STEM-S

NEET-SS



Medical Oncology

GROUP

Essential Notes

PRESENTED BY STEM-S

MASTER INDEX

Medical Oncology Essential Notes

3 parts · 43 chapters · notes pages **1–746**

CONTENTS AT A GLANCE

PART 1 · GENERAL ONCOLOGY 1–105

01 Basics 1
02 Molecular Oncology and Genetics 20
03 Chemotherapy 27
04 Immunotherapy 34
05 Immune Checkpoint Inhibitor–Related Toxicities 44
06 Targeted Therapy 54
07 Radiation Therapy and Radiobiology 62
08 Oncological Emergencies 71
09 Adverse Effects, Supportive Care and Trial Methodology 81
10 Cancer Pain and Symptom Management 91
11 Carcinoma of Unknown Primary 99

PART 2 · HEMATOLOGICAL MALIGNANCIES 106–294

12 Acute Lymphoblastic Leukemia (ALL) 106
13 Acute Myeloid Leukemia (AML) and Related Myeloid Neoplasms 124
14 Chronic Lymphocytic Leukemia (CLL) 140
15 Chronic Myeloid Leukemia (CML) 162
16 Hodgkin Lymphoma 182
17 Non-Hodgkin Lymphoma 201
18 Plasma Cell Neoplasms 226
19 Myeloproliferative Neoplasms 244
20 Hematopoietic Stem Cell Transplantation 264
21 CAR T-Cell Therapy 279

PART 3 · SOLID ORGAN MALIGNANCIES 295–746

22 Thoracic Oncology 295
23 Non-Small Cell Lung Cancer 303
24 Small Cell Lung Cancer 322
25 Thymoma and Mediastinal Neoplasms 337
26 Gastrointestinal Malignancies 352
27 Hepatobiliary Malignancies 365
28 Central Nervous System Oncology 395
29 Head and Neck Oncology 413
30 Breast Cancer: Basics 437
31 Breast Cancer: Neoadjuvant and Adjuvant Therapy 459
32 Breast Cancer: Risk Factors and Diagnosis 479
33 Metastatic Breast Cancer 501
34 Genitourinary Malignancies 516
35 Renal Cell Carcinoma 530
36 Bladder Carcinoma 553
37 Gestational Trophoblastic Neoplasia 574
38 Carcinoma Cervix 599
39 Carcinoma Ovary 621
40 Carcinoma Endometrium 646
41 Soft Tissue Sarcoma 674
42 Bone Sarcoma 697
43 Endocrine Malignancies 719

STEM-S

NEET-SS

Medical Oncology · Essential Notes

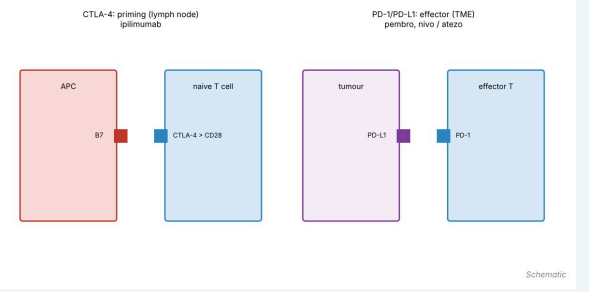


Immune Checkpoint Inhibitor–Related Toxicities

PRESENTED BY STEM-S

1. Pathophysiology & General Management

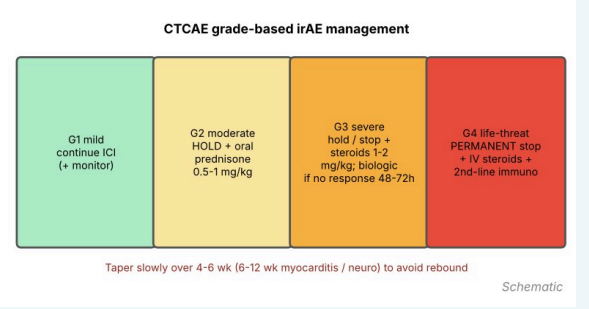
- **ICIs:** anti-CTLA-4 (**ipilimumab**), anti-PD-1 (**pembrolizumab**, **nivolumab**, **cemiplimab**), anti-PD-L1 (**atezolizumab**, **durvalumab**, **avelumab**).
- They uncouple **peripheral immune tolerance**.
- **CTLA-4:** acts in **secondary lymphoid organs** during **T-cell priming**, competing with **CD28** for **B7-1 (CD80) / B7-2 (CD86)**.
- **PD-1 / PD-L1:** acts in **peripheral tissue and the TME** to suppress activated effector T cells.
- Blocking these brakes releases **autoreactive T cells** → irAEs in nearly every organ.
- **Onset: 2-12 weeks** usually; late-onset can occur months after stopping.
- **Combination (ipi + nivo)** markedly increases incidence and severity.



CTLA-4 priming vs PD-1/PD-L1 effector axis

CTCAE grade-based rules

- **Grade 1:** continue ICI with monitoring.
  - Exceptions: **G1 pneumonitis**, **G1 bullous pemphigoid**, **any-grade CNS demyelination** → hold or stop.
- **Grade 2: hold** until ≤ G1; **oral prednisone 0.5-1 mg/kg/day**; rechallenge when tapered to **≤ 10 mg/day**.
- **Grade 3:** hold or permanently stop; **steroids 1-2 mg/kg/day**; if no improvement in **48-72 h**, escalate to **biologic**.
- **Grade 4: permanent discontinuation**; ICU; high-dose IV steroids (pulse **1 g/day** for myocarditis / neuro emergencies) + second-line immunosuppression.



CTCAE grade-based irAE management

3. GI & Pancreatic

- **Colitis:** watery stools, crampy pain, **hematochezia**, **nocturnal diarrhoea**, fever, tachycardia.
- Workup: stool pathogens (**C. diff PCR**, O&P, culture), **faecal calprotectin/lactoferrin + CRP**, **sigmoidoscopy/colonoscopy + biopsy**, CT if peritoneal signs.

Colitis Grade	Stool Frequency / Symptoms	Immunotherapy Action	Systemic & Biologic Management
Grade 1 (Mild)	<4 stools/day over baseline; asymptomatic	Continue (consider holding)	Hydration, loperamide.
Grade 2 (Moderate)	4-6 stools/day; abdominal pain; blood in stool	Hold ICI	Prednisone or IV methylprednisolone 1-2 mg/kg/day. Taper over 4-6 weeks once ≤ G1.
Grade 3 (Severe)	≥ 7 stools/day; severe pain; limiting self-care ADL	Discontinue current combination IO	IV methylprednisolone 1-2 mg/kg/day. No response in 1-2 days → add infliximab or vedolizumab.
Grade 4 (Life-Threatening)	Perforation; toxic megacolon	Discontinue responsible agent	ICU, IV methylprednisolone 1-2 mg/kg/day + immediate infliximab/vedolizumab + surgical consult.

- **Microscopic colitis:** normal mucosa; consider **budesonide 9 mg/day** before systemic steroids in biopsy-proven G2.
- **Steroid-refractory** (no response 24-48 h, or deep ulceration): add **infliximab 5 mg/kg** or **vedolizumab 300 mg**; three infliximab doses (weeks 0, 2, 6) lower recurrence.
- With a biologic, taper steroids fast (**< 2-4 weeks**) to cut dual-immunosuppression infection risk.
- **G3 colitis on combination:** stop the combination; any rechallenge must be **anti-PD-1 / PD-L1 monotherapy only** (CTLA-4 has the highest colitis recurrence).
- **Pancreatitis:** no routine amylase/lipase screening; asymptomatic lipase up to **3× ULN** needs no interruption. **G3** = hold + IV hydration + GI referral; **G4** = permanent stop. **NCCN 1.2026 removed routine steroids** for G3-4 pancreatitis; mainstay is **hydration and supportive care**.

5. Renal: Acute Interstitial Nephritis

- Mostly cell-mediated **acute tubulointerstitial nephritis**; usually asymptomatic (creatinine surveillance); sterile pyuria, microscopic haematuria, low-grade proteinuria.
- Workup: exclude pre/post-renal, urine microscopy (**sterile pyuria**, **eosinophiluria**), stop nephrotoxins, stage by **KDIGO**, biopsy if no response in 5-7 days.

AKI Stage (NCCN/KDIGO)	Creatinine Threshold	Immunotherapy Action	Corticosteroid & Medical Management
Stage 1	1.5-2× baseline OR ≥0.3 mg/dL rise in 48 h	Consider holding ICI	Review nephrotoxins. Creatinine every 3-7 days.
Stage 2	>2-3× baseline	Hold ICI	Nephrology + prednisone 0.5-1 mg/kg/day. No improvement in 5-7 days → biopsy + escalate to 1-2 mg/kg/day.
Stage 3	>3× baseline OR ≥4.0 mg/dL OR RRT	Hold ICI; inpatient	Prednisone or IV methylprednisolone 1-2 mg/kg/day. Taper over 4-6 weeks once Stage 1.

Heads up: In ICI nephritis, avoid PPIs for steroid gastroprotection (PPIs independently trigger AIN); use an H2 blocker (famotidine) instead, and stop NSAIDs.

6. Endocrine

- Endocrine irAEs = **permanent glandular destruction** → rarely need high-dose steroids or permanent stop; manage with **hormone replacement**.
- **Primary hypothyroidism (high TSH, low FT4):** levothyroxine **1.2-1.4 mcg/kg/day** (0.8-1.0 in elderly/CAD); continue ICI.
- **Thyrotoxicosis (low TSH, high FT4):** painless **destructive thyroiditis** releasing preformed hormone; **no antithyroid drugs**; **beta-blockers only**; lasts 4-6 weeks then usually → permanent hypothyroidism.
- **Hypophysitis:** anterior pituitary inflammation (mainly **ACTH, TSH** deficits); headache, fatigue, hyponatraemia, secondary adrenal insufficiency, bitemporal hemianopsia.

Feature	Anti-CTLA-4 Hypophysitis (Ipilimumab)	Anti-PD-1 / Anti-PD-L1 Hypophysitis
Incidence	Significantly higher (~5-10%)	Low (<1%)
Pituitary MRI	Classic gland enlargement and infundibular enhancement	Frequently NORMAL pituitary MRI
Deficits	Multiple hormonal axes (ACTH, TSH, FSH/LH)	Often isolated ACTH deficiency
Mass Effect	Severe headache and visual disturbances common	Rare mass-effect symptoms

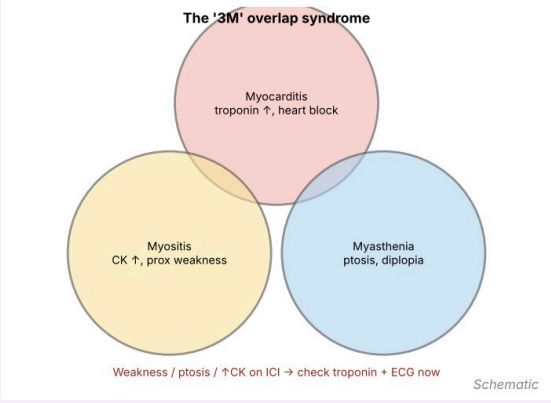
- **Hypophysitis management:** physiological **hydrocortisone 20 mg AM + 10 mg early afternoon** indefinitely; high-dose IV methylprednisolone 1 mg/kg/day **only** for acute visual compromise; **sick-day rules** (double dose 3 days); adrenal crisis = **hydrocortisone 100 mg IV then 50 mg q8h** + saline.

Heads up: In primary hypothyroidism, check serum cortisol first. Giving levothyroxine to an undiagnosed cortisol-deficient patient speeds hepatic cortisol clearance and can trigger a fatal adrenal crisis.

- **ICI type 1 DM:** autoimmune beta-cell destruction, acute hyperglycaemia, DKA, low C-peptide. **No high-dose steroids** (they worsen glycaemia, don't reverse it). Hold ICI only until DKA resolves, then lifelong **basal-bolus insulin**; resume ICI once glucose stable.

7. Cardiovascular: Myocarditis & 3M Overlap

- Fulminant lymphocytic myocarditis; rare (**0.5-1%**) but **40-50% mortality**; onset **1-2 cycles** in; worse with combination and **LAG-3** regimens.
- Workup: **ECG** (heart block, PR/QRS changes, arrhythmia), **troponin + CK-MB + NT-proBNP + total CK**, telemetry, **cardiac MRI (LGE, T1/T2 mapping)**, biopsy if uncertain.
- Management: **permanent stop for G2-4**; ICU + pacing readiness; **pulse methylprednisolone 1 g/day × 3-5 days**, then oral 1 mg/kg/day, taper **6-12 weeks**; refractory (24-48 h) → **abatacept (± ruxolitinib), ATG, alemtuzumab, IVIG, plasmapheresis**.
- High-risk combos: **hs-troponin at baseline and before each of the first 3 cycles**, then every 3 months.



The 3M overlap syndrome

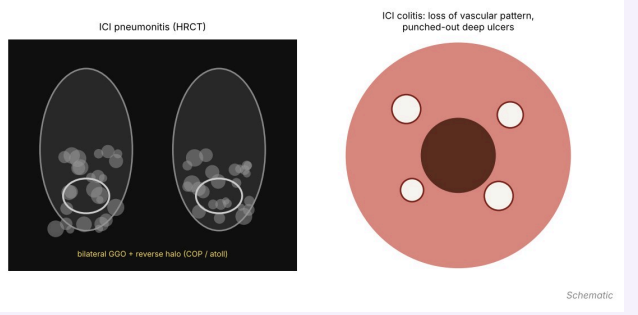
Heads up: The 3M overlap: Myocarditis, Myositis, Myasthenia gravis. Weakness, ptosis or raised CK on an ICI means check troponin and ECG now. Most fatal myocarditis deaths are from conduction block with PRESERVED EF, so a normal echo does not rule it out. Use infliximab with extreme caution if EF is low.

Table 1: GI & Hepatic irAE Management (cont.)

Condition	Diagnostic Hallmark	Initial Steroid Regimen	Preferred 2nd-Line Biologic	Key Exam Test Trap
Myocarditis	Elevated Troponin + ECG Heart Block	IV Methylprednisolone 1 g/day × 3-5d	Abatacept, ATG, IVIG, PLEX	Deaths occur with PRESERVED EF on Echo! Avoid Infliximab if low EF.
Myasthenia Gravis	Fatigable Ptosis / Diplopia + Elevated CK	Prednisone 20 mg/day (Titrate UP)	Rituximab 375 mg/m² wkly × 4	NCCN: Discontinue ICI at G2. Do NOT pulse steroids initially (worsens weakness).
Guillain-Barré	Ascending Areflexia + High CSF Protein	IV Methylprednisolone 1 g/day × 5d + IVIG/PLEX	IVIG or Plasmapheresis	Unlike idiopathic GBS, ICI-GBS REQUIRES pulse steroids alongside IVIG/PLEX.
Encephalitis	Confusion + CSF Lymphocytic Pleocytosis	Empirical IV Acyclovir + IV Methylpred 1-2 mg/kg	Rituximab	Must give empirical IV acyclovir until HSV/VZV PCR is negative.
Demyelination	Spinal Cord Lesion / Transverse Myelitis	IV Methylprednisolone 1 g/day × 3-5d	IVIG or Plasmapheresis	PERMANENTLY DISCONTINUE ICI AFTER ANY-GRADE EVENT.

13. Visual Anchors

- **ICI pneumonitis (HRCT):** bilateral **ground-glass**, peripheral consolidation, subpleural reticular; **COP pattern with reverse halo ("atoll") sign**. Differentiate from hypersensitivity pneumonitis (centrilobular nodules) and radiation pneumonitis (sharp geometric portal borders).
- **ICI colitis (endoscopy):** diffuse erythema, **loss of vascular pattern**, friability, **punched-out deep ulcers** (deep ulceration predicts steroid refractoriness). Histology: neutrophilic infiltrate, crypt abscesses, basal crypt apoptosis.



Pneumonitis HRCT and colitis endoscopy

- **ICI hepatotoxicity (biopsy):** pan-lobular hepatitis, **centrilobular (Zone 3) necrosis**, councilman bodies, **endothelialitis**, dense portal **CD8** infiltrate. Cholestatic: ductopenia, granulomatous cholangitis.

STEM-S

NEET-SS

Medical Oncology · Essential Notes



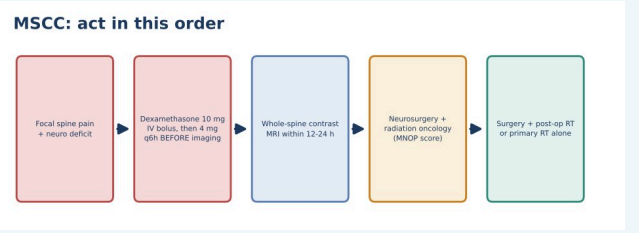
Oncological Emergencies

PRESENTED BY STEM-S

1. Structural and neurologic emergencies

Malignant spinal cord compression (MSCC)

Metastatic tumor in the epidural space, or a collapsed vertebral body, compresses the cord, vascular plexus or nerve roots. Posterior and lateral extension of vertebral metastases (prostate, lung, breast, renal, myeloma) disrupts spinal microcirculation, causing vasogenic edema, ischemia and irreversible axonal injury. The triad is **focal severe spinal pain, progressive bilateral weakness, and sensory/sphincter dysfunction**.



Schematic: MSCC. Illustration only, not a real clinical image.

Pain is the presenting symptom in over 95%, weeks to months before deficits. It is progressive, local to the spine, worse with coughing, sneezing or lying flat, and often radicular. Lesions above the conus give upper motor neuron signs (spasticity, hyperreflexia, extensor plantars); at or below the conus, lower motor neuron signs (flaccidity, hyporeflexia). Bowel/bladder loss, retention and saddle anesthesia mean advanced compromise or cauda equina syndrome. **Contrast MRI of the whole spine** is the gold standard, and the whole axis must be imaged because **up to 30% have noncontiguous asymptomatic lesions**.

- **Step 1:** dexamethasone **10 mg IV bolus, then 4 mg IV q6h** on clinical suspicion. It lowers vasogenic edema, relieves pain and prevents deterioration.
- **Surgery (decompression and stabilization) plus post-op RT:** mechanical instability, unknown histology, progression during RT, or single-level disease in fit patients. It preserves ambulation better than RT alone.
- **Emergency RT as primary therapy:** radiosensitive tumors (lymphoma, myeloma, small cell) or non-surgical candidates.

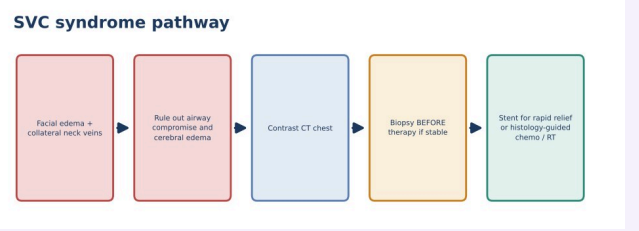
Heads up:

Give dexamethasone before imaging, never after. Plain X-rays show only advanced bony collapse and bone scans (which pick up osteoblastic metastases) miss soft-tissue epidural masses. Do not delay steroids for imaging or biopsy.

Superior vena cava syndrome (SVCS)

Extrinsic compression, invasion or thrombosis of the thin-walled SVC in the narrow right anterior superior mediastinum causes venous hypertension in the head, neck and arms. **SCLC causes 60-70%**, then NSCLC and non-Hodgkin lymphoma. The triad is **facial edema, arm swelling and chest wall collateral veins**. Over days to weeks: dyspnea, orthopnea, facial fullness, cough, hoarseness, dysphagia, plethora, periorbital edema, and **Pemberton sign** (flushing and distress on raising both arms).

Superior vena cava syndrome (SVCS) (cont.)



Schematic: SVCS. Illustration only, not a real clinical image.

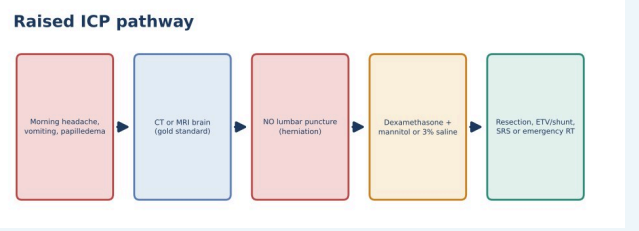
- **Contrast CT chest** shows the obstruction, tumor extent, thrombus and collaterals.
- **Supportive:** head up, oxygen, short-term dexamethasone if airway edema is suspected.
- **Endovascular stenting** relieves symptoms within 24-48 hours (first-line for severe distress or a pending diagnosis).
- **Definitive:** chemotherapy for SCLC and NHL (highly chemosensitive, chemo ± RT); RT or stenting for NSCLC and persistent masses.

Heads up:

In adults SVCS is rarely an immediate surgical or radiation emergency unless there is **central airway compromise or severe cerebral edema**. Get **tissue first** because SCLC, NSCLC and lymphoma are treated differently. If urgent relief is needed while waiting, **stent**.

Raised intracranial pressure and herniation

Tumor, peritumoral vasogenic edema or obstructive hydrocephalus expands intracranial volume beyond compliance. ICP above **150 mm H_2O** impairs perfusion and pushes brain across dural structures. Classic triad: **early-morning headache that wakes the patient**, **nausea/projectile vomiting**, **psychomotor and cognitive slowing**. Headache worsens lying down, coughing or Valsalva. Later: papilledema, sixth nerve palsy, confusion and **Cushing triad** (bradycardia, hypertension, irregular respirations), which signals uncal or tonsillar herniation. CT or MRI shows the mass, T2/FLAIR edema, midline shift and ventricular effacement.



Schematic: raised ICP. Illustration only, not a real clinical image.

- **Dexamethasone 4 mg IV q6h** restores the blood-brain barrier and cuts vasogenic edema.
- **Mannitol 0.5-1.0 g/kg** or **3% saline** for acute deterioration.
- **Definitive:** craniotomy and debulking, ETV or VP shunt for hydrocephalus, or SRS.

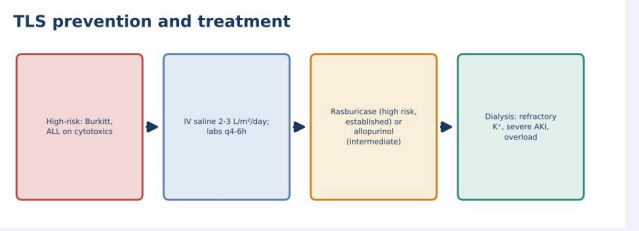
Heads up:

No lumbar puncture with significant mass effect or obstructive hydrocephalus. Dropping spinal pressure creates a gradient that causes fatal transtentorial or tonsillar herniation.

2. Metabolic emergencies

Tumor lysis syndrome (TLS)

Rapid, massive tumor cell death releases ions, proteins and nucleic acids, spontaneously or after cytotoxics, in high-burden disease (**Burkitt lymphoma**, **ALL**). Purines are catabolized by xanthine oxidase to uric acid while potassium and phosphate flood the blood: **hyperkalemia**, **hyperphosphatemia**, **hyperuricemia and secondary hypocalcemia**. Uric acid and calcium-phosphate crystals in the tubules cause AKI; hyperkalemia causes lethal arrhythmias; hypocalcemia causes tetany, carpopedal spasm and seizures.



Schematic: TLS. Illustration only, not a real clinical image.

Cairo-Bishop criteria. Laboratory TLS is ≥ **2** of the following within 3 days before to 7 days after therapy:

- Uric acid ≥ **8.0 mg/dL** (or 25% rise)
- Potassium ≥ **6.0 mEq/L** (or 25% rise)
- Phosphate ≥ **4.5 mg/dL** (adults)
- Calcium ≤ **7.0 mg/dL** (or 25% fall)

Clinical TLS is laboratory TLS plus AKI (creatinine ≥ **1.5 x ULN**), arrhythmia or seizure.

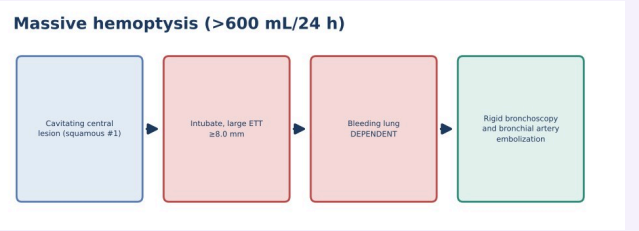
Agent	Mechanism	Key point
Aggressive IV hydration	Renal perfusion, solute clearance	First-line for all risk groups: 2-3 L/m²/day non-dextrose saline, urine output >100 mL/m²/hr
Rasburicase 0.15-0.20 mg/kg IV	Recombinant urate oxidase: uric acid → water-soluble allantoin	High risk or established TLS; works within hours. Contraindicated in G6PD deficiency (severe hemolysis)
Allopurinol 300 mg/day PO	Xanthine oxidase inhibitor	Prophylaxis in low/intermediate risk; does NOT clear existing uric acid

Heads up:

Established TLS with uric acid >12 mg/dL: **rasburicase**, not allopurinol (it only blocks new synthesis). TLS causes **hypocalcemia**, not hypercalcemia. Hyperkalemia: IV insulin/glucose, calcium gluconate for membrane stabilization, loop diuretics. **Hemodialysis** for refractory hyperkalemia, severe hyperphosphatemia, intractable overload or progressive AKI.

Central airway obstruction and massive hemoptysis

Endobronchial growth, extrinsic compression or cavitating necrosis of thoracic tumors (**squamous cell lung carcinoma is #1**). **>50% tracheal obstruction** causes respiratory failure (stridor, orthopnea, suprasternal retractions). Erosion into bronchial arteries causes **massive hemoptysis (>600 mL in 24 h)**, with asphyxiation, hypoxia and collapse.



Schematic: massive hemoptysis. Illustration only, not a real clinical image.

- Intubate with a large single/double-lumen tube, bleeding side **down**. **Bronchial artery embolization** is the definitive non-surgical choice. **Rigid bronchoscopy** with electrocautery, laser or stenting for central obstruction.

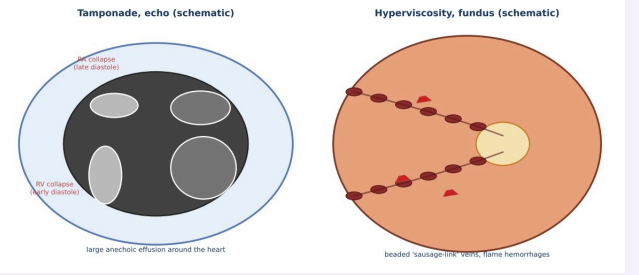
Heads up:

The cause of death is **asphyxiation, not hemorrhagic shock**: protect the healthy lung first (bleeding lung dependent, secure the airway).

5. Comparison tables

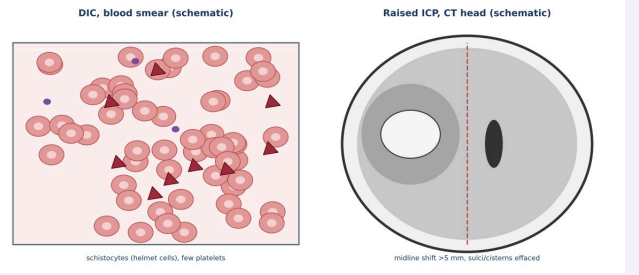
Feature	TLS	Hypercalcemia	SIADH
Mechanism	Massive cell lysis; ion/purine release	PTHrP, osteolysis, calcitriol	Ectopic ADH
Classic tumors	Burkitt, ALL	Squamous lung/H&N, breast, myeloma, RCC	SCLC
Labs	↑ K, ↑ PO_4, ↑ uric acid, ↓ Ca	↑ Ca (>12-14), ↓ PTH, ↑ PTHrP	↓ Na (<135), low plasma osm, high urine Na/osm
Signs	Oliguria, AKI, arrhythmias, tetany	Polyuria, dehydration, constipation, confusion, short QT	Euvolemic hyponatremia, confusion, seizures
First step	IV hydration 2-3 L/m^2/day	Saline 200-300 mL/hr	Fluid restriction (mild) or 3% saline (severe)
Drug	Rasburicase (established); allopurinol (prophylaxis)	Zoledronic acid + calcitonin bridge	Tolvaptan/demeclocycline; treat tumor

- **HVS (fundus):** "sausage-link" or "piston-barrel" retinal veins, disc edema, flame hemorrhages, cotton-wool exudates.



Schematic: tamponade and hyperviscosity (schematic). Illustration only, not a real clinical image.

- **DIC (smear):** schistocytes (helmet cells), thrombocytopenia, nucleated red cells from fibrin-strand microangiopathy.
- **Raised ICP (CT head):** mass with finger-like vasogenic edema; effaced sulci and ventricles, third-ventricle shift **>5 mm**, obliterated suprasellar/ambient cisterns, uncus displaced over the tentorial notch.



Schematic: DIC and raised ICP (schematic). Illustration only, not a real clinical image.

STEM-S

NEET-SS

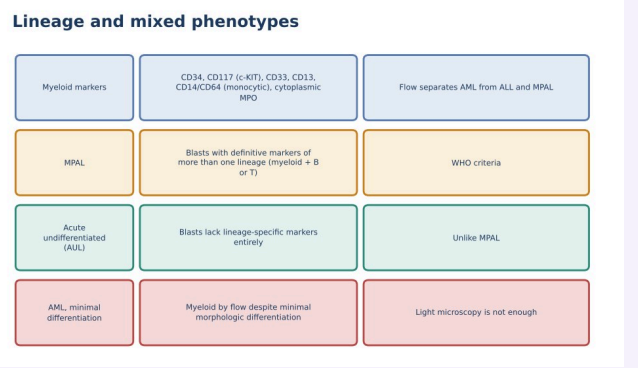
Medical Oncology · Essential Notes



Acute Myeloid Leukemia (AML) and Related Myeloid Neoplasms

PRESENTED BY STEM-S

Lineage immunophenotyping

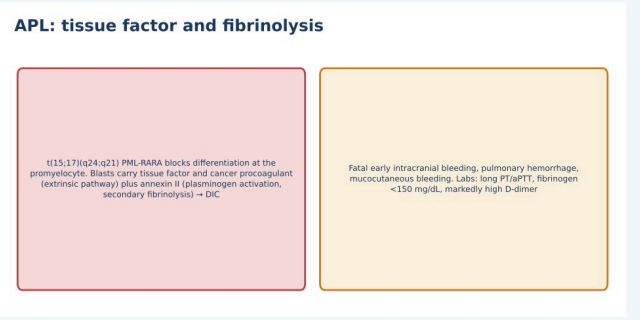


Schematic: lineage. Illustration only, not a real clinical image.

Feature	AML	ALL	MPAL	APL
Cell type	Myeloblasts (Auer rods, MPO+)	Lymphoblasts (TdT+, PAS+)	Dual-lineage blasts	Abnormal promyelocytes (faggot cells)
Flow	CD34, CD117, CD33, CD13, MPO	B: CD19, CD22, CD10. T: CD2, CD3, CD7	Markers for >1 lineage	CD33+, CD13+, MPO+++, often CD34− / HLA-DR−
Cytogenetics	NPM1, FLT3, t(8;21), inv(16), TP53	t(9;22) BCR-ABL1, t(4;11) KMT2A, hyperdiploidy	Variable / complex karyotype	t(15;17)(q24;q21) PML-RARA
Complications	Hyperleukostasis, chloromas	CNS / testicular infiltration	Rapid chemoresistance	Severe DIC, fatal coagulopathy
Frontline	7+3 or HMA + venetoclax	Multi-agent chemo + TKI if Ph+	Acute leukemia induction regimens	Chemo-free ATRA + arsenic trioxide

Hyperleukostasis (usually WBC above about 100 x 10^9/L, more with monocytic AML) causes dyspnea, hypoxia, confusion and visual change from blasts clogging small vessels. Standard teaching: urgent cytoreduction (hydroxyurea, leukapheresis in selected cases) and prompt induction, with caution about transfusing red cells to high Hb values and with TLS prophylaxis. This is not in your source.

Monocytic variants and extramedullary disease (cont.)



Schematic: APL coagulopathy. Illustration only, not a real clinical image.

Risk (PETHEMA/GIMEMA): standard risk is presenting **WBC ≤ 10 x 10^9/L** and high risk is **>10 x 10^9/L**. The presenting WBC is the most important determinant of early hemorrhagic death and relapse, and decides whether a cytoreductive agent (anthracycline or gemtuzumab ozogamicin) is added to ATRA + ATO.



Schematic: APL risk. Illustration only, not a real clinical image.

Heads up:

With DIC and promyelocytes containing stacked Auer rods (**faggot cells**), **start ATRA immediately on clinical suspicion**, before t(15;17) confirmation. Waiting for genetics is a classic distractor that leads to preventable hemorrhagic death.

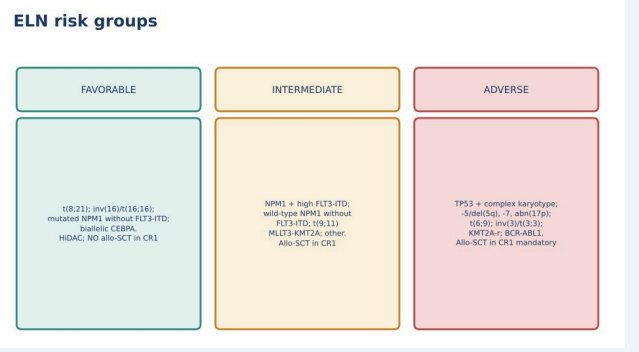


Schematic: APL emergency. Illustration only, not a real clinical image.

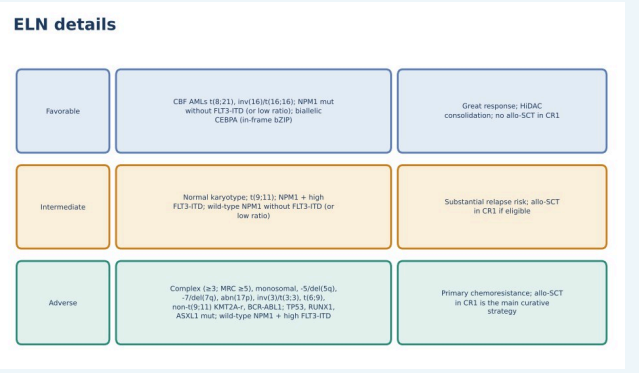
Supportive care in APL DIC is aggressive: platelets kept high (often above 30-50 x 10^9/L) and fibrinogen replaced with cryoprecipitate while ATRA works. Lumbar puncture and central line placement are avoided at presentation because of bleeding risk. These are standard teaching points, not in your source.

4. Cytogenetic and molecular risk (ELN)

Pretreatment cytogenetics and molecular genetics are the **strongest predictors of induction success, relapse risk and survival**, and decide whether chemotherapy alone can cure or an allogeneic transplant is needed.

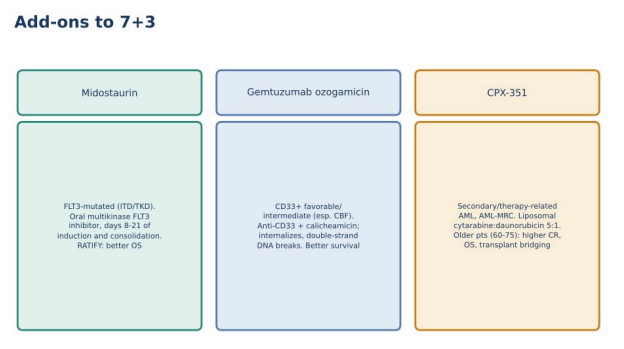


Schematic: ELN groups. Illustration only, not a real clinical image.



Schematic: ELN details. Illustration only, not a real clinical image.

- **Favorable:** CBF AML t(8;21) and inv(16)/t(16;16); mutated **NPM1** without FLT3-ITD (or low allelic ratio); **biallelic mutated CEBPA** (in-frame bZIP). Excellent response; **HiDAC** consolidation; **allo-SCT not indicated in CR1**.
- **Intermediate:** normal karyotype; **t(9;11) MLLT3-KMT2A**; NPM1 mutated with **high** FLT3-ITD ratio; wild-type NPM1 without FLT3-ITD (or low ratio). High relapse risk with chemotherapy alone; **allo-SCT in CR1** for eligible patients.
- **Adverse:** complex karyotype (≥ 3 abnormalities; MRC defines complex as ≥ 5), monosomal karyotype, -5/del(5q), -7/del(7q), abn(17p), inv(3)/t(3;3) (GATA2, MECOM/EVI1), t(6;9) DEK-NUP214, non-t(9;11) KMT2A rearrangements, t(9;22) BCR-ABL1; mutated **TP53** (enriched in t-AML and s-AML), RUNX1, ASXL1; wild-type NPM1 with high FLT3-ITD. Primary chemoresistance with 7+3; **allo-SCT in CR1** is the main curative strategy.



Schematic: add-ons. Illustration only, not a real clinical image.

Heads up:

Idarubicin gives higher complete remission rates than standard-dose daunorubicin, but no consistent overall survival advantage.

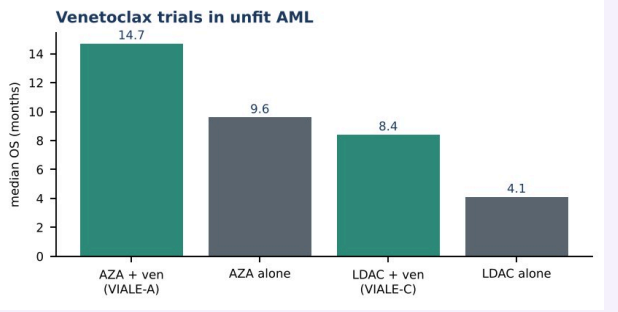
Cytarabine and anthracycline toxicities worth remembering: **high-dose cytarabine** causes cerebellar toxicity (ataxia, nystagmus; risk rises with renal impairment and age) and conjunctivitis (steroid eye drops); anthracyclines cause cardiotoxicity (check ejection fraction). Gemtuzumab can cause hepatic veno-occlusive disease. Standard teaching, not from your source.

Secondary and therapy-related AML

t-AML, AML with myelodysplasia-related changes and AML from MDS resist standard 7+3. **CPX-351** is a liposomal formulation of cytarabine and daunorubicin at a synergistic **5:1 molar ratio**. In patients aged **60-75** with secondary AML it beat 7+3: higher CR rates, better overall survival and more patients bridged to stem cell transplant.

Unfit or elderly patients

Older patients or those with **ECOG ≥ 3** or severe comorbidity cannot tolerate intensive therapy. **Venetoclax** (selective oral BCL-2 inhibitor restoring apoptosis) with a hypomethylating agent (azacitidine or decitabine) is standard. **VIALE-A:** azacitidine + venetoclax median OS **14.7 vs 9.6 months** with azacitidine alone. **VIALE-C:** LDAC + venetoclax **8.4 vs 4.1 months** with LDAC alone.

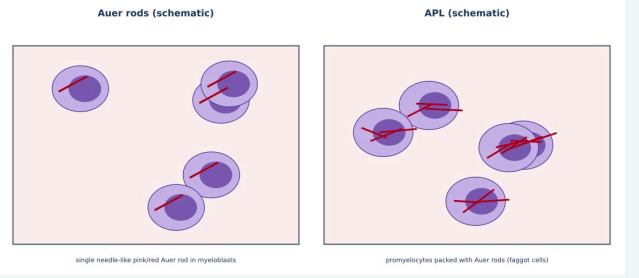


Schematic: median overall survival. Illustration only, not a real clinical image.

7. Visual anchors

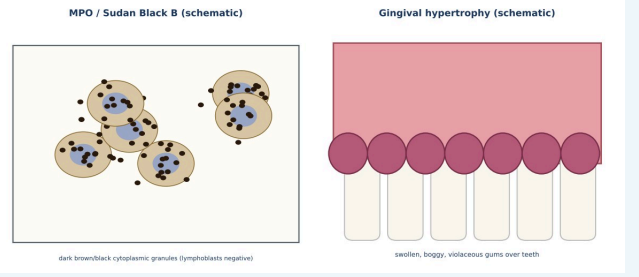
What to recognize on sight. Illustrations only, not real clinical images.

- **Auer rods (Wright-Giemsa):** elongated pink-red needle-like inclusions from fused primary granules containing MPO; **pathognomonic for myeloid lineage**, **never in ALL**.
- **Faggot cells:** promyelocytes with stacked bundles of Auer rods ("bundle of sticks"); pathognomonic for **APL, t(15;17)**.



Schematic: Auer rods and faggot cells. Illustration only, not a real clinical image.

- **MPO and Sudan Black B:** intense dark brown/black cytoplasmic staining confirms myeloid lineage; lymphoblasts are negative.
- **Gingival hypertrophy:** swollen, boggy, violaceous gums, a hallmark of monocytic AML (M4/M5) and KMT2A rearrangement.



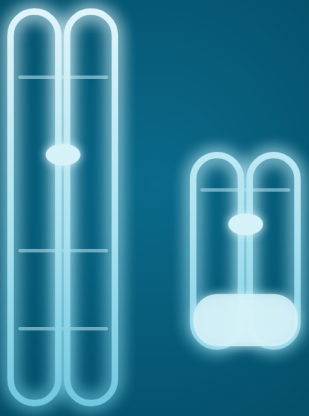
Schematic: MPO stain and gingival hypertrophy. Illustration only, not a real clinical image.

- **Leukemia cutis:** raised violaceous papules or nodules (monocytic AML, KMT2A).
- **Ring sideroblasts (Prussian blue):** erythroid precursors with a perinuclear ring of coarse blue granules covering ≥1/3 of the nuclear circumference (mitochondrial iron overload); marker of **MDS-SF3B1**.

STEM-S

NEET-SS

Medical Oncology · Essential Notes

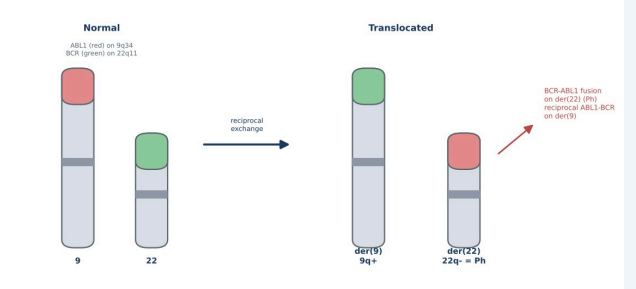


Chronic Myeloid Leukemia (CML)

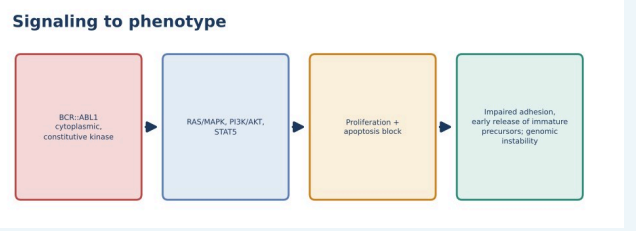
PRESENTED BY STEM-S

1. Pathophysiology and molecular pathogenesis

CML is a clonal myeloproliferative neoplasm that starts in a pluripotent hematopoietic stem cell. Its driver is the **Philadelphia (Ph) chromosome**, found by Nowell and Hungerford in 1960 and later shown to be a balanced reciprocal translocation, **t(9;22)(q34;q11.2)**. The ABL1 proto-oncogene from 9q34 joins the breakpoint cluster region (BCR) on 22q11.2, creating the **BCR::ABL1** fusion gene (the double colon is the newer notation for a fusion). It encodes a constitutively active tyrosine kinase. Wild-type ABL1 (p145) lives mostly in the nucleus and is switched on mainly by DNA damage; the BCR::ABL1 oncoprotein sits **only in the cytoplasm** and is always on.



Schematic: the t(9;22) exchange. Illustration only, not a real clinical image.

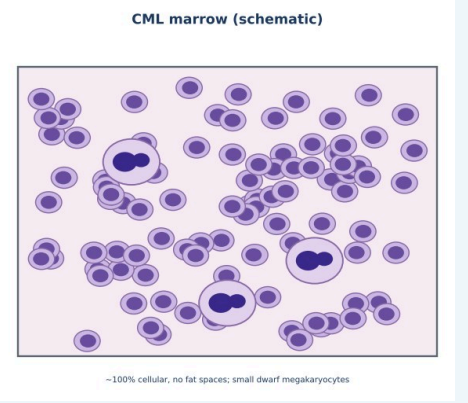


Schematic: signaling. Illustration only, not a real clinical image.

Constant signaling through **RAS/MAPK**, **PI3K/AKT and STAT5** drives uncontrolled proliferation of myeloid progenitors, blocks normal apoptosis, loosens cell-matrix adhesion (so immature precursors leak into the blood too early) and causes progressive genomic instability that sets up secondary mutations and clonal evolution.

Breakpoints and isoforms

Where the break falls in BCR sets the size and activity of the fusion protein. This matters for the diagnosis, for choosing PCR primers and for standardized (International Scale) monitoring.



Schematic: marrow. Illustration only, not a real clinical image.

Heads up:

Marrow fibrosis in CML is secondary and reactive (megakaryocytes release PDGF and TGF-β). It is not a primary feature, does not exclude CML, does not define accelerated phase, and effective TKI therapy reverses it within 3 to 6 months.



Schematic: marrow fibrosis. Illustration only, not a real clinical image.

Karyotype

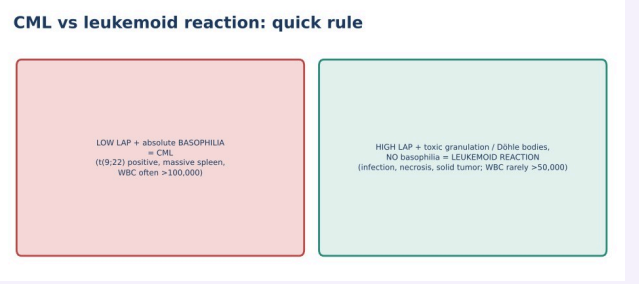
- At least **20 marrow metaphases**: it finds t(9;22) in **85-90%**, picks up variant translocations involving a third chromosome and gives the baseline for ACAs.
- Twenty metaphases give statistical confidence for clonality, detect subtle clonal evolution and give a reliable baseline for monitoring cytogenetic remission.

QR-PCR and FISH

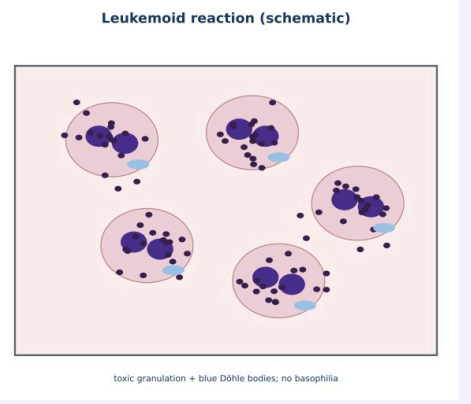
5. Comparative tables

CML vs reactive leukemoid reaction

Feature	CML	Leukemoid reaction
Cause	Clonal stem cell neoplasm	Secondary to severe infection or inflammation
WBC	Typically >100,000/µL	High (>50,000/µL) but rarely >100,000/µL
LAP	Low or zero	Markedly elevated
Absolute basophilia	Present (key differentiator)	Absent
Blasts, promyelocytes	Present (left shift)	Rare or absent; toxic granulation and Döhle bodies
Spleen	Prominent in >70%	Absent or minimal
Ph / BCR::ABL1	Positive (mandatory)	Negative

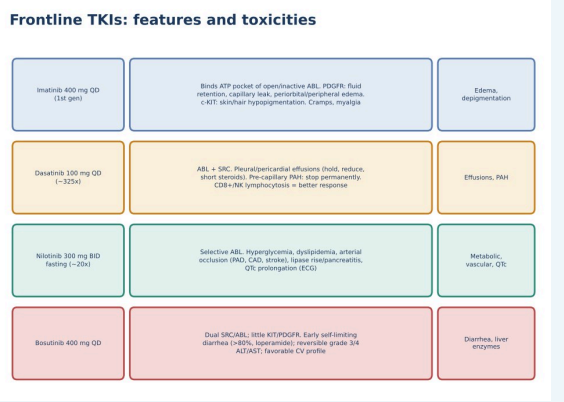


Schematic: quick rule. Illustration only, not a real clinical image.



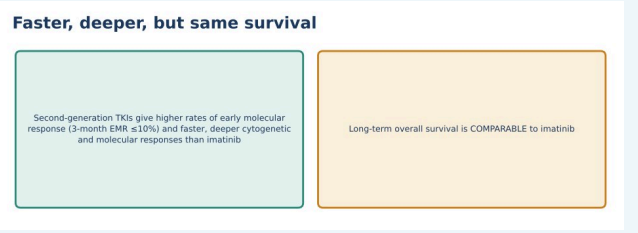
Schematic: leukemoid smear. Illustration only, not a real clinical image.

CML vs Ph-negative MPNs



Schematic: TKI features. Illustration only, not a real clinical image.

Second-generation TKIs



Schematic: second-generation. Illustration only, not a real clinical image.

- **Dasatinib 100 mg daily:** about 325-fold more potent than imatinib; blocks ABL and SRC. **Pleural/pericardial effusions** (hold, reduce dose, short steroid course); **pulmonary arterial hypertension** (permanent stop if confirmed); **therapeutic lymphocytosis** (CD8+ T and NK cell expansion) linked to better response.
- **Nilotinib 300 mg BID on an empty stomach:** about 20-fold more potent, highly selective for ABL. **Hyperglycemia**, **dyslipidemia**, **arterial occlusive events** (PAD, CAD, stroke), **lipase/amylase rise and pancreatitis**, **QTc prolongation** (baseline and periodic ECG). Use with great care in metabolic syndrome, vascular disease or diabetes.
- **Bosutinib 400 mg daily:** dual SRC/ABL, minimal KIT/PDGFR activity. **Early diarrhea** in over 80% (self-limiting, loperamide), reversible grade 3/4 ALT/AST rises; favorable cardiovascular profile like imatinib.

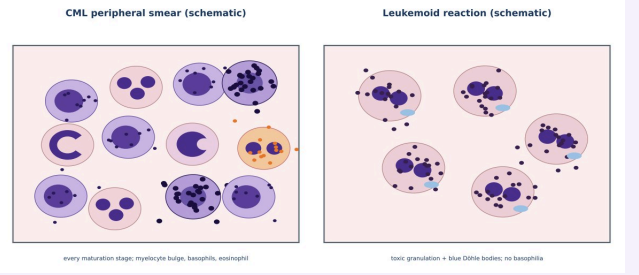
Handy contrast: edema points to imatinib, effusions and PAH point to dasatinib, metabolic and vascular events plus QTc point to nilotinib, diarrhea points to bosutinib, and arterial occlusion points to ponatinib.

Third generation, STAMP and others

10. Visual anchors

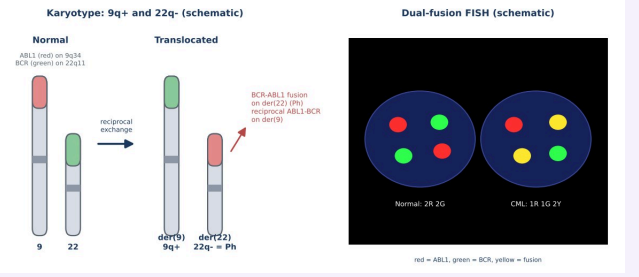
What to recognize on sight. Illustrations only, not real clinical images.

- **Smear, "full spectrum left shift":** every stage of maturation with sparse blasts under 10%, plus prominent absolute **basophils** (coarse purple-black granules hiding the nucleus) and eosinophilia. A leukemoid reaction shows toxic granulation instead.



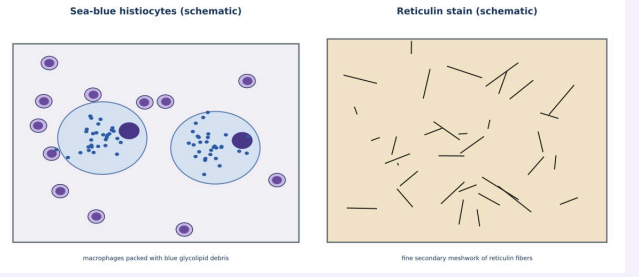
Schematic: CML vs leukemoid smear. Illustration only, not a real clinical image.

- **Karyotype:** the shortened derivative chromosome 22 is the Philadelphia chromosome, from t(9;22)(q34;q11.2).



Schematic: karyotype and FISH. Illustration only, not a real clinical image.

- **Marrow:** hypercellular, G:E >3:1 to 10:1, widened intertrabecular space, and **sea-blue histiocytes (pseudo-Gaucher cells)**, macrophages filled with blue glycolipid debris from cell turnover. **Reticulin** shows a fine secondary meshwork.

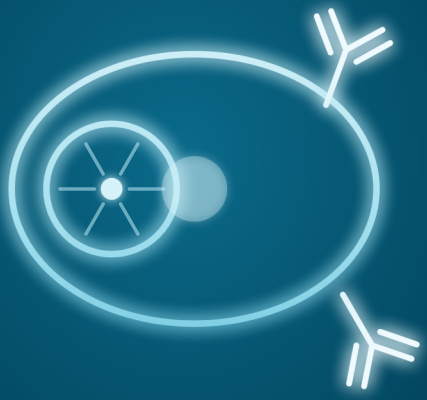


Schematic: histiocytes and reticulin. Illustration only, not a real clinical image.

STEM-S

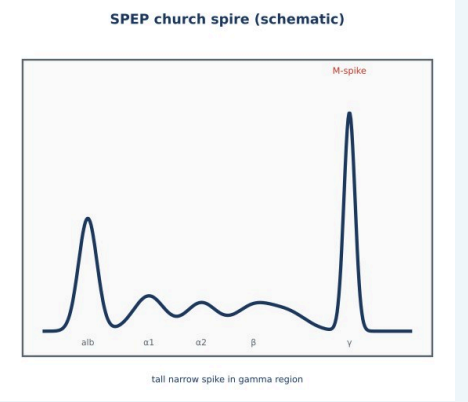
NEET-SS

Medical Oncology · Essential Notes

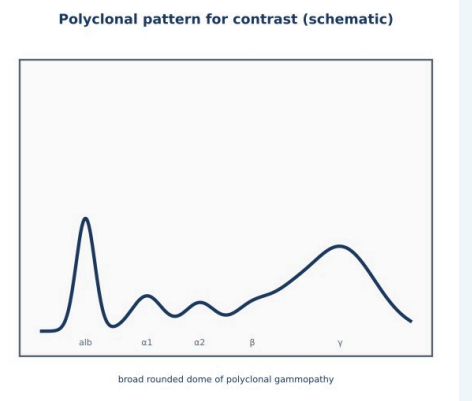


Plasma Cell Neoplasms

PRESENTED BY STEM-S



Schematic: SPEP church spire. Illustration only, not a real clinical image.

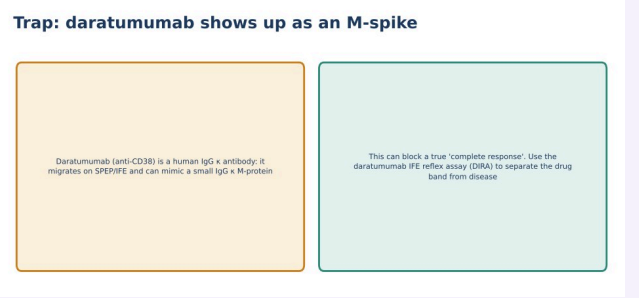


Schematic: polyclonal pattern for contrast. Illustration only, not a real clinical image.

- **Rate nephelometry** gives absolute IgG, IgA and IgM, needed when SPEP is unreliable (beta-region migration, polymerized IgA/IgM).
- **24-hour urine electrophoresis + urine IFE** measure Bence Jones protein; measurable urinary disease is **≥ 200 mg/24 h**.

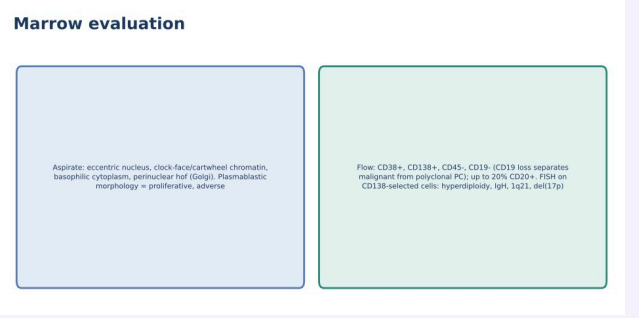
Heads up:

Daratumumab can look like disease. Daratumumab is a human IgG κ antibody, so it migrates on SPEP/IFE and can mimic a small IgG κ M-spike, blocking a true complete response. The daratumumab IFE reflex assay (DIRA) separates the drug band from disease.

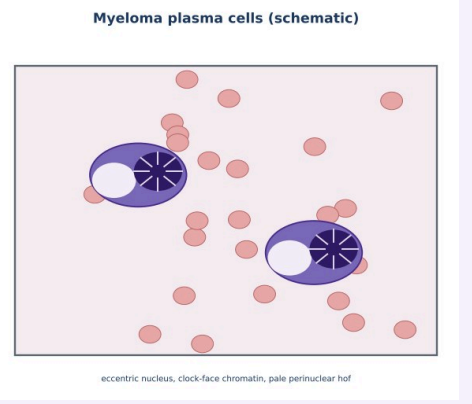


Schematic: daratumumab trap. Illustration only, not a real clinical image.

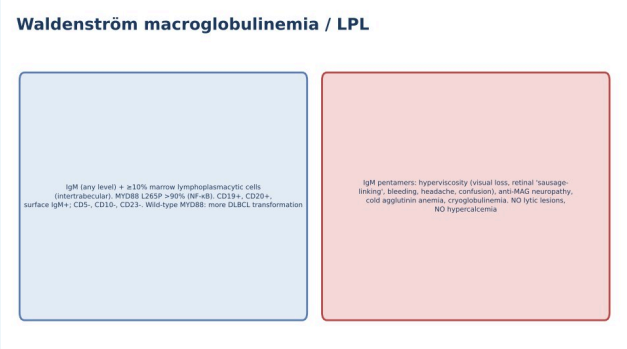
Step 3 and 4: marrow and imaging



Schematic: marrow evaluation. Illustration only, not a real clinical image.



Schematic: myeloma plasma cells. Illustration only, not a real clinical image.



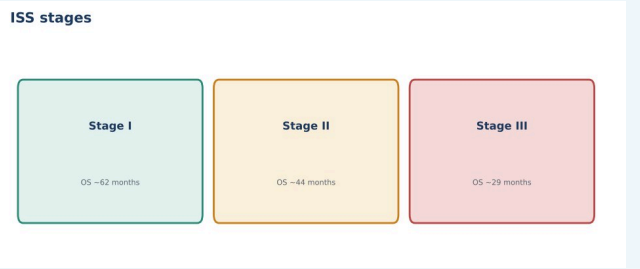
Schematic: Waldenström macroglobulinemia. Illustration only, not a real clinical image.

4. Comparison table

Entity	Monoclonal protein	Marrow	End-organ damage	Key differentiators
Non-IgM MGUS	<3 g/dL	BMPC <10%	None	1%/yr progression; hyperdiploidy or t(11;14)
IgM MGUS	IgM <3 g/dL	LPL <10%	None	No hyperviscosity, organomegaly or nodes
Smoldering MM	≥3 g/dL or urine ≥500 mg/24 h	BMPC 10-60%	None	Mayo 20-2-20; ~25%/yr in first 2 years if high risk
Multiple myeloma	98% (IgG > IgA > light chain only; non-secretory 1-2%)	BMPC ≥10% or plasmacytoma	≥1 CRAB or SLiM	Lytic lesions, cast nephropathy, anemia, hypercalcemia
Solitary plasmacytoma	Absent or small	<10%, normal	None outside lesion	Local RT 40-50 Gy
AL amyloidosis	Monoclonal FLC (mostly λ)	Usually <20%	Nephrotic, cardiac	Congo red apple-green; low voltage ECG; macroglossia
POEMS	Monoclonal λ	Usually <10%	Neuropathy, sclerotic lesions	VEGF high, Castleman disease, hypertrichosis
Waldenström	IgM (any level)	LPL ≥10%	Hyperviscosity, anemia, organomegaly	MYD88 L265P >90%; no lytic lesions; no hypercalcemia

5. Risk stratification and staging

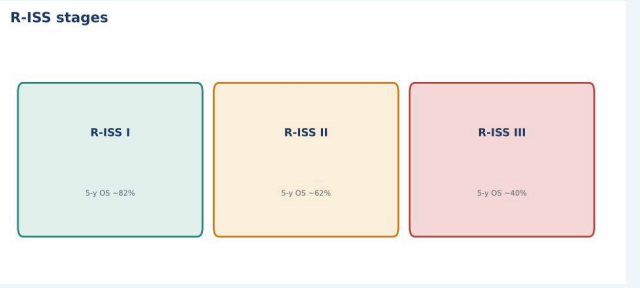
International Staging System



Schematic: ISS. Illustration only, not a real clinical image.

- **ISS I:** β2-microglobulin <3.5 mg/L and albumin ≥ 3.5 g/dL.
- **ISS II:** neither I nor III (for example β2M <3.5 with albumin <3.5, or β2M 3.5-5.5 whatever the albumin).
- **ISS III:** β2-microglobulin ≥ 5.5 mg/L.

Revised ISS (R-ISS)



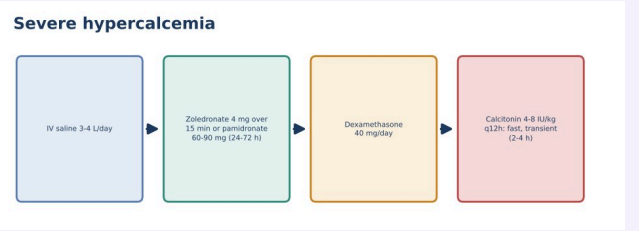
Schematic: R-ISS. Illustration only, not a real clinical image.

- **R-ISS I:** ISS I + standard-risk FISH + normal LDH.
- **R-ISS III:** ISS III + high-risk FISH [t(4;14), t(14;16) or del(17p)] or high LDH.
- **R-ISS II:** *everything between.*

mSMART cytogenetic risk

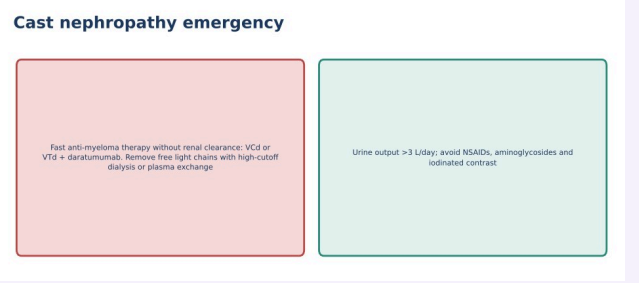
7. Emergencies

Severe hypercalcemia

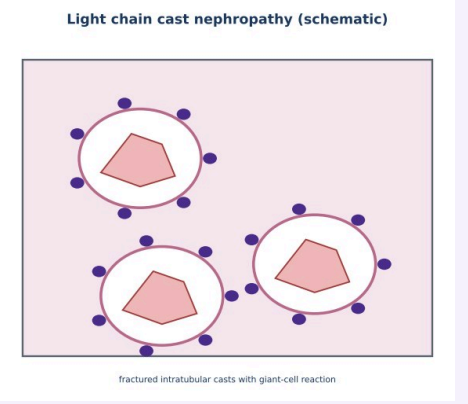


Schematic: hypercalcemia protocol. Illustration only, not a real clinical image.

Cast nephropathy and acute renal failure



Schematic: cast nephropathy emergency. Illustration only, not a real clinical image.



Schematic: light chain cast nephropathy. Illustration only, not a real clinical image.

STEM-S

NEET-SS

Medical Oncology · Essential Notes



Non-Small Cell Lung Cancer

PRESENTED BY STEM-S

CHAPTER INDEX

Non-Small Cell Lung Cancer

Notes pages **303–321** · 19 pages

1 Pathophysiology, Epidemiology & Molecular Oncogenesis 303

- Smoking carcinogenesis 303
- Oncogene-driven (non/light smokers) 303

Origin governs presentation 303

- Divergent genomic landscapes 304

2 Histopathology, Precursor Spectrum & IHC 305

- Adenocarcinoma preinvasive spectrum 305

Squamous & other epithelial subtypes 305

3 Clinical Presentation, Local Invasion & Paraneoplastic 307

Endobronchial / local signs 307

- Direct intrathoracic extension 307
- Metastatic predilections 308

Paraneoplastic syndromes 308

4 Diagnostic & Staging Step-Ladder 309

Anatomic access of modalities 309

5 TNM 8th & 9th Edition Staging 310

T descriptors 310

- N descriptors 311
- M descriptors 311

6 Stage I-II Management & Surgical Paradigms 312

- Lobectomy vs sublobar 312
- Sleeve vs pneumonectomy 312

Medically inoperable Stage I: SBRT vs surgery 313

- Mediastinal lymphadenectomy & Stage II 313
- Adjuvant systemic therapy 313

7 Stage III Multimodality Hierarchy 313

- Resectable IIIA (N2): neoadjuvant paradigm 314
- Unresectable Stage III: concurrent chemoRT + consolidation 314

8 Stage IV Oncogene-Driven NSCLC 315

- Classical EGFR (ex19del ~45%, L858R ~40%) 315
- Uncommon & exon 20 EGFR 315

ALK fusions 315

Other targets 316

9 Stage IV Non-Driver NSCLC 317

- High PD-L1 (≥ 50%) 317
- Low / negative PD-L1 (< 50% or < 1%) 317

Histology-specific restrictions 318

- Second-line and beyond 318

10 Special Scenarios: Oligometastatic & Pleural Effusions 318

Oligometastatic / oligoprogressive 318

- Malignant pleural effusion (MPE) 319

11 Visual Anchors 319

Page numbers match the teal page number printed at the top right of each notes page.

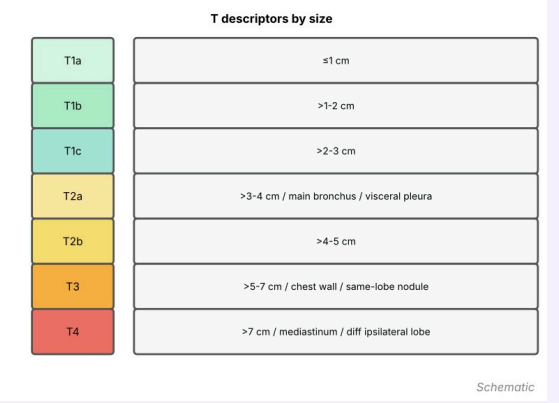
Squamous & other epithelial subtypes (cont.)

Histologic Subtype	Microscopic Architecture	Diagnostic IHC Panel	Molecular Profiling Mandate	Key Clinical Exam Differentiator
Adenocarcinoma	Glandular lumens, acini, papillary cores, lepidic lining, intracytoplasmic mucin	TTF-1 (+), CK7 (+), Napsin-A (+), p40 (−)	Comprehensive NGS mandatory (EGFR, ALK, ROS1, BRAF, MET, RET, KRAS, HER2, NTRK)	Mirror-image IHC to SCC. Actionable drivers common; non-smoker predominance.
Squamous Cell Carcinoma	Keratin pearls, intercellular bridges, sheets of polygonal cells	p40 (+), p63 (+), CK5/6 (+), TTF-1 (−)	NGS not routinely required unless non/light smoker	p40 superior specificity over p63; strongly smoking-associated.
Large-Cell Carcinoma	Sheets of large atypical polygonal cells; no pearls, acini or mucin	Negative for TTF-1, p40, neuroendocrine markers	Routine profiling if adeno markers equivocal	Diagnosis of exclusion on resection only.
Adenocarcinoma in Situ (AIS)	100% lepidic monolayer along septa (≤ 30 mm)	TTF-1 (+), CK7 (+), p40 (−)	Evaluated on resection specimen	Zero invasion; Tis (Stage 0); 100% cure.

Histologic Subtype	Microscopic Architecture	Diagnostic IHC Panel	Molecular Profiling Mandate	Key Clinical Exam Differentiator
Minimally Invasive (MIA)	Predominantly lepidic (≤ 30 mm) with ≤ 5 mm invasive focus	TTF-1 (+), CK7 (+), p40 (−)	Evaluated on resection specimen	Invasive component ≤ 5 mm, no LVI/pleura/STAS; T1mi.
LCNEC	Organoid nesting, rosettes, trabeculae, necrosis, high mitoses	Synaptophysin (+), Chromogranin (+), CD56 (+), Ki-67 >50%	Dual subtypes: SCLC-like (TP53/RB1) vs NSCLC-like (TP53/STK11/KEAP1)	Large cells + nucleoli separate from SCLC.

Heads up: On small biopsies and cytology, don't burn tissue on a big IHC panel. A focused p40 + TTF-1 pair separates squamous (p40+/TTF-1−) from adeno (TTF-1+/p40−) and keeps tissue for molecular testing, avoiding "NSCLC-NOS".

T descriptors (cont.)



T descriptors by size

N descriptors

- **N0:** none. **N1:** ipsilateral peribronchial / hilar (10-14). **N2:** ipsilateral mediastinal / subcarinal (1-9).
  - **9th ed: N2a** single station, **N2b** multiple ipsilateral stations.
- **N3:** contralateral mediastinal/hilar, or any scalene/supraclavicular.

M descriptors

- **M1a:** intrathoracic (malignant pleural/pericardial effusion, contralateral lobe nodule).
- **M1b:** single extrathoracic metastasis in one organ.
- **M1c:** multiple extrathoracic mets. **9th ed: M1c1** one organ system, **M1c2** multiple systems.

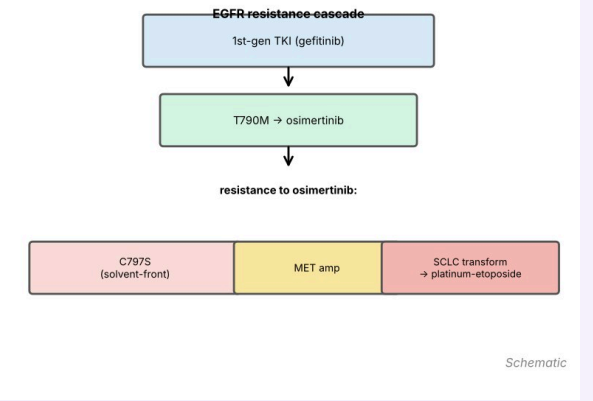
Stage	T Descriptor	N Descriptor	M Descriptor	5-Year Overall Survival Expectation
Stage 0	Tis	N0	M0	Near 100%
Stage IA1	T1a (≤1 cm)	N0	M0	~90%
Stage IA2	T1b (>1-2 cm)	N0	M0	~85%
Stage IA3	T1c (>2-3 cm)	N0	M0	~80%
Stage IB	T2a (>3-4 cm)	N0	M0	~73%
Stage IIA	T2b (>4-5 cm)	N0	M0	~65%
Stage IIB	T1a-T2b / T3	N1 / N0	M0	~56%
Stage IIIA	T1a-T2b / T3 / T4	N2 / N1 / N0-N1	M0	~41%
Stage IIIB	T1a-T2b / T3-T4	N3 / N2	M0	~24%
Stage IIIC	T3-T4	N3	M0	~12%
Stage IVA	Any T	Any N	M1a / M1b	~10%
Stage IVB	Any T	Any N	M1c	<5%

8. Stage IV Oncogene-Driven NSCLC

- NGS + fusion panels are mandatory. With an actionable oncogene, **targeted therapy beats chemo or IO** on ORR, PFS, intracranial control and QoL.

Classical EGFR (ex19del ~45%, L858R ~40%)

- First-line: **osimertinib** (3rd-gen, CNS-active, irreversible).
- **FLAURA:** osimertinib vs gefitinib/erlotinib → PFS **18.9 vs 10.2 mo (HR 0.46)**, OS **36.8 vs 31.8 mo (HR 0.80)**, better CNS control.
- Resistance: 1st-gen fail via **T790M** (→ osimertinib); osimertinib fails via **C797S**, **MET amplification**, or **SCLC transformation** (rebiopsy → platinum-etoposide).



EGFR resistance cascade

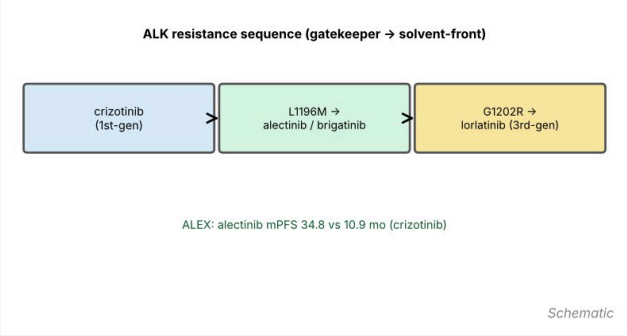
Uncommon & exon 20 EGFR

- **G719X, L861Q, S768I: afatinib** (mPFS ~10.7 mo) or osimertinib.
- **Exon 20 insertions:** resistant to classical 1st/3rd-gen TKIs.
  - **Amivantamab** (EGFR/MET bispecific): CHRYSALIS ORR **40%**, mPFS **8.3 mo**.
  - **Mobocertinib:** ORR **28%**, mPFS **7.3 mo**.

ALK fusions

- **2p inversion** fusing ALK to **EML4**; younger non-smokers, signet-ring adenocarcinoma.
- First-line: **alectinib**, **brigatinib or lorlatinib**.
- **ALEX:** alectinib vs crizotinib PFS **34.8 vs 10.9 mo (HR 0.43)**, 5-yr OS **62.5% vs 45.5%**.
- **ALTA-1L:** brigatinib PFS **24.0 vs 11.0 mo**. **CROWN:** lorlatinib 12-mo PFS **78% vs 39% (HR 0.28)**.
- Resistance: crizotinib → **L1196M** gatekeeper (alectinib/brigatinib/ceritinib) → **G1202R** solvent-front (**lorlatinib**).

ALK fusions (cont.)

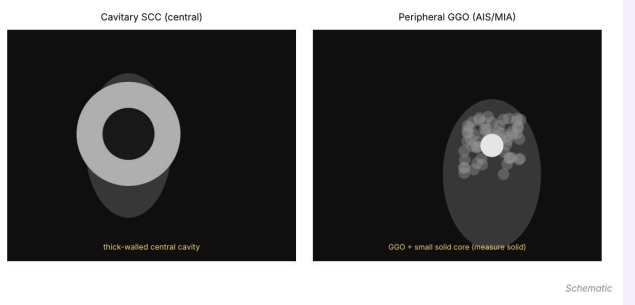


ALK resistance sequence

Other targets

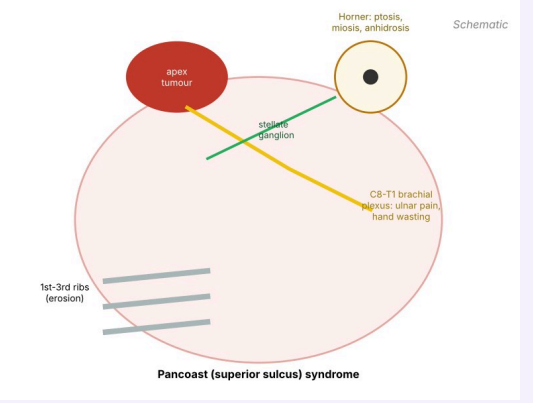
- **ROS1 (CD74-ROS1):** crizotinib (PROFILE 1001 ORR 72%, mPFS 19.3 mo) or entrectinib (CNS); **G2032R** → repotrectinib.
- **BRAF V600E: dabrafenib + trametinib** (ORR 64%, mPFS 10.9 mo).
- **MET exon 14 skipping:** splice-site loss deletes the **CBL** binding juxtamembrane domain → extended MET half-life; **capmatinib** (GEOMETRY ORR 68%, mPFS 12.4 mo) or **tepotinib** (VISION ORR 46%, mPFS 8.5 mo).
- **RET fusions: selpercatinib** (LIBRETTO-001 ORR 85%, mPFS NR) or **pralsetinib** (ARROW ORR 79%, mPFS 13.0 mo).
- **NTRK fusions (< 0.5%): larotrectinib** (ORR 73%, mPFS 35.0 mo) or entrectinib (ORR 57%, mPFS 11.2 mo).
- **KRAS G12C:** covalent switch-II inhibitors **sotorasib** (CodeBreak-100 ORR 37.1%, mPFS 6.8 mo), adagrasib.
- **HER2 exon 20 ins: trastuzumab deruxtecan (T-DXd)**, topo-I payload (DESTINY-Lung01 ORR 55%, mPFS 8.2 mo).

Biomarker Alteration	Prevalence & Patient Profile	Preferred First-Line Targeted Therapy	Landmark Trial	ORR & PFS	Primary Resistance Mechanism
EGFR Exon 19 del / L858R	15-20% (Caucasians), ~50% (East Asians); non-smokers	Osimertinib (3rd-gen)	FLAURA	ORR 80%, mPFS 18.9 mo	EGFR C797S, MET amp, SCLC transformation
EGFR Exon 20 Insertion	1-2%; non-smokers	Amivantamab (EGFR/MET BsAb)	CHRYSALIS	ORR 40%, mPFS 8.3 mo	Secondary mutations, bypass signaling
ALK Fusion	3-5%; younger, light/non-smokers	Alectinib (or Brigatinib, Lorlatinib)	ALEX	ORR 83%, mPFS 34.8 mo	ALK G1202R solvent-front, bypass tracks
ROS1 Fusion	1-2%; light/non-smokers	Crizotinib or Entrectinib	PROFILE 1001	ORR 72-77%, mPFS 19.0-19.3 mo	ROS1 G2032R solvent-front
BRAF V600E	1-2% of adenocarcinomas	Dabrafenib + Trametinib	Planchard et al.	ORR 64%, mPFS 10.9 mo	MAPK reactivation, alternative RTK
MET Exon 14 Skipping	3-4%; older smokers/non-smokers	Capmatinib or Tepotinib	GEOMETRY / VISION	ORR 46-68%, mPFS 8.5-12.4 mo	Second-site MET (D1228, Y1230), KRAS



Cavitary SCC and peripheral GGO

- **Apical sulcus mass with bony destruction (Pancoast):** apical soft-tissue opacity above the clavicle, eroding posterior **first/second/third ribs** and transverse processes. Apical fullness + **Horner** + **C8-T1** pain confirms stellate-ganglion and brachial-plexus involvement.



Pancoast tumour anchor

- **Mediastinal great-vessel compression (SVC syndrome):** bulky right paratracheal/prevascular mass with **slit-like SVC narrowing** and chest-wall/azygos collaterals on contrast CT. Neck vein distension, facial oedema worse bending forward, chest-wall collaterals → urgent tissue diagnosis; **stent or RT only for acute airway/haemodynamic compromise**.

STEM-S

NEET-SS

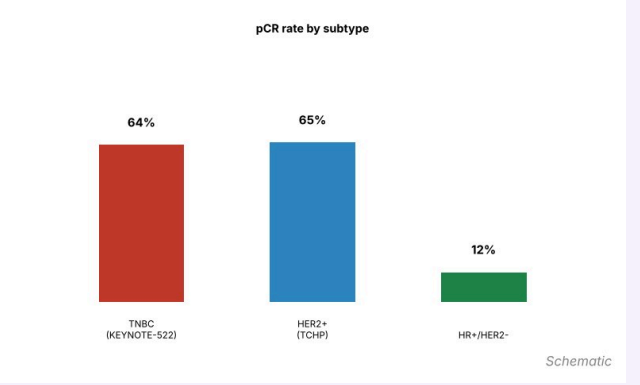
Medical Oncology · Essential Notes



Breast Cancer: Neoadjuvant and Adjuvant Therapy

PRESENTED BY STEM-S

Chemosensitivity Hierarchy



pCR rates by subtype

- **TNBC:** highest chemosensitivity; platinum + immunotherapy regimens reach pCR **>60 to 65%**.
- **HER2-positive:** dual HER2 blockade + taxane reaches pCR **60 to 70%**.
- **HR+/HER2-:** low proliferation, pCR usually **<10 to 15%**; **upfront surgery preferred** for early operable disease to run Oncotype on untreated tissue. Neoadjuvant chemo here is reserved for locally advanced, high-risk node-positive, or downstaging-for-conservation cases.

Standard Neoadjuvant Regimens

- **TNBC (KEYNOTE-522): pembrolizumab** every 3 weeks with **carboplatin + paclitaxel** for 12 weeks, then pembrolizumab with **doxorubicin + cyclophosphamide** (or EC) every 3 weeks for 4 cycles; surgery; then pembrolizumab alone for up to 9 cycles (~1 year). pCR **64.8% vs 51.2%**, EFS HR 0.63, confirmed OS benefit. The intact primary provides neoantigen exposure for T-cell priming.
- **HER2-positive: trastuzumab** (subdomain IV, inhibits PI3K/Akt, ADCC) + **pertuzumab** (subdomain II, blocks HER2-HER3 dimerization). **TCHP** (docetaxel, carboplatin, trastuzumab, pertuzumab) every 3 weeks for 6 cycles avoids anthracycline toxicity; or sequential dose-dense **AC then THP**.
- **Strongly ER+, postmenopausal, frail:** neoadjuvant **aromatase inhibitor** for 4 to 8 months; pCR <10% but clinical response 50 to 70%, enabling conservation in 30 to 40%.

Heads up:

Trastuzumab and doxorubicin must never be given concurrently (synergistic cardiotoxicity and heart failure). Trastuzumab is started only in the taxane phase.

Table 1: Neoadjuvant vs Upfront Surgical Pathway Selection

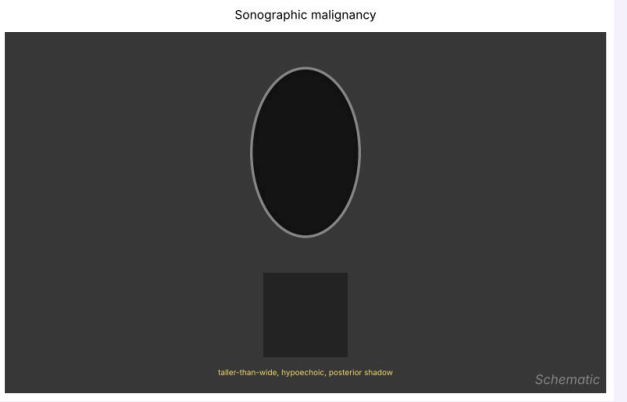
Clinical / Biological Parameter	Preferred: Neoadjuvant Systemic Therapy	Preferred: Upfront Surgical Resection	Key Clinical / Exam Differentiator
Stage II-III Triple-Negative Breast Cancer	Yes (KEYNOTE-522: Chemo + Pembrolizumab)	No	Intact tumor bed required for antigen-driven immune priming; response dictates postoperative capecitabine/olaparib.
Stage II-III HER2-Positive Breast Cancer	Yes (TCHP or AC to THP)	No	Downstages tumor and axilla; pathologic response dictates switching to T-DM1/T-DxD vs continuing trastuzumab.
Small Node-Negative HR+/HER2- (pT1b-T2, cN0)	No	Yes (Primary BCS or Mastectomy)	Preserves untreated surgical specimen for 21-gene Oncotype DX recurrence score to guide chemo omission.
Locally Advanced / Inflammatory Carcinoma (T4, N2-3)	Yes (Mandatory Systemic Induction)	Contraindicated	Surgery upfront in IBC/T4 fails to clear microscopic dermal margins and leads to rapid locoregional recurrence.
Clinical / Biological Parameter	**Preferred: Neoadjuvant Systemic Therapy**	**Preferred: Upfront Surgical Resection**	**Key Clinical / Exam Differentiator**
Large Primary Relative to Breast Volume Desiring BCS	Yes (Tumor Downstaging)	Only if patient desires total mastectomy	Converts patients from inoperable for BCS to lumpectomy candidates.
Biopsy-Proven Involved Axillary Nodes (cN1)	Yes (Targeted Axillary Dissection Candidate)	Only if avoiding neoadjuvant therapy	Downstages axilla to ypN0, safely eliminating the need for morbid complete axillary dissection.

Table 6: Trastuzumab Adjuvant Duration Trials

Trial	Durations Compared	Outcome & Conclusion	Clinical & Board Takeaway
HERA	12 vs 24 months	2 years gave no added DFS/OS benefit over 1 year.	Beyond 12 months adds toxicity without efficacy; 12 months is the ceiling.
ShortHER	12 months vs 9 weeks	9 weeks failed non-inferiority vs 12 months.	Very short courses compromise DFS; 9 weeks is inferior.
PERSEPHONE	12 vs 6 months	6 months non-inferior for DFS with less cardiotoxicity.	Prompted debate on de-escalation in selected low-risk patients.
HORG	12 vs 6 months	6 months failed to confirm non-inferiority.	Contradicted PERSEPHONE; shorter duration cannot be uniformly endorsed.
Global Standard	12 Months (1 Full Year)	Supported by the totality of randomized evidence (NCCN, ASCO, St. Gallen).	12 months remains the non-negotiable global standard.

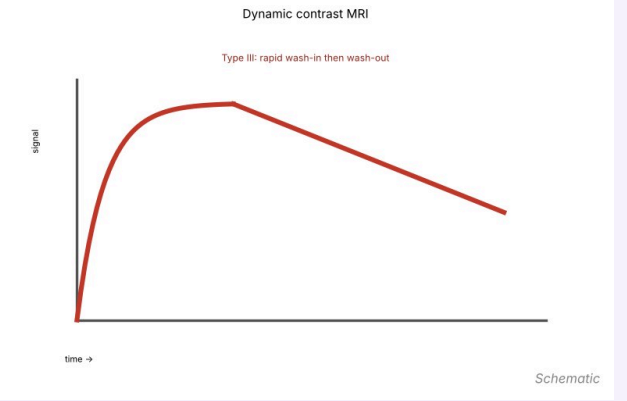
Table 7: Axillary Staging Cutoffs and Anatomical Staging Rules (AJCC 8th Edition)

Staging Category	Precise Millimeter / Quantitative Definition	Anatomic / Clinical Descriptor	Crucial Staging & Exam Pitfall
pT1a	>1.0 mm to <=5.0 mm	Micro-tumor	Often endocrine therapy alone if node-negative and HR+.
pT1b	>5.0 mm to <=10.0 mm	Small invasive tumor	Low threshold for chemo in TNBC; APT regimen if HER2+.
pT1c	>10.0 mm to <=20.0 mm	Intermediate primary tumor	Candidate for Oncotype DX if HR+/HER2- pN0.
pT2	>20.0 mm to <=50.0 mm	Medium primary tumor	T2N0 is Stage IIA; T2N1 is Stage IIB.
pT3	>50.0 mm	Large primary tumor	Defined purely by size; T3N0 is Stage IIB.
T4b	Skin edema, peau d'orange, ulceration, or satellite nodules	Locally advanced, not inflammatory	Distinguish from T4d; does not require rapid onset <3 months.
T4d	Inflammatory Breast Cancer	Clinical: rapid onset (<3 mo) erythema/edema over >=1/3 of breast	BCS absolutely contraindicated; mandates modified radical mastectomy.



Taller-than-wide hypoechoic mass with posterior shadowing

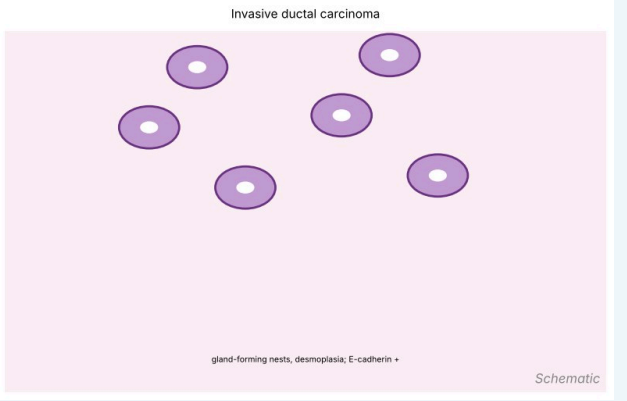
- **Dynamic contrast MRI:** rapid intense early enhancement then **rapid wash-out (Type III curve)** from hyperpermeable angiogenesis.



Type III malignant MRI kinetic curve

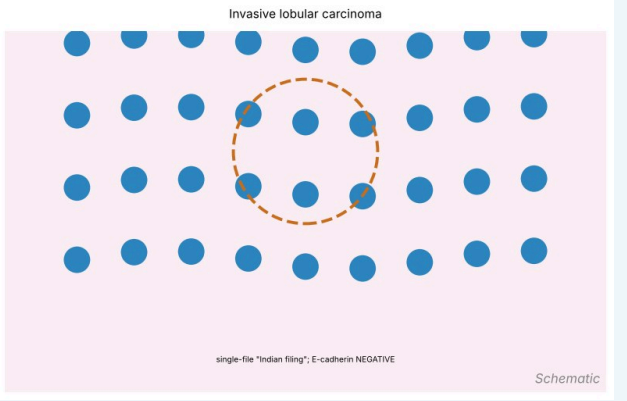
Histopathologic Anchors

- **Invasive ductal carcinoma (NST):** irregular glands, cords, and sheets in dense desmoplastic stroma; atypical nuclei and brisk mitoses; **E-cadherin positive**.



Invasive ductal carcinoma, gland-forming nests

- **Invasive lobular carcinoma:** small uniform cells in **single-file "Indian filing"** with targetoid rings and signet-ring-like vacuoles; **E-cadherin negative (CDH1 loss)**.



Invasive lobular carcinoma, single-file Indian filing

- **Inflammatory breast cancer:** full-thickness dermal punch biopsy shows **tumor emboli plugging dermal lymphatics** (lymphatic embolization, not mere dermal invasion, is the T4d hallmark).

STEM-S

NEET-SS

Medical Oncology · Essential Notes

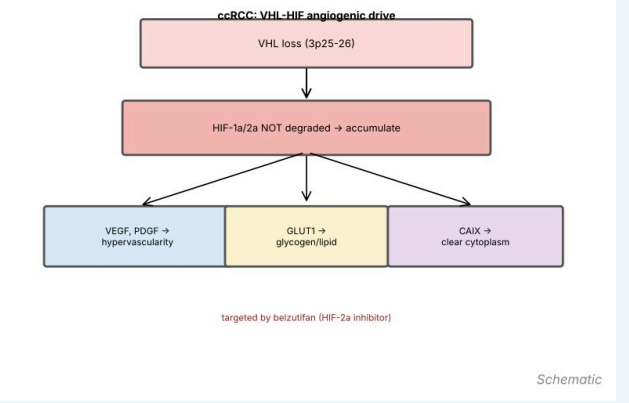


Renal Cell Carcinoma

PRESENTED BY STEM-S

1. Molecular Pathogenesis and Etiologic Mechanisms

Renal cell carcinoma (RCC) is a biologically and histologically heterogeneous group of malignancies arising from the **tubular epithelial cells of the renal cortex**. The molecular story is a story about **oxygen sensing**: in healthy parenchyma, oxygen-sensing machinery balances angiogenesis, erythropoiesis and glycolysis. When genetic lesions disable these brakes, the transformed cell undergoes metabolic reprogramming toward **aerobic glycolysis and constitutive pro-angiogenic signalling**, which directly produces the classic clinical picture: macroscopic hematuria, paraneoplastic erythrocytosis and early vascular invasion.



VHL-HIF-2α oxygen-sensing axis: normoxic degradation vs VHL-loss stabilisation

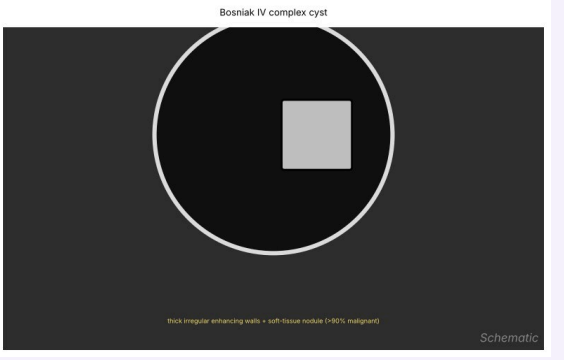
The VHL-HIF-2α Hypoxia Signalling Axis

The hallmark lesion in **clear cell RCC (ccRCC)** (70 to 80% of all renal malignancies) is functional inactivation of the **von Hippel-Lindau (VHL)** tumour suppressor on **chromosome 3p25**. Under normoxia, pVHL is the substrate-recognition component of an **E3 ubiquitin ligase** complex (with **Elongin B, Elongin C, Cullin-2**). Prolyl hydroxylases (PHDs) use molecular oxygen and iron to hydroxylate proline residues on **HIF-α**; hydroxylated HIF-α is bound by pVHL, polyubiquitinated and degraded by the **26S proteasome**.

Imaging Standards (cont.)

- **MRI**: for iodinated-contrast allergy or renal insufficiency, and **superior to CT for defining the cephalad extent of renal-vein/IVC tumour thrombus** and venous-wall invasion.
- **PET**: standard **^{18}F-FDG PET is poor** (physiologic uptake, urinary tracer excretion) and **not recommended**. **^{99m}Tc-sestamibi SPECT/CT** concentrates in mitochondria-rich tumours (83.3% sensitivity, 95.2% specificity), separating **oncocytoma/chromophobe** from clear cell.

The Bosniak Classification of Complex Cystic Masses



Bosniak IV complex cyst, enhancing soft-tissue nodule

Bosniak Category	CT / MRI Morphologic Characteristics	Malignancy Risk	Standard Clinical Management
Category I	Simple benign cyst; hairline-thin wall; no septa, calcification or enhancement; water density (0–20 HU).	<1%	Benign: no follow-up or intervention.
Category II	Minimally complex; fine thin septa (<1 mm); small non-enhancing calcifications; non-enhancing high-density cysts (<3 cm).	<1%	Benign: no follow-up.
Category IIF ("follow-up")	Increased complexity; multiple hairline septa; minimal perceived enhancement; thick/nodular calcification; hyperdense cysts ≥ 3 cm.	~5 to 10%	Surveillance: serial CT/MRI at 6, 12, 24 months.
Category III	Indeterminate complex mass; thickened, irregular or smooth walls/septa with measurable, unequivocal enhancement.	~50%	Surgical excision (partial nephrectomy); active surveillance in select elderly.

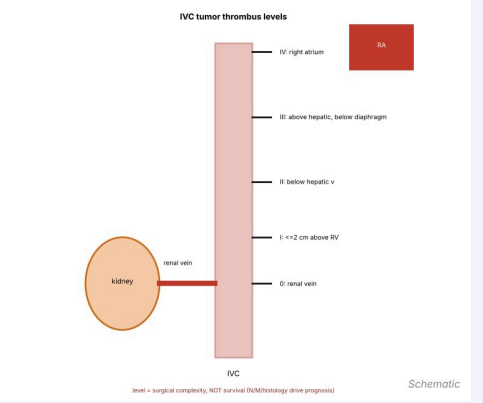
Bosniak Category	CT / MRI Morphologic Characteristics	Malignancy Risk	Standard Clinical Management
Category IV	All Category III features **plus enhancing soft-tissue nodular components** independent of walls/septa.	>90%	Definitive surgical resection (partial or radical nephrectomy).

Heads up:

Two separate "adrenal" fates. **Direct contiguous** spread through the upper pole into the adrenal breaches Gerota and is **T4**. A **separate, non-contiguous** adrenal nodule is hematogenous **M1**. Both are Stage IV, but the T vs M distinction is exactly what the question is testing. And remember **N1 with an organ-confined T1/T2 primary is Stage III**, not Stage I/II.

Venous Tumour Thrombus Architecture (Neves/Novick)

RCC uniquely propagates a **cohesive intraluminal tumour thrombus** from arcuate veins into the renal vein and up the IVC (4 to 10% of cases). Surgical complexity scales with level; **the diaphragm is the critical boundary.**



Neves/Novick thrombus levels 0-IV along the IVC

Level 0 (T3a) renal vein / segmental branches only

↓

Level I (T3b) IVC <=2 cm above renal-vein ostium

↓

Level II (T3b) IVC >2 cm above ostium, BELOW hepatic veins

↓

Level III(T3b) IVC at/above hepatic veins, BELOW diaphragm

↓

∪ · ========== DIAPHRAGM ==========

↓

Level IV (T3c) IVC above diaphragm / into right atrium

Surgery: radical nephrectomy with cavoatrial thrombectomy gives **45 to 70%** 5-year CSS in N0 M0 disease. Level 0–II thrombi allow transabdominal cavotomy with local clamping; **Level III–IV** need liver mobilization (piggyback), veno-venous bypass, or cardiopulmonary bypass with deep hypothermic circulatory arrest.

The Evolving Role of Cytoreductive Nephrectomy (cont.)

Trial Name	Regimen	Mechanism of Action	Hazard Ratio for Overall Survival (95% CI)	Progression-Free Survival (PFS) & Objective Response Rate (ORR)	Clinical Application & Distinct Advantages
CheckMate 214	Nivolumab + Ipilimumab vs Sunitinib	Dual checkpoint blockade (anti-PD-1 + anti-CTLA-4)	mOS HR 0.72 (0.62–0.85)	mPFS 12.3 vs 12.3 mo; ORR 39%; CR 10.7%	Preferred in IMDC intermediate/poor risk; exceptional durability and treatment-free survival; primary progression 18%
KEYNOTE-426	Pembrolizumab + Axitinib vs Sunitinib	Checkpoint + selective VEGFR 1-3 TKI	mOS HR 0.73 (0.60–0.88)	mPFS 15.7 vs 11.1 mo; ORR 60%; CR 10.0%	Broadly active across all IMDC risk; axitinib short-acting, easily titrated
CheckMate 9ER	Nivolumab + Cabozantinib vs Sunitinib	Anti-PD-1 + multi-target TKI (VEGFR2, MET, AXL)	mOS HR 0.66 (0.50–0.87)	mPFS 17.0 vs 8.3 mo; ORR 55%; CR 9.3%	Excellent in bone metastases (MET/AXL); progression rate only 6%

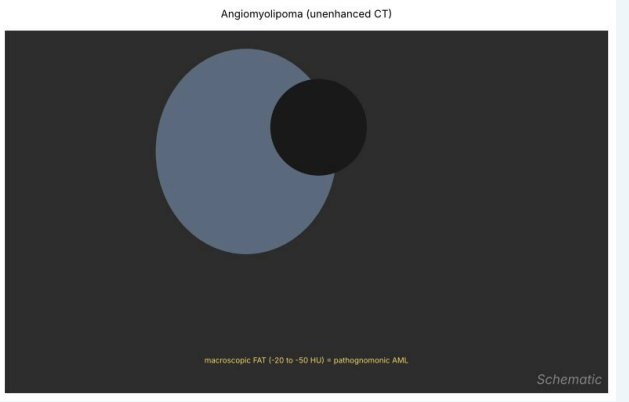
Trial Name	Regimen	Mechanism of Action	Hazard Ratio for Overall Survival (95% CI)	Progression-Free Survival (PFS) & Objective Response Rate (ORR)	Clinical Application & Distinct Advantages
CLEAR	Pembrolizumab + Lenvatinib vs Sunitinib	Anti-PD-1 + multi-target TKI (VEGFR 1-3, FGFR 1-4, RET, KIT)	mOS HR 0.72 (0.55–0.93)	mPFS 23.9 vs 9.2 mo (HR 0.39); ORR 71%; CR 16.1%	Highest ORR and longest PFS of all front-line combinations; ideal for organ-threatening visceral crisis

Doublet selection:

- **Sarcomatoid mandates checkpoint therapy**: inflamed microenvironment, high PD-L1; **ipilimumab + nivolumab** achieves CR approaching 20% and **overrides baseline histology**, even chromophobe.
- **Visceral crisis**: prioritize regression: **lenvatinib + pembrolizumab** (ORR 71%, primary progression ~5%), avoiding the 18% early-progression risk of IO-IO.
- **Active autoimmune disease**: checkpoint inhibitors contraindicated; use **cabozantinib monotherapy** or **lenvatinib + everolimus**.

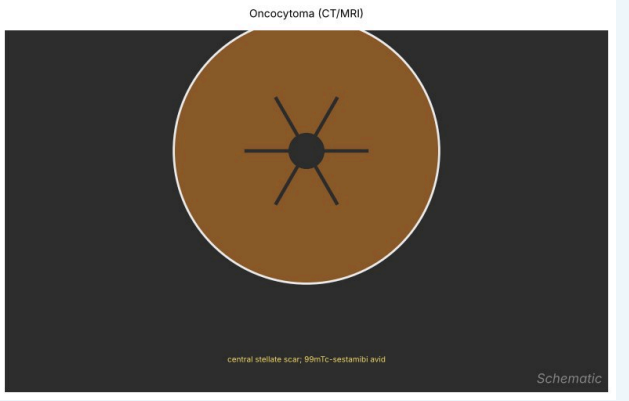
Subsequent Therapy and Molecular Sequencing

- **Post-IO-IO progression**: cross classes to a potent VEGFR-TKI; **cabozantinib** monotherapy is the preferred next-line agent.
- **Belzutifan (HIF-2α)**: after both checkpoint and VEGFR-TKI failure, **LITESPARK-005** showed oral belzutifan (120 mg daily) beat everolimus on PFS (HR 0.75) and ORR (22% vs 4%). It blocks EPO and central oxygen sensing, so it **frequently causes anemia and hypoxia**: if SpO_2 <88% at rest or exertion, **hold and resume at a reduced dose (e.g. 80 mg)** rather than abandoning it.



Angiomyolipoma, macroscopic fat on unenhanced CT

Oncocytoma: well-demarcated cortical mass with a **central non-enhancing stellate scar**; avid ^{99m}Tc-sestamibi uptake (shared by some chromophobe/ccRCC, so not definitive on CT alone).



Oncocytoma, central stellate scar on CT/MRI

Histopathologic Visual Anchors

Type 1 vs Type 2 papillary RCC: Type 1: single layer of small cells, foamy histiocytes in stalks, trisomy 7/17, MET. Type 2: pseudostratified eosinophilic cells, giant nucleoli, FH-negative / 2SC-positive (HLRCC).

STEM-S

NEET-SS

Medical Oncology · Essential Notes



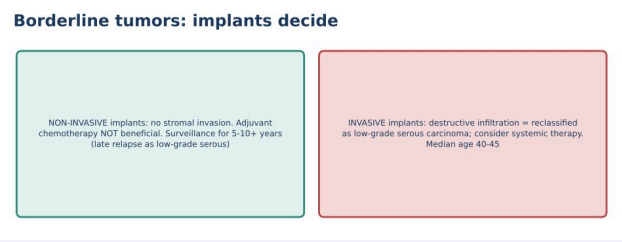
Carcinoma Ovary

PRESENTED BY STEM-S

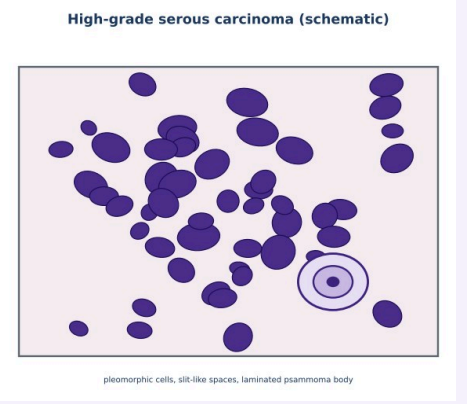
Subtype	Frequency	Drivers	Precursor / associations	Hallmark	Exam feature
HGSC	70-75%	TP53 >95%, BRCA1/2 20-25%, HRD 50%	STIC; HBOC	Marked atypia, psammoma bodies, high mitoses	Chemosensitive upfront; PARP inhibitors work
LGSC	<5%	KRAS, BRAF, NRAS; TP53 wild-type	Serous borderline / cystadenoma	Monomorphic nuclei, micropapillae, low mitoses	Indolent; resistant to chemotherapy
Endometrioid	10%	ARID1A, PTEN, PIK3CA, CTNNB1; MSI	Endometriosis; Lynch	Tubular glands, squamous morules	Synchronous endometrial cancer in 5-10%
Clear cell	5-10%	ARID1A >50%, PIK3CA ~50%, PPP2R1A	Endometriosis	Hobnail cells, clear glycogen-rich cytoplasm	Thromboembolism; platinum-resistant; ipilimumab + nivolumab
Mucinous	1-3%	KRAS; ERBB2 amplification	Mucinous borderline / teratoma	Confluent expansile glands	Unilateral, >10 cm; exclude GI primary

Borderline ovarian tumors

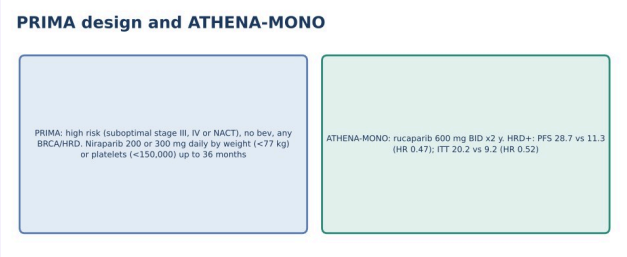
Borderline tumors show proliferation and atypia without destructive stromal invasion. They affect younger women (median 40-45) and are graded by the implant type.



Schematic: borderline tumors: implants decide. Illustration only, not a real clinical image.

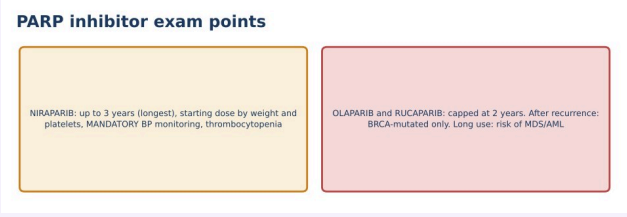


Schematic: high-grade serous histology with a psammoma body. Illustration only, not a real clinical image.

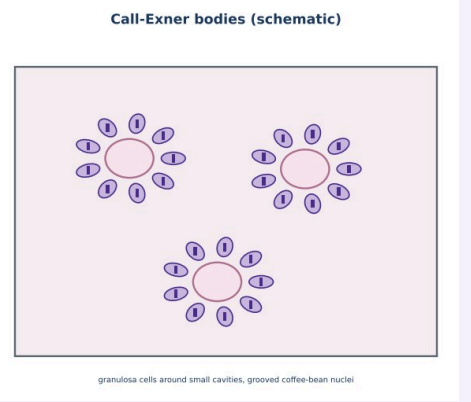


Schematic: PRIMA design and ATHENA-MONO. Illustration only, not a real clinical image.

Trial	Regimen	Biomarker setting	Duration	Toxicity / monitoring
SOLO-1	Olaparib 300 mg BID	Germline or somatic BRCA1/2 only	Up to 2 years	Anemia, nausea, fatigue; blood counts
PAOLA-1	Olaparib 300 mg BID + bevacizumab 15 mg/kg q3w	HRD-positive (BRCAm and BRCA-wt/HRD+)	Olaparib 2 years; bevacizumab 15 months	Hypertension, proteinuria, fatigue; no benefit in HRP
PRIMA	Niraparib 200-300 mg daily	All comers (BRCAm, HRD+, HRP)	Up to 3 years	Thrombocytopenia, anemia; blood pressure monitoring
ATHENA-MONO	Rucaparib 600 mg BID	All comers (best in HRD+, modest in HRP)	Up to 2 years	ALT/AST rise, nausea, anemia, fatigue

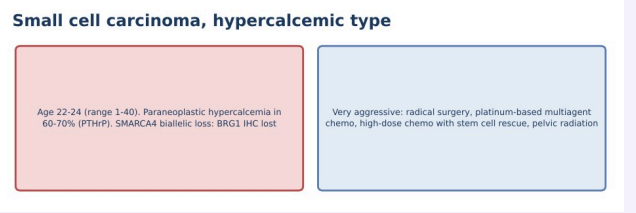


Schematic: PARP inhibitor exam points. Illustration only, not a real clinical image.



Schematic: Call-Exner bodies. Illustration only, not a real clinical image.

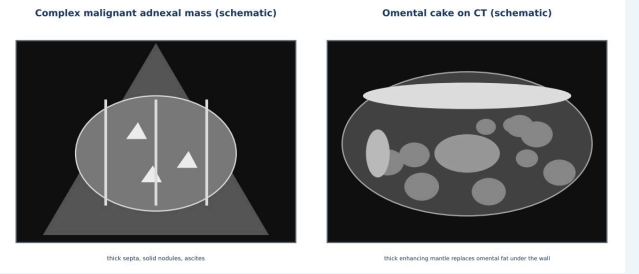
SCCOHT



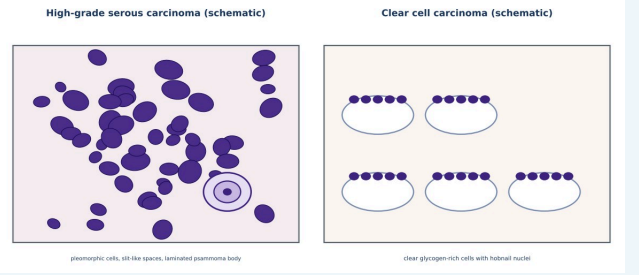
Schematic: small cell carcinoma, hypercalcemic type. Illustration only, not a real clinical image.

Tumor	Lineage	Age	Markers	Hallmark	Feature
Dysgerminoma	Germ cell	15-25	LDH, ALP; ± low β-hCG	Uniform polygonal clear cells, lymphocytic septa	10-15% bilateral; chemosensitive; fertility-sparing surgery
Yolk sac tumor	Germ cell	18-22	AFP very high	Schiller-Duval bodies, hyaline globules	Fast growth, early blood spread; BEP curative
Immature teratoma	Germ cell	15-20	AFP, low β-hCG	Neuroepithelial rosettes	Norris grade 1-3; IA grade 1 observed
Adult granulosa cell	Sex cord-stromal	50-55	Inhibin A and B, estradiol	Call-Exner bodies, coffee-bean nuclei	FOXL2; endometrial cancer risk; late relapse >10-15 y
Sertoli-Leydig	Sex cord-stromal	20-30	Testosterone	Sertoli tubules, Leydig cells with Reinke crystals	Virilization; unilateral
Fibroma	Stromal (benign)	40-60	Normal	Bland spindle cells, collagen	Meigs syndrome; resolves after surgery
SCCOHT	Undifferentiated	20-25	Calcium (PTHrP)	Small round cells, rhabdoid cells, SMARCA4/BRG1 loss	Hypercalcemia in a young woman; very aggressive

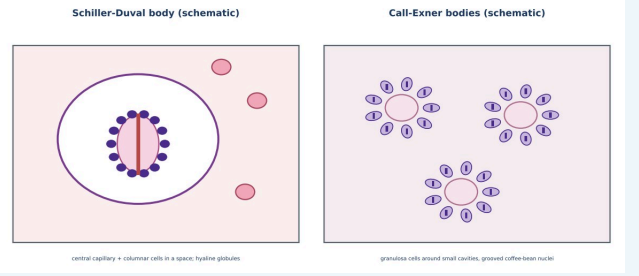
9. Visual anchors



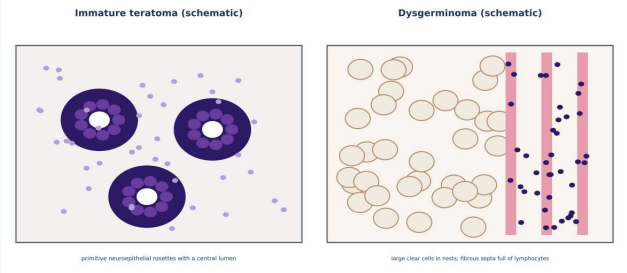
Schematic: complex adnexal mass and omental cake. Illustration only, not a real clinical image.



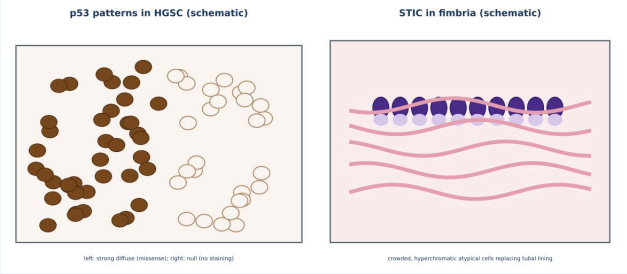
Schematic: high-grade serous and clear cell carcinoma. Illustration only, not a real clinical image.



Schematic: Schiller-Duval and Call-Exner bodies. Illustration only, not a real clinical image.



Schematic: immature teratoma and dysgerminoma. Illustration only, not a real clinical image.



Schematic: p53 patterns and STIC. Illustration only, not a real clinical image.

10. Practice cases

- **Case 1.** Occult STIC found on SEE-FIM after RRSO. **Next step?** Refer to a gynecologic oncologist for staging.
- **Case 2.** Pelvic mass, ascites and right pleural effusion that cleared after the mass was removed; the mass was a fibroma. **Syndrome?** Meigs.
- **Case 3.** Bilateral 8 cm ovarian masses, CA-125 : CEA ratio 10, SATB2 positive. **Likely origin?** Metastatic GI (Krukenberg); do endoscopy.
- **Case 4.** Tumor on the liver capsule with positive 12 mm retroperitoneal node. **Stage?** IIIC (capsule), not IVB.
- **Case 5.** Advanced EOC, R0, normal-looking nodes. **Lymphadenectomy?** No (LION).
- **Case 6.** BRCA-mutated stage III HGSC responding to carboplatin-paclitaxel. **Maintenance?** Olaparib (SOLO-1) or niraparib (PRIMA).
- **Case 7.** Remission, CA-125 rises to 2.5x ULN, normal scan, no symptoms. **Action?** Observe; early chemotherapy gives no survival gain.
- **Case 8.** 19-year-old with a unilateral pelvic mass, very high AFP, Schiller-Duval bodies. **Diagnosis and plan?** Yolk sac tumor: fertility-sparing staged USO then BEP.