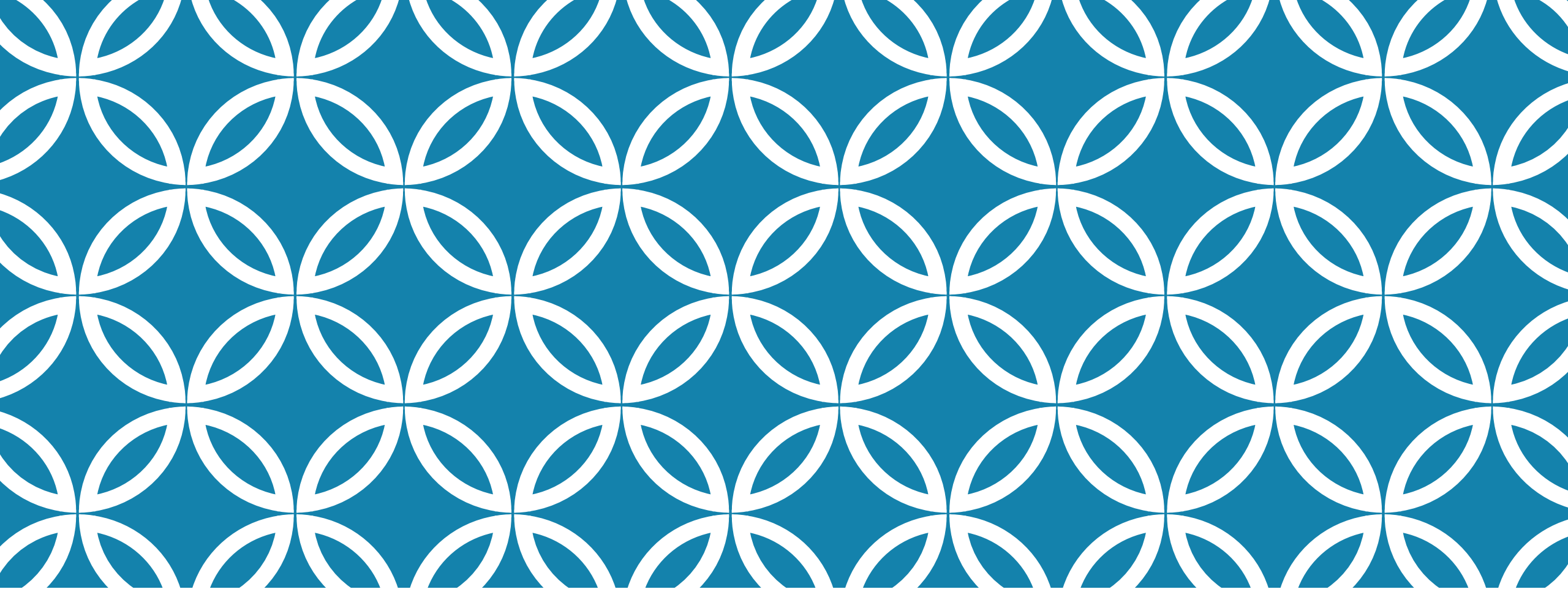




ADNEXAL MASSES

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Gynecologic Oncology



DISCLOSURES

None



OUTLINE

Ovarian cancer statistics

Differential diagnosis

Imaging

Labs

Management

Cases

Current treatments and expectations for your patients with advanced ovarian cancer

OVARIAN CANCER FACTS AND SYMPTOMS

#1 cause of gynecologic cancer deaths

200,000

women in the U.S. are
living with the disease

22,240

women will be
diagnosed each year

1 in 78

a woman's
lifetime risk

14,070

expected fatalities
annually

90%

of diagnosed women
are older than 40



63

median age
of diagnosis



RISK FACTORS



- Family history of ovarian, breast or colon cancers
- Genetic mutations
- Menopause and older age
- Endometriosis



SYMPTOMS TO KNOW

Bloating

Feeling full too quickly

Back pain

Constipation

Difficulty eating

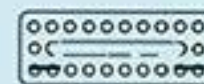
Fatigue

Frequent or
urgent urination

Pain or pressure in the
pelvis or abdomen

Change in
bowel habits

PREVENTIVE FACTORS



Using oral
contraceptives



Tubal ligation
or removal of
fallopian tubes
or ovaries

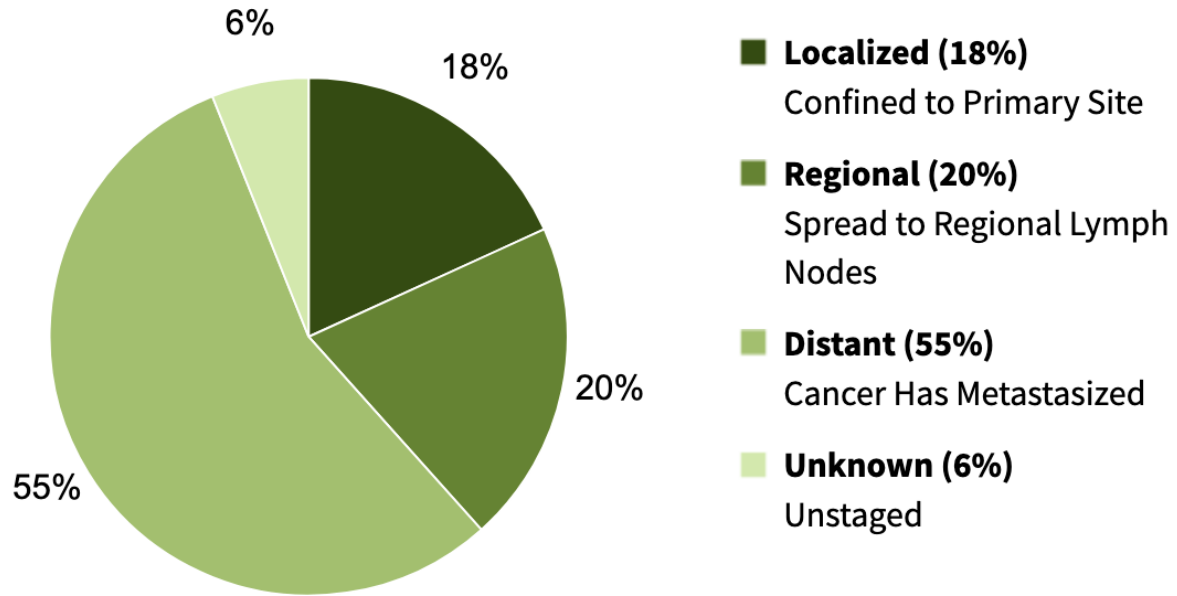


Pregnancy and
breastfeeding

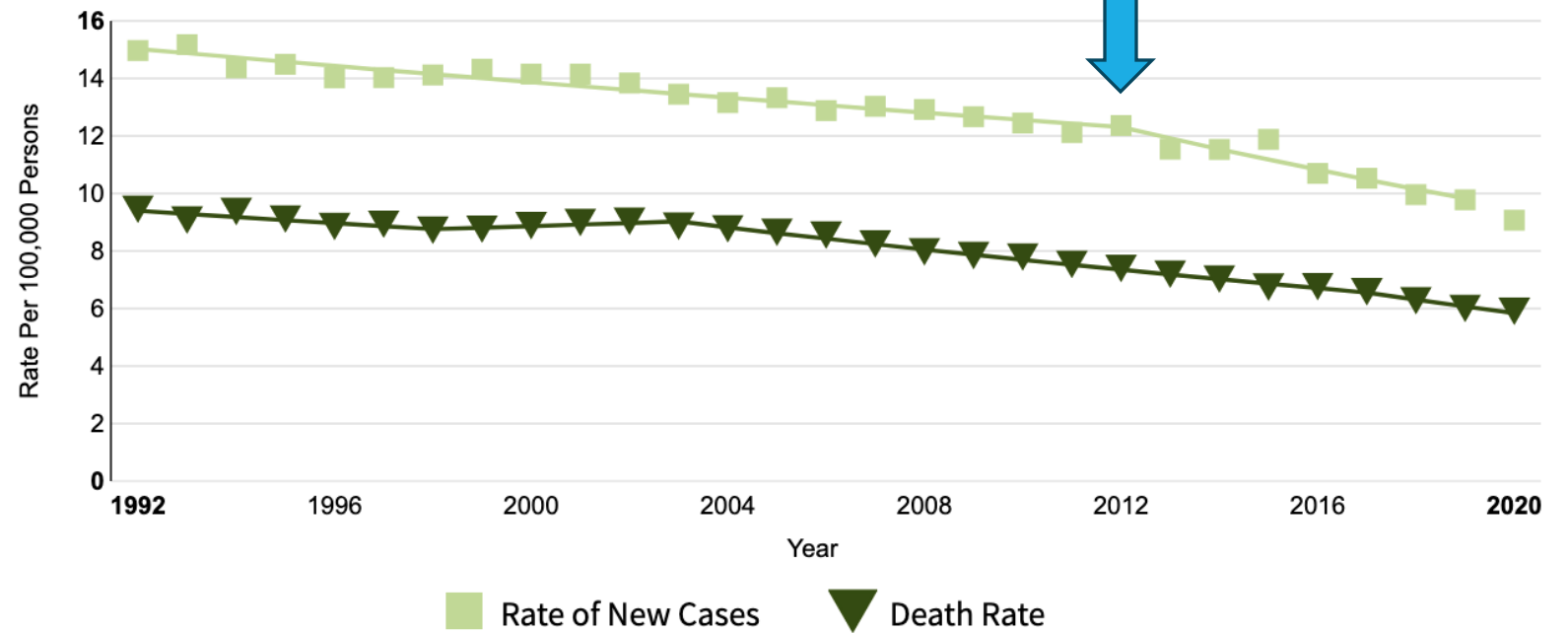
THE UNIVERSITY OF MICHIGAN ROGEL CANCER CENTER

<https://healthblog.uofmhealth.org/cancer-care/ovarian-cancer-symptoms-and-risk-factors-to-know>

Percent of Cases by Stage



- Localized (18%)**
Confined to Primary Site
- Regional (20%)**
Spread to Regional Lymph Nodes
- Distant (55%)**
Cancer Has Metastasized
- Unknown (6%)**
Unstaged



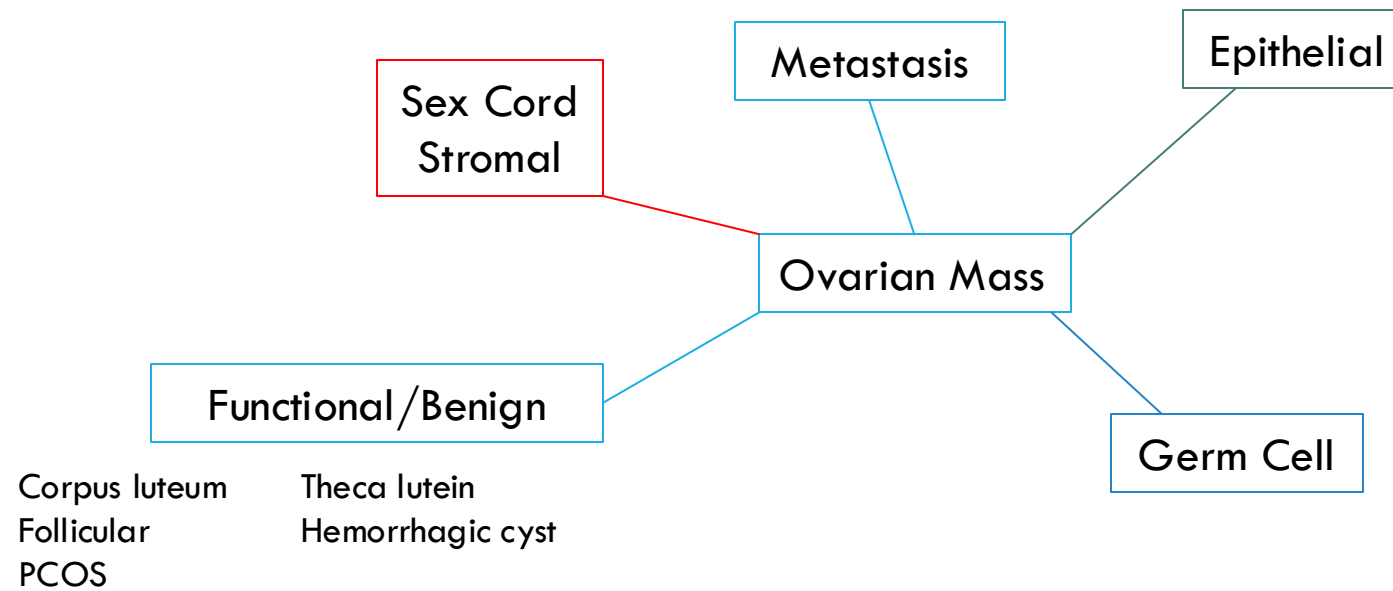
ADNEXAL MASSES: DIFFERENTIAL

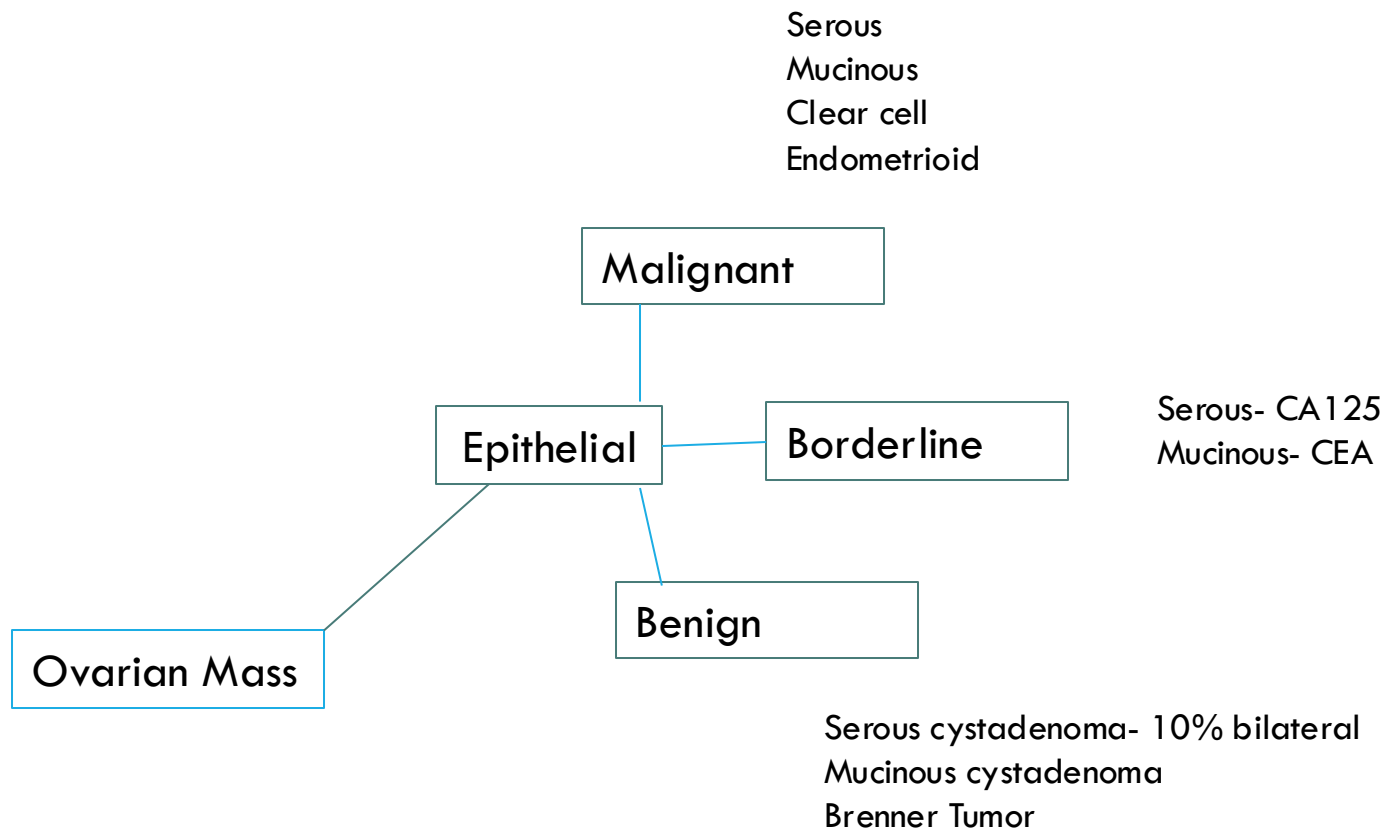
Gynecologic:

- Ovarian
- Fallopian tube
- Uterine

Non-Gynecologic

- Bowel
- Bladder
- Peritoneal/Retroperitoneal



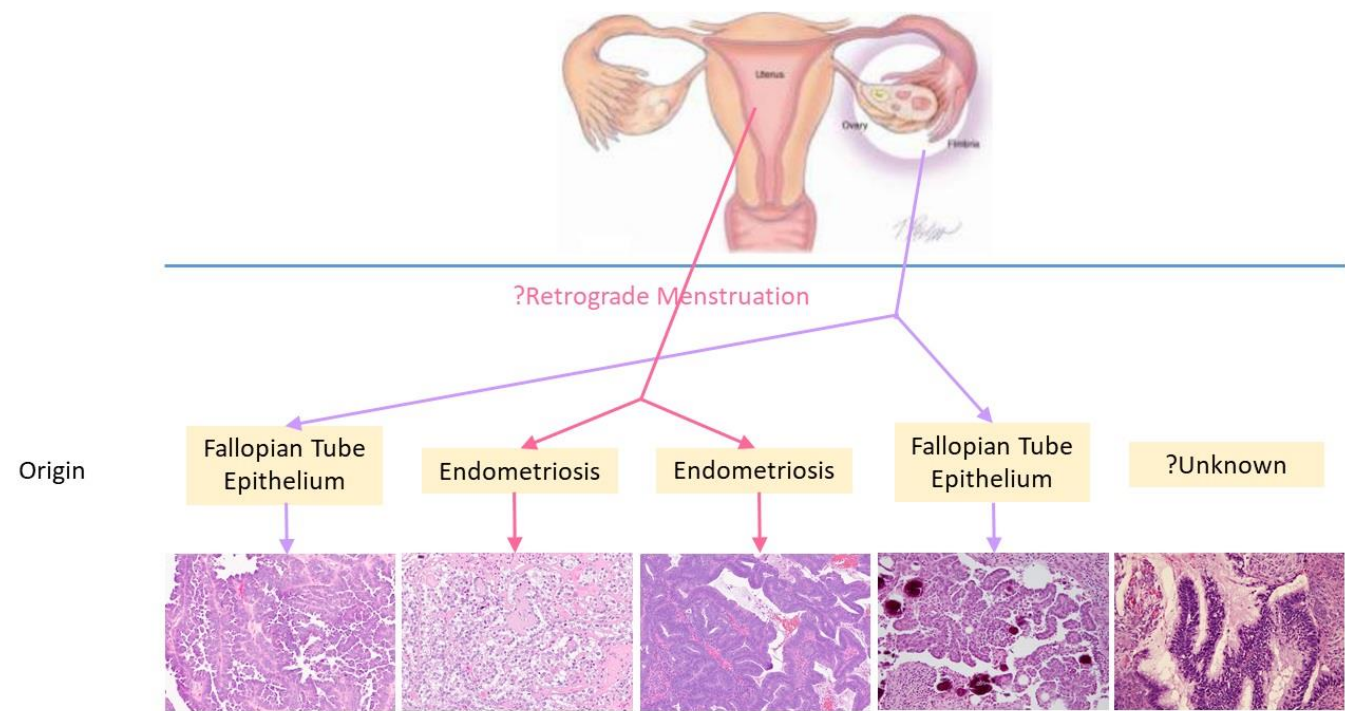


EPITHELIAL TUMORS

Median age at diagnosis (cancer):
63

Most common stage at presentation:
III-IV

Tumor markers:
CA 125, CEA, CA 19-9



	High-Grade Serous Carcinoma	Clear Cell Carcinoma	Endometrioid Carcinoma	Low-Grade Serous Carcinoma	Mucinous Carcinoma
% of all Ovarian Carcinomas	~70%	~10%	~10%	<5%	<5%
Precursor Lesions	Serous tubal intraepithelial carcinoma (STIC)	Clear Cell Borderline Tumor	Endometrioid Borderline Tumor	Serous Borderline Tumor	Mucinous Borderline Tumor
Inherited Syndromes	BRCA1/2, Hereditary Breast and Ovarian Cancer (HBOC)	Lynch Syndrome	Lynch Syndrome	?	?
Common Mutations and Molecular Aberrations	TP53 BRCA1/2 and HRD Chromosomal instability Aneuploidy (100%)	ARID1A PIK3CA CTNNB1 PPP2R1A MSI	PTEN CTNNB1 ARID1A PPP2R1A MSI	KRAS BRAF	KRAS HER2 amplification
Potential Molecular Targeted Therapies	PARP inhibitors, immune checkpoint inhibitors	Tyrosine kinase inhibitors	mTOR inhibitors	MEK1/2 inhibitors	Trastuzumab

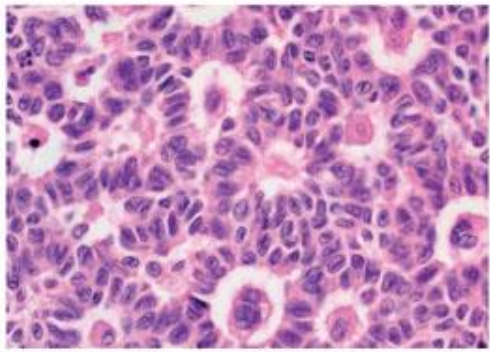
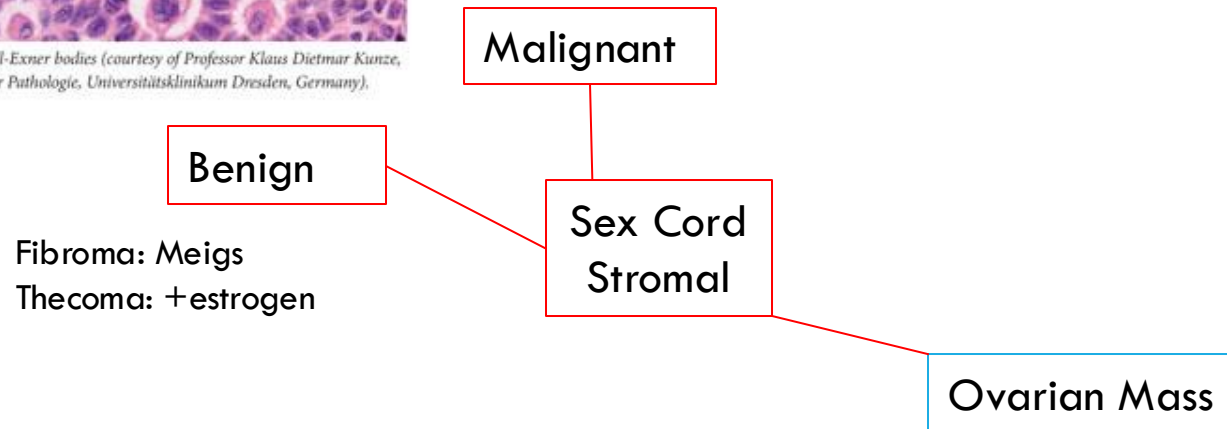


Fig. 1. Call-Exner bodies (courtesy of Professor Klaus Dietmar Kunze, Institut für Pathologie, Universitätsklinikum Dresden, Germany).

Granulosa cell: Call Exner, estrogen, hemoperitoneum
Sertoli Leydig: testosterone



SEX CORD STROMAL TUMORS

Granulosa Cell Tumors

70% of all sex cord stromal tumors

Two subtypes: adult and juvenile

- ~95%: adult type, early post-menopausal, early stage
- 5% juvenile, first 3 decades of life:
 - associated with precocious puberty, are aggressive in advanced-stage disease with recurrence and death occurring within 3 years after diagnosis.

Associated with **endometrial hyperplasia** or **cancer** in **25-50%** and **5-10%** of cases

Tumor markers: Inhibin B

Sertoli-Leydig Cell Tumors

< 0.5% of all ovarian tumors

Typically unilateral tumors and confined to the ovary in 97% of cases

Most often in young women (20 – 30 y/o), who usually become virilized

- hirsutism, temporal balding, deepening of the voice, and enlargement of the clitoris.
- secondary amenorrhea

In a report of 220 cases, only 29 were clinically malignant (~13%)

Testing: testosterone levels

Ovarian Mass

Germ Cell

Benign

Malignant



Dermoid:
20%
bilateral

Immature teratoma: neural elements
Endodermal sinus tumor: AFP
Embryonal carcinoma: hCG + AFP, precocious puberty
Choriocarcinoma: hCG
Dysgerminoma: LDH

GERM CELL TUMORS

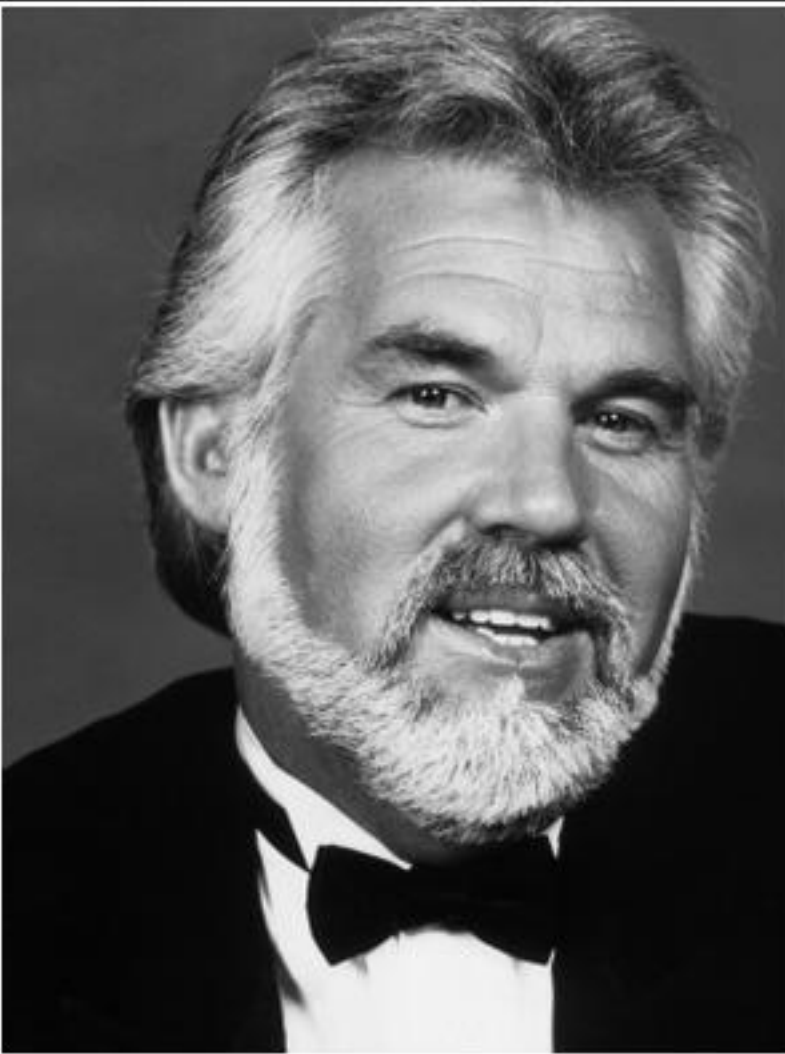
20% of all ovarian tumors (benign and malignant)

- 97% are benign
- 3% are malignant

No known risk factors, although most tumors occur in young women

- 20-30 year olds
- Frequently diagnosed by finding a palpable abdominal mass, often associated with pain

Excellent 5 and 10-year survival rates >91%



You gotta know when to hold'em, know
when to fold'em, know when to walk
away, know when to run. You never
count your money when you're sittin' at
the table, there'll be time enuff for
countin' when the dealin's done.

— *Kenny Rogers* —

AZ QUOTES

WORKUP AND WHEN TO REFER

IMAGING: PELVIC ULTRASOUND

O-RADS

Benign cysts/masses:

- Sensitivity: 95% (76-100%)

Borderline tumors

- Sensitivity: 20% (4-50%)

Malignant tumors

- Sensitivity: 60% (30-80%)
- Specificity: 39.5%

Category	Assessment	Risk of Malignancy (%)
0	Technically incomplete	NA
1	Physiologic, normal	0
2	Almost certainly benign	< 1
3	Low risk	1 to < 10
4	Intermediate risk	10 to < 50
5	High risk	≥ 50

Concerning for malignancy: cystic lesions with solid components: septae, mural nodules, and papillary projections.

- Large solid component
- Wall thickness greater than 3 mm
- Septal thickness greater than 3 mm
- Nodularity
- Necrosis

IMAGING: CT VS MRI

CT

Sensitivity in diagnosing malignancy:
80%

Greatest utility: evaluating for
metastatic spread

- organ or sidewall invasion, peritoneal implants, adenopathy, ascites

Often first imaging from an ED visit

PET CT: sensitivity 55%, specificity 75%,
not recommended for
screening/diagnosis

MRI

Sensitivity in diagnosing malignancy:
100%

Specificity in diagnosing malignancy:
84%

→ Greatest utility:

- Determining origin when unclear
- Further characterization when ultrasound is indeterminate

LABS

Epithelial:

- CA 125, CEA, CA 19-9
- HE4

Germ cell:

- hCG, AFP, LDH

Sex Cord Stromal:

- Inhibin B, Testosterone

Tumor markers depending on age:

<30: all

<50: epithelial, Inhibin B

>50: epithelial

PPV of 2.6% when using a single serum
CA125 level ≥ 35 U/mL

SCORING SYSTEMS

ROCA:

- CA 125 + age + menopausal status
- 6 week repeat ultrasound if increased risk

ROMA:

- CA 125 + HE4 + menopausal status
- Sensitivity: 76-92% (better in postmenopausal), specificity: 75%

RMI (Risk Malignancy Index)

Future Directions: ctDNA

The image shows a mobile application interface for the 'RMI for Ovarian Cancer' calculator. The top navigation bar is teal with a back arrow, the title 'RMI for Ovarian Cancer', and icons for a star and a share button. Below the navigation bar are four tabs: 'CALCULATOR' (highlighted in orange), 'NEXT STEPS', 'EVIDENCE', and 'CREATOR'. A dropdown menu below the tabs shows 'Pearls/Pitfalls'. The main content area is titled 'Ultrasound features' and contains five rows of toggle buttons for 'Multiloculated cysts', 'Solid areas', 'Bilateral lesions', 'Ascites', and 'Intra-abdominal metastases'. The 'Other features' section includes a dropdown for 'Menopausal status' (set to 'Premenopausal or perimenopausal') and a text input for 'Serum CA-125, U/mL' (set to '77'). At the bottom, a teal bar displays the 'RESULT' as '77 points' with the text 'Low risk of malignancy'.

RMI for Ovarian Cancer

CALCULATOR NEXT STEPS EVIDENCE CREATOR

Pearls/Pitfalls

Ultrasound features

Multiloculated cysts No Yes

Solid areas No Yes

Bilateral lesions No Yes

Ascites No Yes

Intra-abdominal metastases No Yes

Other features

Menopausal status
Postmenopausal status =
>1 year of amenorrhea or
age ≥50 years if patient is
status post hysterectomy

Premenopausal or
perimenopausal

Postmenopausal

Serum CA-125, U/mL 77 U/mL

RESULT
77 points Low risk of malignancy

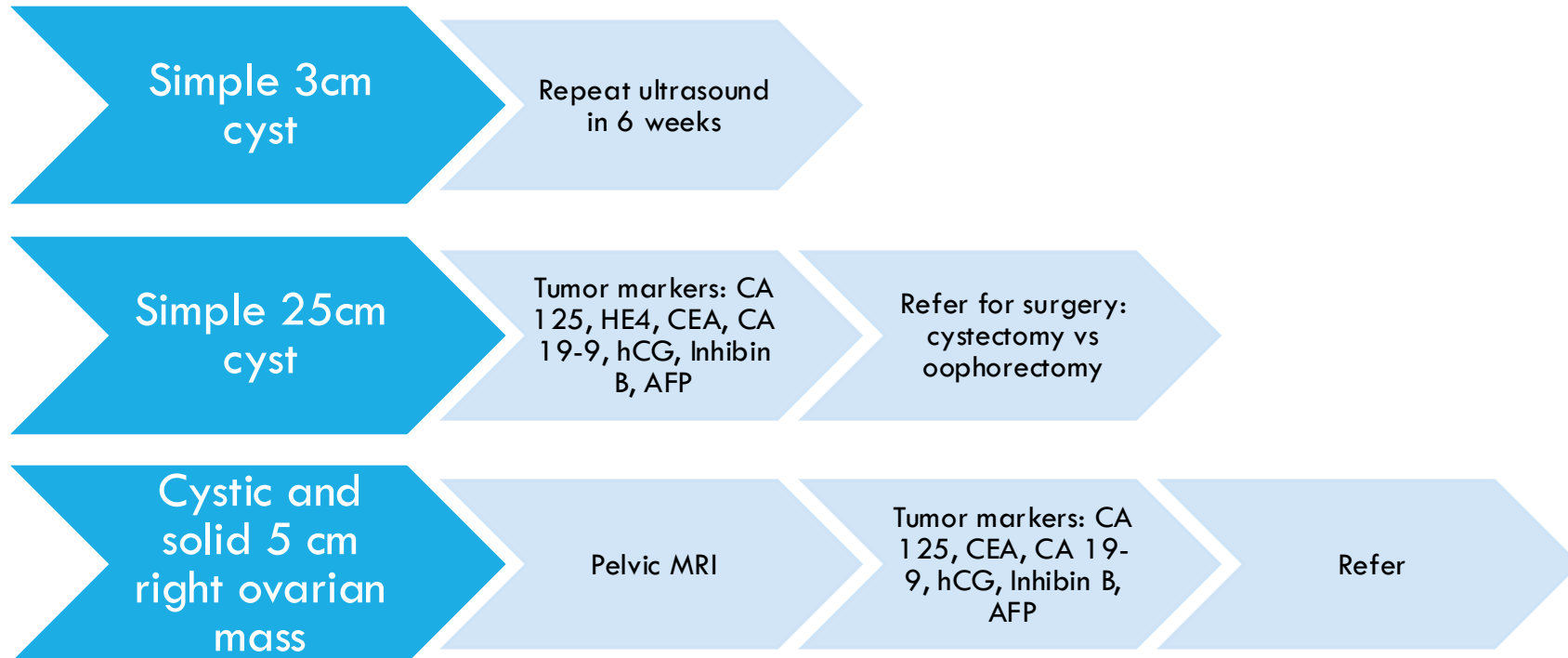
MANAGEMENT: OBSERVATION VS SURGERY

- ☐ Simple
- ☐ Pre-menopausal vs postmenopausal
- ☐ Asymptomatic
- ☐ Size and Trend
- ☐ Tumor markers

CASE #1

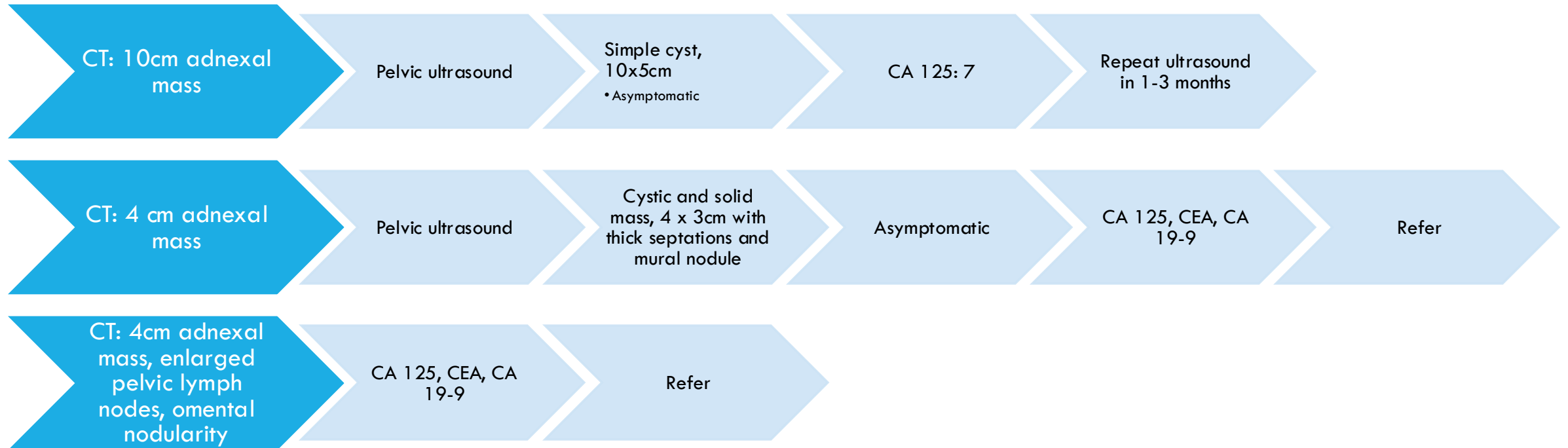
22 year old presents with increasing abdominal distension and discomfort.

- Workup?
- Pelvic ultrasound



CASE #2

67 year old presents to the ED with URI, undergoes CT C/A/P and incidentally found to have an adnexal mass. She follows up with you and asks what she should do next.



CASE #3

68 year old woman was driving back from their winter home in Arizona, noticed increasing shortness of breath and abdominal distension.

She went to the ED and underwent CT C/A/P:

- Massive ascites
- Peritoneal carcinomatosis
- 6cm left adnexal mass, 4cm right adnexal mass
- Lymphadenopathy

MANAGEMENT OF OVARIAN CANCER

Tumor markers, Referral to GYN Oncology

Decision: Primary debulking surgery vs Neoadjuvant chemotherapy

Median OS (mo)	Overall	R0	R1	R2
PDS	29	45	32	26
NACT	30	38	27	25

Strongest predictors for OS

R0 resection – $p < 0.001$

Stage IIIC – $p = 0.001$

Small tumor size preop – $p = 0.001$

Younger age – $p = 0.005$

MANAGEMENT OF OVARIAN CANCER

3-4 cycles chemotherapy (carboplatin + paclitaxel +/- bevacizumab)

Interval debulking surgery

- Hysterectomy, BSO
- Omentectomy
- +/- Bowel resection, cholecystectomy, appendectomy, splenectomy, ostomy
- HIPEC

2-3 cycles chemotherapy

Maintenance

CURRENT OUTCOMES IN OVARIAN CANCER

Median progression free survival for advanced ovarian cancer: 10-50 months

- Mitigating factors:
 - R0 resection with debulking surgery
 - BRCA, HRD: improved response to PARP inhibitors (maintenance), more likely to be platinum-sensitive
- 20-25% will be platinum-refractory
- HIPEC (Hyperthermic Intraperitoneal Chemotherapy):
 - Median PFS 14 vs 10.7 months
 - Median overall survival 46 vs 34 months

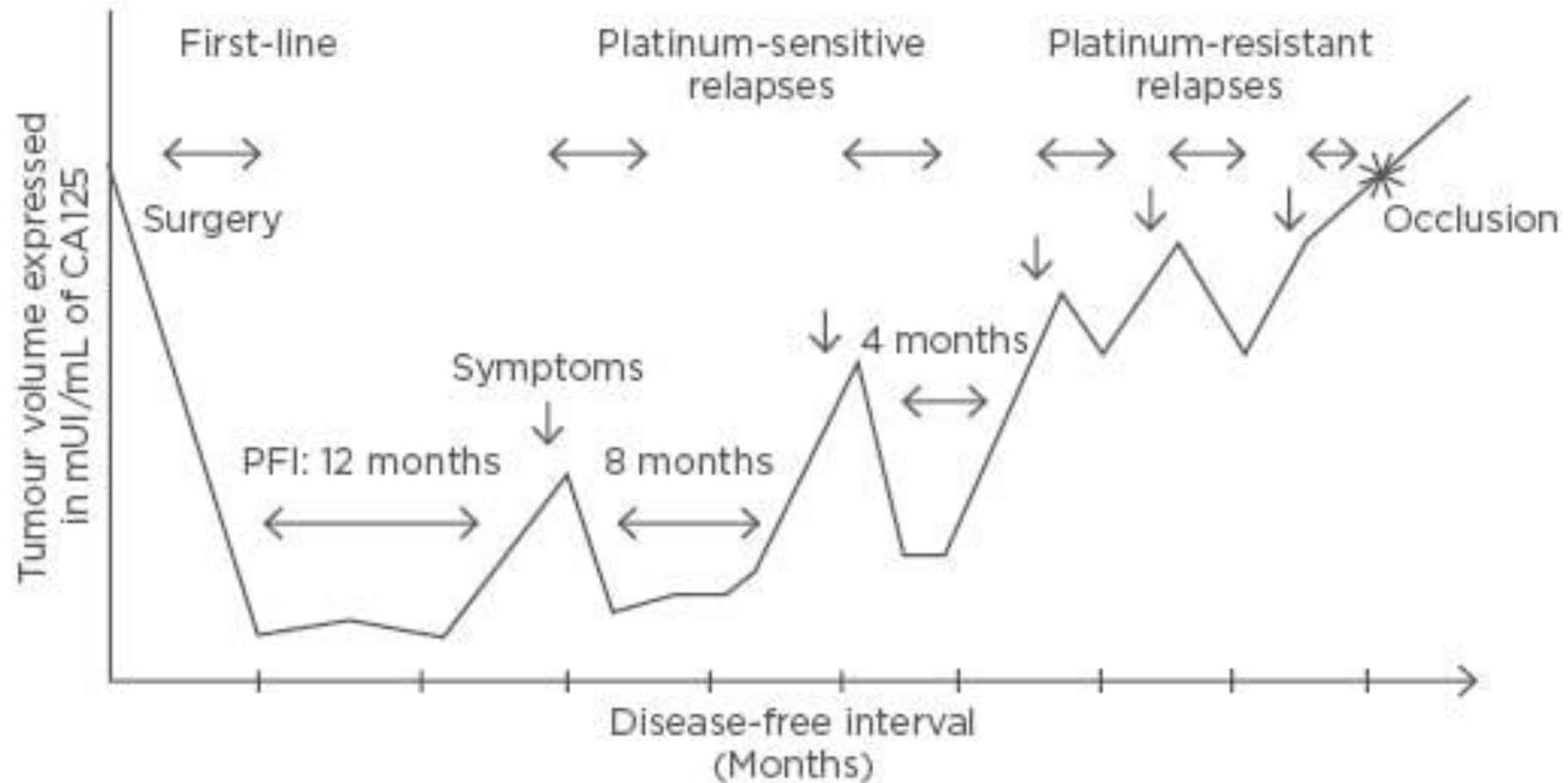
NEW TREATMENTS, NEW SIDE EFFECTS

Bevacizumab: uncontrolled HTN, VTEs, PRES

Mirvetuximab: ocular events

Trastuzumab deruxtrican: ILD

OVARIAN CANCER COURSE



TAKEAWAYS

When in doubt, order an ultrasound

Use tumor markers as an adjunct to imaging

When deciding which imaging to order next, ask yourself:

- Is the ultrasound unclear on the origin? → MRI
- Does the ultrasound have unclear features for malignancy and patient wants to monitor? → MRI
- Does the ultrasound look benign and patient wants to monitor? → ultrasound
- Does the ultrasound look like cancer? → CT C/A/P (staging)

Thank you for whatever workup you feel comfortable doing. When in doubt, refer or call anytime!

QUESTIONS?

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