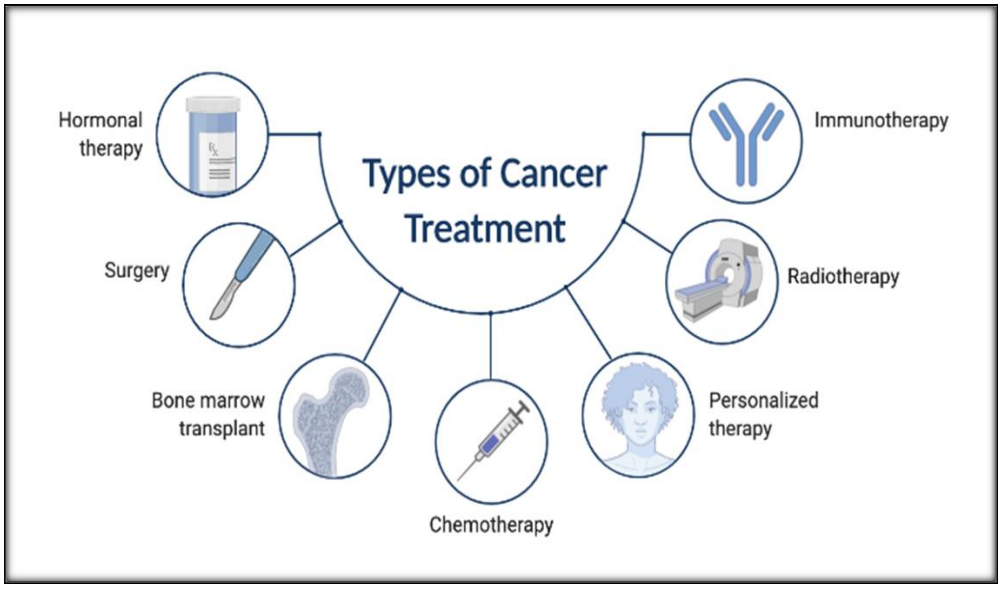

Fig. 6: Treatments of cancer.

❖ **Mechanism of cancer**

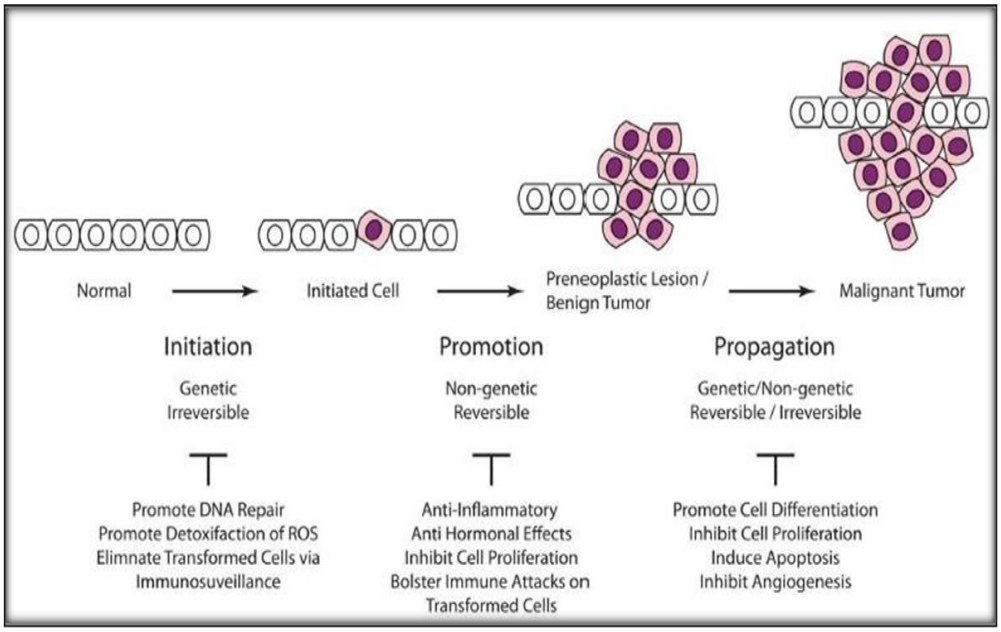

Fig. 7: Mechanism of cancer.

❖ **Novel drugs used in cancer therapy**

1. Tratuzumab deruxtecan

- **Introduction**

Trastuzumab deruxtecan (Brand name Enhertu) is an antibody-drug conjugate used in the treatment of HER2-positive cancers, particularly breast cancer. It combines trastuzumab, a monoclonal antibody that targets the HER2 receptor, with deruxtecan, a cytotoxic chemotherapy agent. This combination allows for targeted delivery of the drug directly to

cancer cells that overexpress HER2, enhancing therapeutic efficacy while minimizing damage to normal tissues.

Trastuzumab deruxtecan has shown promising results in clinical trials, especially for patients who have previously received other HER2-targeted therapies and have progressed in their disease. Its approval has expanded treatment options for advanced breast cancer and other HER2-positive malignancies, improving outcomes for many patients.

- **Features and Properties of trastuzumab deruxtecan**

Alternative Names	DS-8201; DS-8201a; ENHERTU®, fam–trastuzumab deruxtecan; fam-trastuzumab deruxtecanp-nxki;T-DXd
Class	Antineoplastics; Camptothecins; Drug conjugates; Immunoconjugates ; monoclonal antibodies
Target	DNA topoisomerase 1; HER2receptor
Mechanism of action	HER2- directed antibody and DNA topoisomerase 1 inhibitors conjugate
Route of administration	IV infusion
Pharmacodynamics	Multiple- dose administration of trastuzumab deruxtecan 6.4 mg/kgevery 3 weeks (1.2 ×the recommended dosage in HER2- positive metastatic breast cancer) had no clinical relevant effect on the QTc interval in patients with HER2-expressing metastatic breast cancer.
Pharmacokinetics at the recommended dosage in HER2-positive metastatic breast cancer (5.4 mg/kg once every 3 weeks)	Trastuzumab deruxtecan Cmax 122 µg/ml, AUC735µg day/ml. half life ≈ 5.7 days, CL0.42L/day Released topoisomerase inhibitor Cmax 4.4ng/ml, AUC 28ng day/ml, half life ≈ 5.8 days, CL 19.2 L/h
Adverse events Most frequent (>20%)	Nausea, fatigue, vomiting, alopecia, constipation, decreased appetite, anaemia, neutropenia, diarrhoea, leukopenia, cough.
Occasional	Infusion – related reaction, febrile neutropenia
Serious adverse reaction (>1%)	Interstitial lung disease, pneumonia, vomiting, nausea, cellulitis, hypokalaemia, intestinal obstruction
ATC codes WHO ATC code	L01X-X (other antineoplastic agents)
EphMRA ATC code	L1X9(all other antineoplastics)

- **Therapeutic trials**

1. Breast cancer

Trastuzumab deruxtecan showed durable antitumour activity in the phase 2 DESTINY-Breast01 trial in patients with HER2-positive metastatic breast cancer who had been previously treated with ≥ 2 anti-HER2 therapies, including trastuzumab emtansine (NCT03248492). In this trial, patients were randomized to receive trastuzumab deruxtecan 5.4 mg/kg (n = 50), 6.4 mg/kg (n = 48) or 7.4 mg/kg (n = 21) as an intravenous infusion once every 3 weeks in part 1 (pharmacokinetics and dose-finding) of the trial; based on efficacy and tolerability outcomes, the recommended dosage for part 2 was 5.4 mg/kg every 3 weeks [n = 184 (50 patients from part 1 and 134 patients recruited in part and this was administered until unacceptable toxicity or disease progression.

2. Gastric cancer

Treatment with trastuzumab deruxtecan 5.4 or 6.4 mg/kg once every 3 weeks achieved a confirmed ORR (as assessed by the investigators) of 43.2% (19 of 44 evaluable patients) and a DCR of 79.5% in patients with advanced HER2 positive gastric or gastroesophageal junction cancer in a two-part phase 1 trial in patients with heavily pretreated, advanced HER2-expressing tumours (NCT02564900; data cutoff 10 August 2018) . The median time to response was 1.4 months, the median duration of response was 7.0 months, the medianPFS was 5.6 months and the median OS was 12.8 months. Patients from the dose escalation and dose expansion parts who received either dosage regimen were included in this analysis; the median treatment duration was 4.4 months and median follow-up was 5.5 months.

3. Other cancer

In the subgroup of patients with HER2-expressing and/or -mutated NSCLC in the phase 1 trial in heavily pretreated patients with advanced HER2-expressing tumours (NCT02564900), the confirmed ORR was 58.8% and DCR was 88.2% (n = 17 evaluable; data cutoff 10 August 2018); In the subgroup of patients with HER2-expressing advanced colorectal cancer, the ORR was 15.8% (3 of 19 evaluable patients) and DCR was 84.2% (data cutoff 10 August 2018).

- **Ongoing clinical trials**

In addition to DESTINY-Breast01 (NCT03248492) and DESTINY-Gastric01 (NCT03329690), three phase 3 trials of trastuzumab deruxtecan in advanced breast cancer

[DESTINY-Breast02 (NCT03523585), DESTINY-Breast03 (NCT03529110) and DESTINY-Breast04 (NCT03734029)] are underway. Phase 2 trials of trastuzumab deruxtecan that are recruiting include studies in HER2-positive gastric or gastroesophageal junction cancer (NCT04014075), HER2 overexpressing or -mutated NSCLC (NCT03505710), HER2-positive uterine cancer (STATICE; UMIN000029506), HER2-positive biliary tract cancer (HERB; JMA-IIA00423) and HER2-expressing colorectal cancer (NCT03384940). Four phase 1 trials in advanced HER2-expressing solid tumours or breast cancer (NCT02564900, NCT03383692, NCT03368196, NCT03366428) are ongoing. A phase 1/2 trial of trastuzumab deruxtecan in combination with nivolumab in advanced HER2-expressing breast or urothelial cancer (NCT03523572) is recruiting and a phase 1 trial of trastuzumab deruxtecan in combination with pembrolizumab (NCT04042701) in advanced HER2-expressing breast cancer or NSCLC is pending.

- **Current status**

Trastuzumab deruxtecan was granted accelerated approval in the USA on 20 December 2019 for the treatment of adult patients with unresectable or metastatic HER2-positive breast cancer who have received two or more prior antiHER2-based regimens in the metastatic setting. Daiichi Sankyo and Roche are collaborating in the development of a HER2-low companion diagnostic test that will use the VENTANA HER2 (4B5) assay to identify patients with cancers that express low levels of HER2.

1. Talazoparib

- **Introduction**

Talazoparib is a potent oral inhibitor of poly (ADP-ribose) polymerase (PARP), primarily used in the treatment of certain types of breast cancer, particularly those associated with BRCA1 and BRCA2 mutations. By blocking PARP, talazoparib interferes with the DNA repair process in cancer cells, leading to increased DNA damage and ultimately cell death.

It is often prescribed for patients with germline BRCA mutations who have locally advanced or metastatic breast cancer. Clinical trials have demonstrated its efficacy in improving progression-free survival compared to traditional therapies. Common side effects include anemia, fatigue, and nausea, and it requires monitoring for potential hematologic toxicities."

- **Features and Properties of talazoparib**

Alternative names	BMN-673; BMN-673ts; LT 006673; LT-00673; LT-673; MDV-3800; talazoparib tosylate; TALZENNA
Class	Antineoplastics; fluorobenzenes; phthalazines; pyridines; small molecules; triazoles
Mechanism of action	Poly(ADP-ribose) polymerase inhibitor
Route of administration	Oral
Pharmacodynamics	Inhibits the polyadenosine 5'-diphosphoribose polymerase (PARP) enzymes (which play critical role in repairing DNA single-strand breaks) Exhibited selective antitumour activity in vitro and in vivo,targeting tumour cells that were either BRCA1- or BRCA2-deficient
Pharmacokinetics	Exhibited linear pharmacokinetics; may be administered with or without food; median time to a maximum talazoparib concentration was generally 1-2 h post dose
Most frequent adverse event	Anaemia
ATC codes	
WHO ATC code	L01X-X (other antineoplastic agents)
EphMRA ATC code	L1X (all other antineoplastic)
Chemical name	(8S,9R)-5-fluoro-8-(4-fluorophenyl)-9-(1-methyl-1H-1,2,4-triazol-5-yl)-8,9-dihydro-2H-pyrido[4,3,2-de] phthalazin-3(7H)-one

- **Therapeutic trials**

1. Monotherapy

Monotherapy with talazoparib was associated with a significant reduction in the risk of disease progression or death compared with single-agent chemotherapy in patients (aged ≥ 18 years) with locally advanced or metastatic breast cancer and a deleterious or suspected deleterious germline BRCA mutation (detected by the BRACAnalysis CDx assay) participating in a multinational, phaseIII study [NCT01945775 (EMBRACA)].

Talazoparib improved patient-reported outcomes in EMBRACA. For instance, it was significantly more effective than chemotherapy in terms of the estimated overall mean change from baseline in the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ)-Core 30 (C30) global health status (GHS)/quality-of-life (QOL) subscale score [+ 3.0 vs. − 5.4; $p < 0.0001$] and significantly ($p < 0.0001$) delayed the onset of clinically meaningful deterioration compared with chemotherapy [24.3 vs. 6.3 months; HR 0.38 (95% CI 0.26–0.55)]. At baseline, patients in the talazoparib and

chemotherapy groups had a mean EORTC QLQ GHS/ QOL scale score of 61.9 and 60.9. EMBRACA is a randomized, open-label, multinational, phase III study in which 431 patients received talazoparib (n = 287) or single-agent chemotherapy (n = 144) until disease progression, unacceptable toxicity, withdrawal of consent or physician decision. The anti-tumour efficacy of talazoparib monotherapy has also been demonstrated in pilot, phase I (NCT01286987) and II (NCT02286687) studies in patients with germline BRCA mutations in advanced cancers other than breast cancer.

2. Combination therapy

Talazoparib in combination with carboplatin, irinotecan and temozolomide has shown preliminary evidence of anti-tumour activity in patients with solid tumours participating in phase I (NCT02049593; NCT02358200; NCT02392793) studies. It is being evaluated in combination with enzalutamide and temozolomide in patients with solid tumours participating in phase I/II (NCT02116777) and III[NCT03395197 (TALAPRO-2) studies.

- **Ongoing clinical trials**

There are several ongoing phase I/II (NCT01989546; NCT02878785; NCT02116777) and II [NCT03672773; NCT02921919; NCT02286687; NCT03499353; NCT02401347; NCT03148795; NCT03377556; NCT03637491; NCT03565991; NCT03330405 (JAVELIN PARP MEDLEY); NCT02282345; NCT02034916 (ABRAZO)] studies of talazoparib in patients with various solid tumours, including breast cancer and CRPC.

A two-part multicentre, phase III study [NCT03395197 (TALAPRO-2)] is currently recruiting patients with metastatic CRPC and will confirm the starting dose of talazoparib plus enzalutamide in the open-label part of the study and the efficacy of talazoparib plus enzalutamide compared with placebo plus enzalutamide in the randomized, double-blind part of the study. A randomized, open-label, multicentre study [NCT03642132 (B9991030)] evaluating the efficacy of chemotherapy plus avelumab followed by talazoparib plus avelumab, chemotherapy followed by talazoparib and chemotherapy plus bevacizumab followed by bevacizumab in patients with previously untreated histologically confirmed stage III or IV epithelial ovarian, fallopian tube, or primary peritoneal cancer was initiated in July 2018. A randomized, open-label, multinational study [NCT01945775 (EMBRACA)] evaluating the efficacy of talazoparib versus single-agent chemotherapy (chosen by the physician) in patients with locally advanced or metastatic breast cancer with germline BRCA mutations is currently active, but not recruiting. This study was initiated in October 2013,

with data from the primary analysis available.

- **Current status**

Talazoparib received its first global approval on 16 October 2018 for the treatment of adults with deleterious or suspected deleterious germline BRCA -mutated, HER2-negative, locally advanced or metastatic breast cancer in the USA.

3. Ribociclib

- **Introduction**

Ribociclib is an oral, small-molecule inhibitor of cyclindependent kinase (CDK) 4 and 6 that is being developed by Novartis for the treatment of cancer. which are crucial for cell cycle progression. By inhibiting these kinases, ribociclib helps to slow down or stop the growth of cancer cells. Ribociclib is an oral medication used primarily in the treatment of hormone receptor-positive, human epidermal growth factor receptor 2-negative (HR-positive, HER2-negative) breast cancer.

A tablet formulation of ribociclib, in combination with an aromatase inhibitor (letrozole), was approved in the USA in March 2017 as initial endocrine-based therapy for the treatment of postmenopausal women with HR-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer.

- **Features and Properties of ribociclib**

Alternative names	Kisqali; LEE-011
Class	Amides; aminopyridines; antineoplastics; piperazines; pyrimidines; pyrroles; small molecules
Mechanism of action	Cyclin-dependent kinase 4 and 6 inhibitor
Route of administration	Oral
Pharmacodynamics	Reduces cancer cell proliferation by decreasing Rb phosphorylation leading to the G1 phase cell cycle arrest; decreases Ki67 expression; shows synergistic anticancer activity with antiestrogens (e.g. letrozole)
Pharmacokinetics	Tmax 1-5 h; mean plasma effective half -life 32.0 h; mean apparent oral clearance 25.5 L/h; eliminated mainly via faeces
Adverse events (incidence ≥ 35□)	Neutropenia, nausea, infections, fatigue, diarrhoea
Grade 3 or 4 (incidence ≥ 5□)	Neutropenia, leukopenia hypertension, lymphopenia, increased ALT and AST
ATC codes	

WHO ATC code	L01X-E (protein kinase inhibitors)
EphMRA ATC code	L1H (protein kinase inhibitor antineoplastics)
Chemical name	Butanedioic acid—7-cyclopentyl-N,N-dimethyl-2-{[5-(piperazin-1-yl) pyridin-2-yl]amino}-7H-pyrrolo[2,3-d]pyrimidine-6-carboxamide (1/1)

- **Therapeutic trials**

1. Breast cancer

The efficacy and tolerability of ribociclib in patients with advanced breast cancer is being evaluated primarily in the MONALEESA clinical trial programme, which includes three randomized, double-blind, multinational phase III trials: MONALEESA-2 (NCT01958021), MONALEESA3 (NCT02422615) and MONALEESA-7 (NCT02278120).

MONALEESA-2: This trial evaluated ribociclib plus letrozole versus letrozole alone in postmenopausal women with HR+/HER2- breast cancer. Results showed improved progression-free survival (PFS) in the ribociclib group.

MONALEESA-3: Focused on ribociclib combined with fulvestrant in patients with HR+/HER2- breast cancer who had progressed on previous endocrine therapy. The trial demonstrated significant PFS benefits.

MONALEESA-7: This trial studied ribociclib in premenopausal women, combined with tamoxifen or an aromatase inhibitor, showing improved outcomes compared to endocrine therapy alone.

These trials have established ribociclib as a standard treatment option for specific breast cancer populations, emphasizing its efficacy and safety profile.

2. Other cancer

Preliminary clinical activity of single-agent ribociclib has been demonstrated in patients with CDK4/6 pathway activated solid tumours or haematological malignancies in a phase II trial (NCT02187783; SIGNATURE) and in patients with advanced solid tumours and lymphomas in a phase I study (NCT01237236). Ribociclib plus cetuximab (anti-epidermal growth factor receptor monoclonal antibody) showed preliminary antitumour activity in patients with recurrent or metastatic squamous cell carcinoma of the head and neck in a phase I study (EudraCT2014-005371-83).

In a phase Ib/II trial (NCT01781572) in patients with NRAS-mutant melanoma (n=22 evaluable), treatment with ribociclib plus binimetinib [mitogen- activated protein kinase1 and 2 (MEK1/2) inhibitor] produced 5 partial and 4 unconfirmed partial responses, with nine patients achieving stable disease; preliminary estimated PFS was 6.7 months. In a phase Ib/II trial in nine evaluable patients with BRAF- mutant melanoma receiving ribociclib plus encorafenib (BRAFinhibitor), two patients had partial responses and six patients had stable disease. Clinical responses were seen in patients previously treated with BRAF inhibitors.

In a phase I trial (NCT01747876) in paediatric patients with malignant rhabdoid tumours, neuroblastoma or cyclin D-CDK4/6 pathway-activated tumours receiving single agent ribociclib (n=17 evaluable), the best overall response was stable disease, achieved by one patient with primary CNS malignant rhabdoid tumour.

- **Ongoing clinical trials**

1. Breast cancer

The MONALEESA-2,-3,-7 trials in patients with HR-positive, HER2-negative advanced breast cancer are ongoing.

- **Current status**

Ribociclib, in combination with an aromatase inhibitor, received its first global approval on 13 March 2017 in the USAas an initial endocrine-based therapy for the treatment of postmenopausal women with HR-positive, HER2-negative advanced or metastatic breast cancer.

4. Elacestrant

- **Introduction**

Elacetrant is also not a medication used in chemotherapy. It is a member of the group of drugs called selective estrogen receptor degraders (SERDs). These medications function by attaching to the estrogen receptor (ER) in cancer cells and initiating its degradation. Because many breast cancers are driven by estrogen, this activity is significant because it prevents the effects of estrogen on breast cancer cells. Elacestater is especially used to treat hormone receptor-positive, HER2-negative breast cancer, much as CDK4/6 inhibitors like ribociclib. It is intented to be useful in situations where cancers have grown resistant to existing hormone treatments, like selective estrogen receptor modulators or aromatase inhibitors. Clinical trials are now being conducted to evaluate elacestrant, which is given orally as tablets.

- **Features and Properties of elacestrant**

Alternative names	ORSERDU; RAD 1901
Class	Amines; Antineoplastics; Ethers; Small molecules; Tetrahydronaphthalenes
Mechanism of action	Selective estrogen receptor degrader
Route of administration	Oral
Pharmacodynamics	Selectively binds to Erα over Erβ (half maximal inhibitory concentration 48 vs 870 nmol/L); displayed anti-tumour activity in patient-derived ER-positive tumour xenograft models, including those resistant to cyclin-dependent kinase 4/6 inhibitors and those harboring estrogen receptor 1 mutations
Pharmacokinetics	Cmax and AUC values increase more than dose proportionally over a 43-862 mg once daily (i.e. 0.125-2.5-fold the recommended dosage) dosage range; oral bioavailabilityof ≈ 10□ ; time to Cmax of 1-4h; elimination half- life of 30-50 h
Most frequent adverse events	Nausea, fatigue, vomiting and decreased appetite
ATC codes	
WHO ATC code	L02B-A04 (Elacestrant)
EphMRA ATC code	G3X (Other Sex Hormones and Similar Products); L1 (Antineoplastics)
Chemical name	(6R)-6-[2-[ethyl-[[4-[2-(ethylamino)ethyl]phenyl]methyl]amino]-4-methoxyphenyl]-5,6,7,8-tetrahydronaphthalen-2-ol

- **Therapeutic trials**

Monotherapy with oral elacestrant significantly reduced the risk of disease progression or death relative to standard of care (SOC) monotherapy in postmenopausal women and adult men with ER-positive, HER2-negative advanced or metastatic breast cancer participating in a randomized,open-label, multinational phase III study [EMERALD (NCT03778931)].

Phase 1 Trials: Initial studies focused on assessing the safety, tolerability, and pharmacokinetics of elacestrant in patients with advanced ER+ breast cancer. These trials helped establish the optimal dosing and identified preliminary efficacy signals.

Phase 2 Trials: The EMERALD trial, a pivotal phase 2 study, evaluated elacestrant in patients with ER+ breast cancer who had progressed on prior endocrine therapies. Results showed improved progression-free survival compared to standard therapies.

Combination studies: Other trials are exploring elacestrant in combination with targeted

therapies, such as CDK4/6 inhibitors, to enhance its efficacy in resistant breast cancer populations.

- **Ongoing clinical trials**

In addition to the ongoing EMERALD study discussed previously, four phase I/II studies [ELONA (NCT05618613), ELECTRA (NCT05386108), NCT04791384 and ELEVATE (NCT05563220)] are currently recruiting patients, while a phase III study (NCT05512364) and a phase II study [ELCIN (NCT05596409)] are not yet recruiting patients.

- **Current status**

Elacestrant received its first approval on 27 January 2023 for the treatment of postmenopausal women or adult men with ER-positive, HER2-negative, ESR1-mutated (as determined by a US FDA-approved test) advanced or metastatic breast cancer with disease progression following ≥ 1 line of endocrine therapy in the USA.[2–4]

❖ CONCLUSION

Evaluation of Treatment Effectiveness: Physicians assess the degree to which the therapy has reduced or eradicated malignant cells. Typically, biopsies, imaging tests, and other diagnostic instruments are used to do this. Handling and controlling any side effects or issues that may have developed during the course of treatment is known as side effect management.

Lifestyle Guidance: Teaching the patient about lifestyle modifications that can Transition to Follow-Up Care: Arranging for continued surveillance and follow-up visits to manage the long- term effects of therapy and keep an eye out for any recurrence indications. Supporting the patient and their caregivers as they manage the emotional and psychological effects of finishing treatment is known as emotional and psychological support.

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