STEM-S

LAST MINUTE REVISION

LMR NOTES

INI-SS Sample Notes

PRESENTED BY

Stem-S

THE POINTS:

1. Two major histologies of esophageal cancer: **SCC and adenocarcinoma**.
2. **SCC** is more common worldwide; **adenocarcinoma** is rising in Western countries.
3. Major risk factor for **adenocarcinoma**: **Barrett esophagus**.
4. Barrett esophagus = **intestinal metaplasia with goblet cells**.
5. Barrett progression: **GERD → metaplasia → dysplasia → adenocarcinoma**.
6. SCC risk factors: **alcohol + tobacco**.
7. Achalasia increases risk of **esophageal SCC**.
8. Caustic injury predisposes to **SCC**.
9. Most important prognostic factor in esophageal cancer: **lymph node involvement**.
10. Standard treatment for locally advanced disease: **neoadjuvant chemoradiation + surgery**.

2. GASTRIC CANCER

Classification
Lauren classification

- **Intestinal type**
- **Diffuse type**

Feature	Intestinal	Diffuse
Pattern	Gland forming	Infiltrative
Epidemiology	Environmental	Genetic
Risk factors	H. pylori	CDH1 mutation
Spread	Hematogenous	Peritoneal

Sequence

APC mutation → adenoma
KRAS mutation → advanced adenoma
p53 loss → carcinoma

Hereditary Syndromes

Syndrome	Gene	Key features
FAP	APC	1000s polyps
Lynch (HNPCC)	MLH1, MSH2 etc	MSI
Peutz-Jeghers	LKB1	Hamartomas
Juvenile polyposis	SMAD4	GI polyps

HNPCC has **~80% lifetime CRC risk**.

Amsterdam Criteria

- ≥3 relatives with CRC
- ≥2 generations affected
- ≥1 case <50 years
- FAP excluded

Molecular Therapy

- **KRAS/BRAF mutation → no response to EGFR antibodies**
- **MSI-high tumors → respond to checkpoint inhibitors**

5. CHEMOTHERAPY TRIALS

Trial	Regimen	Result	Pearl
NSABP B-15	AC vs CMF	AC superior	Anthracycline standard
CALGB 9344	Paclitaxel added	Improved survival	Taxane standard
BCIRG 006	TCH vs AC-TH	Effective HER2 regimens	TCH less cardiotoxic
GeparTrio	Neoadjuvant chemo	pCR predicts survival	pCR important marker

6. IMMUNOTHERAPY TRIALS (Triple Negative)

Trial	Drug	Result	Pearl
KEYNOTE-522	Pembrolizumab + chemo	Increased pCR	Neoadjuvant immunotherapy
IMpassion130	Atezolizumab + nab-paclitaxel	Improved PFS	TNBC immunotherapy
KEYNOTE-355	Pembrolizumab metastatic	Improved survival	PD-L1 positive TNBC

7. CDK4/6 INHIBITOR TRIALS

Trial	Drug	Setting	Pearl
PALOMA	Palbociclib	Metastatic ER+	First CDK4/6 trial
MONALEESA	Ribociclib	HR+ disease	Improved survival
MONARCH	Abemaciclib	HR+ breast cancer	Adjuvant benefit

8. GENOMIC ASSAY TRIALS

Trial	Test	Key Result	Pearl
TAILORx	Oncotype DX	Avoid chemo in low risk	Genomic testing
MINDACT	MammaPrint	Reduced overtreatment	Precision medicine

8. MANAGEMENT OF DIFFERENT THYROID CANCERS

Cancer	Treatment
Papillary	Total thyroidectomy ± RAI
Follicular	Total thyroidectomy
Medullary	Total thyroidectomy + central node dissection
Anaplastic	Palliative therapy

9. RADIOACTIVE IODINE (RAI)

Indications

- Intermediate or high-risk differentiated thyroid cancer

Mechanism

- Iodine uptake by **thyroid follicular cells**

10. THYROGLOBULIN

Tumor Marker

Use	Purpose
Postoperative monitoring	Detect recurrence
After RAI	Surveillance

11. THYROID CANCER STAGING PEARL

Age cutoff in staging:

Age	Impact
<55 years	Better prognosis
≥55 years	Higher stage

4. FIELD CANCERIZATION

Definition:

Multiple independent tumors due to **chronic carcinogen exposure (tobacco/alcohol)**.

Clinical implication:

- Multiple primary tumors in head and neck region.

5. ORAL CAVITY CANCER

Common Sites

Site	Frequency
Tongue	Most common
Floor of mouth	Second

- **Management**

Stage	Treatment
Early stage	Surgery
Advanced stage	Surgery + RT/CRT

6. OROPHARYNGEAL CANCER

- **HPV-related disease**

Feature	Characteristic
Tumor biology	HPV driven
Prognosis	Better survival
Marker	p16

	Treatment
	RT or surgery
	Chemoradiation

- **TARGETED THERAPY**

Trial	Drug	Result	Pearl
EXTREME Trial	Cetuximab + chemo	Improved survival	First targeted therapy
CheckMate-141	Nivolumab	Improved survival	Immunotherapy standard
KEYNOTE-048	Pembrolizumab	Improved OS	First-line immunotherapy

- **RADIOTHERAPY TRIALS**

Trial	Finding
DAHANCA trials	Accelerated RT improves control
RTOG studies	CRT improves survival

15. MOLECULAR TARGETS

Target	Therapy
EGFR	Cetuximab
PD-1	Nivolumab
PD-L1	Pembrolizumab

16. IMPORTANT POINTS

1. Most common head and neck cancer = **Squamous cell carcinoma**
2. HPV-related cancers arise in **oropharynx**
3. EBV associated cancer = **nasopharyngeal carcinoma**
4. Most important prognostic factor = **nodal metastasis**
5. Glottic cancers present with **hoarseness**
6. Pleomorphic adenoma most common benign salivary tumor
7. Mucoepidermoid carcinoma most common malignant salivary tumor
8. Adenoid cystic carcinoma shows **perineural invasion**
9. RTOG 91-11 established **organ preservation in larynx cancer**
10. EXTREME trial established **cetuximab therapy**

HALLMARKS OF CANCER → TARGETED DRUGS

Hallmark	Key Pathway / Target	Targeted Drugs (Examples)	Cancer Example / Exam Pearl
Sustaining proliferative signaling	EGFR	**Erlotinib, Gefitinib, Osimertinib**	EGFR-mutant lung cancer
	HER2	**Trastuzumab, Pertuzumab, T-DM1**	HER2+ breast cancer
	BCR-ABL	**Imatinib, Dasatinib**	CML
Evading growth suppressors	CDK4/6–RB pathway	**Palbociclib, Ribociclib, Abemaciclib**	HR+ breast cancer
Resisting cell death (apoptosis)	BCL-2	**Venetoclax**	CLL, AML
Enabling replicative immortality	Telomerase	*(No routine clinical drug)*	Exam point: theoretical target
Inducing angiogenesis	VEGF	**Bevacizumab**	CRC, lung
	VEGFR TKI	**Sunitinib, Sorafenib, Pazopanib**	RCC, HCC
Activating invasion & metastasis	MET / ALK	**Crizotinib, Alectinib**	ALK+ lung cancer
Dysregulating cellular metabolism	mTOR	**Everolimus, Temsirolimus**	RCC, NET
Evading immune destruction	PD-1	**Pembrolizumab, Nivolumab**	MSI-H tumors, melanoma
	PD-L1	**Atezolizumab, Durvalumab**	TNBC, biliary
	CTLA-4	**Ipilimumab**	Melanoma
Genome instability & mutation	PARP	**Olaparib, Talazoparib**	BRCA-mutated breast/ovary
Tumor-promoting inflammation	COX / cytokines	*(Indirect role)*	Conceptual, not exam drug

HALLMARKS OF CANCER → DRUG RESISTANCE MECHANISMS

Hallmark Targeted	Therapy Class	Key Resistance Mechanism	Exam Pearl / Trap
Sustaining proliferative signaling	EGFR TKIs	Secondary mutations (EGFR **T790M**)	Osimertinib overcomes T790M
	HER2 inhibitors	HER2 loss / pathway bypass	PI3K activation causes resistance
	BCR-ABL TKIs	Kinase domain mutation (**T315I**)	T315I → resistant to imatinib
Evading growth suppressors	CDK4/6 inhibitors	RB loss / Cyclin E amplification	RB loss = absolute resistance
Resisting apoptosis	BCL-2 inhibitors (Venetoclax)	Upregulation of **MCL-1 / BCL-XL**	Switch to alternate anti-apoptotic protein
Inducing angiogenesis	Anti-VEGF (Bevacizumab)	Alternate pro-angiogenic pathways	Tumor uses FGF, PDGF
Evading immune destruction	PD-1 / PD-L1 inhibitors	Loss of antigen presentation (↓ MHC-I)	β2-microglobulin loss
		Immunosuppressive microenvironment	↑ Tregs, MDSCs
Genome instability & mutation	PARP inhibitors	Restoration of homologous recombination	BRCA reversion mutation
Dysregulated metabolism	mTOR inhibitors	Feedback activation of PI3K-AKT	Pathway redundancy
Invasion & metastasis	ALK / MET inhibitors	Secondary mutations / bypass signaling	Seen in ALK+ lung cancer