คณะแพทยศาสตร์ มหาวิทยาลัยขอนแก่น
FACULTY OF MEDICINE KHON KAEN UNIVERSITY

OVERVIEW OF ONCOLOGY

FOR RESIDENT 2025

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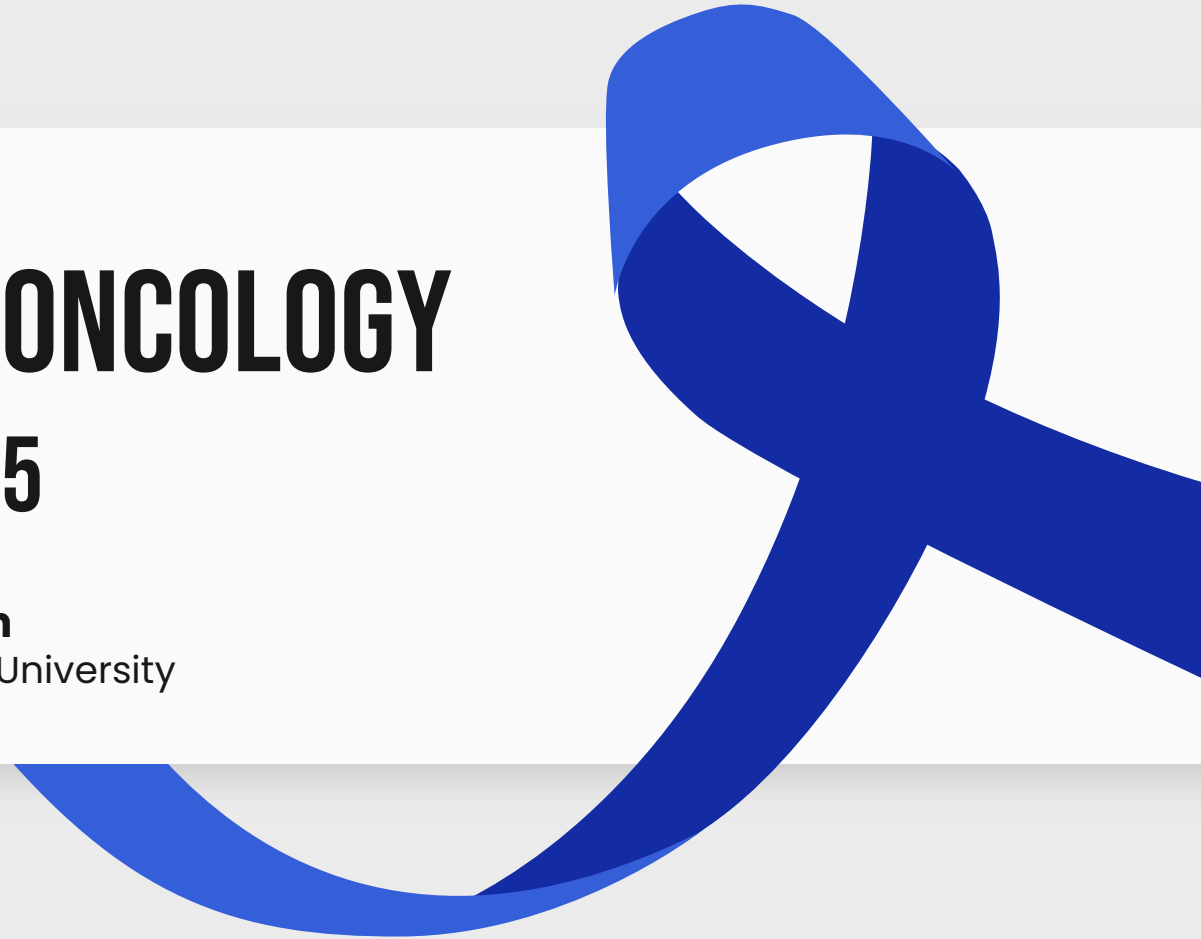

DISCLOSURES

- This academic session is sponsored by Berlin pharmaceutical industry.
- This session is oversimplified framework to guide your learning and cannot replace your lecture and personal reading.
- The information is accurate at the time of presentation and independently from sponsor.

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01

CANCER SCREENING
HEREDITARY CANCER

CANCER SCREENING

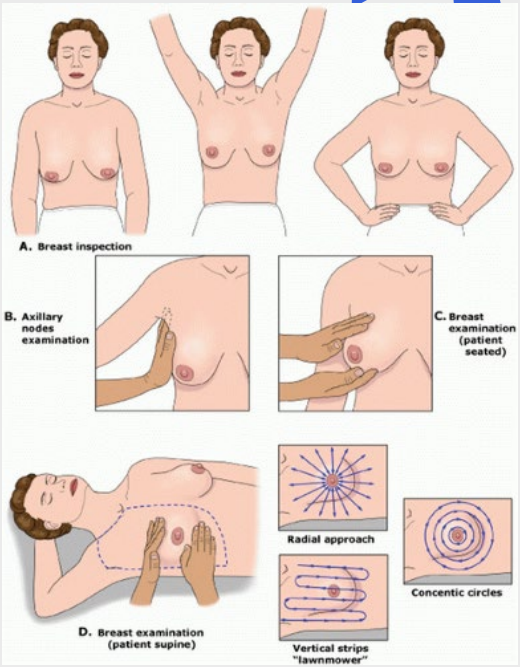
CANCER SCREENING

- **Part of secondary cancer prevention**
- **Cost-effectiveness and effective program**
  : Breast cancer
  : Colorectal cancer
  : Cervical cancer
- **Lung cancer screening using low dose CT is still debatable.**
- **No role of tumor marker in cancer screening**

BREAST CANCER SCREENING

Average risk and asymptomatic

Age	Tool
Age 25 - 39	Clinical Breast Examination q 1-3 yr
Age ≥ 40	Clinical Breast Examination q 1-3 yr Mamogram q 1 yr

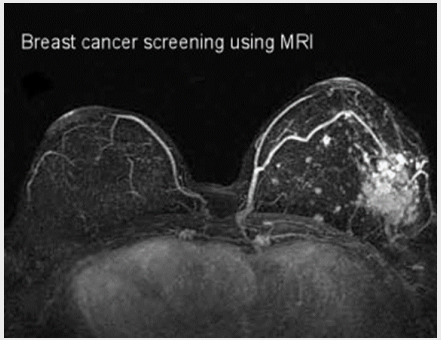


NCCN has not established an upper age limit for screening as long as that individuals in overall good health (some guidelines limit to age of 75)

BREAST CANCER SCREENING

Germline BRCA pathogenic/likely pathogenic

Tool	Starting Age
Cinical Breast Examination every 6-12 months	Age 25
MRI Breast every 1 year	Age 25
Mammogram every 1 year	Age 30 - 75



COLORECTAL CANCER SCREENING

Starting at age of 45–50

Average risk

- Age 45–75 years
- No personal history of adenoma or sessile serrated polyp/sessile serrated lesion or CRC
- No personal history of inflammatory bowel disease (IBD)
- No personal history of high-risk CRC genetic syndromes
- No personal history of cystic fibrosis
- No personal history of childhood cancer
- Negative family history for confirmed advanced adenoma
- Negative family history for CRC

Tools	**Frequency** (normal finding)
Colonoscopy	10 years
Flexible sigmoidoscopy	5 -10 years
CT colonography	5 years
Stool occult blood test	1 year
Multitargeted stool DNA-based testing	3 years

COLORECTAL CANCER SCREENING

Increased risk population

FAMILY HISTORY CRITERIA	SCREENING[fff]	
≥1 first-degree relative with CRC at any age	Colonoscopy beginning at age 40 y or 10 y before earliest diagnosis of CRC, whichever is first	Repeat every 5 y[ddd,fff,ggg,hhh] or if positive, repeat per colonoscopy findings
Second- and third-degree relatives with CRC at any age	Colonoscopy beginning at age 45 y[ddd]	Repeat every 10 y or if positive, repeat per colonoscopy findings
First-degree relative with confirmed advanced adenoma(s) (ie, high-grade dysplasia, ≥1 cm, villous or tubulovillous histology, TSA), or advanced SSPs/SSLs (≥1 cm, any dysplasia) at any age[eee,iii,jjj]	Colonoscopy beginning at age 40 y or at age of onset of adenoma in relative, whichever is first	Repeat every 5–10 y[fff,ggg] or if positive, repeat per colonoscopy findings

CERVICAL CANCER SCREENING

	การตรวจหาเชื้อเอชพีวีกลุ่มความเสี่ยงสูง (High-risk HPV Testing)		การตรวจเซลล์วิทยา (Conventional หรือ Liquid-Based Cytology)
	ตรวจหาเชื้อเอชพีวีกลุ่มความเสี่ยงสูง (แนะนำมากกว่า)	ตรวจหาเชื้อเอชพีวีกลุ่มความเสี่ยงสูงร่วมกับการตรวจเซลล์วิทยา (Co-testing)	
อายุที่เริ่มตรวจ	25 ปี	25 ปี	25 ปี
ความถี่	ทุก 5 ปี	ทุก 5 ปี	ทุก 2 ปี
อายุที่หยุดตรวจ	> 65 ปี ถ้าผลการตรวจปกติ ติดต่อกัน 2 ครั้ง	> 65 ปี ถ้าผลการตรวจปกติ ติดต่อกัน 2 ครั้ง	> 65 ปี ถ้าผลการตรวจปกติ ติดต่อกัน 5 ครั้ง

- สตรีที่อายุน้อยกว่า 25 ปี ไม่แนะนำให้ตรวจคัดกรอง ยกเว้นในสตรีที่มีความเสี่ยงสูง เช่น ติดเชื้อเอชไอวี มีคู่นอนหลายคน เป็นหูดหงอนไก่หรือเป็นโรคติดเชื้อทางเพศสัมพันธ์ เป็นต้น
- สตรีที่ตัดมดลูกพร้อมกับปากมดลูกออกแล้วและไม่มีประวัติ CIN 2-3 หรือ AIS หรือมะเร็งปากมดลูก

LUNG CANCER SCREENING

Only for High-risk population

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2025
Lung Cancer Screening

NCCN Guidelines Index
Table of Contents
Discussion

RISK ASSESSMENT[a,b,c]

- Cigarette smoking history[d]
- Radon exposure[e]
- Occupational exposure[f]
- Cancer history[g]
- Family history of lung cancer in first-degree relatives
- Disease history (chronic obstructive pulmonary disease [COPD] or pulmonary fibrosis)
- Cigarette smoking exposure[h] (second-hand smoke)
- Risk calculator to enhance determination of risk status[i,j]

Patients not eligible for lung cancer screening:

- Symptoms of lung cancer (see NCCN Guidelines for Non-Small Cell Lung Cancer)
- Previous lung cancer (see Surveillance in the NCCN Guidelines for Non-Small Cell Lung Cancer)
- Functional status and/or comorbidity that would prohibit curative intent treatment[k] (see Principles of Surgery in the NCCN Guidelines for Non-Small Cell Lung Cancer and Principles of Radiation Therapy in the NCCN Guidelines for Non-Small Cell Lung Cancer)

RISK STATUS

High risk[i,l,m]
- Age ≥50 y (category 1) and
- ≥20 pack-year history of smoking cigarettes (category 1) or ≥20 year history of smoking cigarettes[1] (category 2B)

→ In candidates for screening, shared patient/provider decision-making is recommended, including a discussion of benefits/risks[c,j]

→ Low-dose CT (LDCT)[n] (category 1)

→ Screening Findings (LCS-2)

* Use low-dose CT
* CXR is not recommended for lung cancer screening

Low risk
- Age <50 y and/or
- <20 pack-year history of smoking cigarettes or <20 year history of smoking cigarettes[1] (category 2B)

→ Lung cancer screening not recommended

HEREDITARY CANCER

HEREDITARY CANCER

Characteristics suspicious for hereditary cancer

- Cancers occurring at **younger ages** than usual
- **More than one type of cancer** in a single person
- Cancers occurring in **both of a pair of organs**
- Cancer occurring in the **sex not usually affected** (e.g. breast cancer in a man)
- **Two or more family members with similar cancer** or cancer syndrome related cancer
- Clinical finding associated with hereditary cancer

Cancer syndrome needed to know

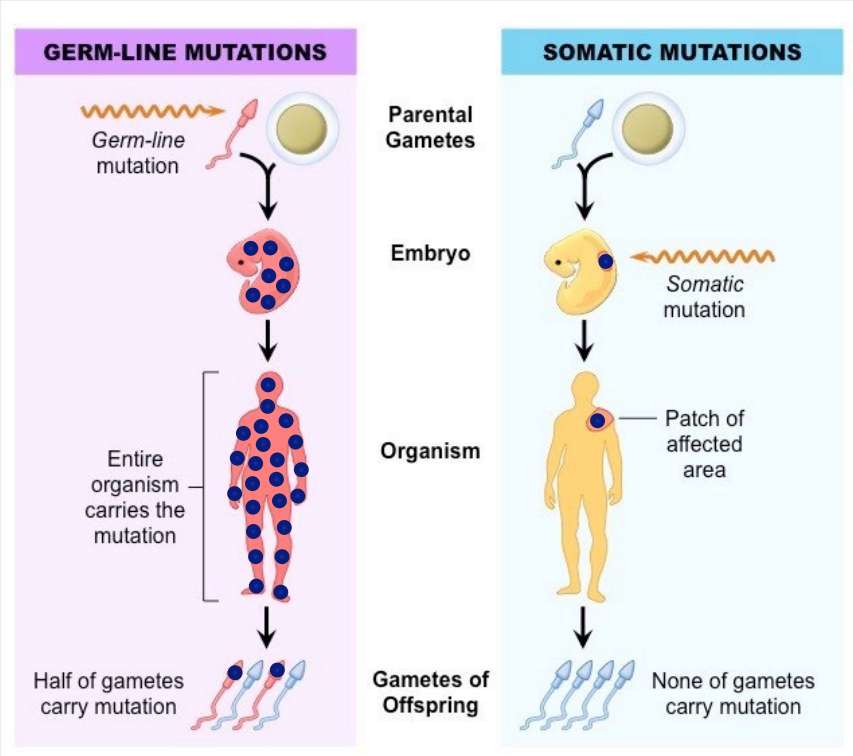
- BRCA-related cancer
- Familial colorectal cancer: FAP, HNPCC

MUTATION

- **Somatic mutations**
  : Occur in a single body cell and cannot be inherited
  : Only tissues derived from mutated cell are affected

- **Germline mutations**
  : Occur in gametes and can be passed onto offspring
  : Every cell in the entire organism will be affected

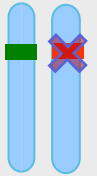
Hereditary cancer



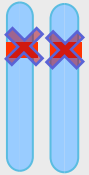
KNUDSON'S TWO HIT HYPOTHESIS

Inherited case

One normal allele
+
One mutant allele
(1st "hit")

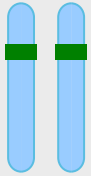


Two mutant alleles
(2nd "hit")



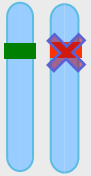
Tumorigenesis

Sporadic case

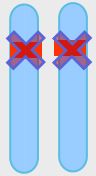


Two normal alleles

One normal allele
+
One mutant allele
(1st "hit")



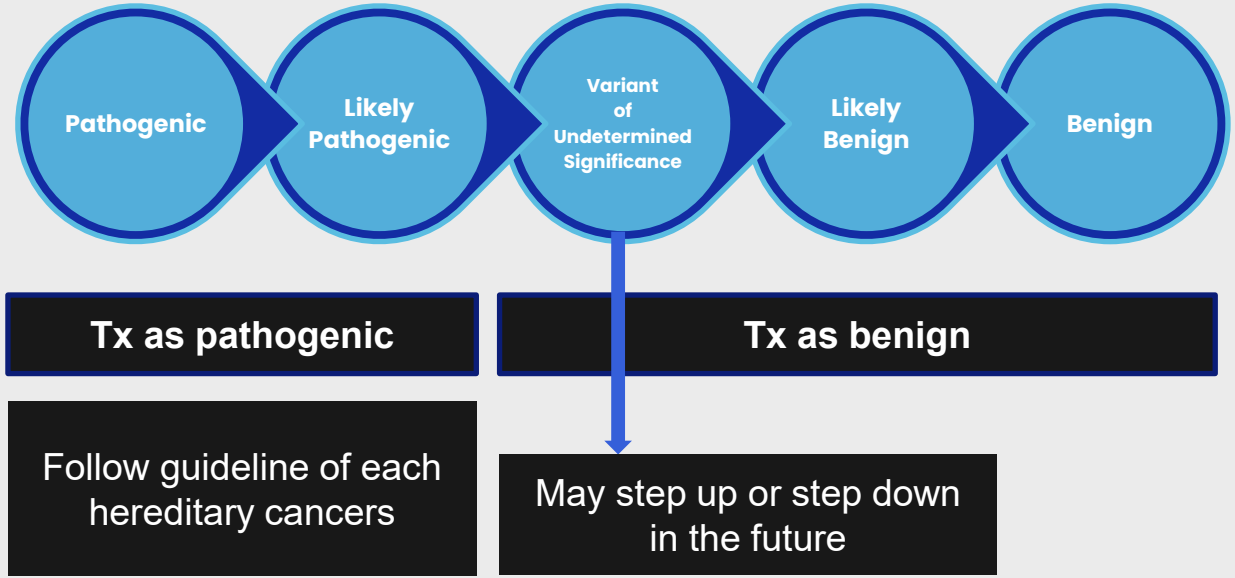
Two mutant alleles
(2nd "hit")



Tumorigenesis

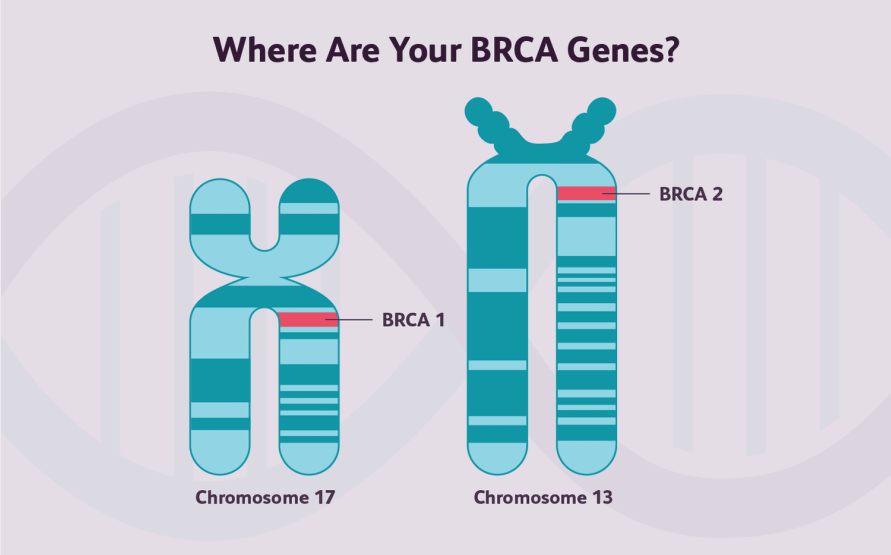
GERMLINE VARIANTS INTERPRETATION

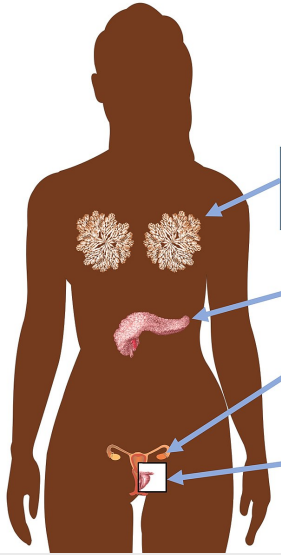
Based on ACMG-AMP Guideline 2015



BRCA-RELATED CANCER

- **BRCA1 and BRCA2** are tumor suppressor genes, involving in DNA repair pathway called homologous recombinant repair.

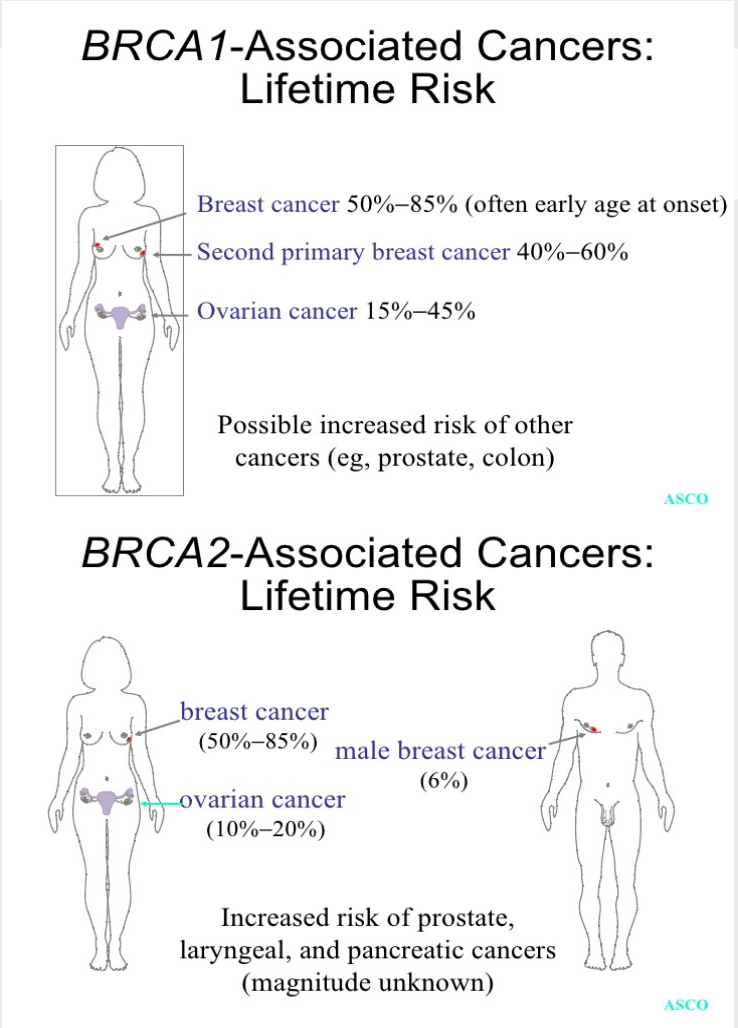




	BRCA1	BRCA2
Breast cancer:	**50% to 65%** Males: 1.2%	**40% to 55%** Males: Up to 9%
Pancreas cancer:	1-3%	2-7%
Ovarian cancer:	**40% to 65%**	**15% to 25%**
Prostate cancer:	9%	15%

BRCA-RELATED CANCER

- Multiple cases of early onset breast cancer
- Ovarian cancer (with family history of breast or ovarian cancer)
- Breast and ovarian cancer in the same woman
- Bilateral breast cancer
- Ashkenazi Jewish heritage
- Male breast cancer



CLINICAL USE BRCA-RELATED CANCER

- **Early cancer screening**
- **Risk-reducing surgery**
  : Prophylactic mastectomy – to reduce risk of breast cancer
  : Prophylactic salpingo-oophorectomy – to reduce risk of ovarian cancer
- **Chemopreventive medication**
  : Antiestrogens for breast cancer
- **Targeted therapy**
  : Use of PARP inhibitor in BRCA-mutated cancer via synthetic lethality pathway
    : Olaparib
    : Rucaparib
    : Niraparib
    : Talazoparib

BRCA-RELATED CANCER

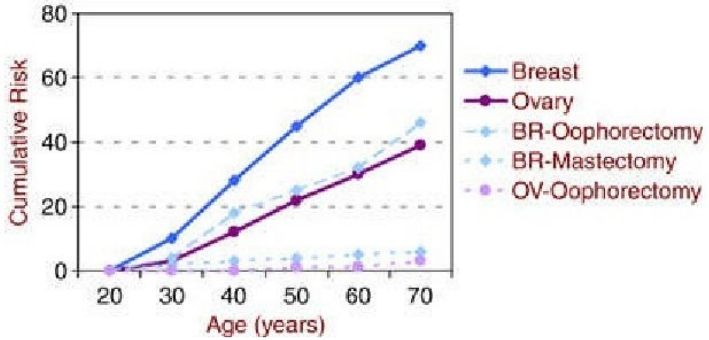
Chemoprevention of Breast Cancer in *BRCA1/2* Carriers

Tamoxifen

Risk reduction of 50% or more
in both *BRCA1* and *BRCA2* carriers

Gronwald J et al, Int J Cancer 2006;118(9):2281-4

Cancer risk reduction with prophylactic surgery



Domchek and Weber, Oncogene 2006; 25:5825-5831

TESTING CRITERIA FOR HIGH-PENETRANCE BREAST CANCER SUSCEPTIBILITY GENES

(Genes such as *BRCA1, BRCA2, CDH1, PALB2, PTEN, STK11,* and *TP53*. See GENE-A)[a,f,g,h,i]

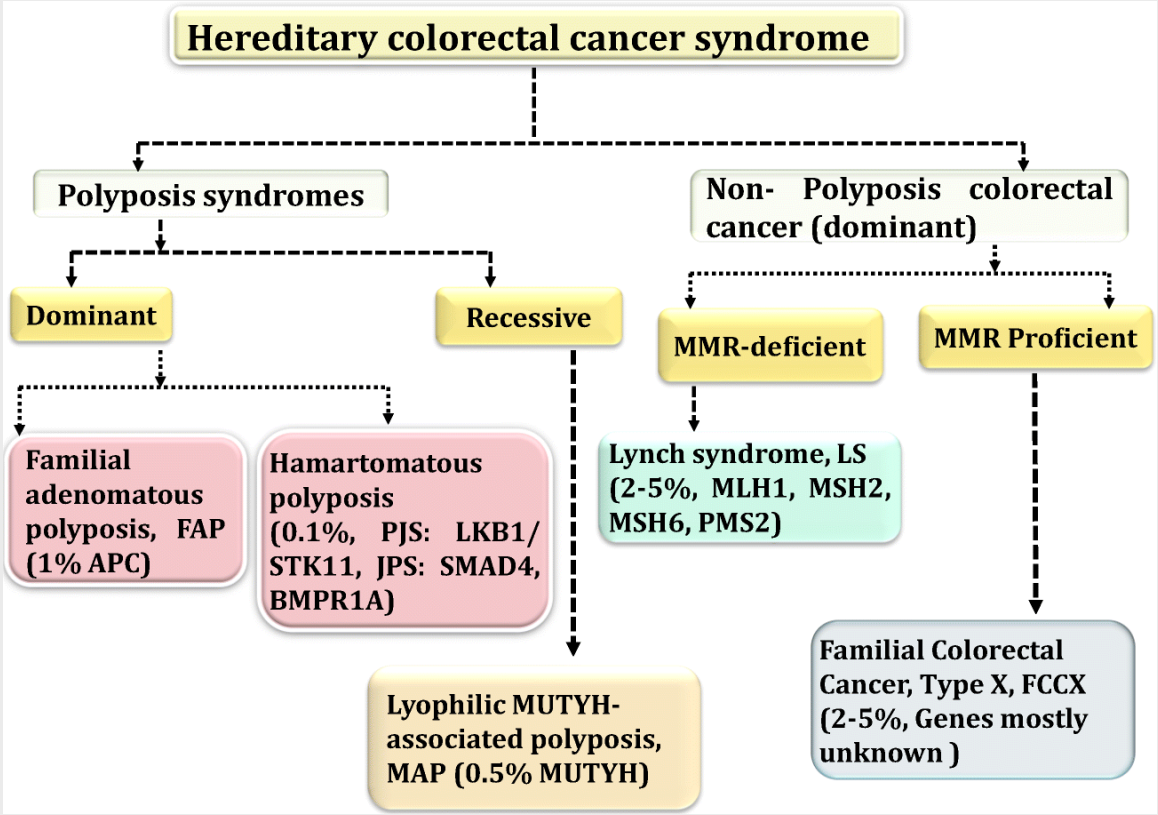
Testing is clinically indicated in the following scenarios:

- See General Testing Criteria on CRIT-1.
- Personal history of breast cancer with specific features:
  - ≤50 y
  - Any age:
    - ◊ Treatment indications
      - – To aid in systemic treatment decisions using PARP inhibitors for breast cancer in the metastatic setting[j,k] (NCCN Guidelines for Breast Cancer)
      - – To aid in adjuvant treatment decisions with olaparib for high-risk,[l] HER2-negative breast cancer[j]
    - ◊ Pathology/histology
      - – Triple-negative breast cancer
      - – Multiple primary breast cancers (synchronous or metachronous)[m]
      - – Lobular breast cancer with personal or family history of diffuse gastric cancer (NCCN Guidelines for Genetic/Familial High-Risk Assessment: Colorectal, Endometrial, and Gastric)
    - ◊ Male breast cancer
    - ◊ Ancestry: Ashkenazi Jewish
  - Any age (continued):
    - ◊ Family history[n]
      - – ≥1 close blood relative[o] with ANY:
        - breast cancer at age ≤50 y
        - male breast cancer
        - ovarian cancer
        - pancreatic cancer
        - prostate cancer with metastatic,[p] or high- or very-high-risk group (Initial Risk Stratification and Staging Workup in NCCN Guidelines for Prostate Cancer)
      - – ≥3 diagnoses of breast and/or prostate cancer (any grade) on the same side of the family including the patient with breast cancer
- Family history criteria: unaffected; or affected but does not meet above criteria
  - Individual with a first- or second-degree blood relative meeting any of the criteria listed above (except unaffected individuals whose relatives meet criteria only for systemic therapy decision-making).[q]
  - Individuals who have a probability >5% of a *BRCA1/2* P/LP variant based on prior probability models (eg, Tyrer-Cuzick, BRCAPro, CanRisk).[r]

Criteria met → GENE-1

If testing criteria not met, consider testing criteria for other hereditary syndromes → If criteria for other hereditary syndromes not met, then cancer screening as per NCCN Screening Guidelines

COLORECTAL CANCER SYNDROME



COLORECTAL CANCER SYNDROME

Syndrome	Gene	Associated cancer
Lynch (HNPCC)	MSH 2, MLH 1, MSH 6, PMS 2 (autosomal dominant)	**Colorectal** cancer(often right-sided), **Endometrial** cancer Stomach, Ovary, Bladder, Urinary tract, Kidney, Gall bladder, Brain, Breast, Small bowel
FAP	APC (autosomal dominant)	**Colorectal cancer (>100 polyp)** Medulloblastoma, Papillary CA thyroid, Hepatoblastoma Pancreatic cancer Gastric and Duodenal cancer

CLINICAL USE OF MMR GENE

- Lynch syndrome
  : MMR gene (MLH1, MSH2, MSH6, PMS2)
- Prognostic biomarker in stage II colon cancer
  : can omit adjuvant chemotherapy
- Predictive biomarker for immunotherapy in advanced CRC

"Amsterdam" Criteria for HNPCC Diagnosis

- 3 relatives with colorectal cancer, where one is 1st degree relative of other two
- 2 generations of colorectal cancer
- 1 colorectal cancer before age 50
- FAP is excluded

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02

PARANEOPLASTIC SYNDROME

PARANEOPLASTIC SYNDROME

- Paraneoplastic syndromes are rare disorders with complex systemic clinical manifestations due to underlying malignancy.
- In paraneoplastic syndromes, the malignant cells do not directly cause symptoms related to metastasis; rather, they generate **autoantibodies, cytokines, hormones, or peptides** that affect multiple organ systems.
- **Symptoms can manifest before or after the diagnosis of cancer.**
- Prompt recognition of these syndromes is critical as it may reveal hidden malignancy, affecting clinical outcomes.

COMMON PARANEOPLASTIC SYNDROME

Cancer	Common Paraneoplastic Syndrome
Small cell lung cancer	Ectopic ACTH SIADH Lambrt-Eaton myasthenic syndrome Cerebellar degeration Limbic encephalitis
Thymoma	Myasthenia gravis Pure red cell aplasia Hypogammaglobulinemia Paraneoplastic pemphigus
Adenocarcinoma of lung	Hypertrophic osteoarthropathy (HOA)
Squamous cell carcinoma	Hypercalcemia (PTHrP-related)

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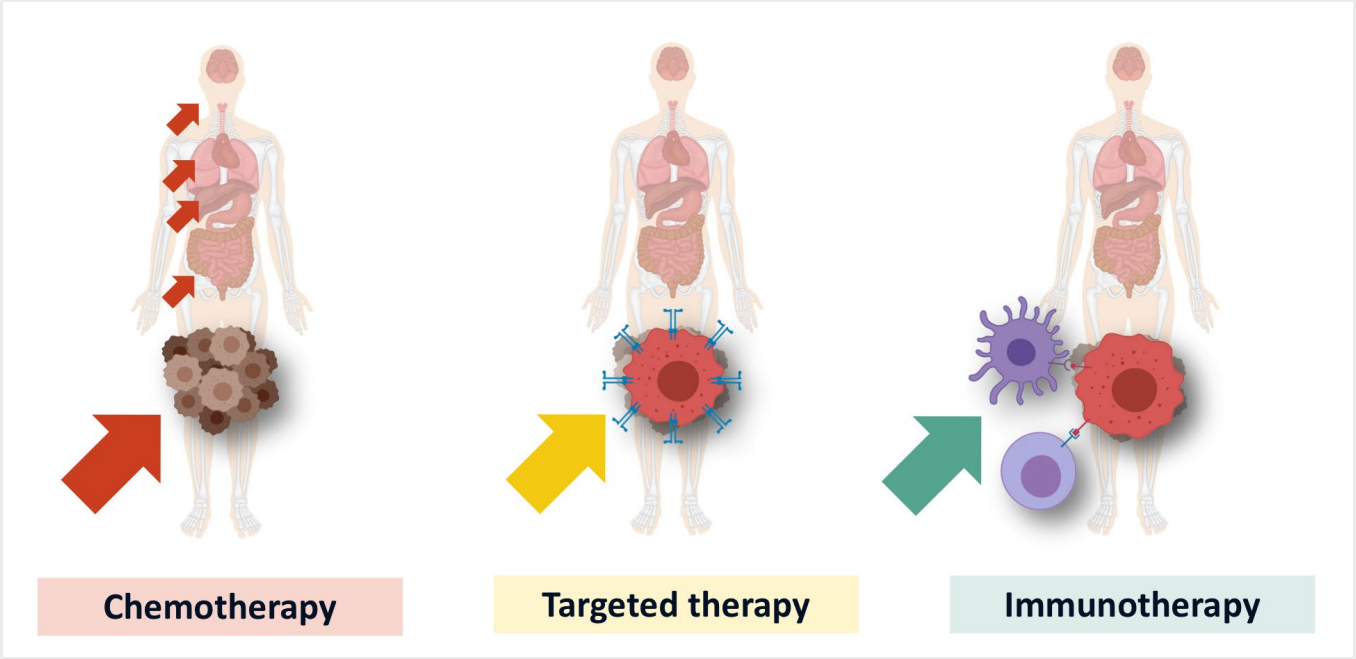
03

COMMON CANCER

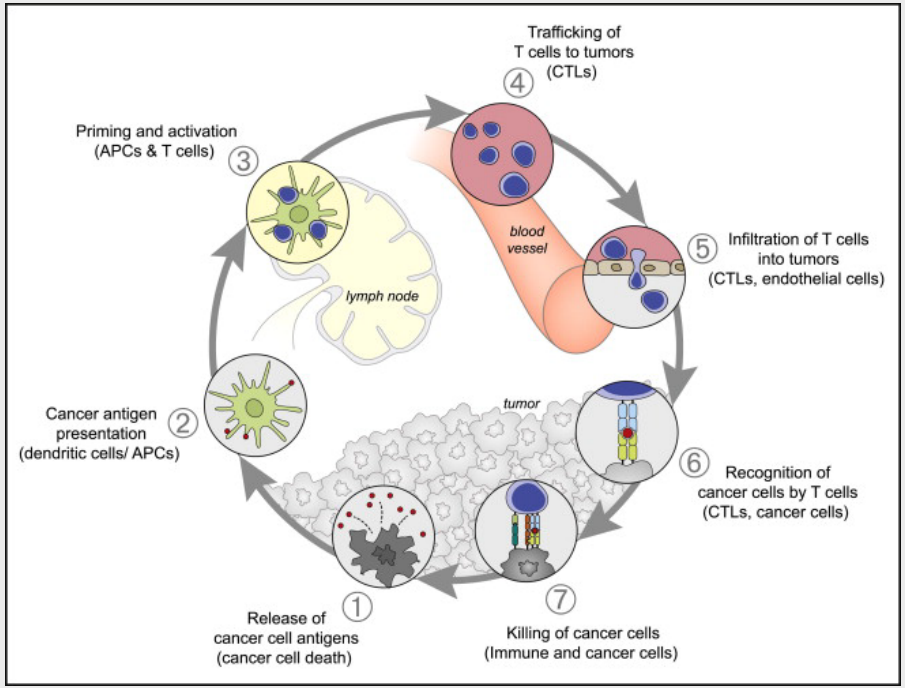
MANAGEMENT

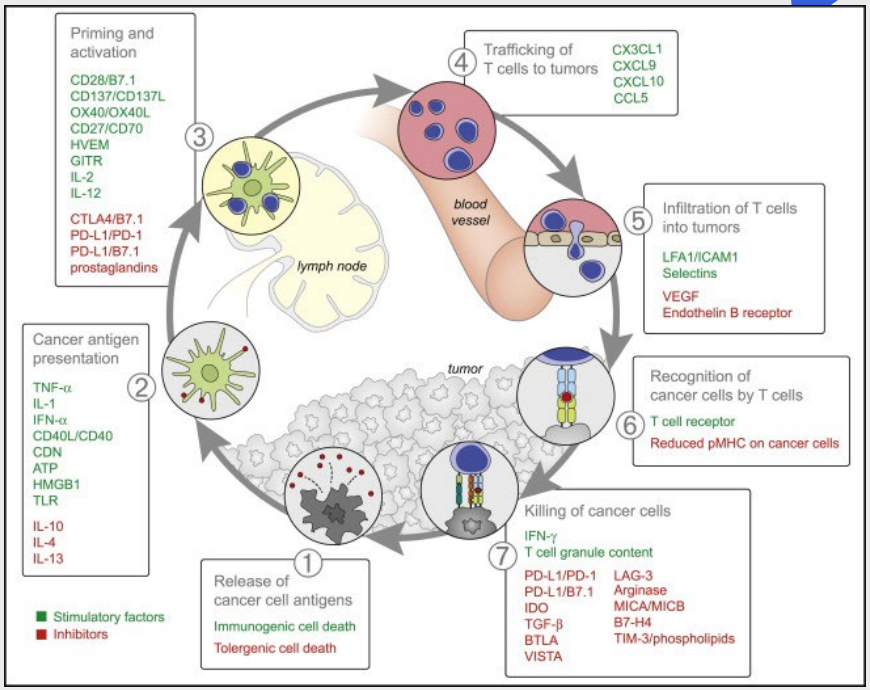
CANCER TREATMENT

CANCER TREATMENT

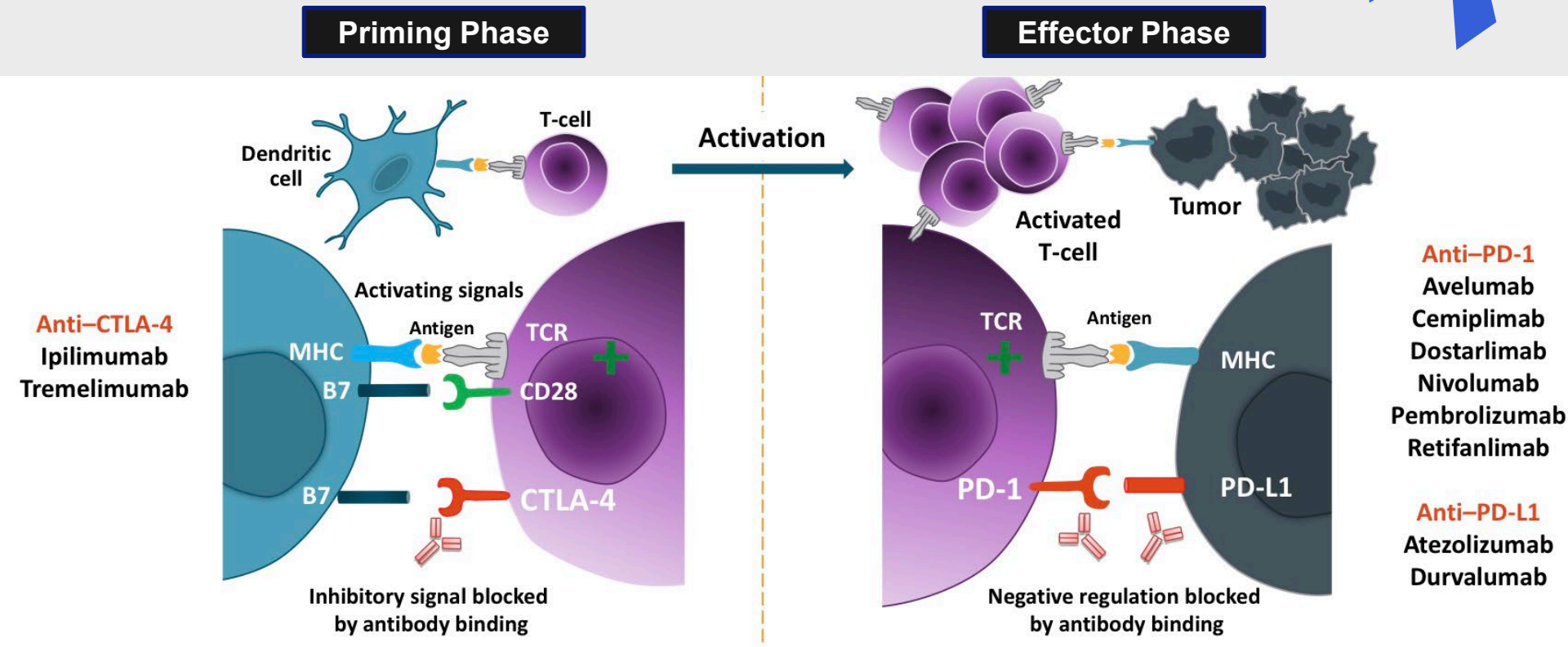


IMMUNOTHERAPY





IMMUNOTHERAPY



BREAST CANCER

BREAST CANCER

SURGERY

Breast conserving surgery
(Wide excision, Lumpectomy)

Mastectomy

CMT

Anthracycline-based
(Doxorubicin, Cyclophosphamide)

Taxane-based
(Docetaxel, Paclitaxel)

Others

RT

Post-op RT

Palliative RT

BREAST CANCER

HORMONAL

SERM: Tamoxifen
(Pre-menopause)

Aromatase inhibitor
: Letrozole, Exemesrane
Anastozole

SERD: Fulvestrant

ANTI-HER2

Trastuzumab
Pertuzumab
Lapatinib
TDM-1
Trastuzumab-deruxtican

OTHERS

CDK4/6 inhibitors:
Ribociclib, Palbociclib,
Abemaciclib

EARLY BREAST CANCER

ADJUVANT TREATMENT AFTER SURGERY (IN BRIEF)

	HORMONE	CMT	ANTI-HER2	RT
HR+ HER2- **Luminal A:** ER+ PR+ Ki67 <20 **Luminal B:** ER+ PR +/- Ki67 > 20	✓	✓		BCS* LN ≥4 T > 5 cm Margin< 1 mm
HR+ HER2+	✓	✓	✓	
HR- HER2+		✓	✓	
HR- HER2- (TRIPLE NEGATIVE)		✓		

*BCS: Breast-conserving surgery

ADVANCED BREAST CANCER

HR+ HER2-

- Visceral crisis : CMT
- No visceral crisis : Hormone +/- CDK4/6 inhibitor

HR- HER2+

- CMT + Anti-HER2

Triple negative

- CMT+/-Immunotherapy: Atezolizumab
- PARP inhibitor in germline BRCA mutation

Visceral crisis

- Severe organ dysfunction/rapid disease progression
- Liver: TB > 1.5x ULN
  (in the absence of biliary tract obstruction)
- Lung: dyspnea at rest
  (after drainage of pleural effusion)

Note:

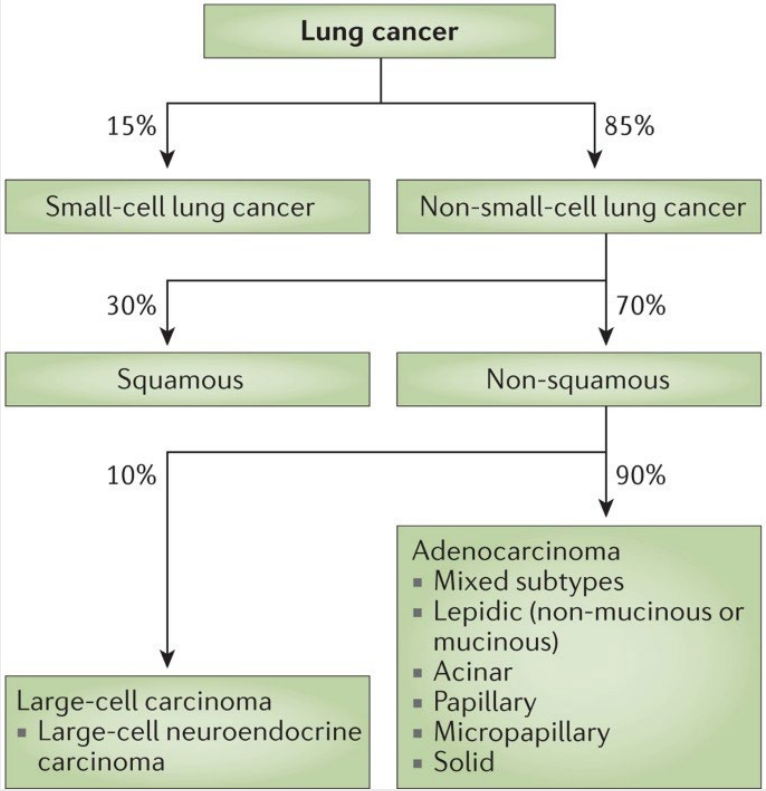
No definite role of surgery and RT in metastatic setting except for palliative symptom control

TREATMENT TOXICITY

	Anthracycline	Anti-HER 2
Mechanism	Type I	Type II
Myocardial effect	Oxidative stress and free radicles	HER2 signaling blockage
Dose-related	Irreversible	Reversible
Risk	Dose-related	No cumulative dose-related
Prevention	Hypertension	Prior/concurrent anthracycline, obesity
	Minimized dose of anthracycline Use of cardioprotective agent	F/U echocardiography Use of cardioprotective agent

LUNG CANCER

LUNG CANCER



Histologic subtypes associated with smoking

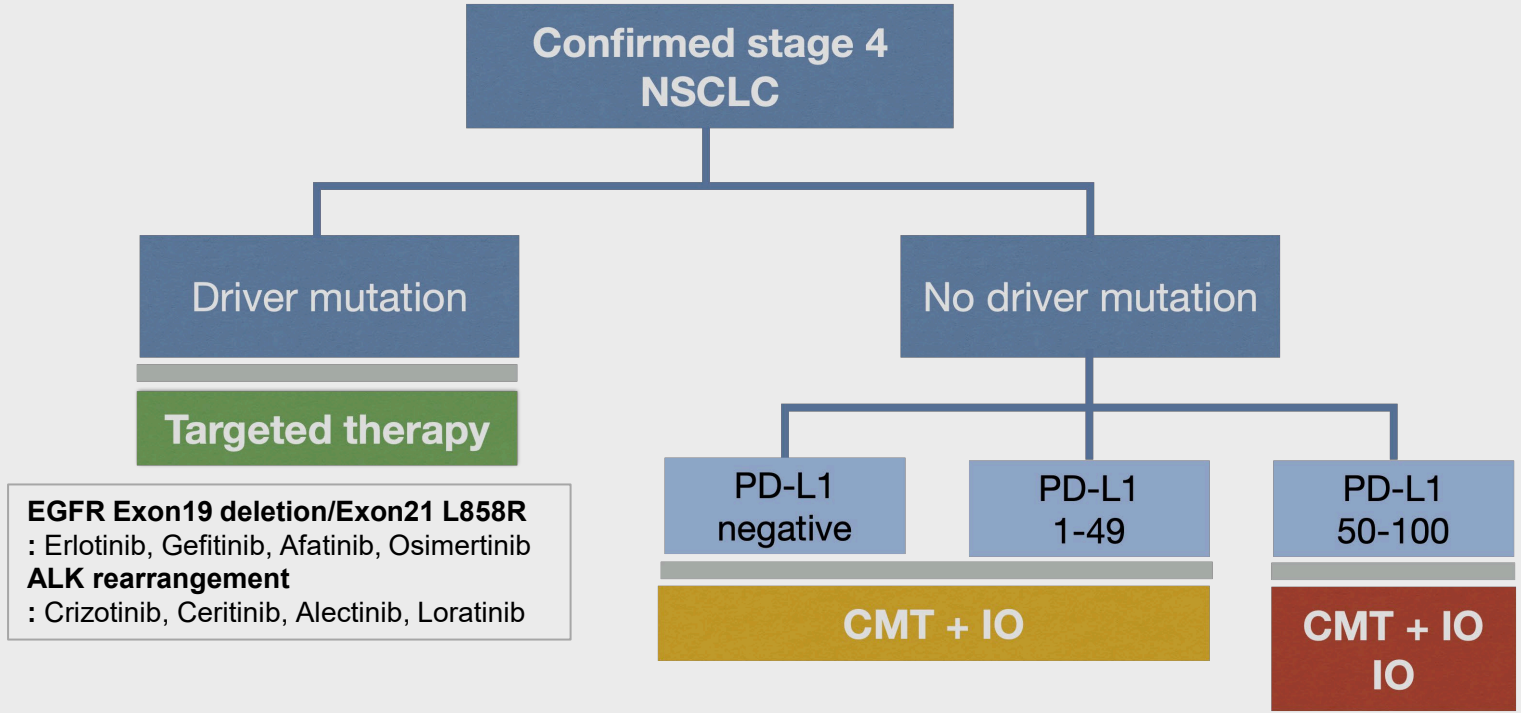
1. **Squamous cell carcinoma**
2. **Large cell carcinoma**
3. **Small cell lung cancer**

NON SMALL CELL LUNG CANCER (CONCEPT)

Stage	Treatment
I	Surgery
II	Surgery + Adjuvant CMT/Immunothepy/Targeted drug (or pre/peri operative strategies)
III	Multidisciplinary team, CCRT followed by Durvalumab (If unresectable)
IV	Systemic treatment

- Adjuvant chemotherapy recommended in tumor size ≥ 4 cm
- Adjuvant osimertinib recommended in resected stage IB – III with EGFR exon 19 del or exon 21 L858R mutation
- Adjuvant alectinib recommened in resected stage IB-III with ALK positive
- Adjuvant immunotherpay recommend in resected II-III without EGFR/ALK mutation
- Peri-operative or neoadjuvant chemotherapy and immunotherapy recommend in stage II-III without EGFR/ALK mutation

NON SMALL CELL LUNG CANCER STAGE IV



NSCLC WITH BRAIN METASTASIS

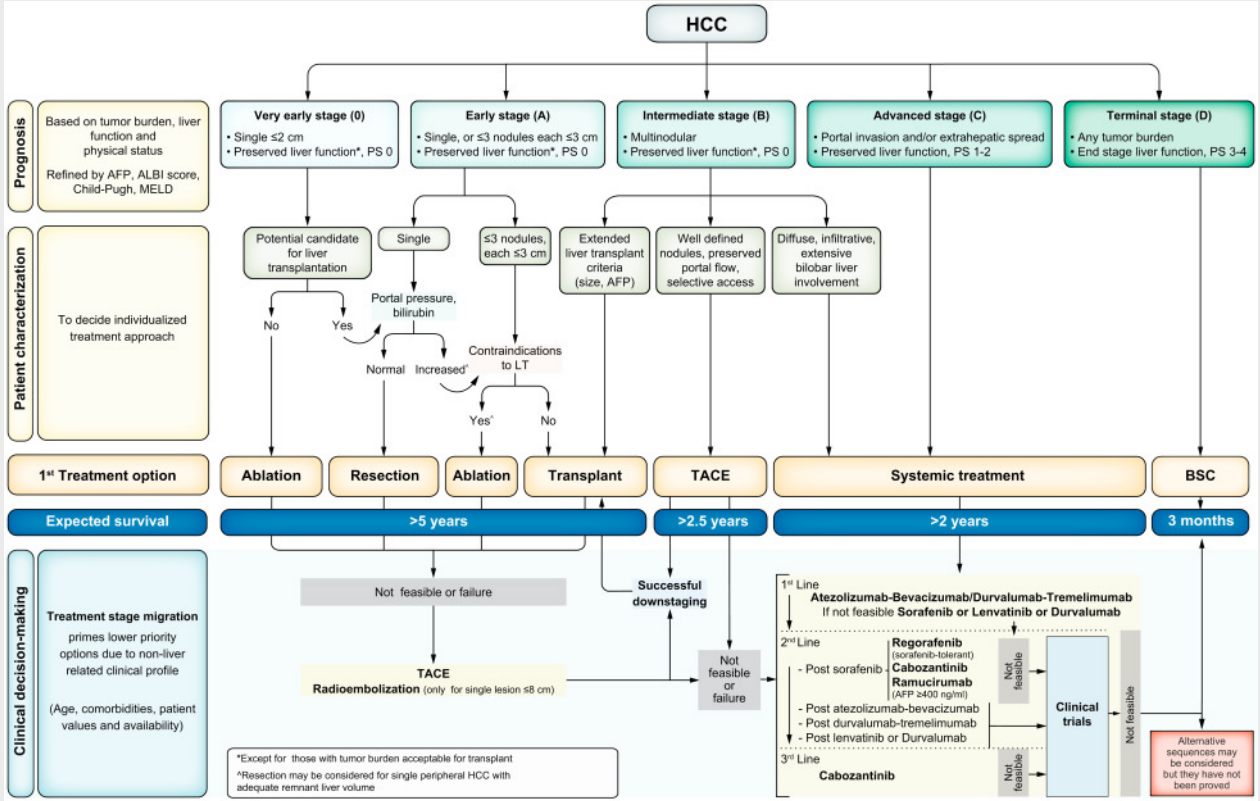
- Surgery may be offered for patients with brain metastases, considering the following factors:
  - Suspected brain metastases without a primary cancer diagnosis.
  - Large tumors with mass effect.
- Patients with symptomatic brain metastases should be offered local therapy (whole brain radiation therapy and/or radiosurgery and/or and/or surgery)
- For patients with asymptomatic brain metastases, local therapy should not be deferred unless patients who received brain-penetrating drug
  - EGFR mutant: Osimertinib
  - ALK-rearrangement: Loratinib, Alectinib, Brigatinib

SMALL CELL LUNG CANCER

- Originated from neuroendocrine cell, accounting for 10-15% of lung cancer
- Rapid growth, tendency to metastasize
- Smoking-related disease, Highly systemic disease
- Paraneoplastic syndrome: SIADH, Ectopic ACTH, LEMG
- Staging: Limited vs. Extensive stage
- Poor prognosis
- **Treatment: Limited stage: CCRT with Cisplatin/Etoposide**
  Extensive stage: Carboplatin/Etoposide + Immunotherapy (Durvalumab/Atezolizumab)

HEPATOCELLULAR CARCINOMA

HEPATOCELLULAR CARCINOMA



Barcelona Clinic Liver cancer (BCLC 2022) guideline

Role of systemic treatment

BCLC-B: Diffuse, infiltrative, extensive billobar liver involvement

BCLC-C: Portal invasion and/or extrahepatic spread, preserved liver function, Performance 1-2

HEPATOCELLULAR CARCINOMA

Systemic treatment

First-line

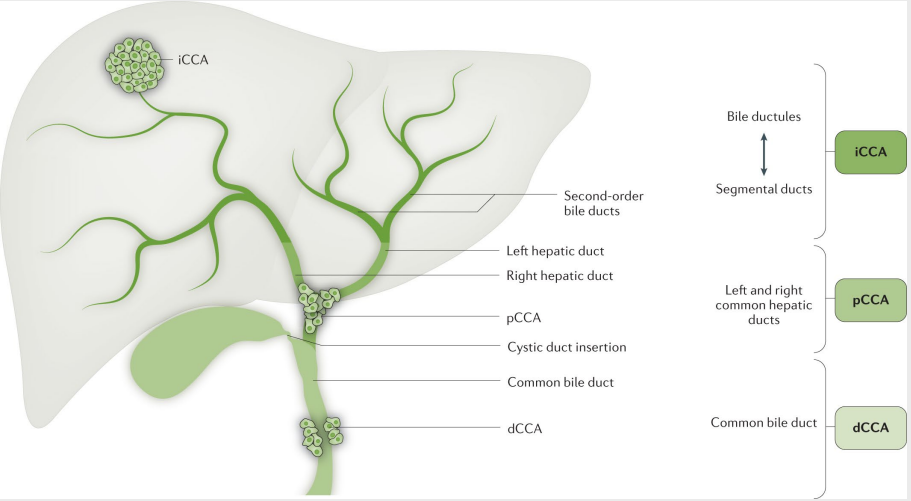
- Bevacizumab + Atezolizumab, Durvalumab + Tremelimumab (preferred)
- Sorafenib, Lenvatinib
- Durvalumab

Second-line

- Targeted drugs: Regorafenib, Carbozantinib, Ramucirumab
- Immunotherapy: Nivolumab+Ipiliumumab, Pembrolizumab

CHOLANGIOCARCINOMA

CHOLANGIOCARCINOMA



- Malignant tumor of bile duct epithelium (cholangiocyte)
- Classified by anatomy into
  - Intrahepatic CCA
  - Peri-hilar CCA
  - Distal CCA
- Etiology
  - Fluke-related
    : Opisthorchis viverrine (Southeast Asia)
    : Clonorchis sinensis (Korea, China)
  - Non-fluke-related
    : No identifiable-cause
- Classified by anatomy into
- Targetable mutation: IDH1 mutation, FGFR2 fusion, HER2 amplification

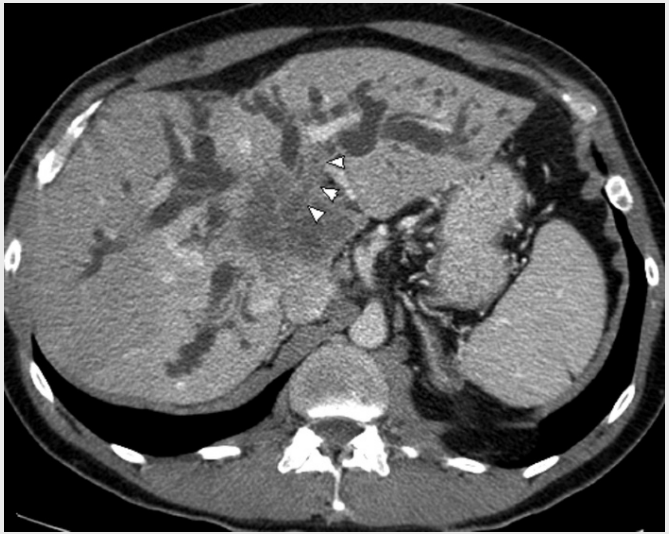
CLINICAL PRESENTATION

Clinical Presentation

- Obstructive jaundice
  (esp. in peri-hilar and distal CCA)
- Right upper quadrant pain
- Chronic dyspepsia
- Anorexia, weight loss

Investigation

- US: liver mass, IHD dilatation
- CT abdomen: Hypodense lesion, subcapsular retraction, perilesional bile duct dilatation



TREATMENT

Resectable (localized disease)

- Curative aim
- Surgery followed by adjuvant capecitabine

Unresectable (locally advanced, distant metastasis)

- Palliative aim
- Biliary drainage
- Systemic therapy (CMT +/- IO)
    - Cisplatin + Gemcitabine + Durvalumab/Pembrolizumab
    - Cisplatin + Gemcitabine
    - Targeted therapy
      (second line setting if driver mutation detected: FGFR2, IDH1, HER2)

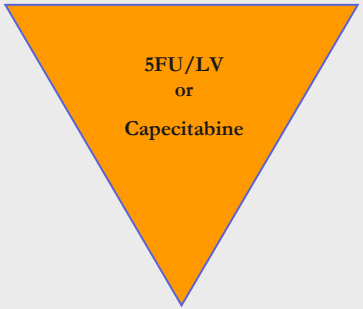
COLORECTAL CANCER

COLON CANCER

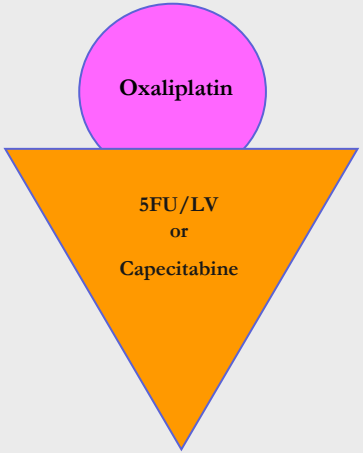
Stage	Treatment
I	Surgery
II	Surgery (+ Adjuvant 5FU in high risk patient)
III	Surgery + Adjuvant FOLFOX
IV	Surgery + Metastasectomy + Adjuvant CMT in oligometastic setting Palliatice CMT + targeted agent in unresectable case

- **High risk stage 2**
  - T4, poorly differentiated histology, bowel perforation/obstruction, closed/positive margin
  - Inadequate LN sampling (<12 LN)
  - Lymphovascular invasion, Perineural imvasion
- **Consider RT in rectal cancer**

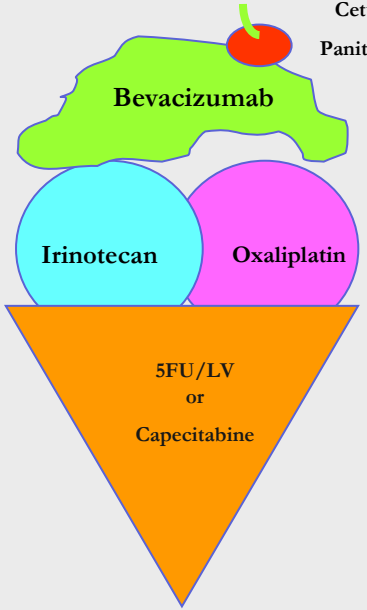
CMT IN COLON CANCER



Stage 2



Stage 3



Stage 4

PALLIATIVE CMT IN COLON CANCER

1. **Single agent 5FU + LV** (can be replaced by oral Capecitabine)

2. **Better regimen (Doublet/Triplet Chemo)**
   - 2.1 Oxaliplatin + 5FU/LV : FOLFOX
   - 2.2 Irinotecan+ 5FU/LV : FOLFIRI
   - 2.3 Oxaliplatin + Irinotecan+ 5FU/LV : FOLFOXIRI

3. **Best regimen (Targeted therapy + Chemotherapy)**
   - 3.1 For RAS/BRAF WT and left-sided tumor
     : FOLFOX/FOLFIRI + Cetuximab/Panitumumab
   - 3.2 Others
     : FOLFOX/FOFIRI + Bevacizumab, FOLFOXIRI + Bevacizumab
     : Cetuximab + Encorafenib in second line setting for BRAF V600E mutant

GERM CELL TUMOR

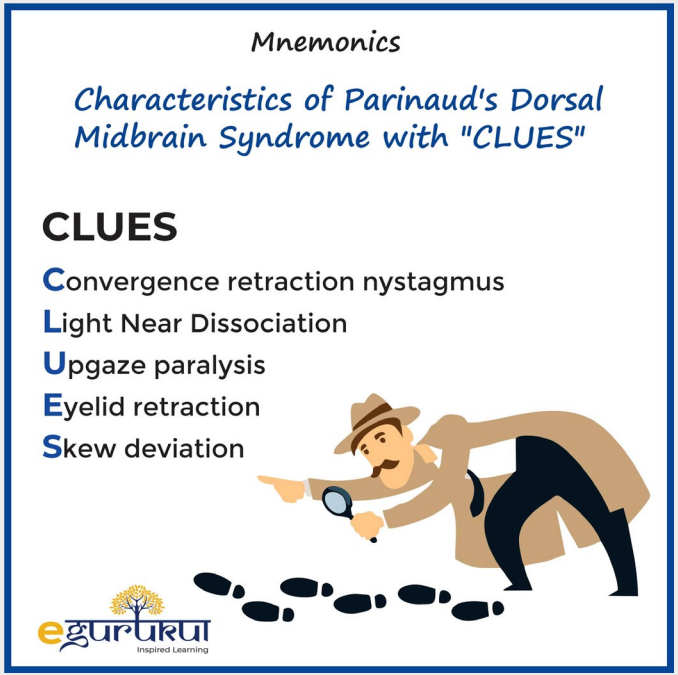
GERM CELL TUMOR

- **Malignancy of primodial germ cell**
- **Primary gonadal site (Testicular) 95%**
- **Relatively rare for extragonadal sites**
  : midline mass, mediastinum, retroperitoneum, pineal gland
- **Common in Male, Age : 20-40 yr**
- **Chemosensitive tumor**
- **Risk factors**
  : Cryptorchidism, Hypospadias, Klinefelter's syndrome (mediastinal GCT), i(12p)

CLINICAL PRESENTATION

- Testicular mass

  : Painless mass (almost always unilateral)
- Retroperitoneal mass
  : Back pain, Palpable mass
- Mediastinal mass
  : SVC syndrome, RS symptom
- Intracranial mass (Pineal/Pituitary)
  : Parinaud syndrome, DI, Hydrocephalus, Hypopituarism
- Gynecomastia
  : high level of hCG



TUMOR MARKER

		Beta-hCG	AFP
Seminoma		Mildly elevated ↑	Never rising
Non-seminoma	Embryonal cell carcinoma	↑	↑
	Choriocarcinoma	↑↑↑	⟷
	Yolk sac tumor	⟷	↑↑↑
	Teratoma	⟷	⟷
	Mixed germ cell tumor	↑	↑

False positive AFP: HCC, Hepatoid variant adenocarcinoma, Cirrhosis
False positive Beta-hCG: Marijauna, Gestational trophoblastic neoplasm, Malignancy, Marijauna

CMT IN ADVANCED GERM CELL TUMOR

Standard therapy: BEP x 4 cycles

Cisplatin 20 mg/m² d 1-5
Etoposide 100 mg/m² d 1-5
Bleomycin 30 IU d 1,8,15
Q 3 weeks

Alternative therapy: VIP x 4 cycles

Cisplatin 20 mg/m² d 1-5
Etoposide 75 mg/m² d 1-5
Ifosfamide 1200 mg/m² d 1-5
Q 3 weeks

BEP regimen

- Bleomycin : pulmonary fibrosis
- Etoposide : hypersensitivity and cardiotoxicity
- Cisplatin : N/V, renal toxic, neuropathy

Prefer VIP to BEP if underlying lung disease or plan to RT chest

GIST

GASTRO INTESTINAL STROMAL TUMOR (GIST)

- Spindle cell neoplasm of the gastrointestinal tract
- Originated from interstitial cell of Cajal
- Presentation: accidental finding from CT/EGD, mass effect, GI bleeding
- Primary site : Stomach, small bowel, rectum, mesentery, retroperitoneum
- Common metastasis site: Liver
- IHC : Positive for CD117 (C-kit), DOG-1

- **Rx : Early stage > Surgery** (+ adjuvant imatinib for 3 years)

  : Advanced > Tyrosine kinase inhibitor : Imatinib

- GIST is chemoresistant tumor, no role of conventional chemotherapy !

PROSTATE CANCER

PROSTATE CANCER

Clinical

Locally advanced : LUTs, Bladder outlet obstruction, Hematuria

Advanced : Bone pain (Blastic bone metastasis), Cord compression, Myelophthisis

Lab: PSA > 4 + Abnormal digital rectal exam

Risk stratification : PSA, Gleason and T-stage

Pathology : Adenocarcinoma, CK7-, CK20-, PSA+, NKX 3.1+

TREATMENT

Local disease

– Low risk: radical prostatectomy or RT

– Intermediate risk : radical prostatectomy with pelvic LN dissection or RT

– High/Very high : RT with long-term ADT or radical prostatectomy with pelvic LN dissection

Locally advanced : Rx as high risk

Metastasis : ADT, Novel anti-androgen, CMT

* ADT: Androgen Deprivation treatment

TREATMENT

Androgen deprivation therapy (ADT)

- Bilateral orchidectomy
- LHRH analogues : leuprolide, goserelin, buserelin

Novel anti-androgen treatment

- CYP-17 inhibitor: abiraterone
- New generation anti-androgen: enzalutamide, apalutamide, apalutamide, darolutamide

SIDE EFFECT OF ADT

Less sexual desire

Impotence

Hot flush

Breast tenderness and growth of breast tissue

Osteoporosis

Anemia

Decreased mental sharpness

Loss of muscle mass

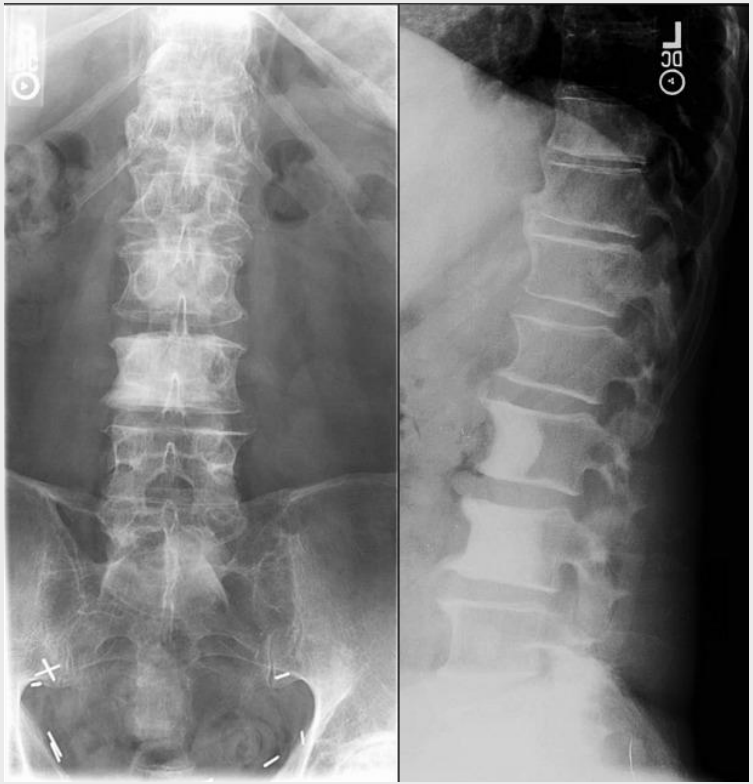
Weight gain

Fatigue

Hypercholesterol

Depression

BONE METASTASIS IN PROSTATE CANCER



- Mostly osteoblastic lesion
- Relate to level of PSA
- Bone pain
- Fracture
- Malignant cord compression
- Rx :
  - Local RT
  - Bisphosphonate or Denosumab

04

CANCER OF UNKNOWN PRIMARY

CANCER OF UNKNOWN PRIMARY

IHC marker for determining cell lineage

Markers*	Most Likely Cell Lineage
Pan-keratin (AE1/AE3 & CAM5.2)	Carcinoma
CK5/6, p63/p40	Squamous cell carcinoma
S100, SOX10	Melanoma
LCA± CD20± CD3±	Lymphoma
OCT3/4± SALL4±	Germ cell tumor
WT1, calretinin, mesothelin, D2-40	Mesothelial tumor

*These markers are not uniformly specific or sensitive and can be present on other tumors.

CANCER OF UNKNOWN PRIMARY

IHC marker for Adenocarcinoma

CK7+ 20+ "CUP-O"

- **C**holangiocarcinoma
- **U**rothelial carcinoma
- **P**ancreatic carcinoma
- **O**varian cancer

CK7+ 20- "Upper thorax"

- **Thyroid**
- **Breast**
- **Lung**
- **Pancreas, CCA, Ovary (non-mucinous)**

CK7- 20+ "GI malignancy"

- **Colorectal cancer**
- **Gastric cancer**
- **Merkel**

CK7- 20-

- **Prostate**
- **HCC**
- **RCC**
- **Squamous cell**

CANCER OF UNKNOWN PRIMARY

IHC marker for Adenocarcinoma, CK7+ 20-

CK7+ 20- "Upper thorax"

- **Thyroid**
- **Breast**
- **Lung**
- **Pancreas, CCA, Ovary (non-mucinous)**

Cancer	Additional positive IHC
Thyroid	TTF-1, Thyroglobulin
Breast	GATA3, Mammaglobulin, GDCFP-15
Lung	TTF-1, Napsin A

CANCER OF UNKNOWN PRIMARY

Primary markers	Cancer type	Additional markers to consider
CK7+,CK20-	Lung [NSCLC (adenocarcinoma) and SCLC]	TTF1, SMARCA4, synaptophysin
	Thyroid	Thyroglobulin, TTF1, PAX8
	Breast	GATA3, SOX10, ER, PgR, Mammaglobin, BRST1
	Upper GI, pancreaticobiliary	CDX2, CK19, SMAD4, ARID1A, BAP1
	Endometrial, endocervical, ovary (serous)	PAX8, ER, PgR, WT1, p53
	Renal (papillary)	PAX8, PAX2, racemase, CD10
	Salivary gland	GATA3, S100, SOX10, AR, HER2
	Bladder	GATA3, p63
CK7+, CK20+	Bladder	GATA3, p63
	Upper GI, pancreaticobiliary	CDX2, CK19, SMAD4, ARID1A, BAP1
	Rectum	CDX2, SATB2
CK7-, CK20+	Colorectal, upper GI	CDX2, SATB2
	Merkel cell	Synaptophysin
CK7-, CK20-	Renal	PAX8, PAX2, racemase, CD10
	Hepatocellular	Arginase1, HepPar1
	Germ cell	SALL4, PLAP
	Prostate	PSMA, NKX3.1
	Gastric	CDX2
	SCLC	TTF1, SMARCB1, synaptophysin
	Adrenal cortical	SF1, calretinin, inhibin
	Neuroendocrine	INSM1, synaptophysin
	Squamous cell	p40, p63, CK5/6

FAVORABLE CUP

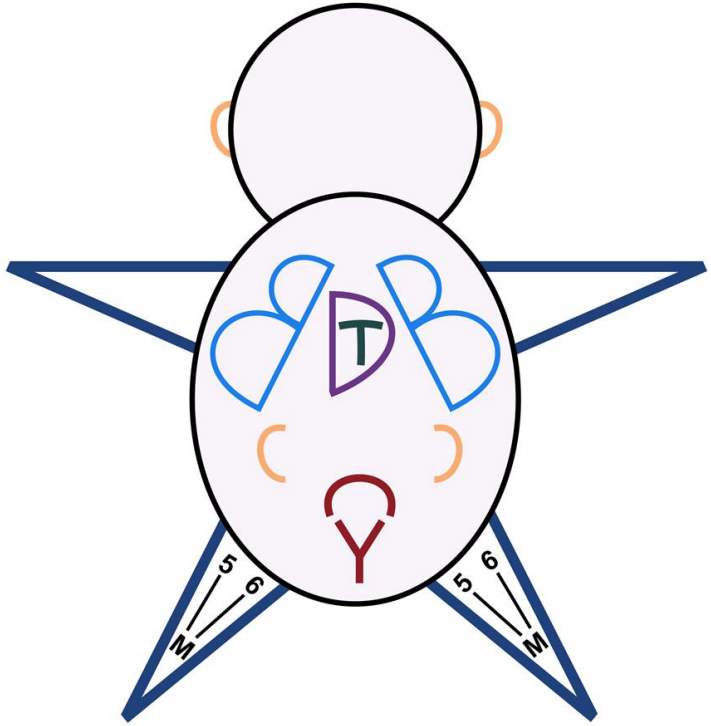
Histologic type	Clinical feature	Treatment recommendation
Adenocarcinoma	Women with isolated axillary adenopathy	Treat as stage II breast cancer
	Women with peritoneal carcinomatosis	Treat as stage III ovarian cancer
	Men with elevated PSA or blastic bone metastases	Treat as advanced prostate cancer
Adenocarcinoma or PDC	Single metastatic lesion	Definitive local therapy (resection and/or radiation therapy)
Squamous cell	Cervical adenopathy	Treat as head and neck cancer with involved neck nodes
	Inguinal adenopathy	Inguinal node dissection Consider concurrent radiation therapy/chemotherapy (as in locally advanced cervical cancer)
Poorly differentiated carcinoma	Young men with midline tumor or elevated hCG/AFP	Treat as extragonadal germ cell tumor
	Other clinical presentations	Empiric platinum/paclitaxel chemotherapy
Poorly differentiated neuroendocrine carcinoma	Diverse clinical presentations	Treat with platinum/etoposide or paclitaxel/platinum/etoposide

05

SIDE EFFECTS

OF SYSTEMIC THERAPY

SIDE EFFECT OF CHEMOTHERAPY



Cisplatin and Carboplatin
- ototoxicity
- nephrotoxicity

Vincristine
- peripheral neuropathy

Bleomycin and Busulfan
- pulmonary fibrosis

Trastuzumab and Doxorubicin
- cardiotoxicity

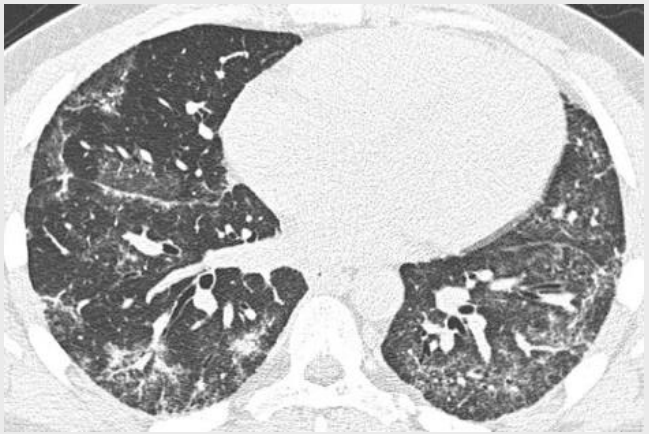
Cyclophosphamide
- hemorrhagic cystitis

Methotrexate, 5-FU, and 6-MP
- myelosuppression

PULMONARY TOXICITIES

Bleomycin

- Induces reactive oxygen radicals
- Acute- Pneumonitis, ARDs
- Late – Lung fibrosis



CARDIOTOXICITIES

5-FU
- Coronary spasm

Osimertinib
- QT prolongation

Anti-VEGF
- Hypertension, bleeding, thrombosis

CARDIOTOXICITIES: CARDIOMYOPATHY

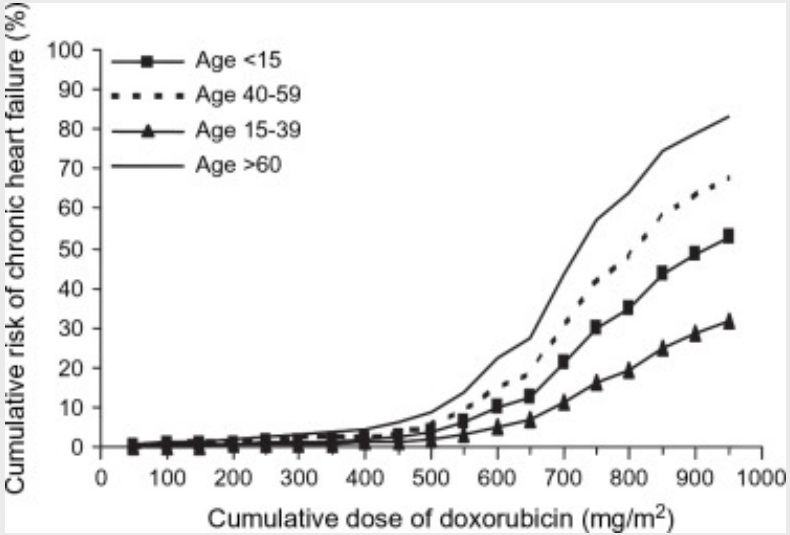
Doxorubicin

- Dose dependent, Irreversible
- Should not exceed cumulative dose of 350-450 mg/m^2

Trastuzumab

- Dose independent, Reversible

Follow up echocardiography is mandated !



RENAL TOXICITIES

Cisplatin
- Renal tubular damage (Fanconi syndrome)
- AKI
- SIADH

Cyclophosphamide
- Hemorrhagic cystitis from its active metabolite ”acrolein”
- Prevention: mesna

Anti-VEGF
- Proteinuria

NEURO TOXICITIES

Oxaliplatin

- Acute – sensitive to cold
- Late - dose dependent peripheral neuropathyneuropathy

Taxane (Paclitaxel, Docetaxel) **/ Vincristine**
: Peripheral neuropathy

Ifosfamide, MTX : Encephalopathy

GI TOXICITIES

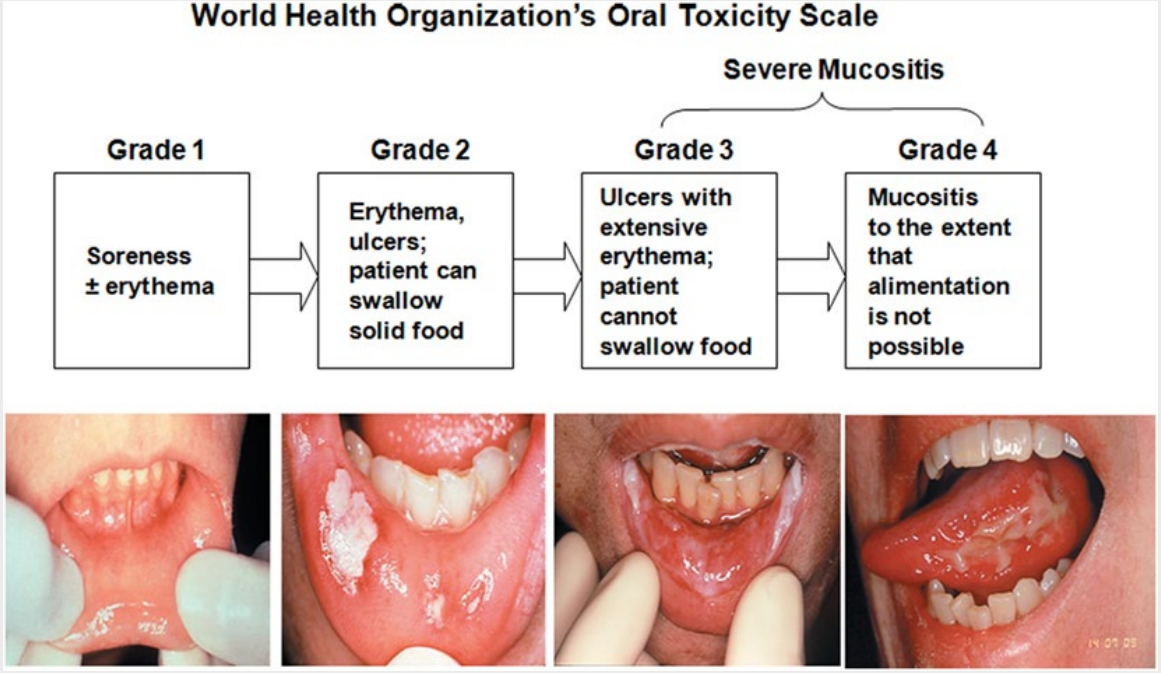
5-FU, Capecitabine

- Mucositis, diarrhea

Oxaliplatin
: Veno-occlusive disease (blue liver)

Irinotecan
: Acute diarrhea (parasympathetic effect)
: Late diarrhea from metabolite
: Steatohepatitis (yellow liver)

MUCOSITIS



Chemotherapy
MTX, 5-FU, Cyclophosphamide, Docetaxel, Doxorubicin, Paclitaxel,
Targeted therapy
Everolimus, Sorafenib

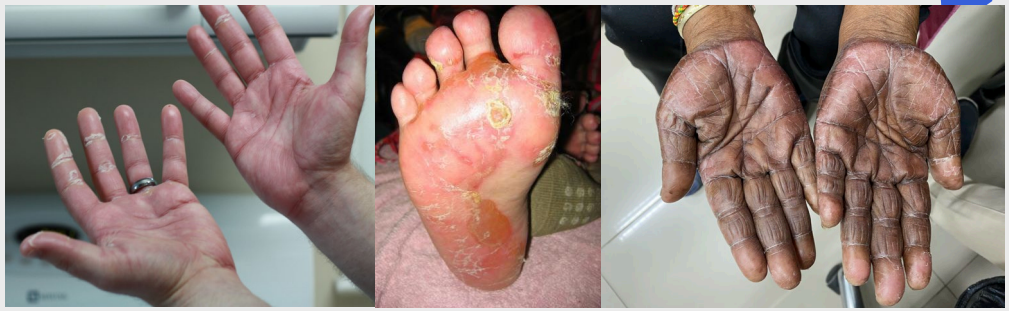
Prevent
: Ice chip for 5-FU

Rx
: Systemic analgesic therapy with narcotics

SKIN TOXICITIES

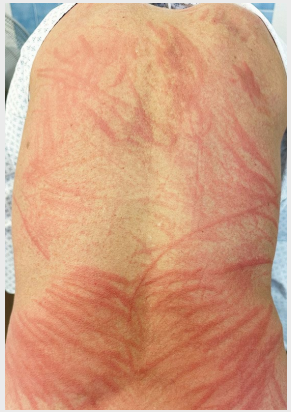
Hand-foot syndrome and Hand foot skin reaction

- Capecitabine
- Tyrosine kinase inhibitor



Flagellate erythema

- Bleomycin



PRIDE SYNDROME: ANTI-EGFR

PRIDE syndrome

- **P**apulopustular (acneiform) rash and/or paronychia
- **R**egulatory abnormalities of hair growth
- **I**tching
- **D**ryness (xerosis)
- **E**GFR inhibitors: Erlotinib, gefitinib, Osimertinib, Panitumumab, Cetuximab

Others

- Mucositis
- Photosensitivity

SECONDARY LEUKEMIA

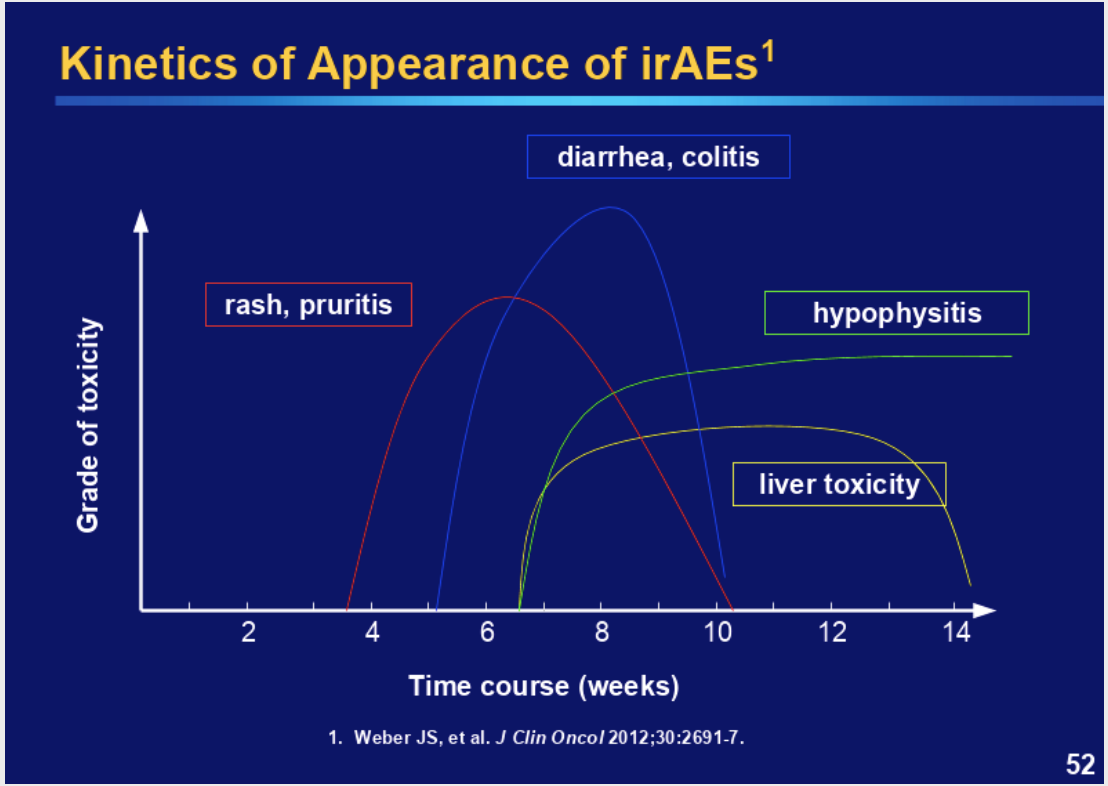
Cyclophosphamide/Ifosfamide

- AML in 5-7 yrs
- MDS
- -5, -7 del
- AML: M1, M2

Etoposide

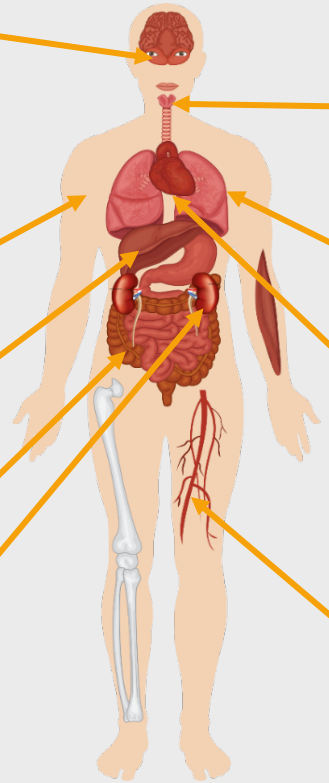
- AML in 1-3 yrs
- t(11q23)
- AML: M4, M5

IMMUNOTHERAPY



- Immunotherapy functions by enhancing host immune system ability to clear cancer cell but it can also lead to immune mediated damage to healthy native tissue called Immune-related Adverse Events (irAEs)

IMMUNOTHERAPY



Eye
- Uveitis
- Iritis

Skin
- Dermatitis exfoliative
- Vitiligo
- Alopecia

Hepatic
- Hepatitis, autoimmune

Gastrointestinal
- Colitis

Renal
- Nephritis

Endocrine
- Hypo- or hyperthyroidism
- Adrenal insufficiency
- Hypophysitis

Pulmonary
- Pneumonitis (< 5% incidence)

Cardiac
- Myocarditis

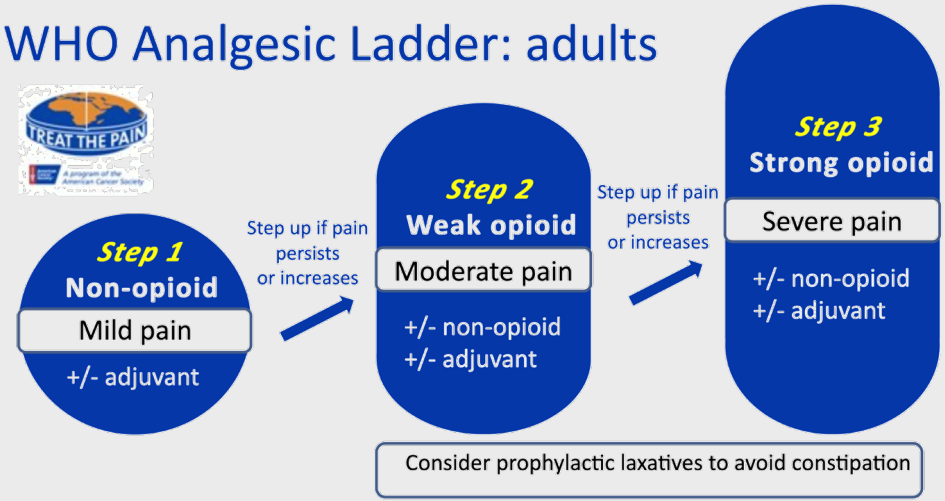
Neurologic
- Neuropathy
- Guillain-Barre
- Myasthenia gravis–like syndrome

06

PALLIATIVE CARE

CANCER PAIN MANAGEMENT

WHO Analgesic Ladder: adults



Non-opioids	ibuprofen or other NSAID, paracetamol (acetaminophen), or aspirin
Weak opioids	codeine, tramadol, or low-dose morphine
Strong opioids	morphine, fentanyl, oxycodone, hydromorphone, buprenorphine
Adjuvants	antidepressant, anticonvulsant, antispasmodic, muscle relaxant, bisphosphonate, or corticosteroid

Combining an opioid and non-opioid is effective, but do not combine drugs of the same class.

Time doses based on drug half-life ("dose by the clock"); do not wait for pain to recur

Adapted by Treat the Pain from World Health Organization http://www.who.int/cancer/palliative/painladder/en/ (accessed 7 November 2019)

Numerical rating scale

Mild	1 2 3
Moderate	4 5 6
Severe	7 8 9 10

OPIOID USAGE

- Starting with short-acting opioid, morphine IR/syrup 5-7.5 mg as needed
- If ≥ 4 dose needed per day, consider long-acting background opioid on total dose using previous 24 hr
- Consider pain adjunctive medication e.g. TCA/anti-convulsant in neuropathic pain

Breakthrogh dose : 10-20% of background dose

If breakthrough dose using ≥ 4 dose per day,
reset new background dose and breakthrough dose

PAIN CRISIS MANAGEMENT

- Use intravenous bolus (peak effect 15 min) or subcutaneous route (peak effect 30 min)
- For opioid naïve: 2-5 mg of morphine
  For opioid tolerant: 10-20% of total opioid taken in previous 24 hr

If pain unchanged, increased dose by 50-100%

If pain decreased but inadequately controlled, repeat same dose

If pain improved and adequately controlled, continue current dose as needed

OPIOD CONVERSION

Before	Conversion Factor	After
Morphine po 60 mg	**÷ 3**	**Morphine IV** 20 mg
Morphine po 60 mg	**=**	**Kapanol** 60 mg
Morphine po 60 mg		**Fentanyl patch** 25 mcg/hr
Fentanyl IV	=	**Fentanyl patch**

DYSPNEA CRISIS

- **Use intravenous/subcutaneous route**
- **Non-specific measure**
  - Calm reassurance
  - Positioning
  - Oxygen
  - Opioids
  - Possibly sedative: midazolam, lorazepam

DEATH RATTLE

- **Positioning**
- **Antisecretory agents**
  - Atropine 0.4-0.8 mg SC q 1 hr PRN
  - Atropine eye drop 1% 4 drops SL q 4 hr PRN
- **Consider suctioning if secretions are**
  - Distressing
  - Proximal
  - Accessible

Overview of Oncology 2025
For Resident

THANK YOU

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