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A SCIENTIFIC ANALYSIS REPORT ON THE EXTENSIVE RESEARCH OF ANTI-CANCER MEDICATIONS AND, ITS COMPREHENSIVE STUDIES

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ABSTRACT

Conventional anticancer medications have some limitations related or linked to their poor water solubility and poor pharmacokinetics, these drawbacks which can result in serious majour unpleasant side effects and patient multidrug resistance. Which has hampered the development of chemotherapy and leading to critical/crucial therapy profile. It's crucial to understand that not all cancer treatments and medications function in the same manner, some cancer treatments, such as: targeted therapy, hormone therapy, and immunotherapy, operate in a different way, so the study is much more important when it comes to the treatment of cancer. Melamine toxicity, and its evaluation for causing cancer or as a carcinogen is also significant along with new development of therapeutics.

KEYWORDS: Cancer medication, Chemotherapy, Melamine, Anticancer, development of cancer tumour, Carcinogen.

I. INTRODUCTION

II. Cancerous cells proliferate out of control as a result of a build-up of abnormalities that disrupt numerous cells regulating processes

II.a. Understanding the disease

Every time a new cell is created, it goes through the same process to develop into a mature (or fully functional) cell. The procedure, which has several phases, is known as the cell cycle.

Chemotherapy is used to make the cell cycle to act normally than that of the malfunctioned or numerous multiplications of cells abnormally inside the body.

Chemotherapy medications target abnormal growth of the cells at various cell cycle stages inside the body or the affected body part or the organ. Knowing how these medications function enables doctors to foresee which medications would likely interact well. Based on the timing of the cell phases, doctors can also determine how frequently doses of each medication should be administered.

Chemotherapy is only useful in not hormone sensitive and in progressive tumours. Uterine sarcomas are a rare and heterogeneous group of tumours. Therefore, no clinical guidelines are available for this entity. These often-aggressive tumours are hardly responding to systemic and radiation therapy.[7]

Most cancers fall into one of three main groups: carcinomas, sarcomas, and leukemias or lymphomas. Carcinomas, which include approximately 90% of human cancers, are malignancies of epithelial cells. Sarcomas, which are rare in humans, are solid tumours of connective tissues, such as: muscle, bone, cartilage, and the fibrous tissue. Leukemias and, lymphomas, which account for approximately 8% of human malignancies, arise from the blood-forming cells and, from cells of the immune system, respectively. Tumours are further classified according to tissue of origin (e.g., lung or breast carcinomas) and, the type of cell involved. For example, fibrosarcomas arise from fibroblasts, and erythroid leukemias from precursors of erythrocytes (red blood cells).[6]

II.a.i. Glossary of a term, sarcoma: a cancer of cells of connective tissue.

II.b. Melamine and its toxicity

***II.b.1. Synonyms*:** Cyanuramide; cyanurotriamide; cyanurotriamine; isomelamine; triaminotriazine; 2,4,6-triaminotriazine; triamino-*s*-triazine; 2,4,6-triamino-1,3,5-triazine; 2,4,6-*s*-triazinetriamine; 1,3,5-triazine-2,4,6(1H,3H,5H)-triimine.

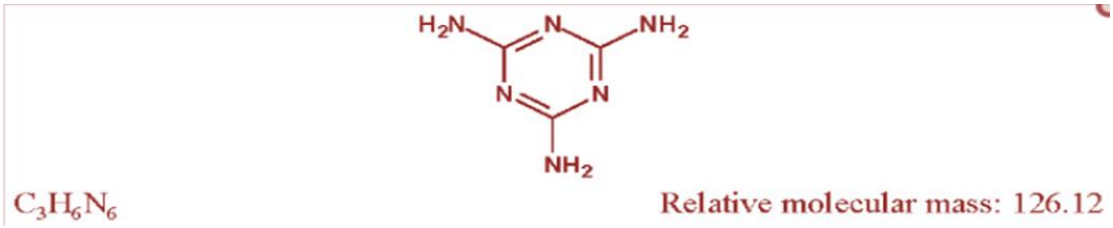


Figure 1: Structure of melamine.[50]

II.b.2. Animal carcinogenicity data

Melamine has been studied for carcinogenicity in mice and, rats of each sex by oral administration. It produced urinary bladder and, ureteral carcinomas in male rats but only urinary bladder hyperplasia in male mice. The occurrence of urinary bladder tumours in male rats correlated strictly with calculus formation and, exposure to high doses. The dose dependence was confirmed by subsequent studies in male rats in which concomitant administration of sodium chloride to increase urinary output resulted in a decreased tumour yield.[50]

III. Tumour: cancer results in a malignant tumour

A tumour is an abnormal growth of body tissue. Tumours can be cancerous (malignant) or noncancerous (benign).[2]

Mutations brought on by a carcinogen or carcinogenic substances start with the onset of development of the tumours. Both benign and malignant tumours are classified according to the type of cell from which they arise.

III.a. A malignant tumour of the uterus

Malignant uterine tumours are responsible for up to 9% of all new cancer cases and for 4.5% of all cancer related deaths in women. The three important uterine cancers are endometrial cancers, uterine sarcomas and cervical cancers. Endometrial cancers are typically found in elderly women and, are > 70% hormone sensitive (type I); type II is often less differentiated and, not hormone sensitive.[7]

III.b. Causes of the tumour

Tumours often develop when the cells in the body divide and, expand excessively. The body normally regulates the growth and, the division of cells. Older cells are replaced by new ones, or new functions are carried out by new cells. Damaged or unnecessary cells expire to create a space of replacement with the healthy cells. A tumour may develop if the balance between

cell growth and, death is upset/disturbed. Such as: disturbance in the normal functioning due to an effect of chemical contact, change in hormones, continuous use of food preservatives, due flesh of animals, a chemical substance such as: hormones from the higher vertebrates animal flesh like: Beef (*boeuf)*, Chicken, Pork, Mutton (*mouton)*, Venison (*cerf)*, rabbit meat, **white meat,** turkey breast, **australus, Camel loin, ostrich tenderloin, Horse meat, Veal,** Squab, Carabeef, Chevon, bat meat, cat barbecue or churrasquinho de gato, barbecued bat and any flesh that may have different nucleic acid signals than that of the human body may also target to the over growth or abnormal growth of cells in normal human body. Such substances are also called as: **carcinogen,** including the flesh of the higher vertebrates.

Figure 2: Flesh of bat.

IV. Some examples of associated diseases with consumption of flesh: It has been speculated that megabats may be the natural reservoir of Ebolavirus, SARS-CoV, though the evidence has been called "far from decisive".[3]

IV.a. Toxins: Eating fruit bats is also linked to a neurological disease called lytico-bodig disease.[3]

V. Other related information on meats: In December 2018, the dog and cat meat trade prohibition act of 2018 was signed into federal law making the consumption of cat meat illegal and punishable by a fine of $5,000. Previous to that bill, consuming cat meat was legal in 44 states.[4] It was passed by the Senate as part of the 2018 Farm Bill on December 11th, 2018. The House passed the reconciled Farm Bill on December 12th 2018. On December 20th, 2018, President Donald Trump signed it into law. Enacted by the 115th United States of America Congress.[5] Similar allegations were made in 2016 for similar type of flesh consumption in Chennai, India.[4] By prohibiting the killing of animals, diseases that are spread through the consumption of their flesh can be controlled and also be prevented. One such example associated with it is the spread of pandemic of

2019, SARS-CoV-2, SARS-CoV-1. **Other conditions may include:** digestive track cancer, colon cancer, abdominal bleeding, anal fissures, dirty stinking mouth, bleeding rectum, and neurologically associated brain strokes. **Refer figure 8,9,10,11 below of this article.**

Chemotherapy medications work well on cancer cells because the cancer cells more frequently gets divided; quickly than healthy ones. Chemotherapy medications, however, are unable to distinguish between cancer cells and, healthy ones. This implies that both cancer cells and, healthy cells suffer damage, which results in adverse outcomes. Every time chemo is administered, a delicate balance must be struck between eliminating the cancer cells and, protecting the healthy cells in order to treat or control the condition (to lessen side effects).

The benefit of chemotherapy is that most healthy cells will eventually recover from chemo's negative effects. However, because they are altered (not normal) cells, cancer cells typically do not recover from the effects of chemotherapy. Chemotherapy is effective in killing a variety of cancer cells because of this.

VI. Tumours due to DNA malfunctioning

VI.a. Malfunctioning DNA[17]

Tumours develop as a result of DNA malfunction, particularly in genes that affect how well cells can control their own growth. Additionally, some faulty genes can impede unhealthy cells from eliminating themselves to make way for fresh, healthy ones.

"The regulation of cell death is so important, as per reports of " Dr. Garcia. "If your programmed cell death is altered, the cell does not know when it's time to die and persists. If the cell learns how to block that, and it develops the ability to proliferate, tumours grow more rapidly." Some of these mutations lead to rapid, unchecked growth, producing tumours that may spread quickly and damage nearby organs and tissues. "Malignant cells have the ability to produce enzymes that dissolve the native tissue. This is known as invasiveness," as per; Dr. Garcia reports. Other mutations are less aggressive, forming slow-growing tumours that are not cancerous. "Benign tumours don't generally invade," Dr. Garcia report stated. "They usually push the normal tissue to the side."

Many people carry benign tumours their entire life. Nevi, or moles, are types of benign tumours that may never need treatment. Other types of benign tumours include:

i. **Adenomas**: These bumps form on the surfaces of G-I tract. "A colon polyp, a classic adenoma, has only a 1 percent chance of becoming cancer in the patient's lifetime," says Jeffrey Weber, MD, Gastroenterologist at a hospital-Phoenix.
ii. **Fibromas**: These tumours of connective tissue may be found in any organ. Fibroid tumours are named for where they form in the body, such as: 1. uterine fibroids.
iii. **Desmoid tumour**: These are often more aggressive than most benign tumours and, may invade nearby tissue and, organs. But they do not metastasize.
iv. **Haemangiomas**: These tumours are a collection of blood vessel cells in the skin or internal organs. They may appear on the skin as a birthmark-like discolouration and, often disappear on their own.
v. **Lipomas**: These soft, round, fatty tumours are often found on the neck or shoulders.
vi. **Leiomyomas**: The most common gynaecologic tumour, may be found in the uterus. Their growth is fuelled by hormones.

VII. Diagnosis

Diagnosis can be achieved by vaginal ultrasound and by histology after hysteroscopy and curettage of the uterine cavity.[7]

Although surgical staging is the primary method of assessing prognostic factors in endometrial cancer, cross-sectional imaging may help in treatment planning by providing information about factors such as: the depth of myometrial invasion, cervical involvement, and nodal status. The pre-treatment evaluation of cervical cancer traditionally has consisted of clinical evaluation, laboratory tests, and conventional radiographic studies, but more advanced imaging methods allow additional insights into the morphologic and metabolic features of cervical cancer. This article reviews the applications of modern imaging modalities in the assessment of endometrial cancer and, the cervical cancer and, their impact on treatment planning and, post-treatment follow-up.[9]

Ultrasonography plays a central role in the management of patients with gynaecological disorders. It is widely available and, is a relatively inexpensive imaging tool. In certain circumstances, its diagnostic accuracy may match that of MRI.[10]

VIII. Therapy:

Therapy of choice is the stage related radical hysterectomy (incl. lymph node dissection). Postoperatively and, at progressive stages endocrine and, radiation therapies can be useful.[7]

Therefore, radical tumour surgery plays the main therapeutic role. Cervical carcinomas are usually growing on an underlying chronic infection with oncogenic HPV subtypes. Important co-factors for carcinogenesis are: tobacco smoking, an immunodeficiency and chronic genital infections are the other causes. Cervical carcinomas and their precursor lesions are easily accessible for screening tests. Many tumours are detected in early tumour stages. Preoperatively diagnostic procedures are performed to examine local and, distant tumour growth. In early stages a radical hysterectomy (incl. pelvine (+paraaortal) lymphonodectomy) and in rare cases a uterus preserving surgery should be performed. Alternatively, a primary radio-chemotherapy can be applied. Patients with tumours in stages > or = FIGO IIb receive a primary combined radio-chemotherapy.[7]

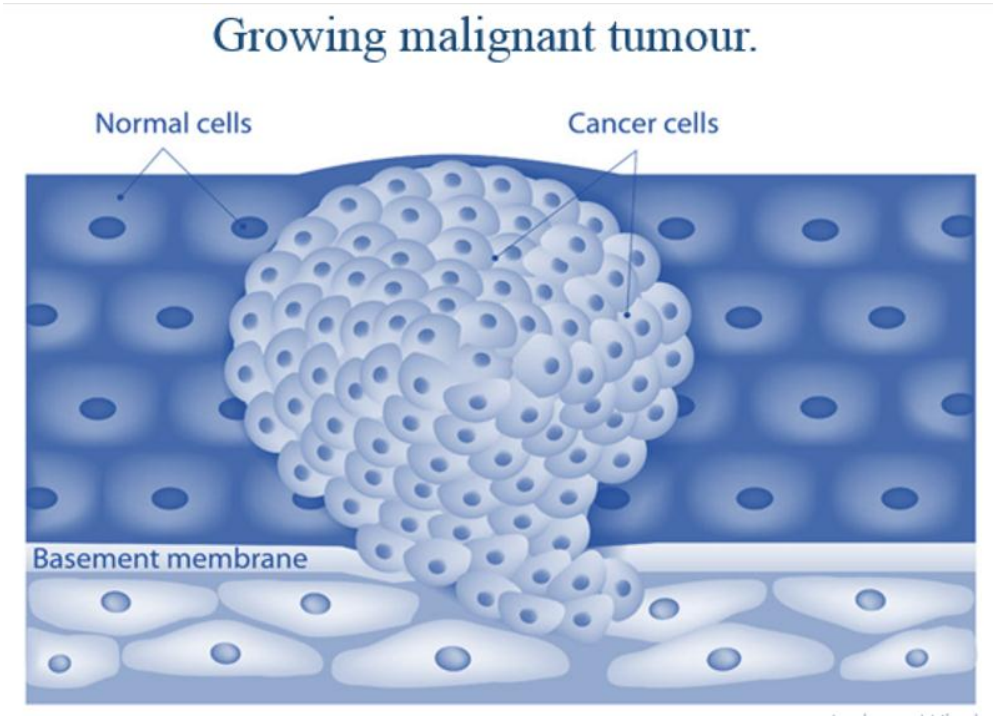
IX. Snippets

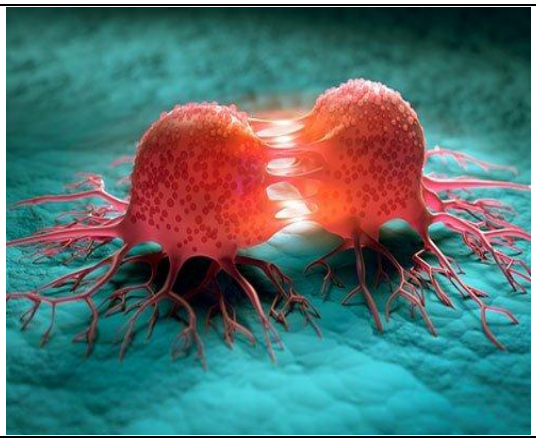
Malignant uterine tumours can affect the corpus or the cervix. The endometrial carcinoma with its different histological subtypes counts for most of the malignomas of the uterine body. But the rare category of uterine sarcomas (carcinosarcomas, leiomyosarcomas as well as endometrial stromal sarcomas) also belongs to this group. Cervical cancer presents an own entity, regarding both histology and, therapeutic options. Endometrial cancer is the most common genital malignoma. Histologically, the endometrial cancer can be subdivided in two groups: type I is hormonal sensitive and well differentiated, type II represents an undifferentiated aggressive tumour with poor prognosis. In general, the patient is elderly. Due to the main symptom - abnormal vaginal bleeding - endometrial cancer is detected in an early stage in about 75% of all patients. First choice in therapy is stage related surgery. Follow-up schemes have not proved yet to improve survival, therefore clear guidelines are missing. National and, international groups recommend regular follow-up visits to detect the early vaginal vault relapse which is curable. Cervical cancer is mainly a squamous cell carcinoma and, oncogenic Human Papilloma Virus (HPV) associated.[8]

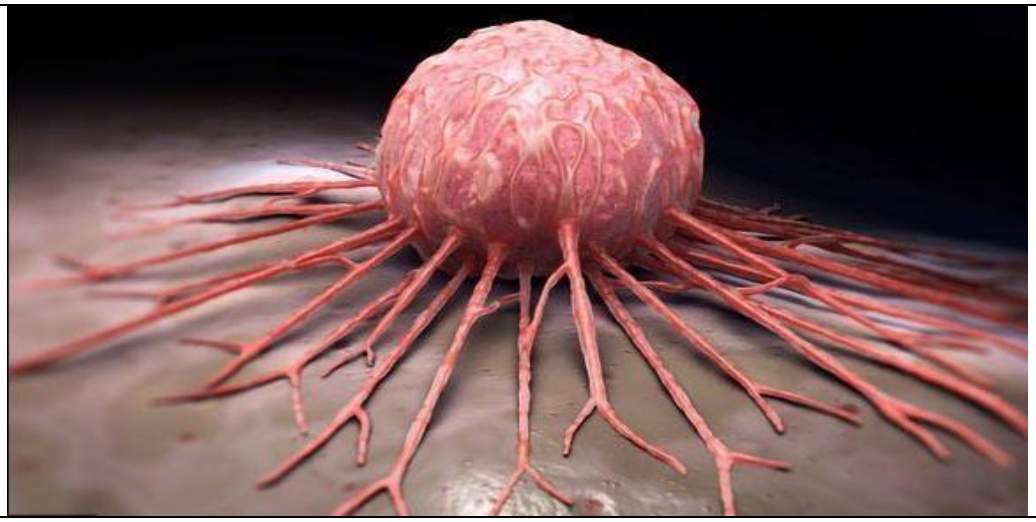
X. *General scientific statement on cancer therapy*

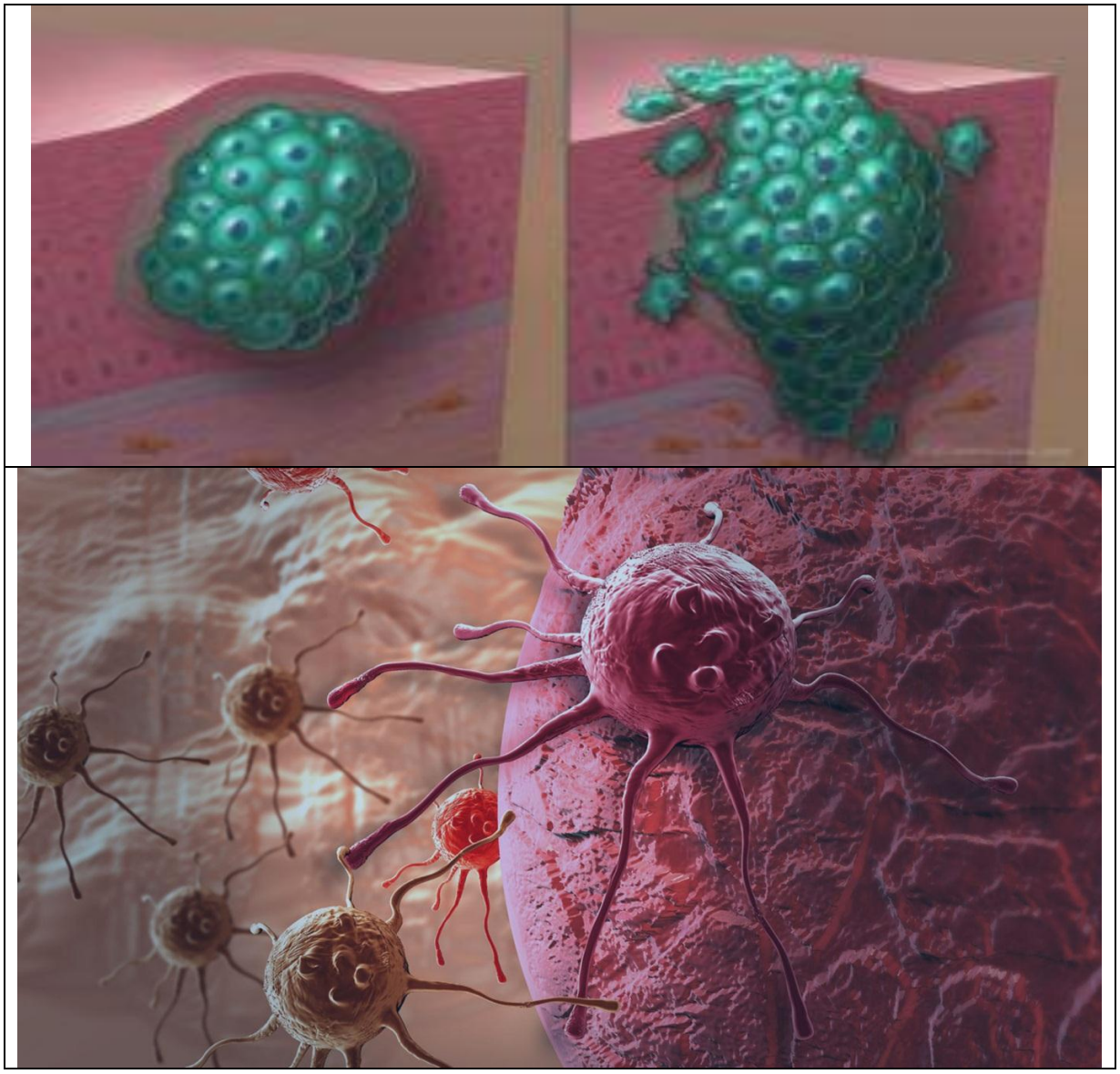
Cancer is treated with a variety of chemotherapy agents or chemo medicines, either alone or in conjunction with other medications or therapies. These medications range greatly in terms of their chemical make-up (what they are composed of), how they are prescribed and, the way they are administered, how effective they are at treating particular cancer types, and any potential adverse effects of these drugs or medications.[1]

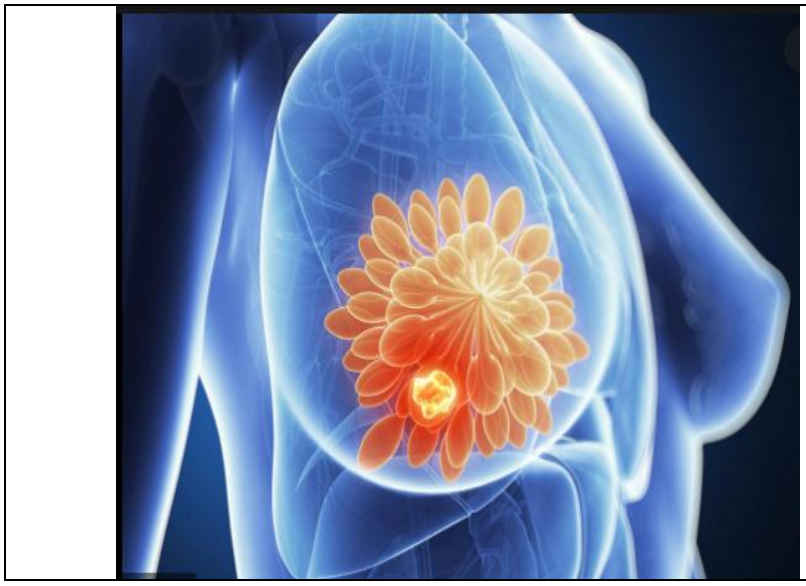
XI. Cancer study from the images











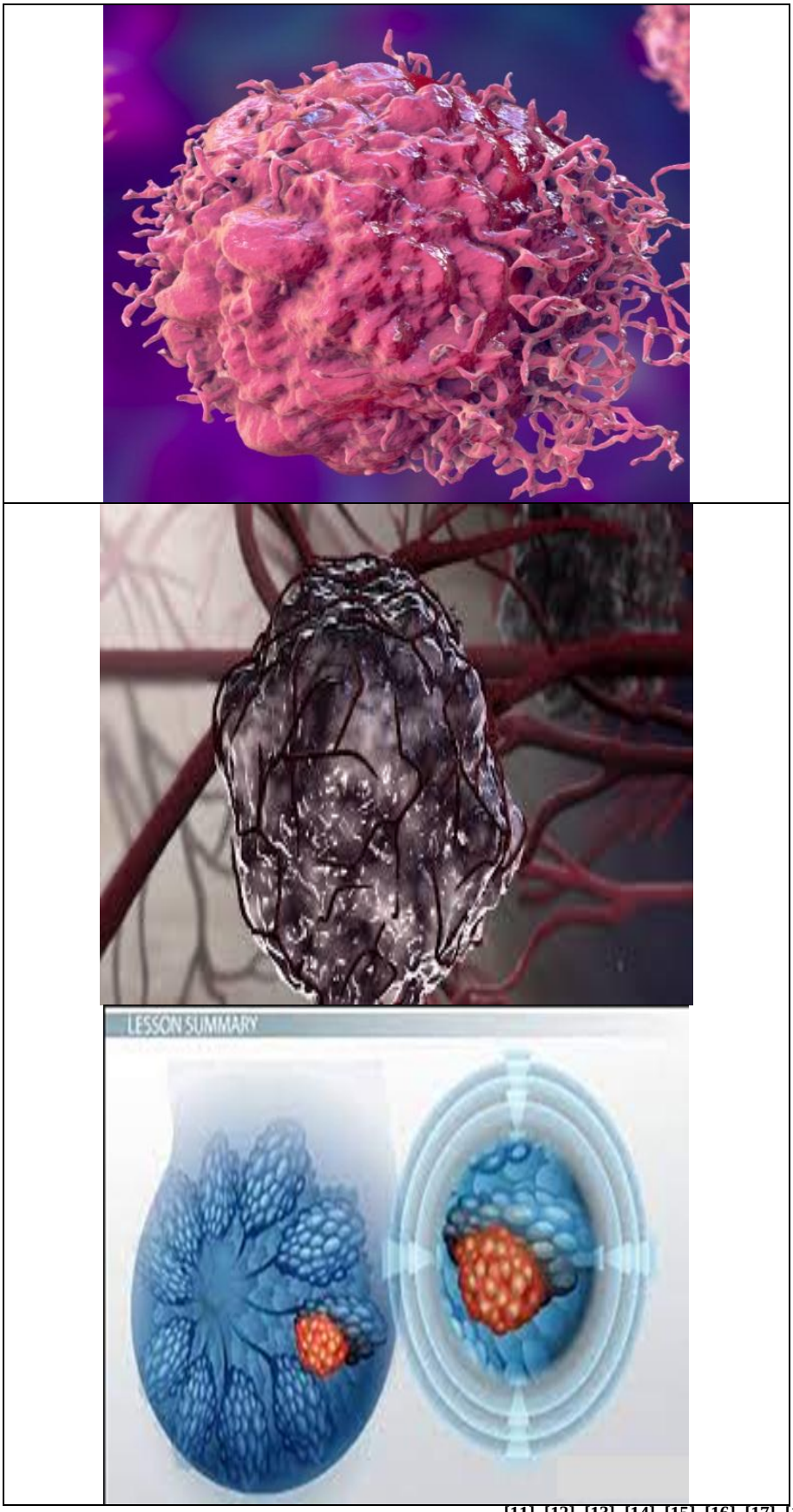


Figure 3: Image of tumour causing cell division.[11], [12], [13], [14], [15], [16], [17], [18], [19]

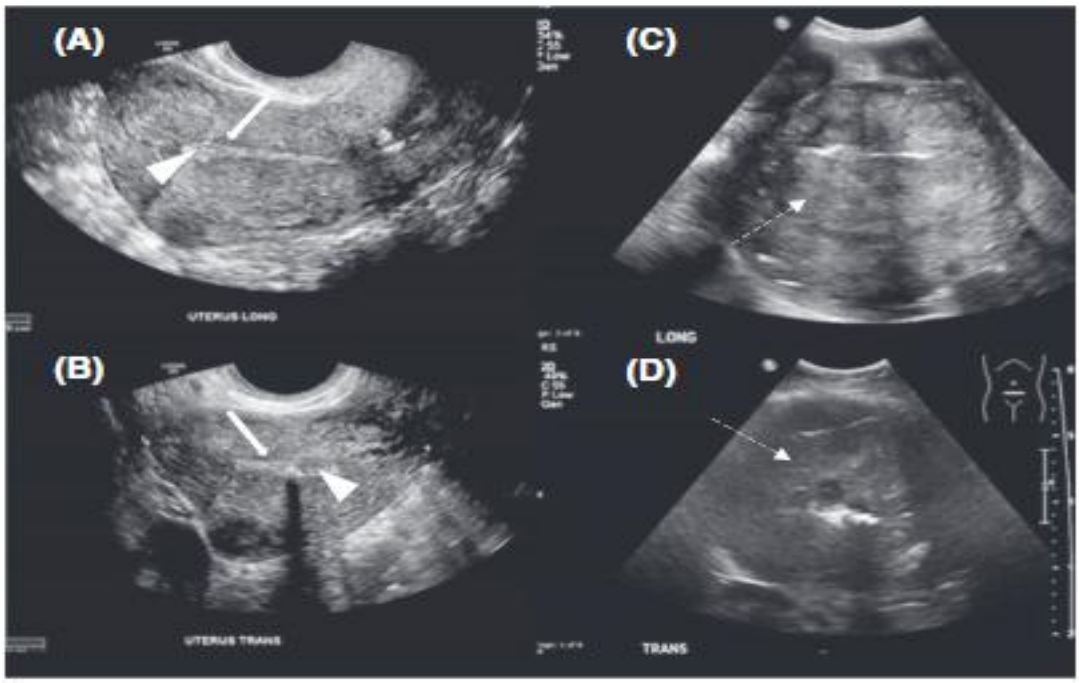


Figure 4: Ultrasound scans of a normal uterus. Transvaginal ultrasound scans of (A) sagittal plane (long) and (B) axial plane (Trans) with normal, thin, uniform echogenic endometrium (arrowheads) and sub-endometrial hypoechoic halo (solid arrows). Transabdominal ultrasound scans of endometrial carcinoma in sagittal plane (C) and axial plane (D). Note the cause of heterogeneous echogenicity due to haemorrhage and, necrosis.[10]

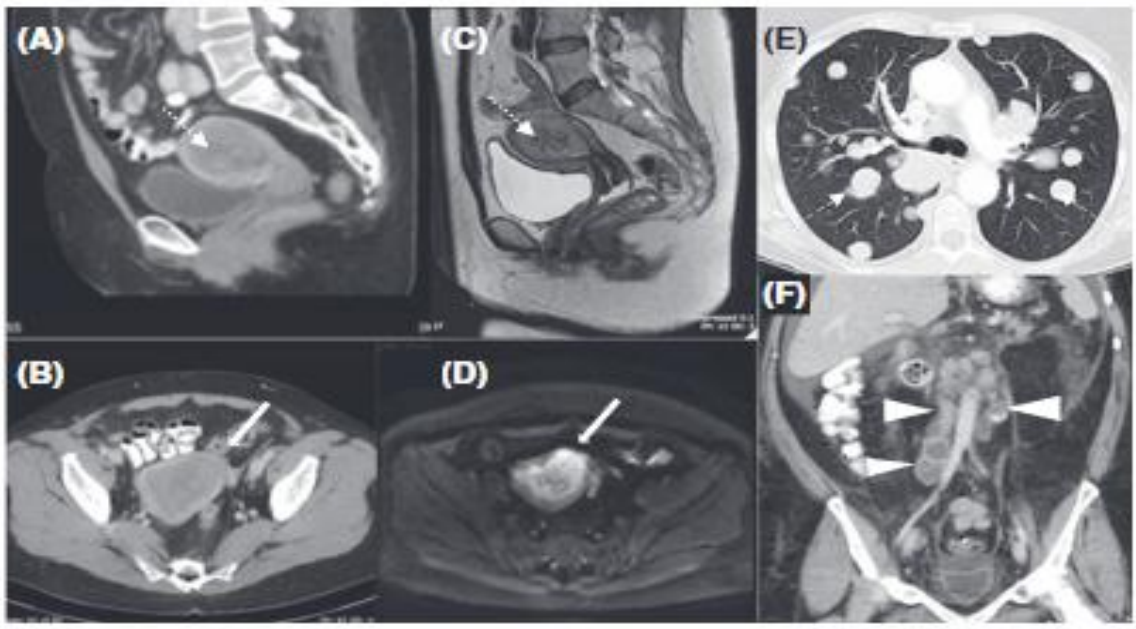


Figure 5: Computed tomography (A: sagittal plane, B: axial plane) and MRI (C: sagittal T2, D: axial diffusion- weighted) in the same patient with endometrial

carcinoma distending the endometrial cavity (dotted arrows) and deep myometrial invasion (solid arrows). E: Axial CT chest with multiple "cannonball" pulmonary metastases (dashed arrows). F: Coronal CT abdomen demonstrating multiple para-aortic necrotic lymph node metastases.[10]

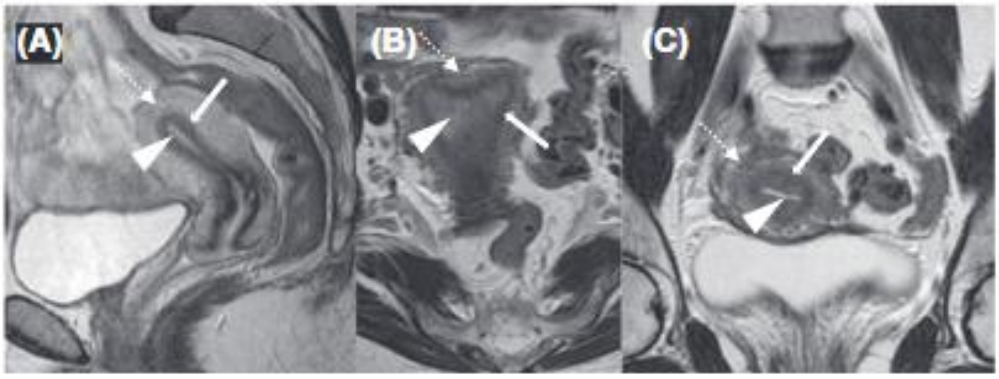


Figure 6: Normal zonal anatomy on T2- weighted MRI in (A) sagittal, (B) axial, and (C) coronal planes demonstrating high signal (bright) endometrium (arrowheads), low signal (darker) junctional zone or inner myometrium (solid white arrows), and intermediate signal (grey) outer myometrium.[10]

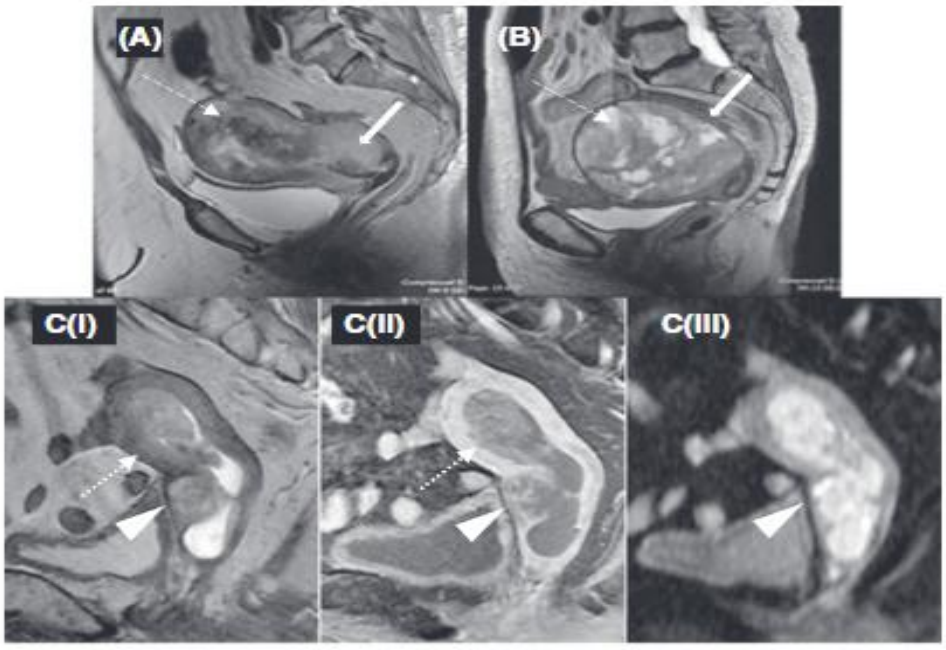


Figure 7: Deep myometrial invasion on MRI: (A) Sagittal T2 demonstrating obvious deep myoinvasion with heterogeneous tumour obliterating the normal uterine zonal anatomy (dashed arrow) and invading cervical stroma (solid arrow). (B) Pitfall of MRI myometrial invasion assessment: large polypoid tumour stretches and thins the

myometrium (dashed arrow) with age- related loss of normal zonal anatomy (solid arrow), pathology confirming no evidence of deep myoinvasion. (C) Multiparametric MRI improving staging accuracy: equivocal depth of myoinvasion and cervical stromal involvement on sagittal T2 (C.i). Dynamic T1 fat saturated post contrast (C.ii) shows disruption of subendometrial stripe at anterior midbody of uterus (dotted arrow) confirming myoinvasion. Cervical mucosal enhancement preserved posteriorly but disrupted anteriorly (arrowhead) confirming stromal invasion. Diffusion- weighted imaging (C.iii) highlights tumour extent and deep cervical stromal invasion but absence of bladder wall invasion.[10]

XII. **Anatomical removal of tumours:** It is important to remove the tumours to safe the unwanted growth of cells in the human body.

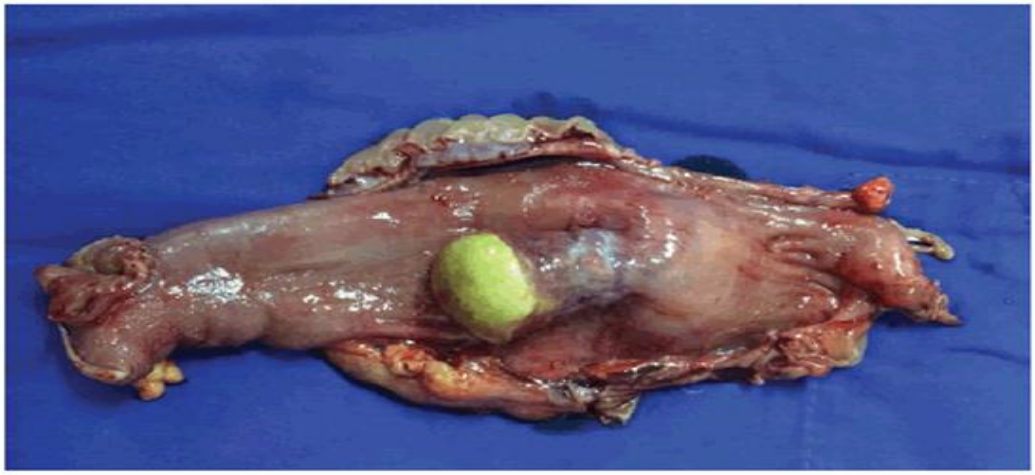


Figure 8: Stromal tumour resection.[20]

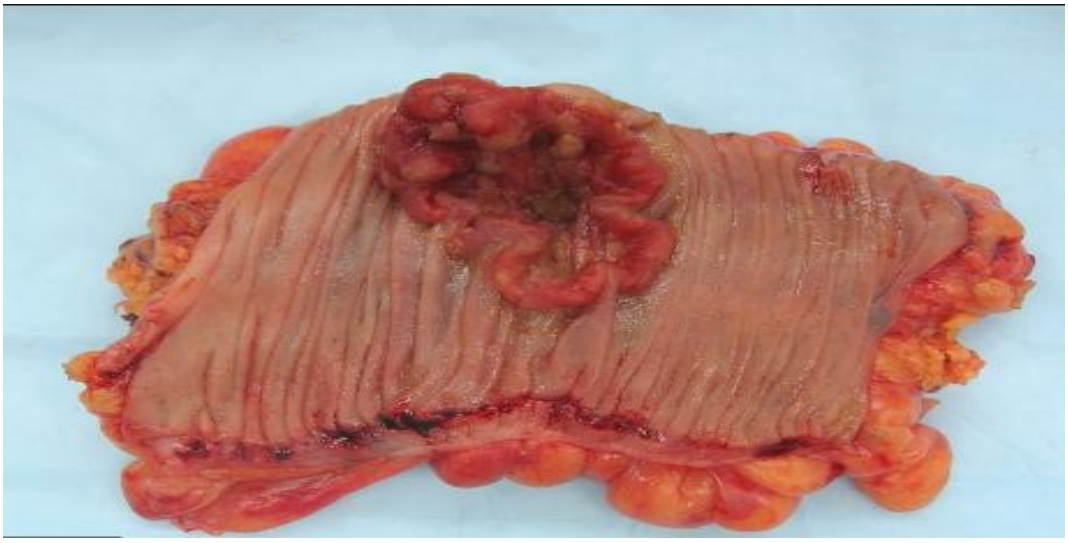


Figure 9: Organoids personalise cancer treatment.

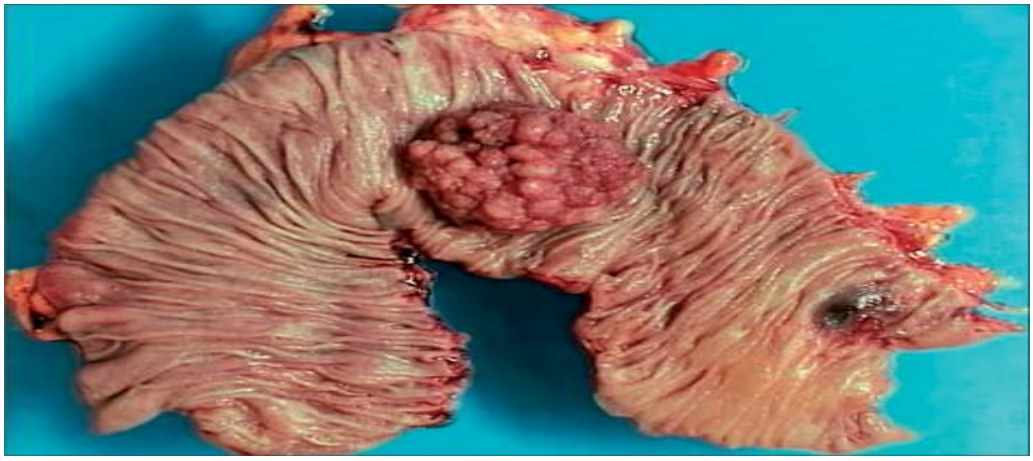


Figure 10: Oestrogen and the colon: potential mechanisms for cancer prevention.[22]

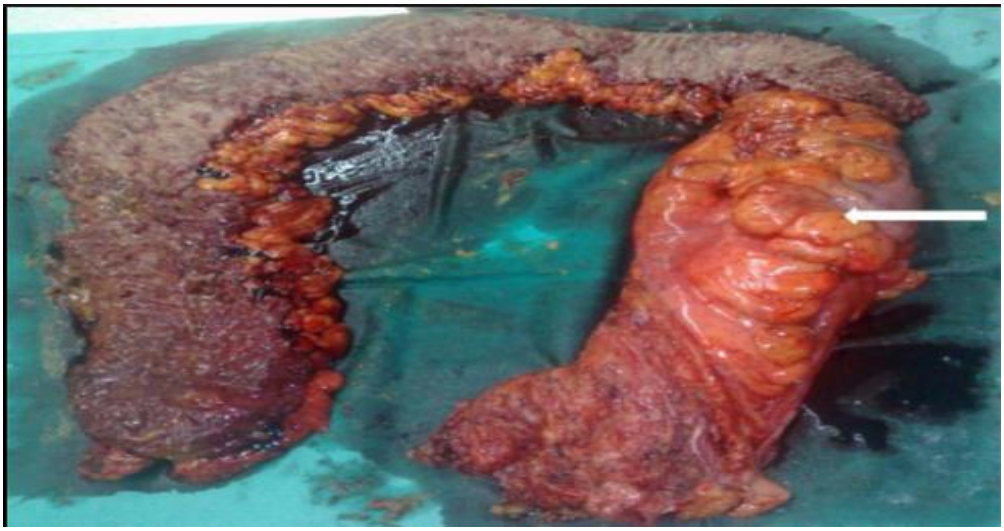


Figure 11: Operative specimen showing multiple polyps throughout the colon.

XIII. Oncology (Cancer) / hematologic malignancies approval notifications[24,25]

FDA approves durvalumab for locally advanced or metastatic biliary tract cancer on September 2, 2022, the Food and Drug Administration approved durvalumab (Imfinzi, AstraZeneca UK Limited) in combination with gemcitabine and cisplatin for adult patients with locally advanced or metastatic biliary tract cancer (BTC).

Efficacy was evaluated in TOPAZ-1 (NCT03875235), a randomised, double-blind, placebo-controlled, multiregional trial that enrolled 685 patients with histologically confirmed locally advanced unresectable or metastatic BTC who had not previously received systemic therapy for advanced disease.

Trial demographics were as follows: 56% Asian, 37% White, 2% Black, and 4% other race; 7% Hispanic or Latino; 50% male and 50% female; median age was 64 years (range 20-85) and 47% were 65 years or older. Fifty-six percent had intrahepatic cholangiocarcinoma, 25% had gallbladder cancer, and 19% had extrahepatic cholangiocarcinoma.

XIV. Patients were randomised 1:1 to receive

Durvalumab 1,500 mg on Day 1+ gemcitabine 1,000 mg/m2 and cisplatin 25 mg/m2 on days 1 and 8 of each 21-day cycle up to 8 cycles, followed by durvalumab 1,500 mg every 4 weeks, or placebo on day 1+ gemcitabine 1,000 mg/m2 and, cisplatin 25 mg/m2 on days 1 and 8 of each 21-day cycle up to 8 cycles, followed by placebo every 4 weeks.

Durvalumab or placebo were continued until disease progression or unacceptable toxicity. Treatment was permitted beyond disease progression if the patient was clinically stable and, deriving clinical benefit, as determined by the investigator.

The majour efficacy outcome measure was overall survival (OS). Tumour assessments were conducted every 6 weeks for the first 24 weeks, then every 8 weeks until confirmed objective disease progression. A statistically significant improvement in OS was demonstrated in patients randomised to receive durvalumab with gemcitabine and cisplatin compared to those randomised to receive placebo with gemcitabine and cisplatin. Median OS was 12.8 months (95% CI: 11.1, 14) and 11.5 months (95% CI: 10.1, 12.5) in the durvalumab and placebo arms, respectively (hazard ratio 0.80; 95% CI: 0.66, 0.97, p=0.021). The median progression-free survival was 7.2 months (95% CI: 6.7, 7.4) and 5.7 months (95% CI: 5.6, 6.7) in the durvalumab and, placebo arms, respectively. Investigator-assessed overall response rate was 27% (95% CI: 22% - 32%) and 19% (95% CI: 15%-23%) in the durvalumab and placebo arms, respectively.

The most common (≥20%) adverse reactions occurring in patients were fatigue, nausea, constipation, decreased appetite, abdominal pain, rash, and pyrexia.

The recommended durvalumab dose is 1,500 mg every 3 weeks for patients with a body weight ≥30 kg when given with gemcitabine and, cisplatin, followed by 1,500 mg every 4 weeks as a single agent until disease progression or unacceptable toxicity. For patients with a body weight <30 kg, the recommended dose is 20 mg/kg every 3 weeks with gemcitabine and, cisplatin followed by 20 mg/kg every 4 weeks until disease progression or unacceptable toxicity.

XV. Myeloid and lymphoid neoplasms with eosinophilia and abnormalities of *PDGFRA*, *PDGFRB* or *FGFR1*[26]

PDGFR$^{\beta}$-positive myeloid neoplasms are rare. Marked leukocytosis (over 100×10^{9}/L) with marked eosinophilia (over 10%) has been rarely described in myeloid neoplasms associated with PDGFR$^{\beta}$ rearrangement.[27]

The World Health Organisation (WHO) created a new category for myeloid and lymphoid neoplasms with eosinophilia and, alterations of PDGFRA, PDGFRB, or FGFR1 in their 2008 classification of malignancies of hematopoietic and lymphoid organs. Numerous of these instances exhibit myeloproliferative neoplasms, frequently accompanied by eosinophilia. However, neoplasms connected to PDGFRA rearrangement can manifest as T lymphoblastic lymphoma or acute myeloid leukaemia with eosinophilia. In addition to acute myeloid leukaemia or T lymphoblastic lymphoma, which both exhibit eosinophilia, neoplasms linked to FGFR1 rearrangement have also been reported to change into either T lymphoblasts or B lymphoblasts in chronic eosinophilic leukaemia. Because of the prominent lymphoid component these disorders have been assigned, in the WHO classification, to a specific category rather than being categorised as a myeloproliferative neoplasm. However, it should be noted that BCR-ABL1-positive chronic myelogenous leukemia is accepted as a bona fide myeloproliferative neoplasm and yet it too can undergo lymphoblastic transformation and even present as acute lymphoblastic leukemia with the underlying chronic myelogenous leukemia being revealed only after remission has been achieved.

XVI. Study of case report[27]

We report a case of 37-year-old man with myeloid neoplasm associated with PDGFRβ rearrangement who presented with marked eosinophilia of 13.3% and, leukocytosis with WBC count of 189×109/L. He was found to have PDGFRβ locus rearrangement at 5q32-33 by fluorescent in situ hybridisation (FISH). He responded very well to low-dose imatinib therapy. To the best of the knowledge to this degree of hypereosinophilia and leukocytosis in

a young adult was reported only once previously. Using low dose therapy in treating this condition has rarely been reported and has not been clearly defined. Our case demonstrated that low dose imatinib therapy can be as effective as high dose imatinib therapy in treating PDGFRβ-positive myeloid neoplasms.

XVII. Case study conclusions

The patient presented with very high WBC and eosinophil count rarely reported in a young adult with PDGFRβ-rearranged myeloid neoplasm. The recognition of this rare presentation as a manifestation of PDGFRβ-gene translocation is important, and equally important that low-dose imatinib (100 mg/day) might have the same effect as higher dose imatinib (400 mg/day). Eosinophilia, Myeloid Neoplasm, PDGFRβ rearrangement.

XVIII. Snippet

Myeloid and lymphoid neoplasms with eosinophilia and abnormalities of *platelet-derived growth factor receptor alpha* (*PDGFRA*), *platelet-derived growth factor receptor beta* (*PDGFRB*), and *fibroblast growth factor receptor-1* (*FGFR1*) are a group of hematologic neoplasms resulting from the formation of abnormal fusion genes that encode constitutively activated tyrosine kinases. These entities are now separated into their own majour category in the 2008 World Health Organisation classification of haematolymphoid tumours. Although eosinophilia is characteristic of these diseases, the clinical presentation of the three entities is variable. Conventional cytogenetics (karyotyping) will detect the majourity of abnormalities involving *PDGFRB* and *FGFR1*, but florescence *in situ* hybridisation (FISH)/molecular studies are required to detect *factor interacting with PAP* (*FIP1L1*)–*PDGFRA* as the characteristic 4q12 interstitial deletion is cryptic. Imatinib mesylate (imatinib) is the first-line therapy for patients with abnormalities of *PDGFRA/B*, whereas patients with *FGFR1* fusions are resistant to this therapy and carry a poor prognosis. The discovery of novel gene rearrangements associated with eosinophilia will further guide our understanding of the molecular pathobiology of these diseases and aid in the development of small-molecule inhibitors that inhibit deregulated haematopoiesis.[28]

XIX. Fusion genes and corresponding cytogenetic abnormalities in patients with myeloid and lymphoid neoplasms with eosinophilia and, abnormalities of *PDGFRA*, *PDGFRB*, and *FGFR1*.[28] *Table -1*.

PDGFRA	
FIP1L1–PDGFRA	del(4)(q12q12) *(cryptic)
BCR–PDGFRA	t(4;22)(q12;q11)
KIF5B–PDGFRA	Complex karyotype including: del(3)(p21), add(4)(q12),–10,13q?,+der(?)
CDK5RAP2–PDGFRA	ins(9;4)(q33;q12q25)
ETV6–PDGFRA	t(4;12)(q12;p13)
STRN–PDGFRA	***t(2;4)(p24;q12)***
PDGFRB	
ETV6–PDGFRB	t(5;12)(q33;p13)
WDR48–PDGFRB	t(1;3;5)(p36;p21;q33)
GPIAP1–PDGFRB	***der(1)t(1;5)(p34;q33), der(5)t(1;5)(p34;q15), der(11)ins(11;5)(p12;q15q33)***
TPM3–PDGFRB	t(1;5)(q21;q33)
PDE4DIP–PDGFRB	t(1;5)(q23;q33)
PRKG2–PDGFRB	t(4;5;5)(q23;q31;q33)
GOLGA4–PDGFRB	***t(3;5)(p21–25;q31–35)***
HIP1–PDGFRB	***t(5;7)(q33;q11.2)***
CCDC6–PDGFRB	***t(5;10)(q33;q21)***
GIT2–PDGFRB	***t(5;12)(q31–33;q24)***
NIN–PDGFRB	***t(5;14)(q33;q24)***
KIAA1509–PDGFRB	***t(5;14)(q33;q32)***
CEV14–PDGFRB	***t(5;14)(q33;q32)***
TP53BP1–PDGFRB	***t(5;15)(q33;q22)***
NDE1–PDGFRB	***t(5;16)(q33;p13)***
RABEP1–PDGFRB	***t(5;17)(q33;p13)***
SPECC1–PDGFRB	***t(5;17)(q33;p11.2)***
CEP85L–PDGFRB	***t(5;6)(q33–34;q23)***
KANK1–PDGFRB	t(5;9)(q31–32;p22–?24.3)
FGFR1	
ZNF198–FGFR1	t(8;13)(p11;q12)
CEP110–FGFR1	t(8;9)(p11;q33)
FGFR1OP1–FGFR1	t(6;8)(q27;p11–12)
TRIM24–FGFR1	t(7;8)(q34;p11)
BCR–FGFR1	t(8;22)(p11;q11)
MYO18A–FGFR1	t(8;17)(p11;q23)
HERVK–FGFR1	t(8;19)(p12;q13.3)
FGFR1OP2–FGFR1	ins(12;8)(p11;p11p22)
LRRFIP1–FGFR1	t(2;8)(q37;p11)
CPSF6–FGFR1	t(8;12)(p11;q15)/dic(8;12)(p11;p11)
NUP98–FGFR1	t(8;11)(p11;p15)
Not specified	t(3;8;9)(p25;p21;q34)
TPR–FGFR1	t(1;8)(q25;p11.2)
CUX1–FGFR1	t(7;8)(q22;p11)

Myeloid and, lymphoid neoplasms with eosinophilia and, abnormalities of *PDGFRB* usually present with leukocytosis with anaemia and, thrombocytopenia with progressive disease. Neutrophilia, basophilia (sometimes marked), and, eosinophilia are variable. Monocytosis is often present as many patients show features similar to CMML. The bone marrow is hypercellular with increased reticulin fibrosis (Figure **1**2). Mast cell aggregates may be seen in this entity as well.

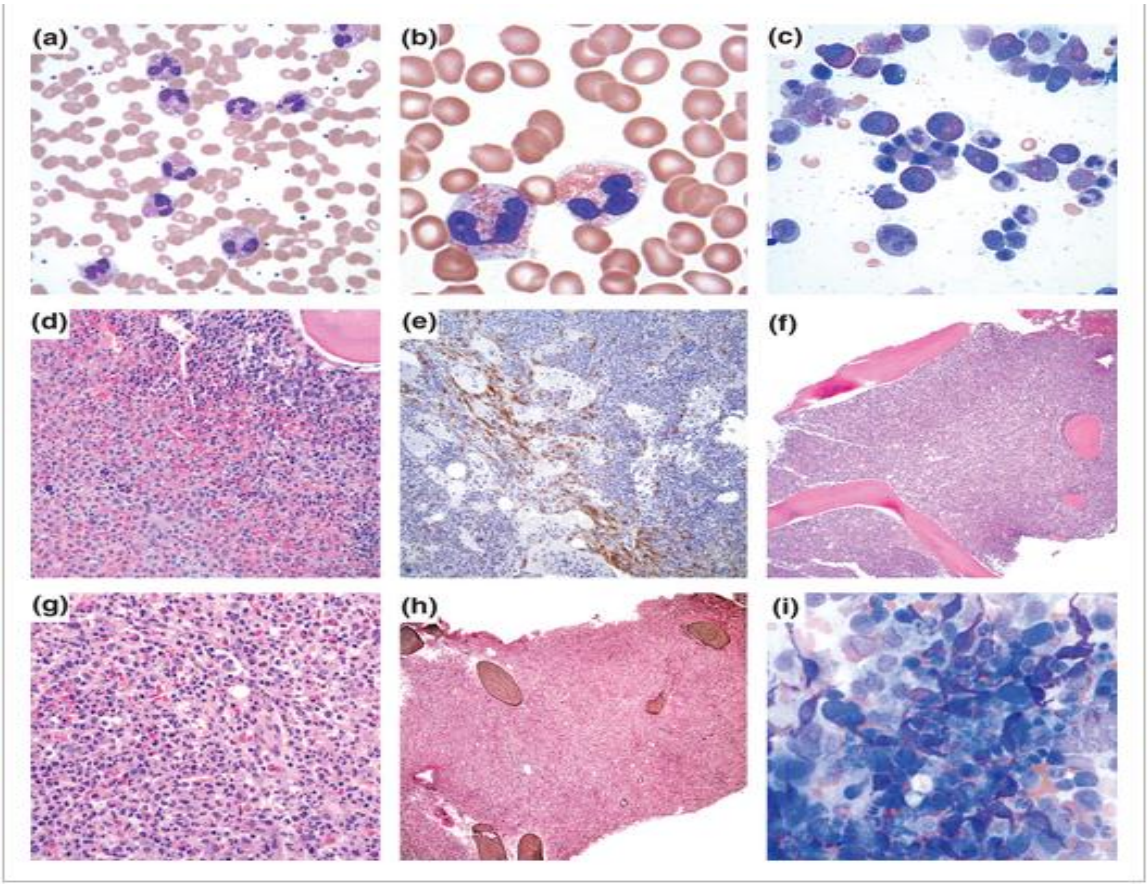


Figure 12: Morphologic findings in patients with myeloid and lymphoid neoplasms with eosinophilia and abnormalities of PDGFRA, PDGFRB, and FGFR1: (a) Peripheral blood smears typically show marked eosinophilia as in this patient (Giemsa–Wright stain, original magnification, 400×); (b) eosinophils may show morphologic abnormalities such as: cytoplasmic vacuoles or sparse granules as seen in this case with PDGFRA rearrangement (Giemsa–Wright stain, original magnification, 1000×); (c) similar to peripheral blood smears, aspirate smears will often show eosinophilia (Giemsa–Wright stain, original magnification, 400×); (d): commonly in cases with rearrangements of PDGFRA or PDGFRB, pale-staining cells with spindled morphology can be appreciated in loose clusters (noted here abutting trabecular bone), consistent with an abnormal mast cell proliferation as seen in this patient with PDGFRA

rearrangement (haematoxylin and eosin stain, original magnification, 200×); (e) CD25 can aberrantly highlight these atypical mast cells (CD25 immunohistochemical stain, original magnification, 200×); (f) bone marrow biopsies will typically be hypercellular as seen in this case with PDGFRB rearrangement (haematoxylin and eosin stain, original magnification, 40×); (g) this case shows myeloid hyperplasia with eosinophilia and dilated sinuses (haematoxylin and eosin stain, original magnification, 400×); (h) marrow fibrosis is a common feature (reticulin histochemical stain, original magnification, 40×); (i) very few cases with FGFR1 rearrangements have been reported with an associated atypical mast cell proliferation including this case; note the numerous mast cells with atypical spindled morphology (Giemsa–Wright stain, original magnification, 600×).

XX. FDA approves pemigatinib for relapsed or refractory myeloid/lymphoid neoplasms with FGFR1 rearrangement[25,29]

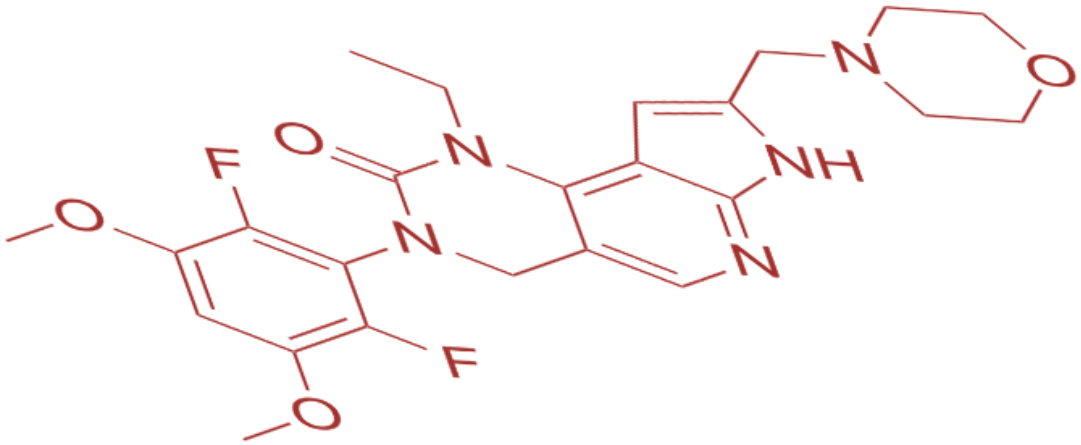


Figure 13: Structure of Pemigatinib.[46]

On August 26, 2022, the Food and, Drug Administration approved pemigatinib (Pemazyre, Incyte Corporation) for adults with relapsed or refractory myeloid/lymphoid neoplasms (MLNs) with fibroblast growth factor **receptor 1** (FGFR1) rearrangement.

Efficacy was evaluated in **FIGHT-203** (NCT03011372), a multicentre open-label, single-arm trial that included 28 patients with relapsed or refractory MLNs with FGFR1 rearrangement. Eligible patients were either not candidates for or have relapsed after allogeneic hematopoietic stem cell transplantation (allo-HSCT) or after a disease modifying therapy (e.g., chemotherapy). Pemigatinib was administered until disease progression, unacceptable toxicity, or until patients were able to receive allo-HSCT.

Selected demographics and, baseline characteristics were: median age of 65 years (range, 39 to 78); 64% female; 68% White, 3.6% Black or African American, 11% Asian, and 3.6% American Indian/Alaska Native; and 88% ECOG performance status of 0 or 1.

Efficacy was established based on complete response (CR) rates per the response criteria relevant to the morphologic disease type. Of the 18 patients with chronic phase in the marrow with or without extramedullary disease (EMD), 14 achieved CR (78%; 95% CI: 52, 94). The median time-to-CR was 104 days (range, 44 to 435). The median duration was not reached (range: 1+ to 988+ days). Of the 4 patients with blast phase in the marrow with or without EMD, 2 achieved CR (duration: 1+ and 94 days). Of 3 patients with EMD only, 1 achieved a CR (duration: 64+ days). For all 28 patients (including 3 patients without evidence of morphologic disease), the complete cytogenetic response rate was 79% (22/28; 95% CI: 59, 92).

The most common (≥20%) adverse reactions occurring in patients were hyperphosphatemia, nail toxicity, alopecia, stomatitis, diarrhoea, dry eye, fatigue, rash abdominal pain, anaemia, constipation, dry mouth, epistaxis, serous retinal detachment, extremity pain, decreased appetite, dry skin, dyspepsia, back pain, nausea, blurred vision, peripheral oedema, and dizziness.

The most common (≥10%) Grade 3 or 4 laboratory abnormalities were decreased phosphate, decreased lymphocytes, decreased leukocytes, decreased platelets, increased alanine aminotransferase, and decreased neutrophils.

The recommended pemigatinib dose is 13.5 mg orally once daily on a continuous basis until disease progression or unacceptable toxicity.

XXI. Graft vs. host disease: Also called: GVHD, runt disease.

A condition that occurs when donor bone marrow or stem cells attack the recipient.

Graft-versus-host disease can occur at any time after a transplant. However, it's more common after the marrow has started to make healthy cells. The condition can be mild or severe.

Symptoms vary based on how long someone has had the condition, but may include mouth ulcers, abdominal pain and rash.

Treatment includes medication to suppress the immune system, such as: i. steroids.

XXII. Graft versus host disease, additional information: chronic and acute

Graft versus host disease (GvHD) is a condition that might occur after an allogeneic transplant. In GvHD, the donated bone marrow or peripheral blood stem cells view the recipient's body as foreign, and the donated cells/bone marrow attack the body.

There are two forms of GvHD: i. Acute graft versus host disease (aGvHD). ii. Chronic graft versus host disease (cGvHD). As an allogeneic transplant recipient, you might experience either form of GvHD, both forms, or neither.[31] Graft-versus-host disease (GVHD) is a potentially serious complication of allogeneic stem cell transplantation and reduced-intensity allogeneic stem cell transplantation. During allogeneic stem cell transplantation, a patient receives stem cells from a donor or donated umbilical cord blood. GVHD occurs when the donor's T cells (the graft) view the patient's healthy cells (the host) as foreign, and attack and damage them. Graft-versus-host disease can be mild, moderate or severe. In some cases, it can be life-threatening.[32]

XXIII. Summarised as

Chronic graft versus host disease **(GVHD)** is a complication that can occur after a stem cell or bone marrow transplant in which the newly transplanted donor cells attack the transplant recipient's body. Symptoms may include skin rash, mouth sores, dry eyes, liver inflammation, and development of scar tissue in the skin and joints, and damage to the lungs. The exact cause of chronic GVHD is unknown. It likely results from a complex immune-mediated interaction between the donor and the recipient cells.[30] **(GARD).**

XXIV. Some common medications that are given to prevent GVHD include[32]

I. Abatacept (Orencia®),
II. Antithymocyte globulin (ATG),
III. Alemtuzumab (Campath®),
IV. Belumosudil (Rezurock™),
V. Corticosteroids (methylprednisolone or prednisone),
VI. Cyclophosphamide (Cytoxan®),
VII. Cyclosporine,
VIII. Methotrexate (Trexall®),
IX. Mycophenolate mofetil (CellCept®),
X. Sirolimus (Rapamune®),
XI. Tacrolimus (Prograf®).

FDA approves ibrutinib for paediatric patients with chronic graft versus host disease, including a new oral suspension on **August 24, 2022,** the **Food and Drug Administration**

approved **ibrutinib** (Imbruvica, Pharmacyclics LLC) for paediatric patients ≥ 1 year of age with chronic graft versus host disease **(cGVHD)** after failure of 1 or more lines of systemic therapy. Formulations include capsules, tablets, and, oral suspension.

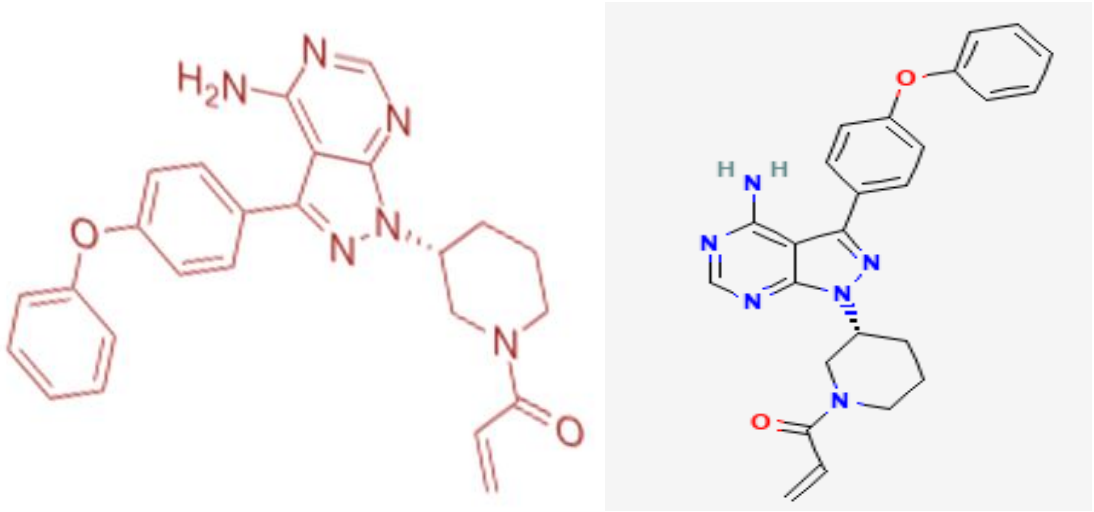


Figure 14: Structure of Ibrutinib.[47]

Efficacy was evaluated in iMAGINE **(NCT03790332)**, an open-label, multi-centre, single-arm trial of ibrutinib for paediatric and, young adult patients 1 year to less than 22 years old with moderate or severe **cGVHD**. The trial included 47 patients who required additional therapy after failure of 1 or more lines of systemic therapy. Patients were excluded if single organ genitourinary involvement was the only manifestation of **cGVHD**.

The median age of patients was 13 years (range, 1 to 19). Selected demographics of the 47 patients were as follows: 70% male, 36% White, 9% Black or African American, 55% other or unreported.

The main efficacy outcome measure was overall response rate (ORR) through Week 25. ORR included complete response or partial responses according to the 2014 NIH Consensus Development Project Response Criteria. ORR by Week 25 was 60% (95% CI: 44, 74). The median duration of response was 5.3 months (95% CI: 2.8, 8.8). The median time from first response to death or new systemic therapies for **cGVHD** was 14.8 months (95% CI: 4.6, not evaluable).

The most common (≥20%) adverse reactions, including; laboratory abnormalities, were: anaemia, musculoskeletal pain, pyrexia, diarrhoea, pneumonia, abdominal pain, stomatitis, thrombocytopenia, and, headache.

The recommended dosage of IMBRUVICA for patients 12 years of age and older with **cGVHD** is 420 mg orally once daily, and for patients 1 to less than 12 years of age with **cGVHD** is 240 mg/m^2 orally once daily (up to a dose of 420 mg), until **cGVHD** progression, recurrence of an underlying malignancy, or unacceptable toxicity.[33]

XXV. Trastuzumab deruxtecan in *HER2*-Mutant non–small-cell lung cancer

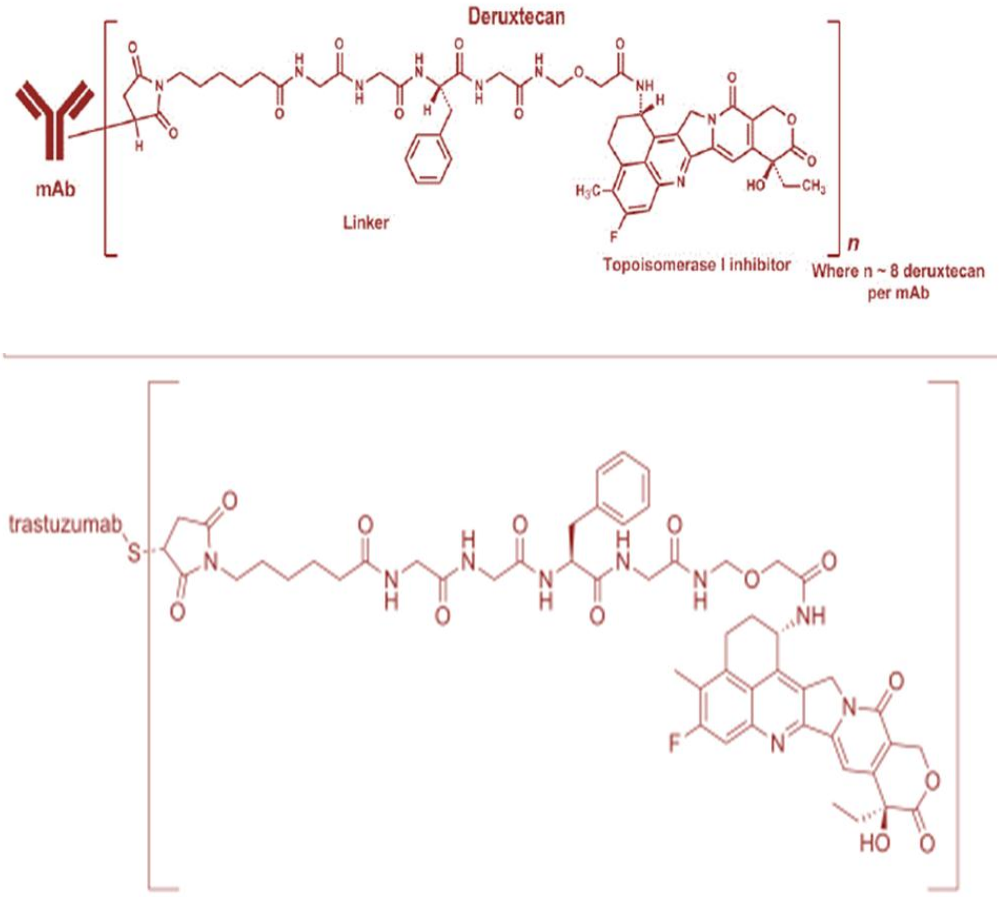


Figure 15: Structure of Trastuzumab deruxtecan.[48]

The lungs are a pair of cone-shaped breathing organs in the chest. The lungs bring oxygen into the body as you breathe in. They release carbon dioxide, a waste product of the body's cells, as you breathe out. Each lung has sections called lobes. The left lung has two lobes. The right lung is slightly larger and, has three lobes. The two tubes called bronchi lead from the trachea (windpipe) to the right and the left lungs. The bronchi are sometimes also involved in lung cancer. Tiny air sacs called alveoli and, small tubes called bronchioles make up the inside of the lungs.[35]

The majority of non–small-cell lung cancers (NSCLCs) are caused by oncogenic alterations, and the development of targeted therapies has contributed to a substantial reduction in mortality from NSCLC in recent years.1,2 mutations in the gene encoding human epidermal growth factor receptor 2 (HER2, also called ERBB2) drive approximately 3% of non-squamous NSCLCs and are associated with female sex, never-smoking history, and a poor prognosis, as well as with a slightly younger age and higher incidence of brain metastases than NSCLC without HER2 mutations or with other mutations.

Although HER2 targeting has transformed the treatment of patients with breast and, gastric cancers, HER2-targeted therapies have not been approved for patients with NSCLC. Therefore, patients with HER2-mutant NSCLC are currently treated with standard chemotherapy or immunotherapy, which have limited activity as second- or later-line treatment.[34]

1. Non-small cell lung cancer is a disease in which malignant (cancer) cells form in the tissues of the lung.
2. There are several types of non-small cell lung cancer.
3. Smoking is the majour risk factor for non-small cell lung cancer.
4. Signs of non-small cell lung cancer include a cough that doesn't go away and results in the shortness of the breath.
5. Tests that examine the lungs are used to diagnose and stage non-small cell lung cancer.
6. If lung cancer is suspected, a biopsy is done.
7. Certain factors affect prognosis (chance of recovery) and, treatment options.
8. For most patients with non-small cell lung cancer, current treatments do not cure the cancer.[35]

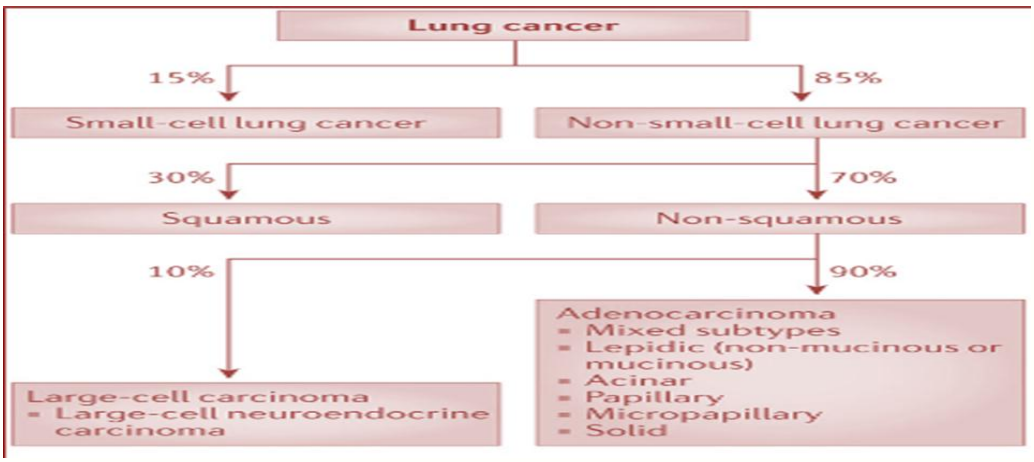


Figure 16: Lung cancer study.

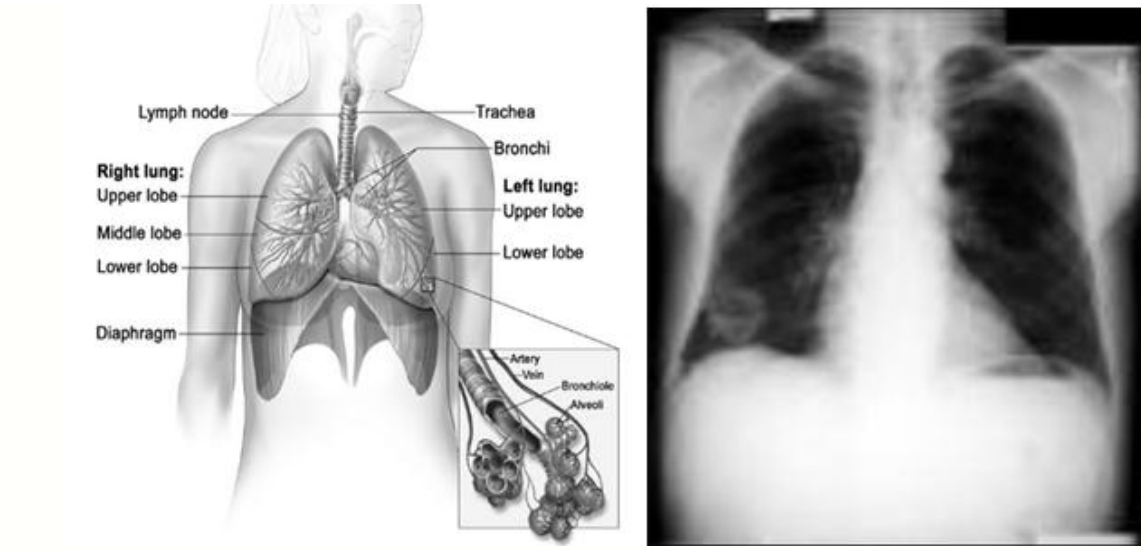


Figure 17: Anatomy of the respiratory system, showing the trachea and both lungs and their lobes and airways. Lymph nodes and the diaphragm are also shown. Oxygen is inhaled into the lungs and passes through the thin membranes of the alveoli and, into the bloodstream. And an x-ray image for diagnostic purposes.[35,36,42]

XXVI. Risk factors for lung cancer include the following[35]

I. Smoking cigarettes, pipes, or cigars, now or in the past. This is the most important risk factor for lung cancer. The earlier in life a person starts smoking, the more often a person smokes, and the more years a person smokes, the greater the risk of lung cancer.

II. Being exposed to second-hand smoke. (Inhaling secondhand smoke is called involuntary or passive smoking. Also called **environmental tobacco smoke and ETS**.)

III. Being exposed to asbestos, arsenic, chromium, beryllium, nickel, soot, or tar in the workplace.

XXVI.a. Being exposed to radiation from any of the following

I. Radiation therapy to the breast or chest.

II. Radon in the home or workplace.

III. Imaging tests such as: CT scans.

IV. Being infected with the human immunodeficiency virus (HIV).

V. Atomic bomb radiation.

VI. Living where there is air pollution.

VII. Taking beta carotene supplements and being a heavy smoker.

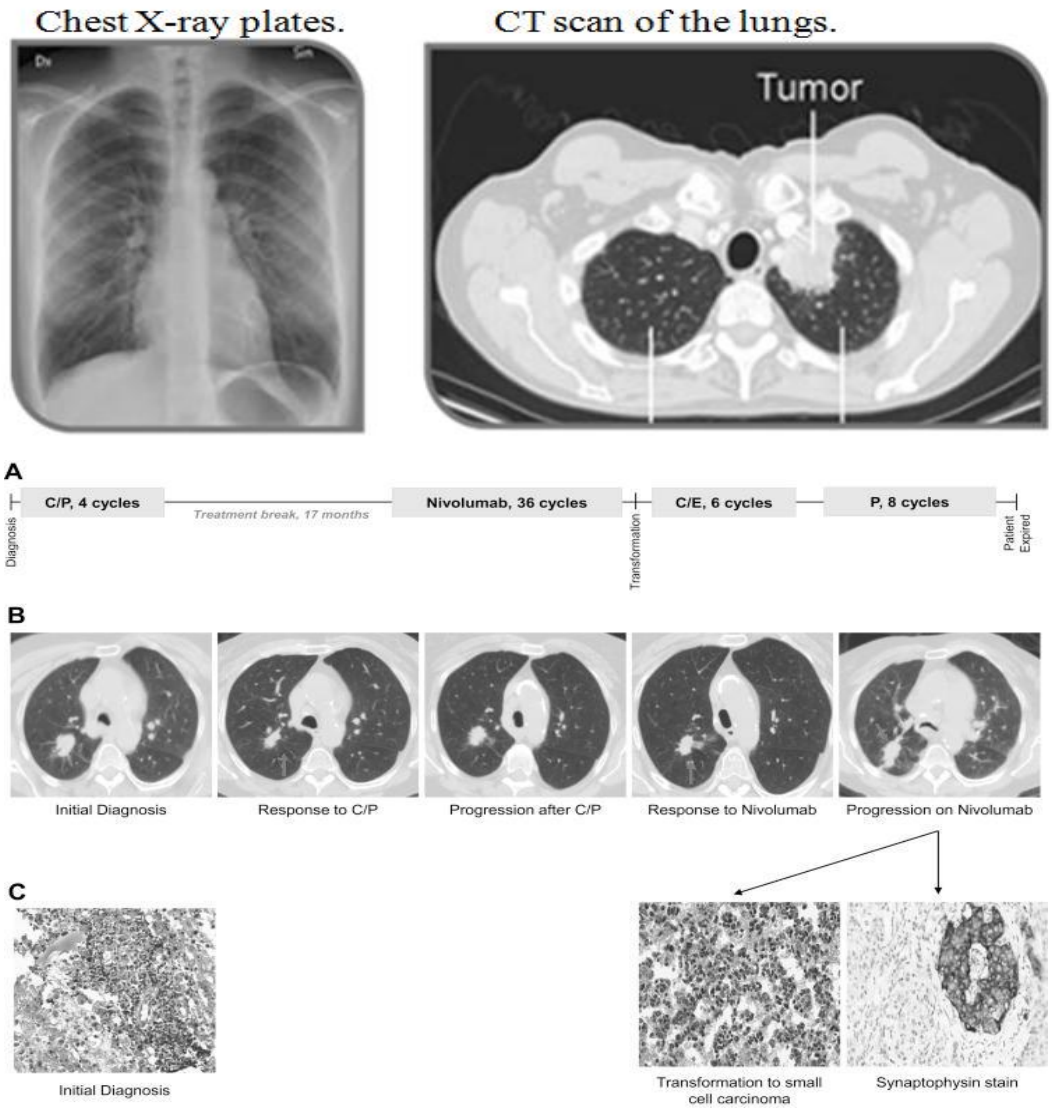
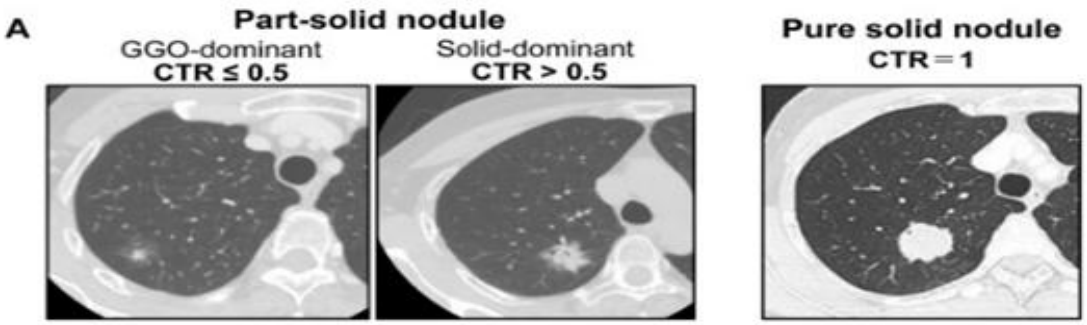


Figure 18: Advanced NSCLC (non-small cell lung cancer), Small Cell Lung Cancer Transformation as a mechanism of resistance to PD-1 therapy in KRAS-Mutant Lung Adenocarcinoma.[37,38]



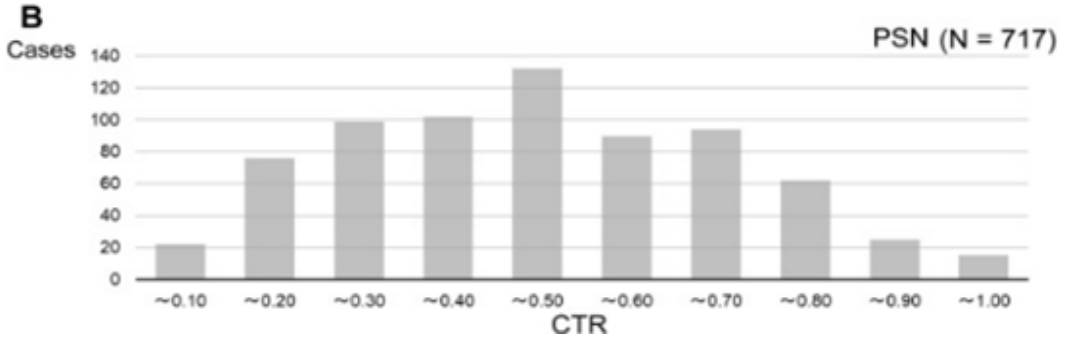


Figure 19: A) Representative computed tomography images of pure solid nodules, solid-dominant PSNs, and GGO-dominant PSNs. (B) Histogram of the distribution of CTR of PSNs. CTR, consolidation-to-tumour ratio; GGO, ground-glass opacity; PSN, part-solid nodule.

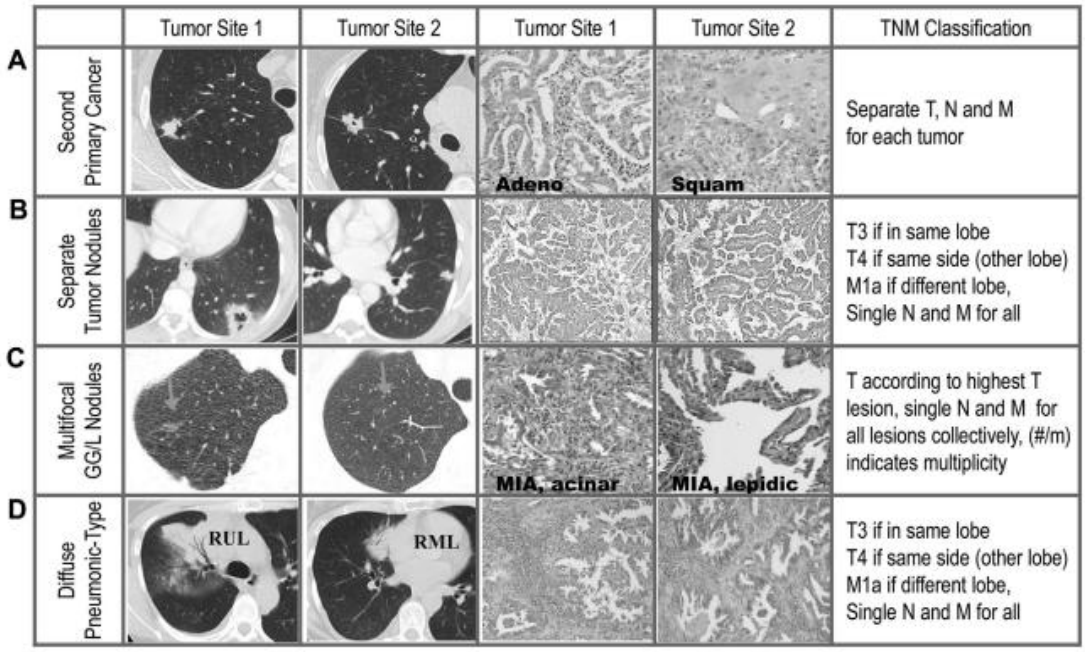


Figure 20: Representative examples of four patterns of disease that manifest multiple pulmonary sites of lung cancer. (A) Second primary cancers. A patient with two primary lung cancers in the RUL. CT images of each in the left two panels; corresponding microscopic images showing an adenocarcinoma and a squamous carcinoma in the next two panels. Note that most second primary cancers are of the same (not a different) histologic type. (B) Separate tumour nodules. A patient with a separate tumour nodule of the same histotype as the index tumour. The left panels show CT images of each lesion; the right panels show the corresponding microscopic images. (C) Multifocal GG/L lung cancer. A patient with multifocal GG/L tumours in the right

upper lobe (who had other GG/L tumours in other lobes). Arrows point to two GG/L tumours on CT in the left two panels; the next two panels show corresponding microscopic images (both were adenocarcinoma with a prominent lepidic component, although with different other adenocarcinoma subtypes). These tumours are classified together as GG/L tumours regardless of such secondary differences. (D) Pneumonic-type lung cancer. A patient with pneumonic-type lung cancer (this patient also had focal sites of disease in the RLL). The left panels show CT images of the RUL and RML with the typical regional areas with a ground glass and consolidative appearance; the next panels show the corresponding microscopic images. Adeno, adenocarcinoma; CT, computed tomography; GG/L tumours, tumours with prominent ground glass (imaging) or lepidic (histologic) features; MIA, minimally invasive adenocarcinoma; RLL, right lower lobe; RML, right middle lobe; RUL, right upper lobe; Squam, squamous cell carcinoma.[43]

FDA granted accelerated approval to fam-trastuzumab deruxtecan-nxki for HER2-mutant non-small cell lung cancer. On **August 11, 2022**, the Food and Drug Administration granted accelerated approval to fam-trastuzumab deruxtecan-nxki (Enhertu, Daiichi Sankyo, Inc.) for adult patients with unresectable or metastatic non-small cell lung cancer (NSCLC) whose tumours have activating human epidermal growth factor receptor 2 HER2 (ERBB2) mutations, as detected by an FDA-approved test, and who have received a prior systemic therapy. This is the first drug approved for HER2-mutant NSCLC.

FDA also approved the Life Technologies Corporation's Oncomine™ Dx Target Test (tissue) and the Guardant Health, Inc.'s Guardant360® CDx (plasma) as companion diagnostics for Enhertu. If no mutation is detected in a plasma specimen, the tumour tissue should be tested.

Enhertu was evaluated at a 6.4 mg/kg dose (n=152) across multiple trials and at a 5.4 mg/kg dose (n=102) in a randomised dose-finding trial. Response rates were consistent across dose levels. Increased rates of interstitial lung disease/pneumonitis were observed at the higher dose. The efficacy results of the approved recommended dose of 5.4 mg/kg given intravenously every 3 weeks are described below:

Efficacy for accelerated approval was based on DESTINY-Lung02, a multicentre, multi-cohort, randomised, blinded, dose-optimisation trial. Eligible patients were required to have unresectable or metastatic HER2-mutant non-squamous NSCLC with disease progression after prior systemic therapy. Patients were selected for treatment with Enhertu based on the

presence of activating HER2 (ERBB2) mutations in a tumour specimen. Patients received Enhertu 5.4 mg/kg by intravenous infusion, every 3 weeks until unacceptable toxicity or disease progression.

Of the 52 patients in the primary efficacy population DESTINY-Lung02, the median age was 58 years (range 30 to 78), 69% were female; 79% were Asian, 12% were White, and 10% were of other races. The majour efficacy outcome measures were confirmed objective response rate (ORR) as assessed by blinded independent central review using RECIST v1.1 and duration of response (DOR). The confirmed ORR was 58% (95% CI: 43, 71) and the median DOR was 8.7 months (95% CI: 7.1, not estimable [NE]).

The most common (≥20%) adverse reactions, including laboratory abnormalities, were nausea, decreased white blood cell count, decreased haemoglobin, decreased neutrophil count, decreased lymphocyte count, decreased platelet count, decreased albumin, increased aspartate aminotransferase, increased alanine aminotransferase, fatigue, constipation, decreased appetite, vomiting, increased alkaline phosphatase, and alopecia. The prescribing information includes a Boxed Warning advising health professionals of the risk of interstitial lung disease and embryo-foetal toxicity.[44]

XXVII. Some common phytoconstituents that help fight cancer[52]

XXVII. a. Anticancer properties of certain herbal compounds

a.i. Polyphenols

Polyphenols' cytotoxicity on a variety of cancer cells has been demonstrated, and their antioxidant properties have been determined.

Polyphenolic compounds, which include flavonoids, tannins, curcumin, resveratrol, and gallacatechins, are all anticancer compounds. Resveratrol can be found in a variety of foods, including peanuts, grapes, and red wine. Green tea contains gallacatechins. Polyphenols, which are natural antioxidants, are thought to improve health and reduce the risk of cancer. Polyphenols are thought to have apoptosis-inducing and anticancer properties that can be used. Polyphenols are thought to initiate apoptosis by regulating the mobilisation of copper ions that are bound to chromatin, thereby causing DNA fragmentation. Resveratrol was found to be capable of DNA degradation in the presence of Cu (II). Plant polyphenols can also interfere with proteins found in cancer cells, promoting their growth. Polyphenols that regulate acetylation, methylation, or phosphorylation via direct bonding can have an effect on

cancer agents. Curcumin-treated cancer cells, for example, have been shown to suppress Tumor Necrosis Factor (TNF) expression via interaction with various stimuli.

a.ii. Flavonoids

Flavonoids are polyphenolic compounds that belong to a large family of secondary metabolites found in plants, with over 10,000 known structures. They are physiologically active plant agents that are gaining scientific interest due to their potential health benefits.

a.iii. Brassinosteroids

Brassinosteroids (BRs) are naturally occurring compounds found in plants that regulate cell growth and differentiation, elongation of stem and root cells, and other functions such as: resistance and, tolerance to disease and the condition of stress. BRs are also used to regulate plant senescence. They are required for plant development and growth. BRs are another naturally occurring compound that has shown therapeutic value in the fight against cancer.

Two natural BRs were used in studies with cancerous cells to demonstrate the anticancer properties of these compounds. 28-homocastasterone (28-homoCS) and, 24-epibrassinolide (24-epiBL) have been shown to be effective at micromolar concentrations and have anticancer effects on various cancer cell lines.

Table 2: Information on anticancer agents.

Anticancer agent.	**Isolated or derived from:**	**Compound activity**.	**Research and clinical development**.
Sulphoraphane,	Isotiocynanate in cruciferous vegetables *Brassica.*	Induces phase 2 detoxification enzymes; inhibits tumor growth in breast cancers; antiproliferate effects	Clinical trials with cruciferous vegetable preparations containing sulphoraphane administered orally.
Paclitaxel (Taxol),	Taxane; *Taxus brevifolia* L.	Microtubule disruptor; block mitosis; induce apoptosis; microtubules are polymerized and stabilized; disruption of spindle formation; inhibition of translational machinery	In clinical trials; Phase I-III; early treatment settings; non-small cell lung cancer, breast cancer, ovarian cancer, Kaposi sarcoma. Alternative drug administration research and development using nanoparticles, nanocochealtes, and

			nanoliposomes.
Epipodophyllotoxin,	*Podophyllum peltatum* L.; Podophyllotoxin isomer.	Pro-apoptotic effects; cell cycle interference	Trials for lymphomas and testicular cancer.
Vincristine,	*Catharanthus roseus* G. Don; **Vinca alkaloids**.	Anti-mitotic; microtubule inhibitor; bind to β-tubulin; microtubule stabilizers or destabilizers; pro-apoptotic properties and induce cell cycle arrest; anti-tumour activity	In clinical trials for lymphomas, sarcomas, and leukemias.
Vinblastine,			In clinical trials for testicular cancer, Hodgkin's disease, and lymphoma.
Vinorelbine,			Single and combination trials for non-small cell lung cancer; Phase I-III.
Vindesine,			Clinical trials for acute lymphocytic leukaemia.
Vinflunine,			Clinical trials for activity against solid tumors; Phase III clinical trials.
Pomiferin,	Isoflavonoid isolatated from *Maclura pomifera; Dereeis Malaccensis.*	Pro-apoptotic effects; DNA fragmentation; inhibits oxidative damage of DNA; antioxidant activity; inhibits histone deacetylases; cytotoxicity of cancer cells	Six human cancer cell lines were inhibited in their growth: ACHN (kidney), NCI-H23 (lung), PC-3 (prostate), MDA-MB-231 (breast), LOX-IMVI (melanoma), and HCT-15 (colon).
Epigallacotechin-3-gallate,	**Catechin**; green tea.	Antioxidant; decrease DNA damage from oxidative stress; anti-proliferative effects; inhibition of specific kinases; inhibit carcinogenesis induced chemically or by UV	Prostate cancer clinical trials; Phase I clinical study for oral dose administration.
Combretastatin A-4 phosphate,	Water-soluble analogue of combretastatin; *Combretum caffrum.*	Anti-angiogenic; vasuclar shut-down of tumors; tumor necrosis	Early trials; mimics developed; clinical and preclinical trials.
Roscovitine,	Derived from olomucine; *Raphanus sativus* L. (*Brassicaceae*).	Inhibition of cyclin dependent kinases; reduction of cell cycle progression	Phase II clinical trials in Europe.

Flavopiridol,	Synthetic flavonoid derivative; rohitukine based structure; *Dysoxylum binectariferum*Hook.f. (*Meliaceae*).	Anti-inflammatory; immunamodulatory activity; tyrosine kinase activyt; growth inhibitory effects	Clinical trials in solid tumours, lymphomas, and leukemias in phases I and II.
Noscapine,	Opium poppy (*Papaver somniferum*).	Antiproliferative properties; microtubule interfering; inhibits tumour growth and progression	Phase I and Phase II clinical trials; limited progression due to drug solubility; drug analogue and nanotechnology research.

XXVIII. List of Abbreviations

1. Computed tomography, (CT),
2. positron emission tomography, (PET),
3. sentinel lymph node, (SLN),
4. the Cancer Genome Atlas (TCGA),
5. chronic myelomonocytic leukemia (CMML)
6. acute myeloid leukemia (AML),
7. B-lymphoblastic leukemia/lymphoma (B-ALL),
8. chronic myeloid leukemia (CML),
9. systemic mastocytosis (SM),
10. genetic and rare diseases information centre (GARD),
11. HLA (human leukocyte antigen)
12. graft-versus-host disease (GVHD),
13. consolidation-to-tumour ratio (CTR),
14. part-solid nodules (PSNs), (40)
15. overall survival (OS,). (39)
16. tumour, node, and metastasis (TNM).

XXIX. CONCLUSION

There are many different types of cancer in the human population, but they all share similar characteristics or genotypes, such as: insensitivity to signals that inhibit cell growth, allowing them to replicate indefinitely. Apoptosis is avoided and never induced in cancer cells, and angiogenesis is maintained within the tumour tissue, allowing cancer cells to survive. Plant-derived compounds have been shown to inhibit cancer cell activity by inhibiting cell proliferation and, inducing apoptotic cell death. Cancer has been a constant battle around the world, with much progress in cures and, preventative therapies. The disease is characterised by cells in the human body that are constantly multiplying and, cannot be controlled or stopped. As a result, malignant cells form tumours that have the potential to spread. Therefore, it is found that the cancer is a disease that affects the entire human population of

its cause. Chemotherapy, radiotherapy, and chemically derived drugs are currently used as treatments. Chemotherapy, for example, can put patients under a lot of stress and harm their health. As a result, there is a focus on using alternative cancer treatments and therapies. There is an ongoing need for new therapies to treat and prevent this potentially fatal disease. Herbal medicines have been used and, continue to be used as the primary source of medical treatment in developing countries for many years. Plants have been used in medicine for centuries because of their natural antiseptic properties. As a result, research has focused on the potential properties and, applications of terrestrial/marine plant extracts for the development of potential nanomaterial-based drugs for treatment of diseases such as: cancer. Many plant species are already being used to treat or prevent cancer development. Multiple researchers have identified plant species with anticancer properties, with a particular emphasis on those used in herbal medicine in developing countries. Therefore, natural-derived compounds are attracting scientific and, research attention because they are thought to have fewer toxic side effects than current treatments such as: the chemotherapy. Chemically derived epigenetic drugs such as: 5-azacytidine (azacitidine; Vidaza) and, 5-aza-2'-deoxycytidine (decitbine; Dacogen) which are both DNMTi 11 and HDACi such as: i. suberoyanilde hydroxamic acid (SAHA, Vorinostat, Zolinza) and FK228 (Romidespin, Istodax) have been developed and, tested. However, developing a chemically derived drug that is non-toxic to normal cells while being specific to cancer cell cytotoxicity is difficult. As a result, development and, research into naturally derived compounds for anticancer treatment are in high demand, with a particular emphasis on those derived from plant species and, their natural products. From the above foregoing study conducted it can be concluded that there are many new developments in the therapy using newer approved drugs, approved with clinical trials and, proved safety for its usage. (FDA approved drugs such as:

i. Durvalumab. Durvalumab; which is an antineoplastic monoclonal antibody used to treat urothelial carcinoma and, locally advanced, unresectable non-small cell lung cancer. (ibid-45) With chemical formula: protein chemical formula:$C_{6502}H_{10018}N_{1742}O_{2024}S_{42;}$ Protein average weight: 146300.0 Da. **ii. Pemigatinib**: Pemigatinib, sold under the brand name Pemazyre, is an anti-cancer medication used for the treatment of bile duct cancer. Pemigatinib works by blocking FGFR2 in tumour cells to prevent them from growing and spreading. Pemigatinib belongs to a group of medicines called protein kinase inhibitors. **iii. Ibrutinib:** Ibrutinib: it is sold under the brand name Imbruvica among others, is a small molecule drug that inhibits B-cell proliferation and, survival by irreversibly binding the protein Bruton's tyrosine kinase. Blocking BTK inhibits the B-cell receptor pathway, which is often aberrantly active in B cell

cancers. **Formula:** $C_{25}H_{24}N_6O_2$, Ibrutinib is in a class of medications called kinase inhibitors. It works by blocking the action of the abnormal protein that signals cancer cells to multiply. This helps stop the spread of cancer cells. **ENHERTU** is FDA-approved for the treatment of several types of cancer Fam-trastuzumab deruxtecan-nxki injection is used to treat HER2-positive metastatic (cancer that has spread to other parts of the body) breast cancer or whose cancer cannot be removed with surgery in patients who have previously received an anti-HER2 breast cancer treatment for metastatic disease or have breast cancer that has come back during or within 6 months of completing treatment for early-stage breast cancer.

Cancer is the leading cause of death in young as well as adults, therefore proper diagnosis, recommendation of dosage regimen; good therapy profile is one of the extensive requirements for the development of such therapy profiles for the treatment of the cancers amongst patients.

A strategy for the detection and, the treatment of cancer is an essential part of any comprehensive cancer control strategy that are a part of the clinical trials as well as a part of NDA process along with therapy profiles in the patients, and volunteers involved in the trials for the process in filing of NDA. Its primary objective is to either completely cure cancer patients or greatly extend their lives while ensuring a high quality of life. A diagnostic and, treatment plan should never be created in a vacuum if it is to be effective. It must be connected to a programme for early detection in order to identify patients when they are still treatable and, more likely to be cured. Additionally, it needs to be combined with a palliative care programme to provide patients with advanced cancers who are no longer candidates for treatment with enough comfort from their physical, emotional, and spiritual suffering. Additionally, programmes should have a component aimed at raising awareness about cancer risk factors and, the importance of taking preventative actions to avoid contracting cancer. This programme includes food habits, carcinogens in the food and drug substances, or intake of carcinogens from different materials such as:

i. Melamine, $C_3H_6N_6$. released in the food or water through the servings. Melamine is a white solid in appearance, that is soluble in water. In one large-scale application, melamine is combined with formaldehyde and other agents to produce melamine resins.

This white solid is a trimer of cyanamide, with a 1,3,5-triazine skeleton. Like cyanamide, it contains 67% nitrogen by mass, and its derivatives have fire retardant properties due to its release of nitrogen gas when burned or charred. Melamine can be combined with

formaldehyde and other agents to produce melamine resins. **a. Chronic toxicity:** Ingestion of melamine may lead to reproductive damage, or bladder or kidney stones, which can lead to bladder cancer. A study in 1953 reported that dogs fed 3% melamine for a year had the following changes in their urine: reduced specific gravity, increased output, melamine crystalluria, and protein and occult blood. Ibid.[49] Melamine as a chemicals substance that cause tumours of the kidney or urinary bladder in rodents. Ibid.[50] From the study it is also clear that newer research development in anti-cancer studies have been successful in clinical trials and, its phases. Studies have also demonstrated that the FDA approved the NDA and regarded it as a safe medicine for use. The plant kingdom produces naturally occurring secondary metabolites that are being studied/investigated for anticancer properties, which could lead to the development of new clinical drugs. With the success of these compounds that have been developed into standard cancer treatments, new technologies are emerging to further develop the field. Nanoparticles for nanomedicines, for example, aim to improve the anticancer activities of plant-derived drugs by controlling the release of the compound and, investigating new methods of administration. *Catharanthus roseus,* of the Apocynaceae, also known as *Vinca rosea*, is indigenous to Madagascar, Europe and India and also, in United States of America, Australia. Along with its anti-cancer properties it is used as: antidysentric, antihaemorrhagic, diuretic and, wound healing, also as a tea in treatment of diabetes. The majour component that the *Vinca rosea* have are: indole alkaloids. Example: vinca-leucoblastine, leurosine, leurosidine, leurocristine as an anti-cancer drug isolated or derived from *Catharanthus roseus. Catharanthus roseus* have of about majour 20 dimeric indole-dihydroindole alkaloids that have oncolytic activity. The Vinblastin is the majour indole alkaloid which have a specific part named catharanthine and, dihydroindole alkaloid part named as vindoline. Other effective chemicals include: ajamalicine, locherine and, tetrahydroalstonine. The dose of Vincristine sulphate is 10 to 30 µg/Kg intravenously with significant high dosing of 2 mg. Also, Vinblastine sulphate; 100 µg/Kg of body weight have been very effective oncolytic agents to treat several types of cancer. Dosage regimens of such, herbal based preparation that includes *Catherantus roseus* phytoconstituents are: tablets, syrups, gels, sachets, creams, jellies, polyherbal jams etc are majour preparations of such kind for the anti-cancer remedy. Today's plant-derived anticancer agents fall into four categories: vinca alkaloids (vinblastine, vincristine, and vindesine), epipodophyllotoxins (etoposide and teniposide), taxanes (paclitaxel and docetaxel), and camptothecin derivatives (camptotecin and irinotecan). Ibidem, idem 51. Thus, curing to cancer with such significant strategy-based drug medicine models are very effective with appropriate development in the

dosage forms as mentioned above in the conclusion section and as well in the **table 2** of this scientific content article structured for understanding of the current and, the recent advanced treatment in the market or hospitals for a particular cancer treatment in a patient.

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XXXII. REFERENCE

1. https://www.cancer.org/treatment/treatments-and-side-effects/treatment-types/chemotherapy/how-chemotherapy-drugs-work.html [Accessed on: September, 4-2022].
2. https://medlineplus.gov/ency/article/001310.htm [Accessed on: September, 4- 2022].
3. https://en.wikipedia.org/wiki/Bat_as_food [Accessed on: September, 4- 2022].
4. https://en.wikipedia.org/wiki/Cat_meat#:~:text=Cat%20meat%20is%20meat%20prepared,desperation%20during%20wartime%20or%20poverty. [Accessed on: September, 4-2022].
5. https://en.wikipedia.org/wiki/Dog_and_Cat_Meat_Trade_Prohibition_Act_of_2018 [Accessed on: September, 4- 2022].
6. Cooper GM. The Cell: A Molecular Approach. 2nd edition. Sunderland (MA): Sinauer Associates; 2000. The Development and Causes of Cancer. Available from: https://www.ncbi.nlm.nih.gov/books/NBK9963/
7. Mundhenke C, Bauerschlag D, Fischer D, Friedrich M, Maass N. Maligne Tumoren des Uterus [Malignant tumors of the uterus]. Ther Umsch, 2007 Jul; 64(7): 381-8. German. doi: 10.1024/0040-5930.64.7.381. PMID: 17948755.

8. Johann S, Mueller MD. Korpuskarzinom / Zervixkarzinom [Follow-up after malignant tumours of the uterus (cancer of the uterine corpus / cervical cancer)]. Ther Umsch, 2008 Jun; 65(6): 341-6. German. doi: 10.1024/0040-5930.65.6.341. PMID: 18622958.
9. Akin O, Mironov S, Pandit-Taskar N, Hann LE. Imaging of uterine cancer. Radiol Clin North Am., 2007 Jan; 45(1): 167-82. doi: 10.1016/j.rcl.2006.10.009. PMID: 17157628.
10. Yin Lin, M., Dobrotwir, A. and McNally, O., 2018. Role of imaging in the routine management of endometrial cancer. *International journal of gynecology and obstertrics.*, [online] pp.109-117. Available at: <https://obgyn.onlinelibrary.wiley.com/doi/epdf/10.1002/ijgo.12618> [Accessed on: September, 4- 2022].
11. http://surl.li/cwrzz [Accessed on: September, 4- 2022].
12. http://surl.li/cwsas [Accessed on: September, 4- 2022].
13. http://surl.li/cwsbc [Accessed on: September, 4- 2022].
14. http://surl.li/cwsbm [Accessed on: September, 4- 2022].
15. http://surl.li/cwsby [Accessed on: September, 4- 2022].
16. http://surl.li/cwscy [Accessed on: September, 4- 2022].
17. https://www.cancercenter.com/community/blog/2017/12/whats-the-difference-benign-and-malignant-tumors [Accessed on: September, 3- 2022].
18. http://surl.li/cwsff [Accessed on: September, 3- 2022].
19. http://surl.li/cwsil [Accessed on: September, 3- 2022].
20. http://surl.li/cwskl [Accessed on: September, 3- 2022].
21. http://surl.li/cwskr [Accessed on: September, 3- 2022].
22. https://www.google.com/imgres?imgurl=https%3A%2F%2Fels-jbs-prod-cdn.jbs.elsevierhealth.com%2Fcms%2Fattachment%2F2001025812%2F2003898473%2Fgr1.jpg&imgrefurl=https%3A%2F%2Fwww.thelancet.com%2Fjournals%2Flanonc%2Farticle%2FPIIS1470204508701001%2Ffulltext&tbnid=7_3WgOXIiL9VCM&vet=12ahUKEwij3_3_-fX5AhVF_jgGHUfiBe0QxiAoAXoECAAQGQ..i&docid=WNrU8hEmk0UPSM&w=470&h=362&itg=1&q=cancer%20tumor%20images&ved=2ahUKEwij3_3_-fX5AhVF_jgGHUfiBe0QxiAoAXoECAAQGQ [Accessed on: September, 3- 2022].
23. http://surl.li/cwslw [Accessed on: September, 3- 2022].
24. https://www.fda.gov/drugs/resources-information-approved-drugs/oncology-cancer-hematologic-malignancies-approval-

notifications#:~:text=On%20August%2020%2C%202020%2C%20the,to%20three%20lines%20of%20therapy. [Accessed on: September, 3- 2022].

25. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-durvalumab-locally-advanced-or-metastatic-biliary-tract-cancer [Accessed on: September, 4- 2022].
26. Bain BJ. Myeloid and lymphoid neoplasms with eosinophilia and abnormalities of PDGFRA, PDGFRB or FGFR1. Haematologica, 2010 May; 95(5): 696-8. doi: 10.3324/haematol.2009.021675. PMID: 20442440; PMCID: PMC2864371.
27. Andrei M, Bandarchuk A, Abdelmalek C, Kundra A, Gotlieb V, Wang JC. PDGFRβ-Rearranged Myeloid Neoplasm with Marked Eosinophilia in a 37-Year-Old Man; And a Literature Review. Am J Case Rep., 2017 Feb 17; 18: 173-180. doi: 10.12659/ajcr.900623. PMID: 28209946; PMCID: PMC5325042.
28. Savage., N., George., T. and Gotlib., J., 2013. Myeloid neoplasms associated with eosinophilia and rearrangement of PDGFRA, PDGFRB, and FGFR1: a review. *International journal of laboratory hematology. The official journal of the international society for laboratory hematology*, 35(5): 491-500.
29. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-pemigatinib-relapsed-or-refractory-myeloidlymphoid-neoplasms-fgfr1-rearrangement [Accessed on: September, 4- 2022].
30. https://rarediseases.info.nih.gov/diseases/10964/chronic-graft-versus-host-disease [Accessed on: September, 4- 2022].
31. https://my.clevelandclinic.org/health/diseases/10255-graft-vs-host-disease-an-overview-in-bone-marrow-transplant [Accessed on: September, 4- 2022].
32. https://www.lls.org/treatment/types-treatment/stem-cell-transplantation/graft-versus-host-disease [Accessed on: September, 4- 2022].
33. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-ibrutinib-pediatric-patients-chronic-graft-versus-host-disease-including-new-oral [Accessed on: September, 4- 2022].
34. *Bob T. Li, Egbert F. Smit, Yasushi Goto, The new England journal of medicine.*, 2022. Trastuzumab Deruxtecan in HER2-Mutant Non–Small-Cell Lung Cancer. pp.241-251. DOI: 10.1056/NEJMoa2112431
35. https://rb.gy/bvrltr [Accessed on: September, 4- 2022].

36. https://encrypted-tbn0.gstatic.com/images?q=tbn:ANd9GcSHslyBEoSBkmXOWrjuc_mR_pwjox5bR0milLNtIaHg&s [Accessed on: September, 4- 2022].
37. https://rb.gy/iczrca [Accessed on: September, 4- 2022].
38. https://bit.ly/3ANtwQT [Accessed on: September, 4- 2022].
39. https://www.jtocrr.org/article/S2666-3643%2822%2900004-2/fulltext [Accessed on: September, 4- 2022].
40. https://www.jtocrr.org/article/S2666-3643%2822%2900004-2/fulltext [Accessed on: September, 4- 2022].
41. https://rb.gy/gpx1qp [Accessed on: September, 4- 2022].
42. https://rb.gy/hqcdes [Accessed on: September, 4- 2022].
43. https://bit.ly/3cKJUtw [Accessed on: September, 4- 2022].
44. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-fam-trastuzumab-deruxtecan-nxki-her2-mutant-non-small-cell-lung [Accessed on: September, 4- 2022].
45. https://rb.gy/bvagnr [Accessed on: September, 4- 2022].
46. https://rb.gy/jxwdss [Accessed on: September, 4- 2022].
47. https://rb.gy/fvh1x2 [Accessed on: September, 4- 2022].
48. https://www.rxlist.com/enhertu-drug.htm [Accessed on: September, 4- 2022].
49. https://en.wikipedia.org/wiki/Melamine [Accessed on: September, 1- 2022].
50. IARC Working Group on the Evaluation of Carcinogenic Risks to Humans. Some Chemicals that Cause Tumours of the Kidney or Urinary Bladder in Rodents and Some Other Substances. Lyon (FR): International Agency for Research on Cancer; 1999. (IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, No. 73.) Melamine. Available from: https://www.ncbi.nlm.nih.gov/books/NBK402098/
51. https://www.globalpubresearch.com/catharanthus-roseus [Accessed on: September, 5-2022].
52. https://newisolatedphytocompounds.blogspot.com/2022/09/plant-compounds-with-anticancer.html [Accessed on: September, 5-2022].