Medical Update: Ovarian Cancer 2018

How is our definition of Ovarian Cancer changing?

Ovarian Cancer Alliance of Oregon and Southwest Washington

and

Compass Oncology

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Ovarian Cancer Definitions

Ovarian Cancer

- *What is it?*
- *Who gets it?*
- *How is it treated?*
- *How successful is treatment?*

Ovarian Cancer Definitions

Ovarian Cancer

- *Definitions of Past*
- *Definition of each woman's cancer*
- *Definitions of where we are at today*
- *New definitions for now and the Future*

Definitions / Terminology

What is Ovarian Cancer ?

Each woman's ovarian cancer is unique

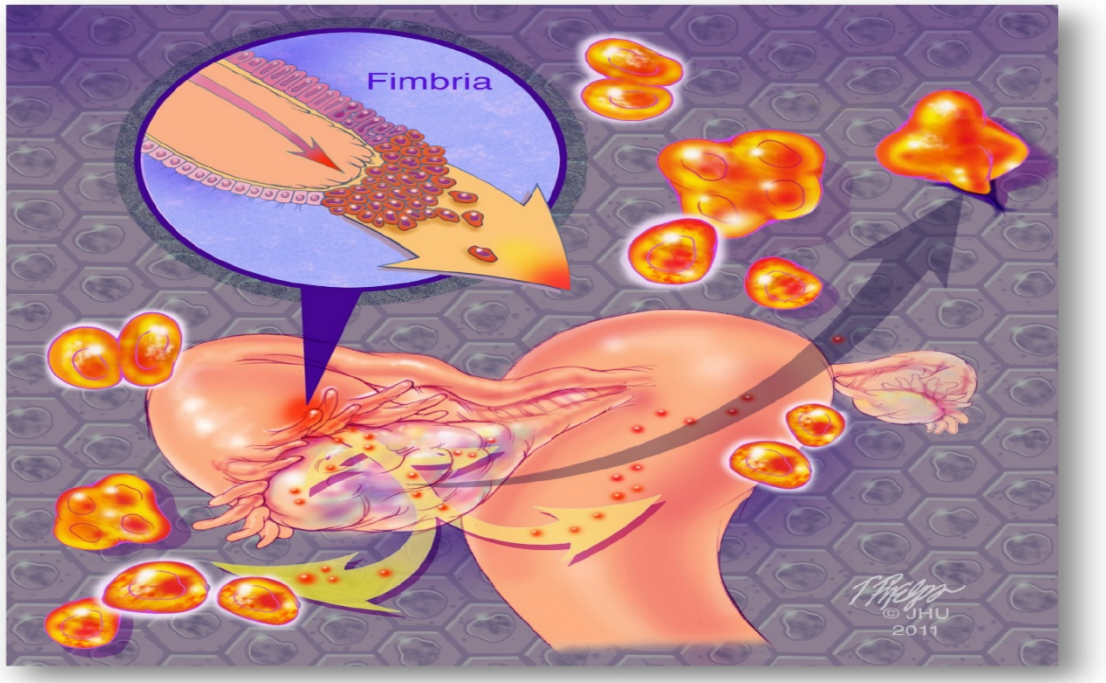
Where does *Epithelial Ovarian Cancer* come from?

Hint – not from the ovary

What is Ovarian Cancer ?

Where does ovarian cancer come from?

The fallopian tube



What is the "*Biology of Ovarian Cancer*"

Each woman's ovarian cancer is unique

Classic Epithelial Ovarian Cancer

What does it look like?

How much cancer is found at diagnosis?

How easy is it to surgically remove?

How does it respond to chemotherapy?

What is the *"Biology of Ovarian Cancer"*

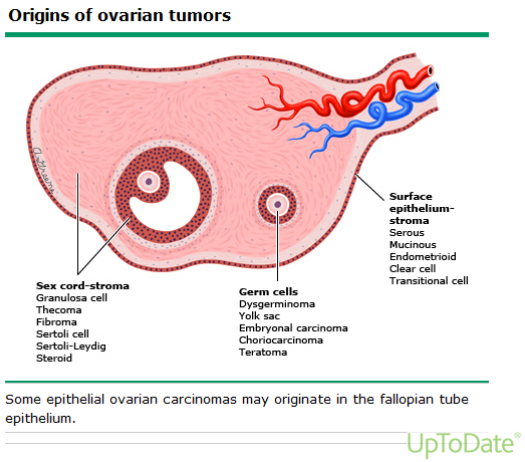
What does it look like?

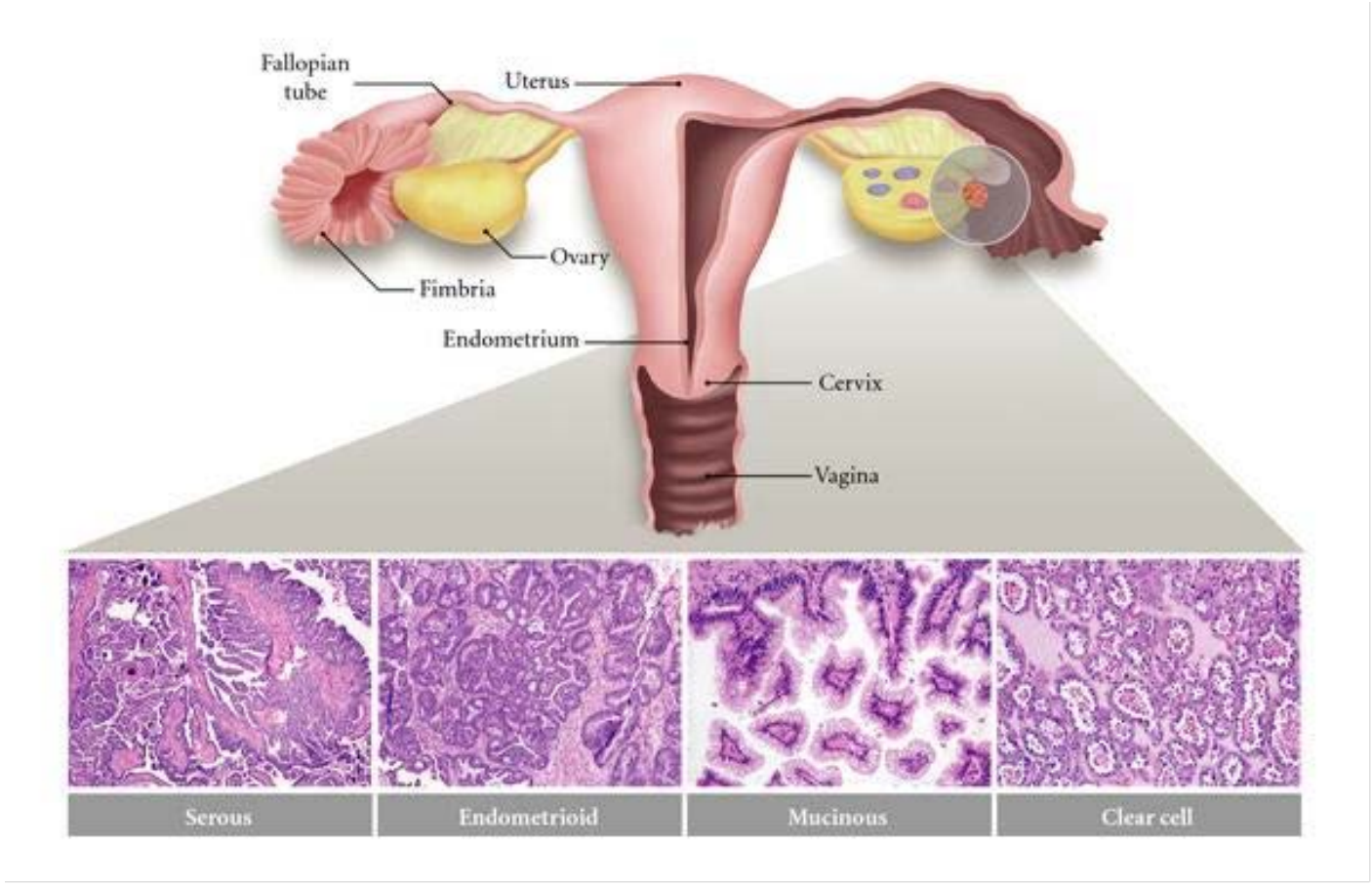
Histology –

What the cancer cells look like under the microscope

→ 75% High Grade Serous Carcinoma

Biology of Ovarian Cancer





What is the "*Biology of Ovarian Cancer*"

How much cancer is found at diagnosis?

Stage →**where cancer cells are found in the body**

75% Advanced Stage

the cancer has spread throughout abdomen / lung fluid

What is the *"Biology of Ovarian Cancer"*

How easy is it to surgically remove?

Extent of Disease

Before resectable/unresectable

After

Complete (microscopic)

Optimal (< 1cm)

Suboptimal (> 1cm)

What is the "*Biology of Ovarian Cancer*"

How does it respond to chemotherapy

Platinum sensitive vs resistant

How long does the response last

Response complete vs partial

What is the "*Biology of Ovarian Cancer*"

Is there a genetic mutation responsible for the cancer?

>15 % Germline mutation (familial based)

??? (100%) Somatic Mutation (tumor based)

(Hint—Targeted Therapy)

Percentage of Women with Ovarian Cancer who should undergo BRCA testing

100%

- Provide prognostic information regarding ovarian cancer
- Influences Treatment Options (Parp inhibitors)
- Influences Surveillance for other cancers (esp. breast)
- Significantly impact prevention of cancers in other family members

"No woman with BRCA1 or 2 gene mutation should ever die of ovarian or breast cancer if <u>all 30 year old women</u> were tested."

Mary-Claire King, PhD

March 20, 2016

SGO ABOG Lecturer, San Diego

Ovarian Cancer Treatment

Which is first -- surgery and / or chemotherapy?

Surgery 1st –Tumor Reductive Surgery

or

Chemotherapy 1st – Neoadjuvant Chemotherapy

Ovarian Cancer Treatment

How do we decide surgery and / or chemotherapy?

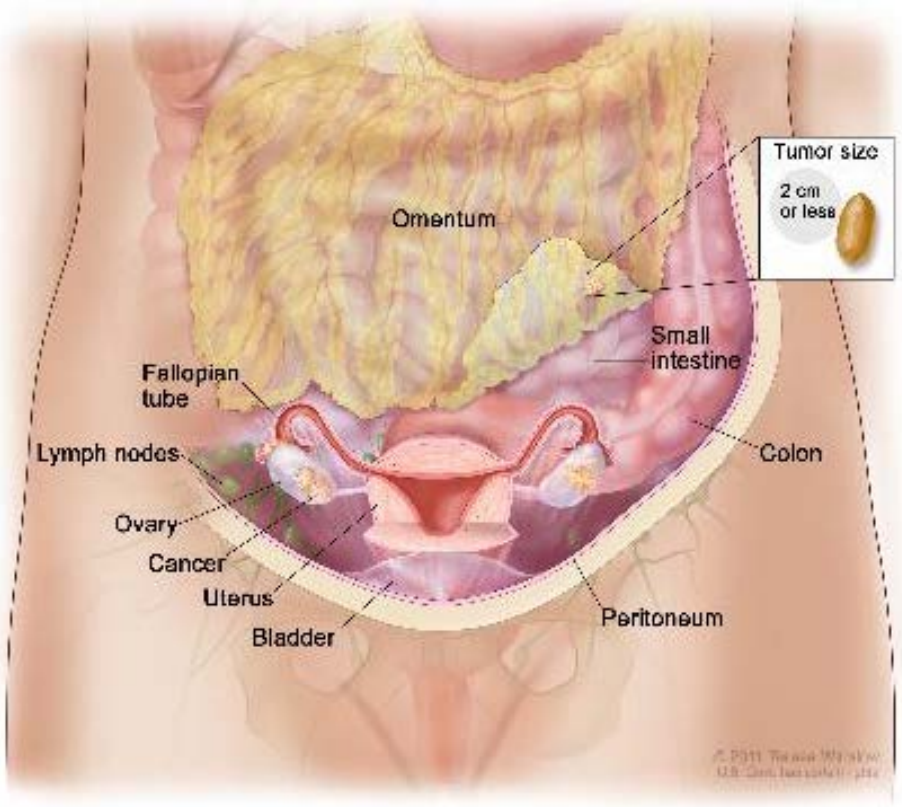
- Assessment by Gynecologic Oncologist
- Extent of the Disease
- Functional Status

Ovarian Cancer Treatment

What is removed?

- **REMOVE ALL VISIBLE CANCER** :
  - **Resection of Pelvic Tumor**: uterus + ovaries + fallopian tubes
  - **Omentectomy**
  - Possible bowel, lymph nodes, skin of the inside of the abdominal cavity (
  - Intraperitoneal Port Placement
- Surgery by Gynecologic Oncologist results in better survival outcomes
  - ***High volume surgeons at High Volume Facilities***

What is the Omentum?



Definitions / Terminology

What is Standard of Care Treatment?

The treatment approach that is considered the optimal treatment that has been scientifically studied as is superior other treatment options.

1st Line Treatment

Surgery and Chemotherapy

Components

- Carboplatin + Taxol Chemotherapy
- Consultation with Gynecologic Oncologist
- Surgery by Gynecologic Oncologist
- Consideration for Intraperitoneal Chemotherapy

Definitions / Terminology

Primary Treatment – 1st line

After first line treatment

Cancer surveillance –Observation (standard of care)

Maintenance /Consolidation–
continuing with current treatment component

Switch Maintenance—after complete response, then maintenance treatment with a **different drug**

Definitions / Terminology

What happens if / when Ovarian Cancer recurs?

Treatment Choices depend on

Timing is (almost) everything

Progression Free Interval
Platinum sensitivity--

Functional status
Prior treatments / residual toxicities
Goals of treatment
Acceptable toxicities

Eligibility for Clinical Trial

Definitions / Terminology

Treatment terms

What are treatment options for recurrent cancer?

Current chemotherapy -- single agent vs multiple agents

- Carboplatin / Cisplatin
- Liposomal Doxorubicin
- Gemcitabine
- Topotecan
- Taxanes

Biologics –Bevacizumab

Targeted--Parp inhibitors **

***If BRCA+ and /or platinum sensitive*

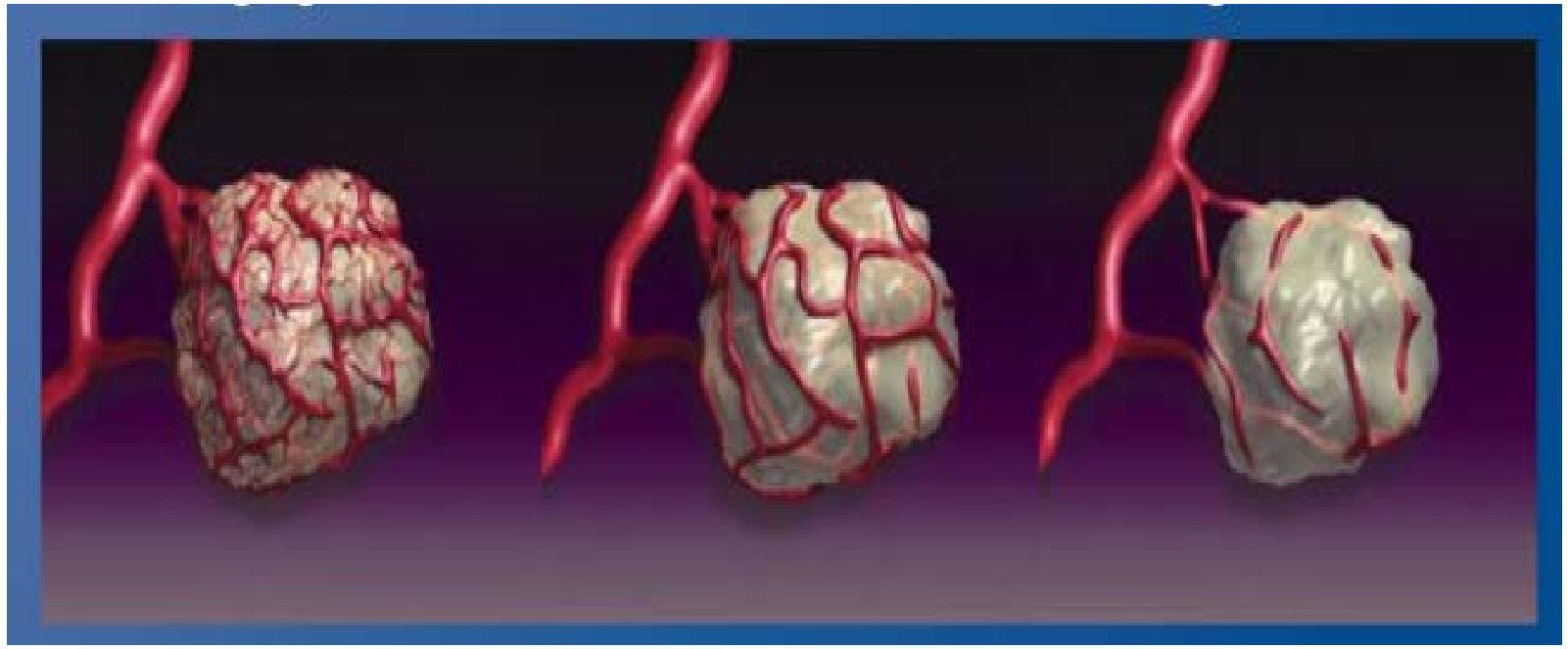
Definitions / Terminology

Treatment terms

What are Biologics

–Angiogenesis inhibitors

Bevacizumab, Cedarinib



Bevacizumab (Avastin)

Angiogenesis Inhibitor

- One of the first 'biologic' treatments for ovarian cancer
- Effective in several other cancers (colon, breast, lung)
- Intravenous every 2-3 weeks
- Limited side effects (symptoms) but significant potential toxicities (risk to health)

Research with Bevacizumab and Ovarian Cancer

- "1st line" Ovarian Cancer Treatment
- Maintenance Treatment
- Recurrent Disease

What are PARP Inhibitors?

Parp inhibitors work to inhibit a Parp DNA Repair Mechanism.

Alone they are affective in controlling Ovarian Cancer in women with a BRCA mutation.

OR

Clinical Trials are looking at the combination of Parp Inhibitors and other cancer treatment drugs to also help control Ovarian Cancer in women who are BRCA negative

It all starts with healthy cells replicating themselves……

During replication, a cell needs to *duplicate it's DNA*.

Duplicating the DNA is very complex and mistakes happen.

If mistakes during the duplication of the DNA, the cell's have built in repair mechanisms—these are DNA Repair Pathways

Healthy cells have two different *DNA repair pathways*.

Homologous Recombination (BRCA pathway)

Base Excision Repair (Parp pathway)

What are the current PARP Inhibitors?

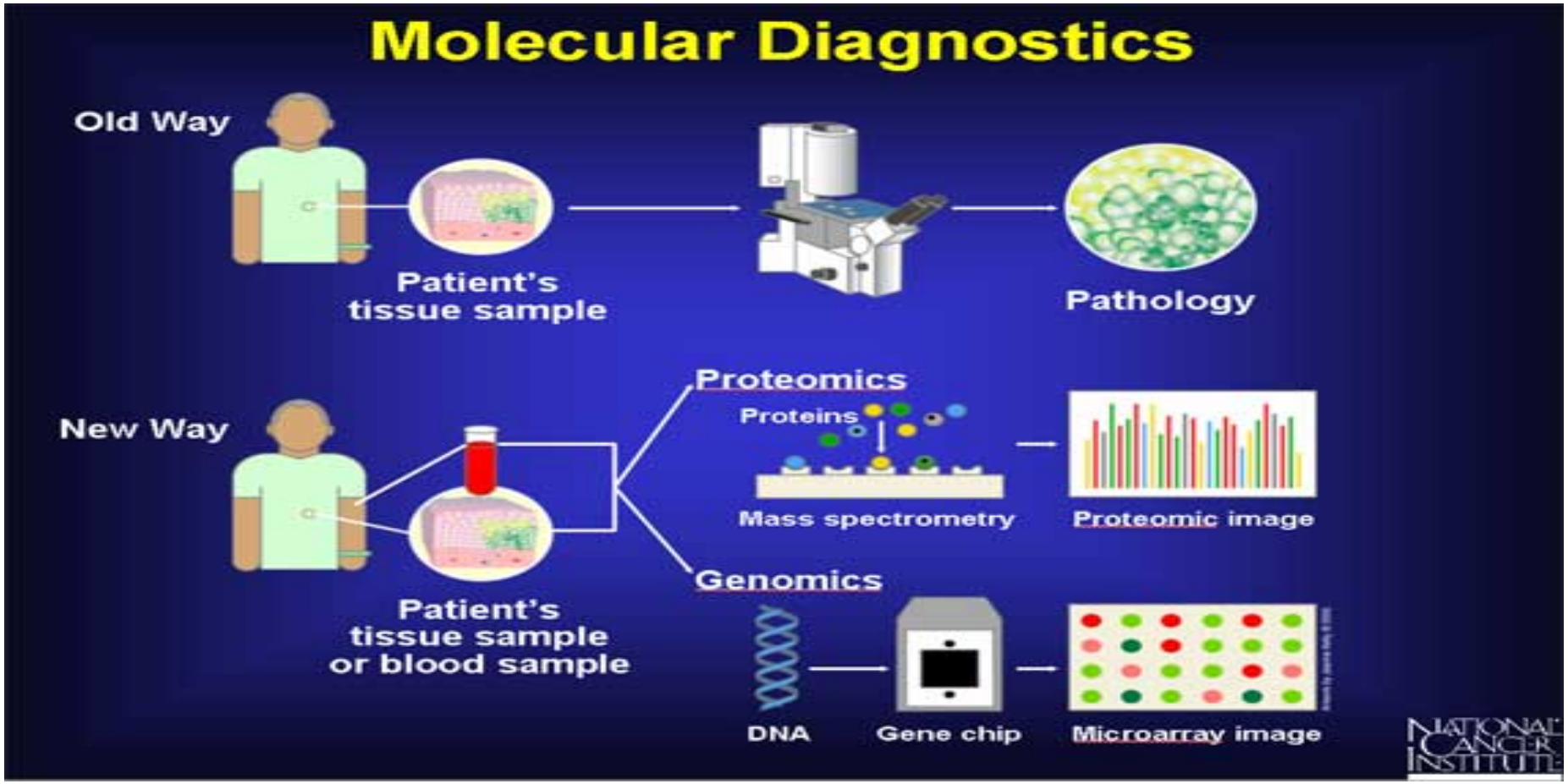
- **Olaparib**
- **Rucaparib**
- **Niraparib**
- **Veliparib**
- **Talazoparib**

What is Target Therapy?

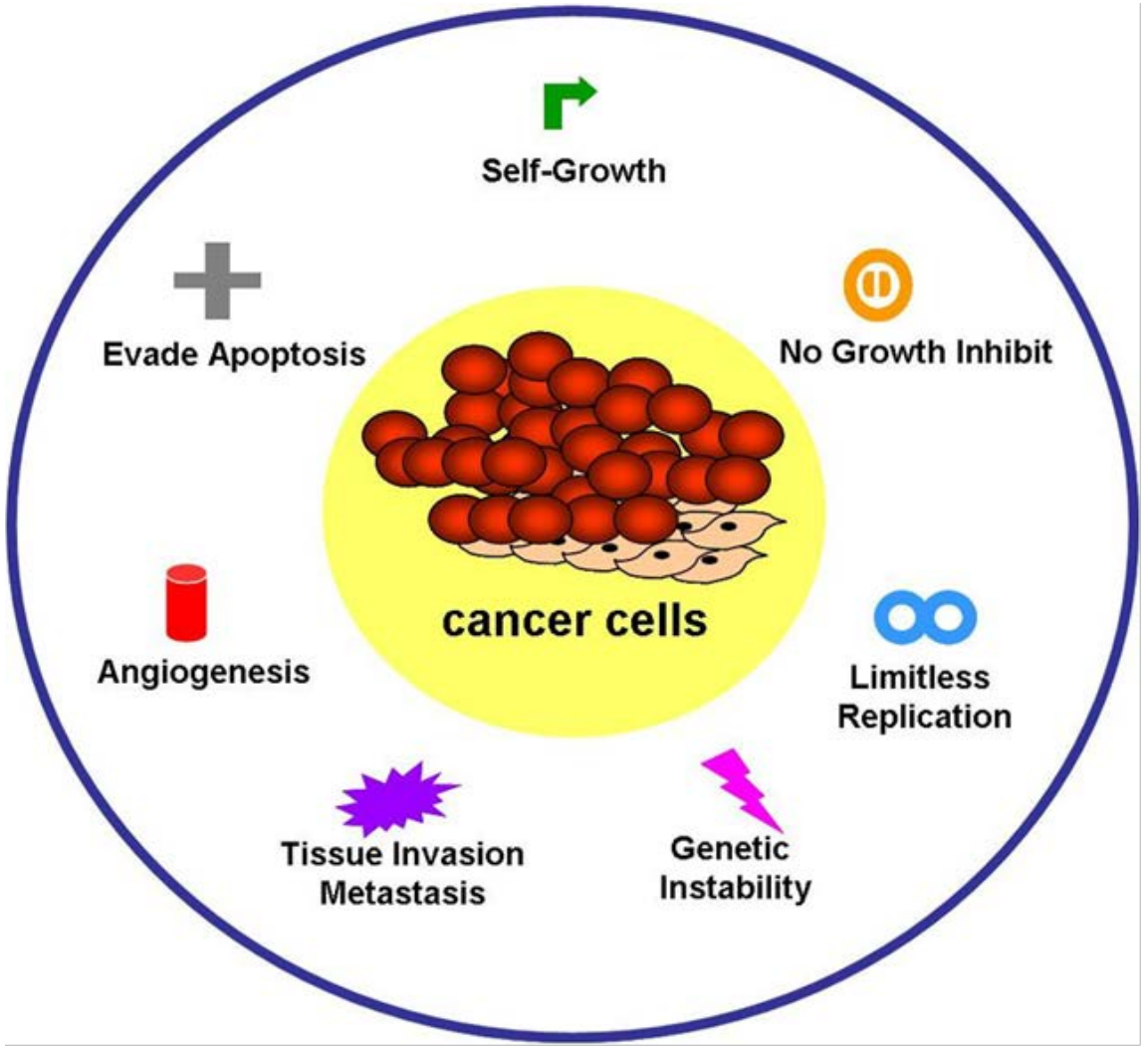
Using the molecular profile of the cancer determine the treatment options.

One of the oldest targeted therapies is the anti-estrogen drug Tamoxifen in breast cancer.

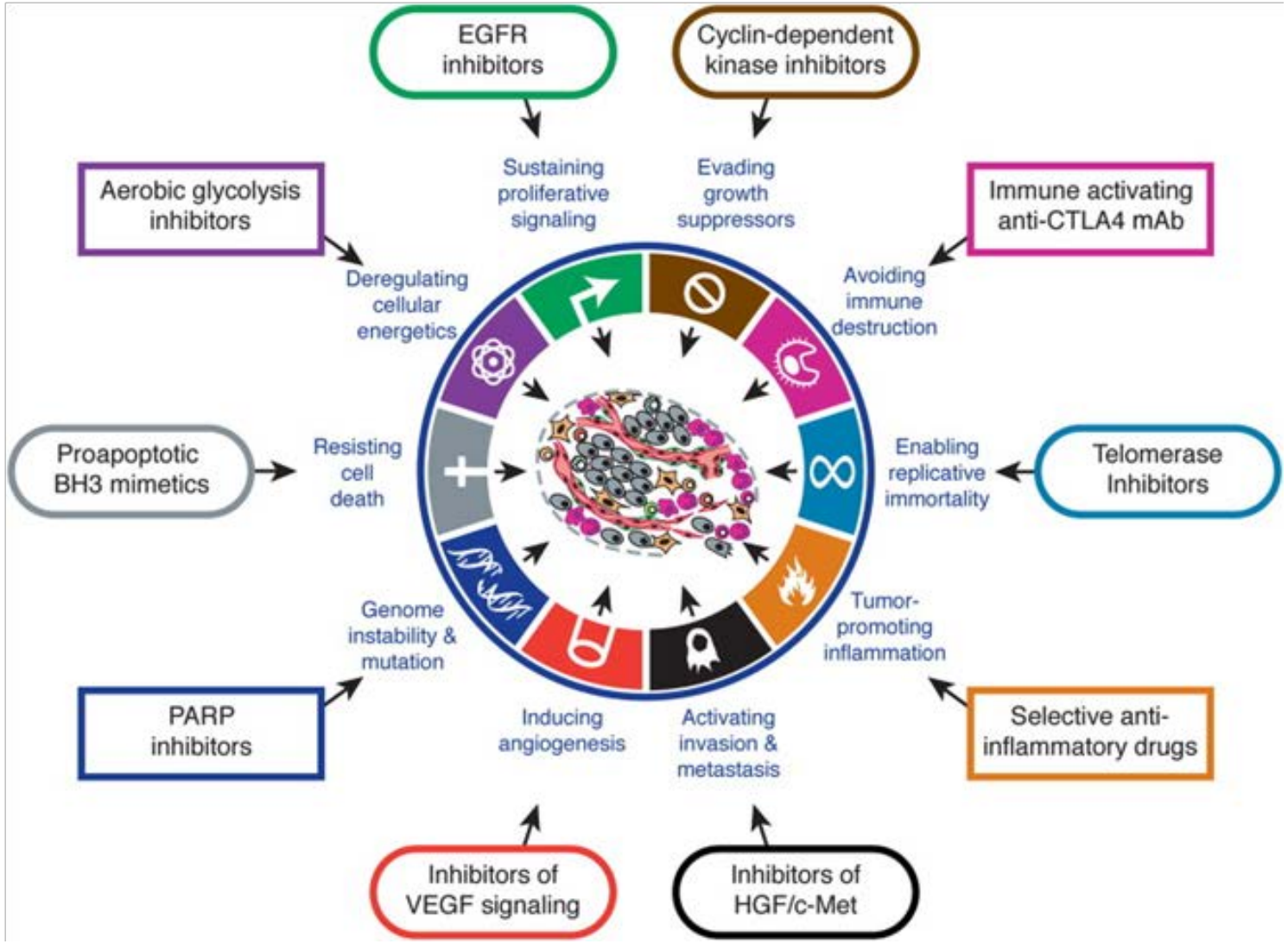
What is Molecular Profiling?



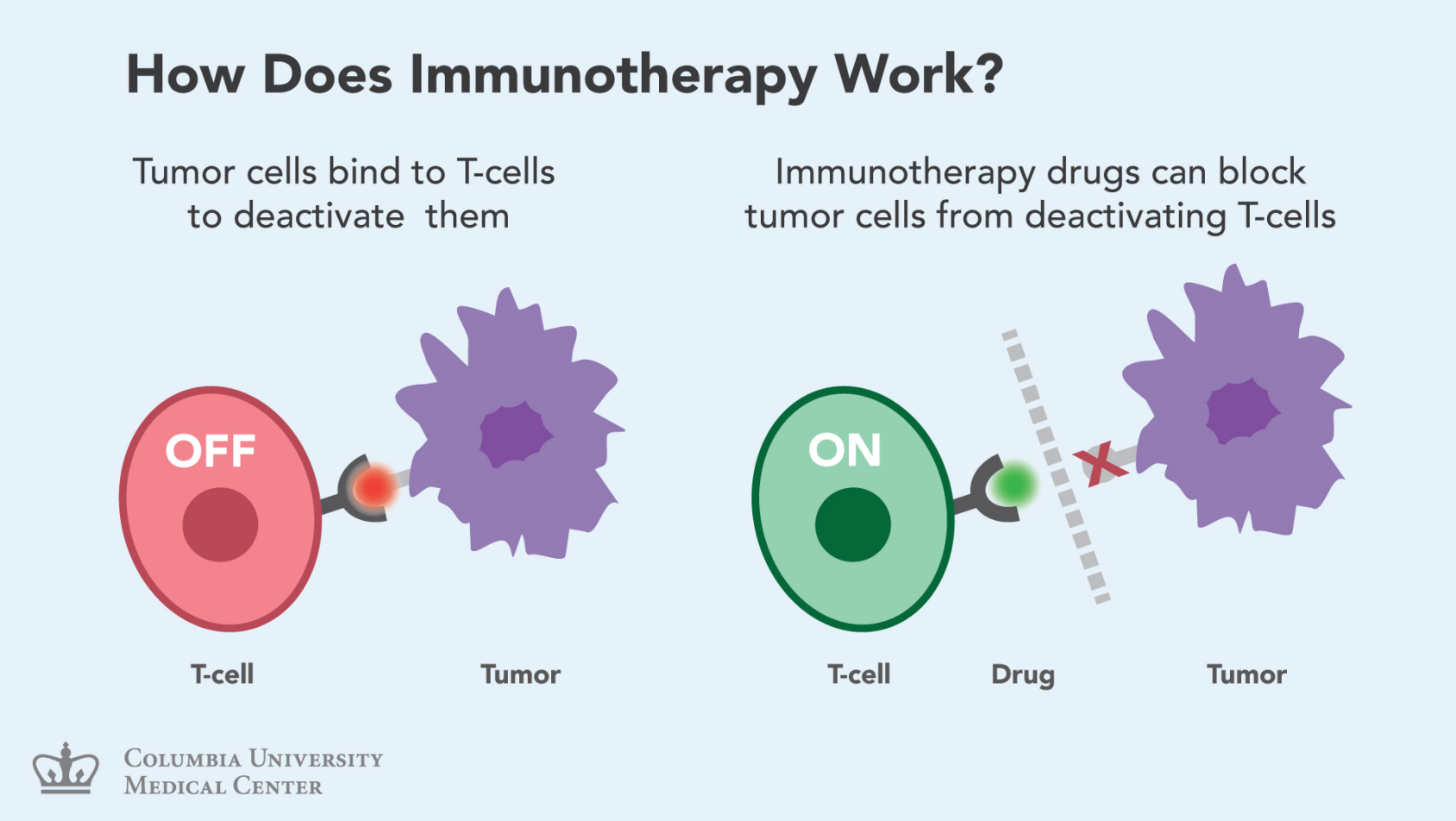
Cancer Cell Function which may be altered



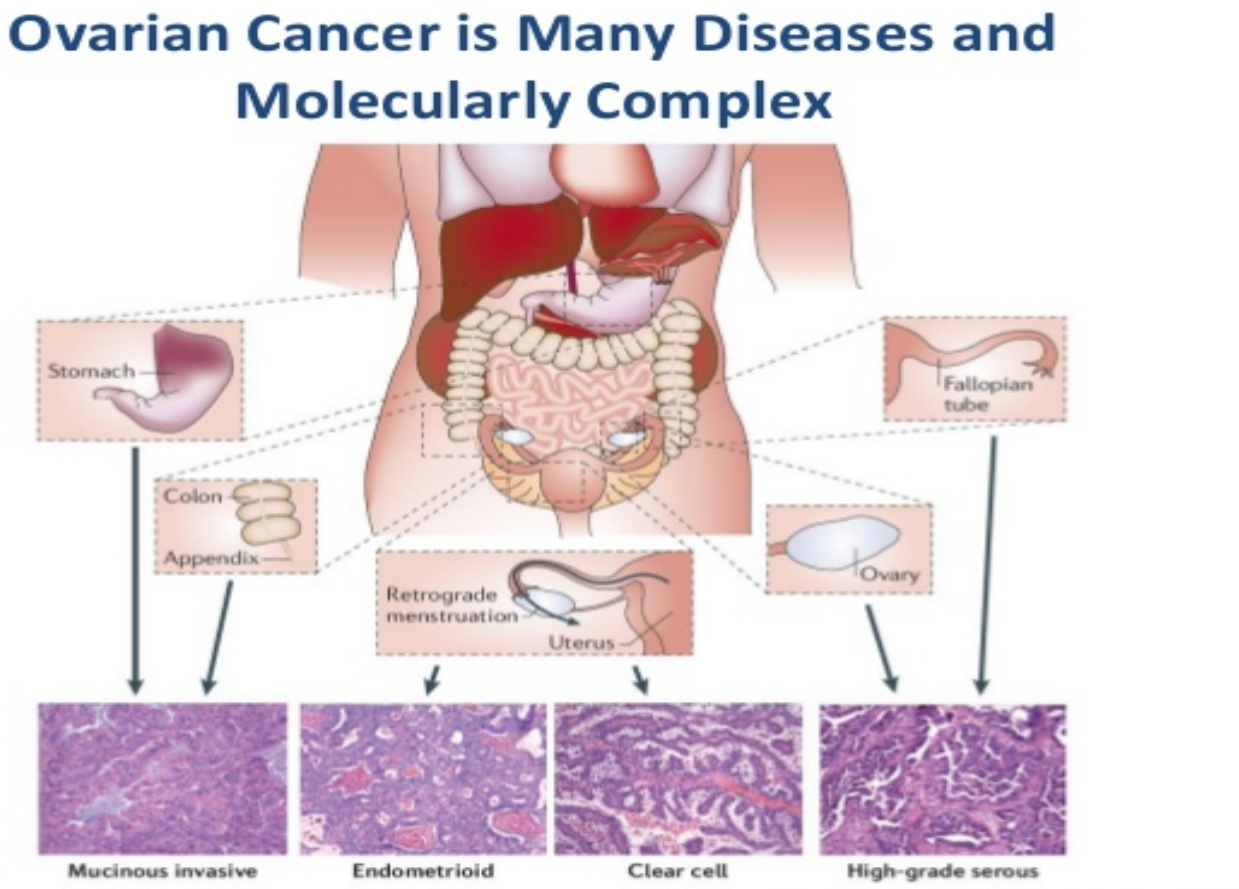
Treatment Strategies related to Cancer Function



What Is Immunotherapy

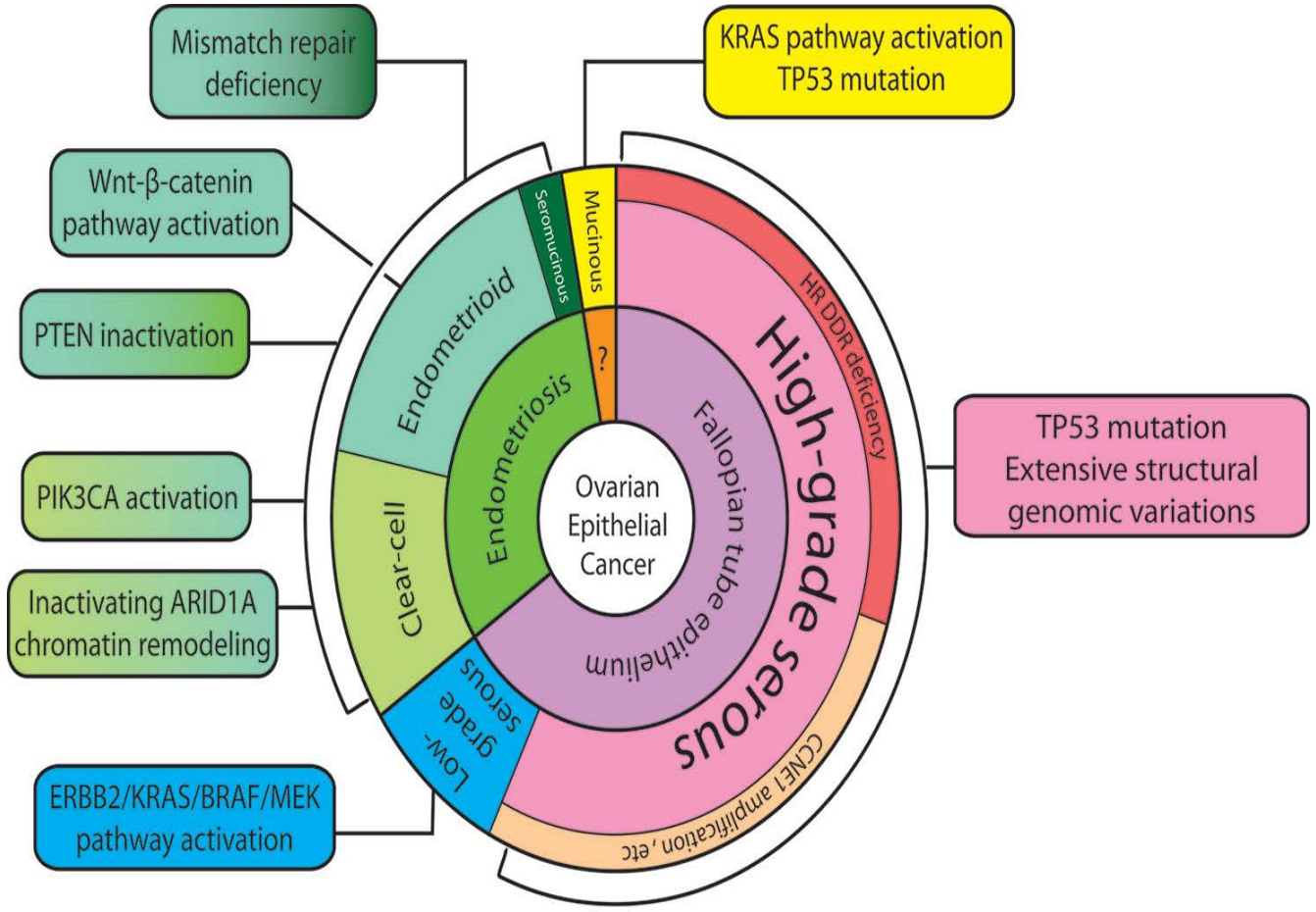


Definitions / Terminology



Vaughan S, et al.: Nature Reviews 2011

What targets are there for Ovarian Cancer?



New Targeted Therapies

- Bevacizumab (Avastin)
- Bortezomib (Velcade)
- Ceritinib (Zykadia)
- Ipilimumab (Yervoy)
- Nivolumab (Opdivo)
- Olaparib (Lynparza)
- Pazopanib (Votrient)
- Pembrolizumab (Keytruda)
- Pertuzumab (Perjeta)
- Temsirolimus (Torisel)
- Trametinib (Mekinist)
- Trebananib
- Veliparib
- Rucaparib
- Avelumab
- Binimetinib
- Niraparib
- VB-111
- Vanucizumab
- Selinexor

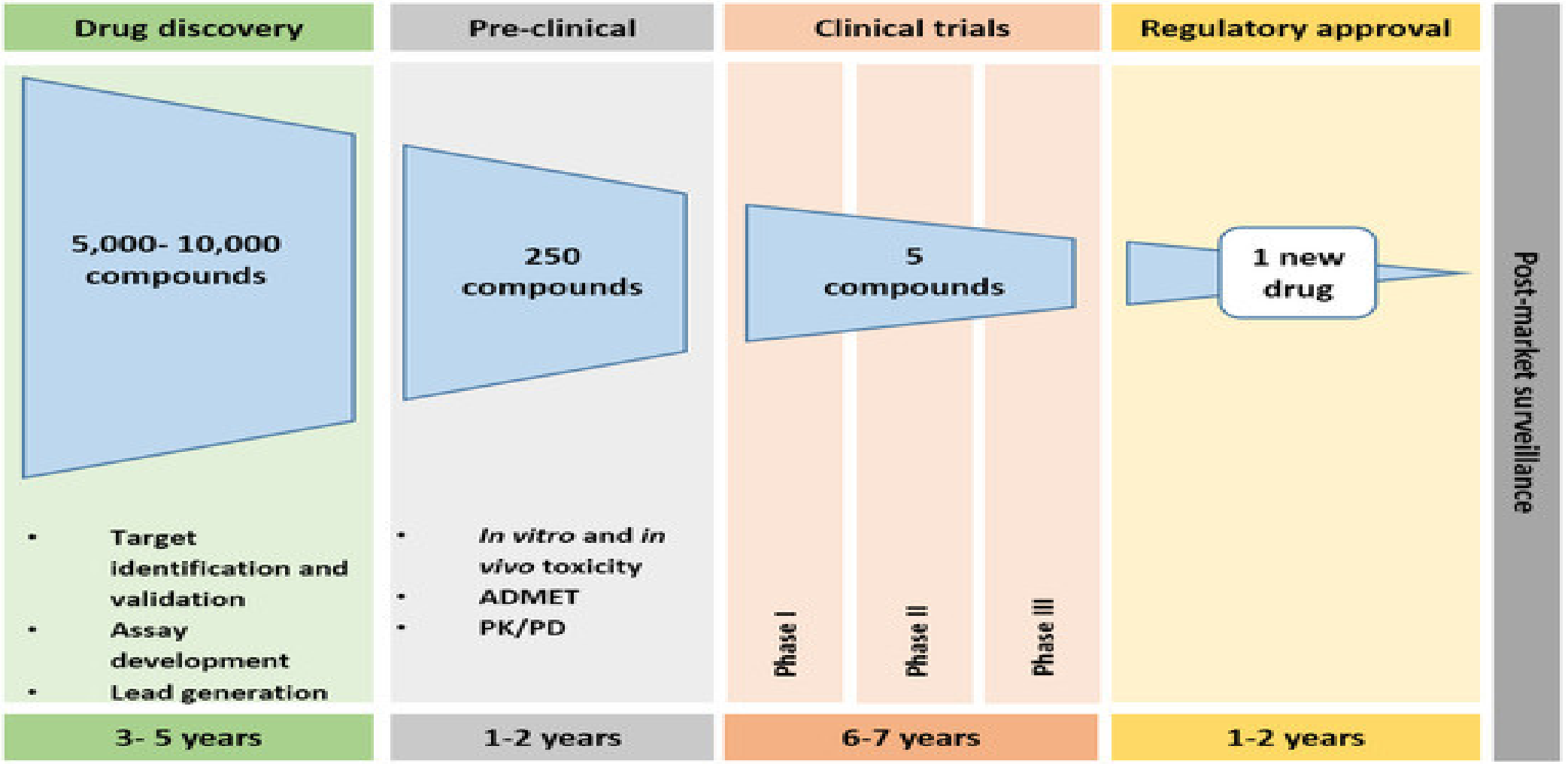
What are Clinical Trials?

Research Studies performed to test new, potentially beneficial medical interventions on people.

Various Types of Cancer Research Trials

- Prevention Trials
- Screening Trials
- Diagnostic Trails
- Treatment Trials
- Quality of Life / Supportive Care Trials
- Genetics Trials

Research from conception to drug



Clinical Trials

- Phase I -- Is the treatment safe?
- Phase II Does the treatment work?
- Phase III Is it better than what's already available?
- FDA Approval
- Phase IV What else do we need to know?

Eligibility for Clinical Trials

- Type of Cancer / Stage / Histology
- Current status of the cancer
- Any prior treatments
- Measurable disease (RECRIST)

- Functional Status
- Other health Issues / other cancer diagnosis

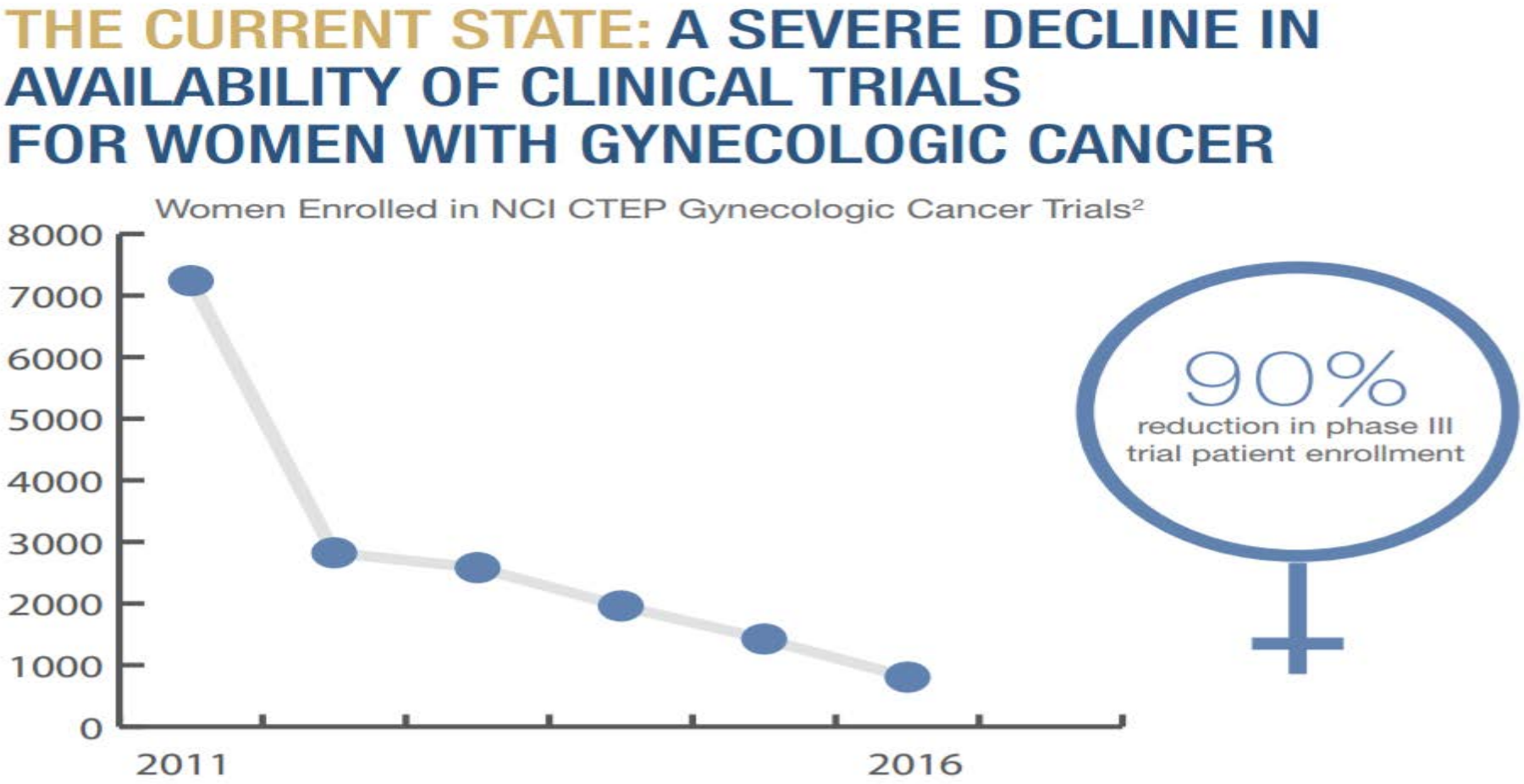
Eligibility for Clinical Trials

- Type of Cancer / Stage / Histology
- Current status of the cancer
- Any prior treatments
- Measurable disease (RECRIST)
    - Tissue Biopsy
    - Molecular Profiling
    - Targeted therapies
- Genetics
- Functional Status
- Other health Issues / other cancer diagnosis

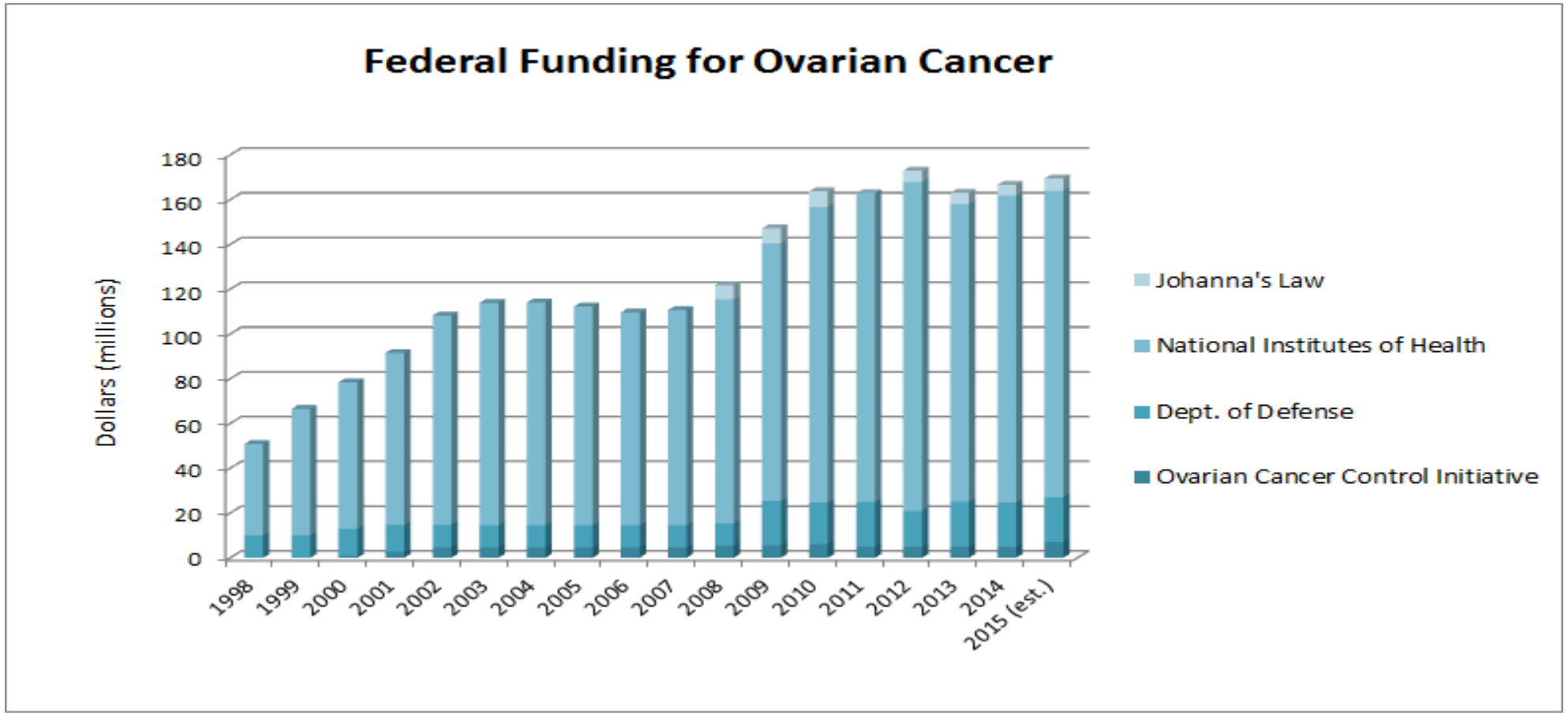
Who pays for Clinical Trials?

- Government
- Private Foundations (Ovarian Cancer Research Fund)
- Pharma

Who pays for Clinical Trials?



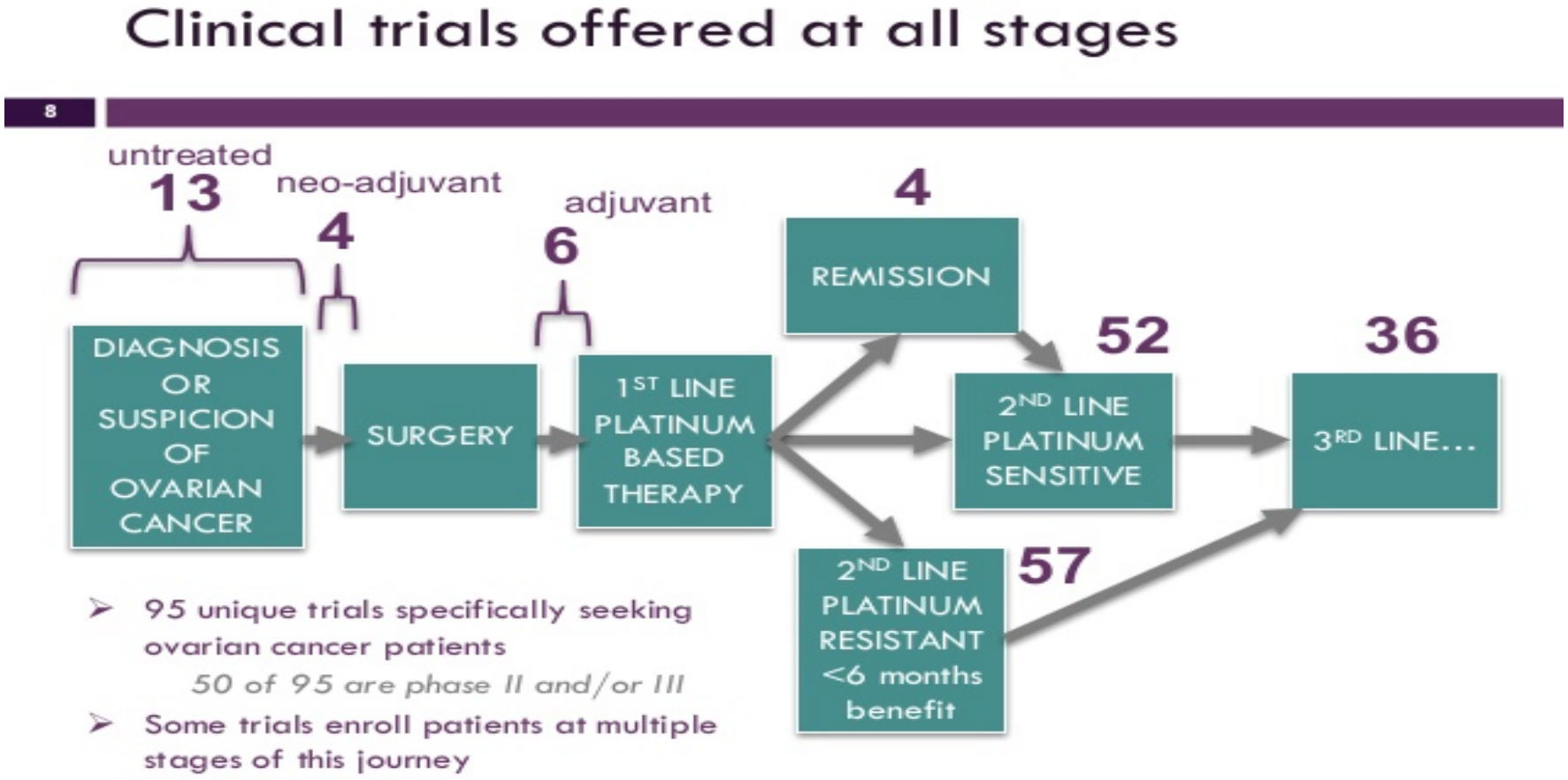
Who pays for Clinical Trials?



Are there Many Clinical Trials?

- 50 Phase II or III studies specifically for ovarian cancer
- 45 Phase I trials specifically for ovarian cancer patients
- Hundreds of general Phase 1 trials

Are there Many Clinical Trials?



Pharma / Private Industry

Immunotherapy Studies

- **Compass Oncology**
  - 1st line (with Carbo / Taxol)
    - additional treatment and / or maintenance
  - ATEZOLIZUMAB (open)
  - AVELUMAB IN COMBINATION WITH (PARP) INHIBITOR TALAZOPARIB (opening soon)

Other immunotherapy

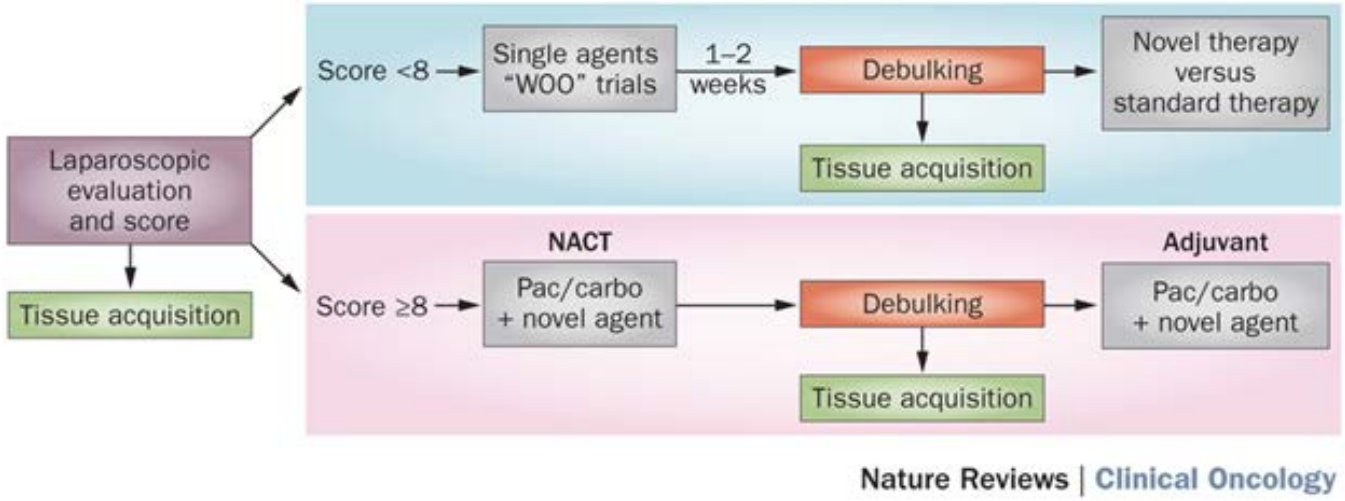
- **Cancer vaccines:**
  - **Vaccines are substances put into the body to start an immune response to help prevent or treat cancer.**

Large Research Programs

- The Cancer Genome Atlas (**TCGA**)
- **MATCH** – Molecular Analysis for Therapy Choice Trial
    - 2 % of targets have ‘actionable drugs’
- ‘**Actionable Drugs’ --***Multicenter Ovarian Cancer Research—*
    - Angiogenesis Studies = 6
    - Parp Inhibitors = 9
    - Immunomodulators = 2
    - Antibody drug conjugates = 1
    - 38 New drugs in the pipeline through Pharma

Sharing and Integrating the Latest Research

- MD Anderson Cancer Center Moon Shot Program (2012)
- APOLLO – adaptive patient-oriented platform longitudinal learning and optimization.
    - Integrating clinical information with translational data from research to accelerate adaptation of the newest information available in real times.
- Anderson Algorithm



Nature Reviews | Clinical Oncology

Early Detection

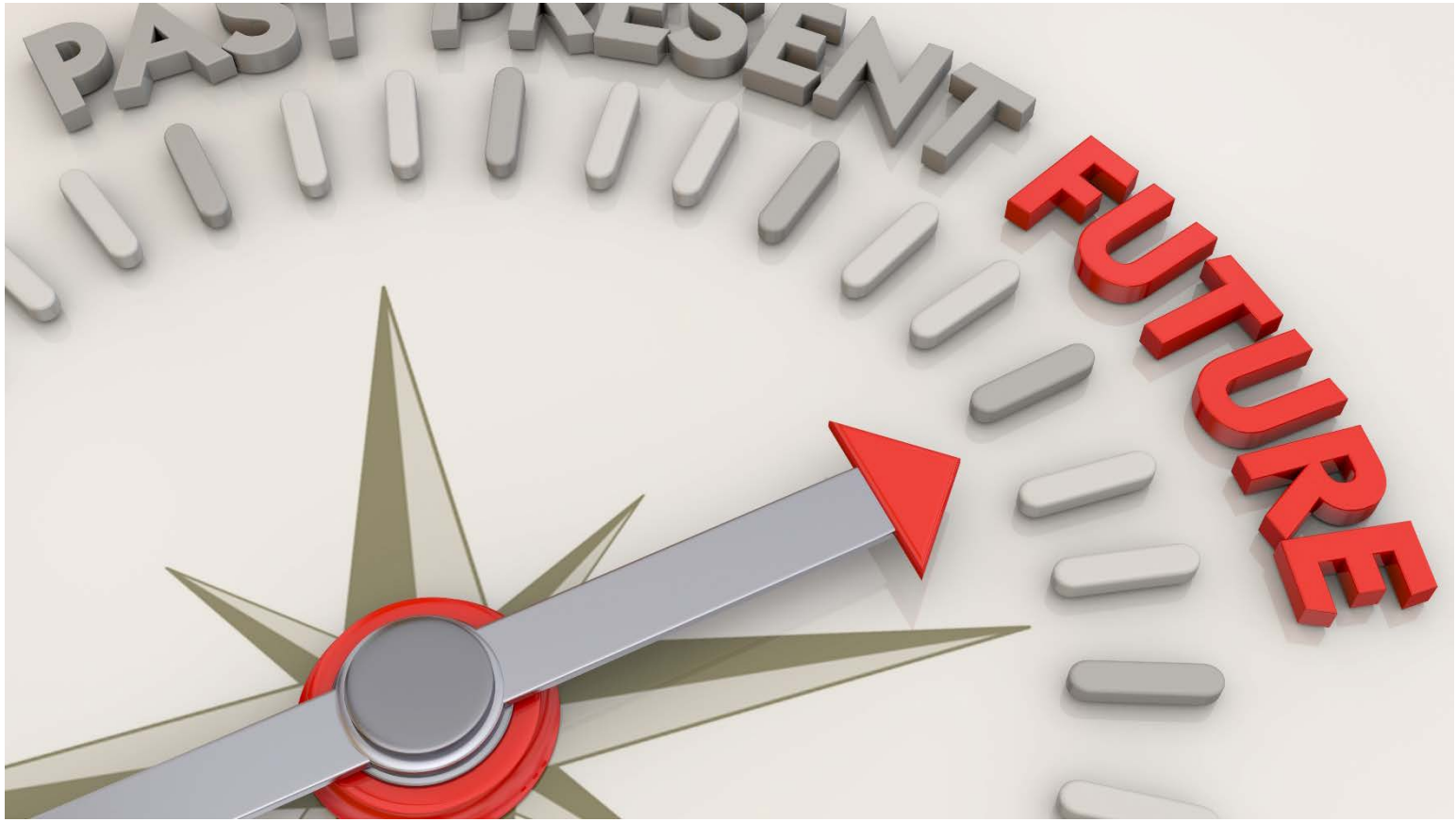
- 6 – Develop Early Detection Strategies
  - extend beyond *current* imaging modalities and biomarkers
    - CA125 and Transvaginal Ultrasound have not had substantial impact on mortality from ovarian cancer in the general or high risk populations.
  - New methods of ***cytology*** (pap, endometrial) to detect pre cancer or early cancer
  - New ***Blood tests*** to detect new, unique proteins or combination of proteins

Conclusion--Some Key Messages that are ready for D&I

- Current methods for early detection in the general or high-risk population do not have substantial impact on mortality.
- Proven preventive strategies exist.
- All women with invasive ovarian cancer should receive germline genetic testing.
- Genetic counseling and testing for the first-degree relatives of women with a hereditary cancer syndrome or germline mutation.
- Uniform implementation of the standard of care and the inclusion of supportive care across the survivorship trajectory.

Conclusion

- **Major changes are occurring in Cancer Care**
  - ***Prevention → Early Detection →Primary Treatment → Recurrent / Chronic Disease***
- **Novel approaches to treating cancer**
  - ***Research into many different approaches to cancer***
  - ***Personalized Medicine—***
    - developing treatments based on the individual and the cancer itself
- **Focus on Quality of Life**
  - **Treatment tolerance and toxicities**
  - **Emotional / social aspects of cancer diagnosis**
  - **Palliative Care and End of Life**



Thank you