Oncology for the General Practitioner

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Faculty of Health Sciences

Fakulteit Gesondheidswetenskappe
Lefapha la Disaense tša Maphelo

Topics

Non surgical modalities and treatments

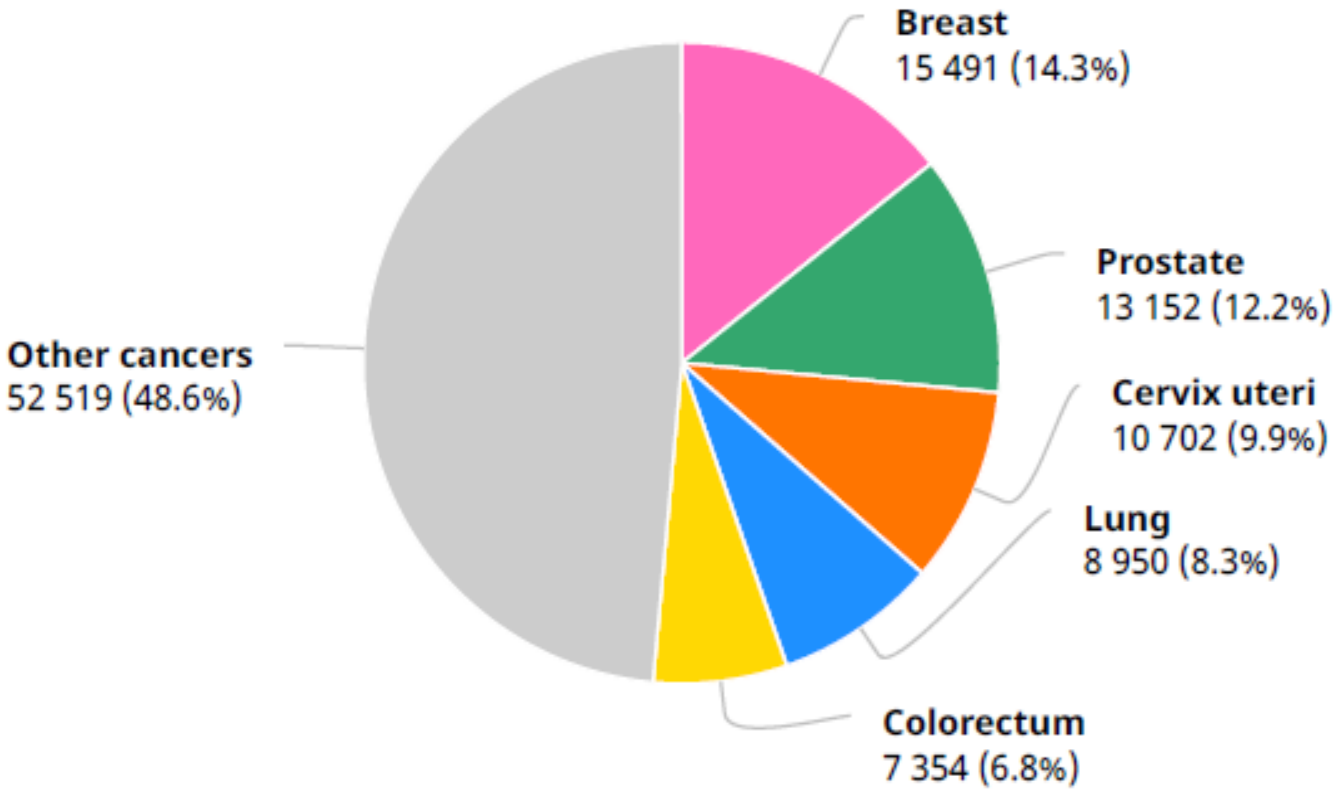
- Cancer in South Africa
- Diagnostic imaging modalities and rationale
- Systemic therapies
  - Cancer genomics and role in guiding treatment
  - Targeted therapies
  - Immunotherapies
- Radiotherapy
  - Modalities
  - Improvements of technology

Topics

- Treatment approaches in common cancers
  - Breast cancer
  - Cervical cancer
  - Prostate cancer
  - Lung cancer
  - Colorectal cancer
  - Oligometastatic disease

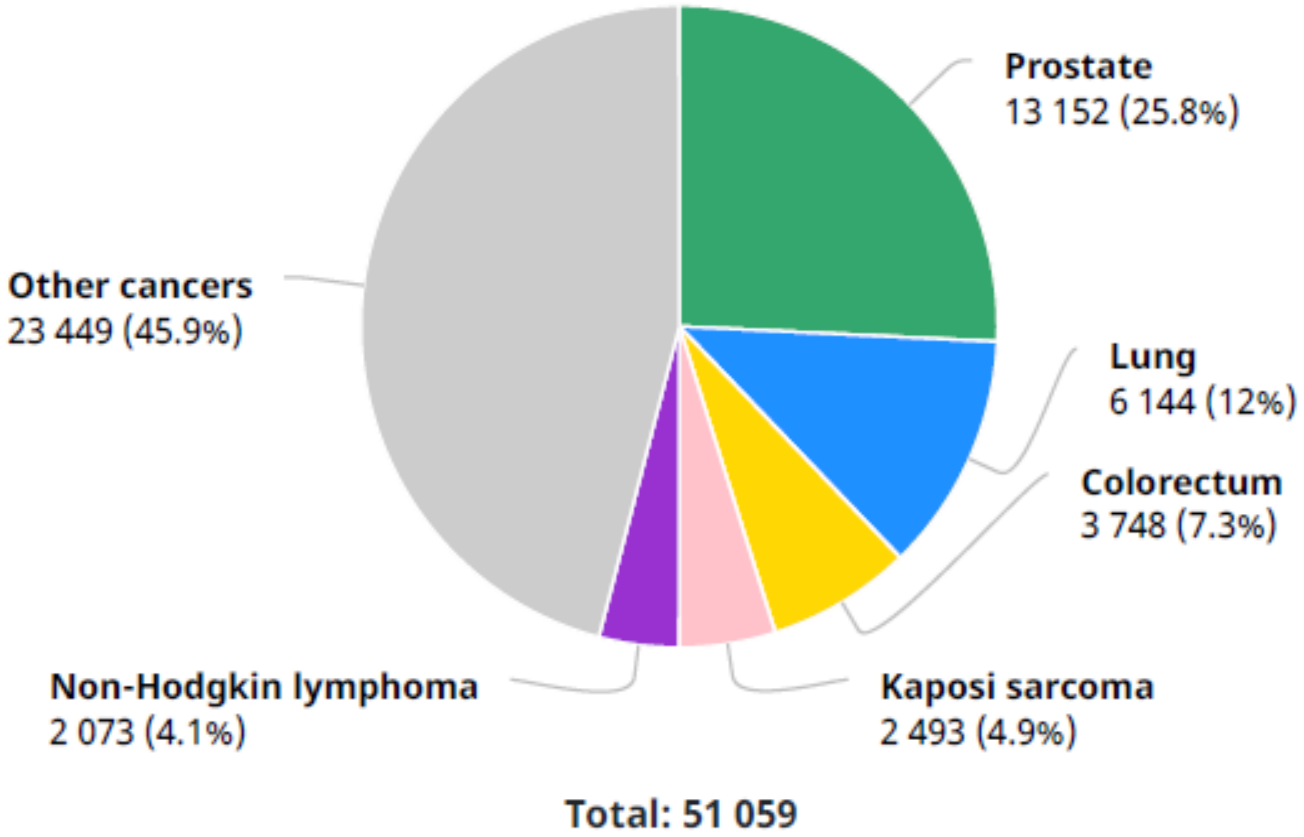
- Oncological emergencies

Number of new cases in 2020, both sexes, all ages



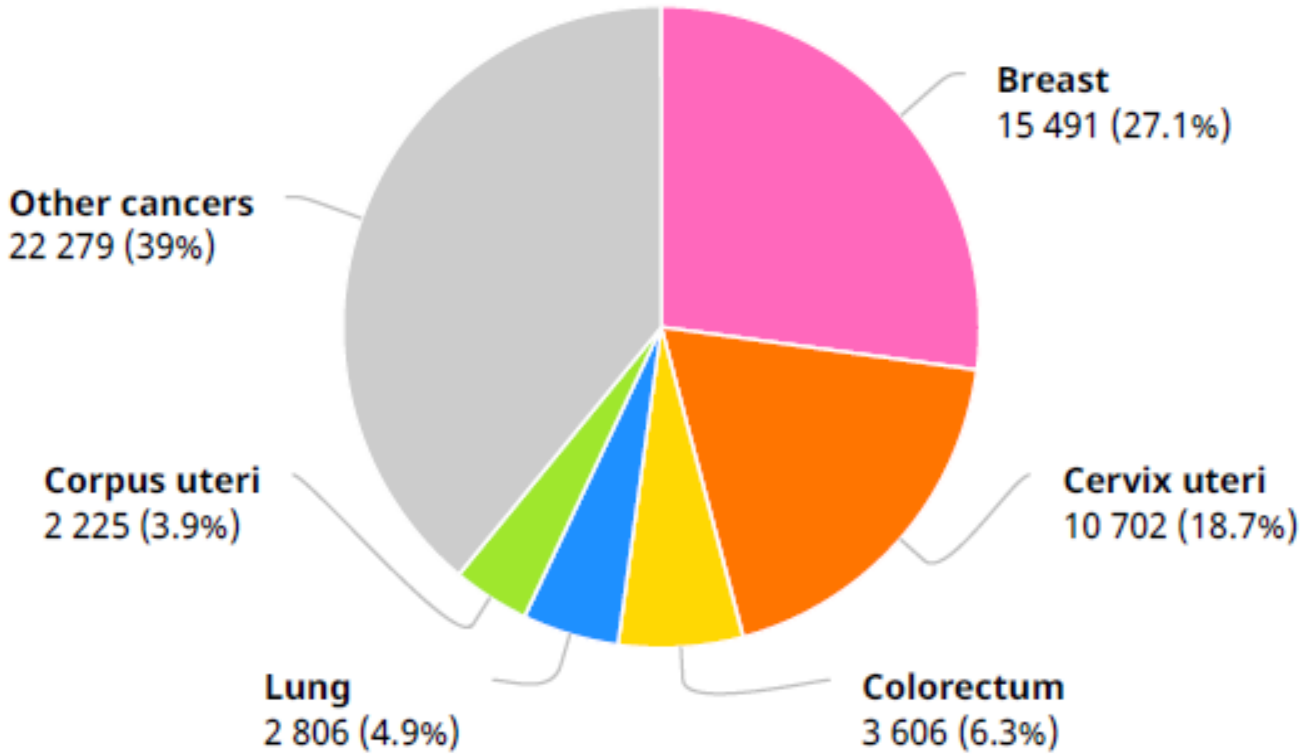
Total: 108 168

Number of new cases in 2020, males, all ages



Total: 51 059

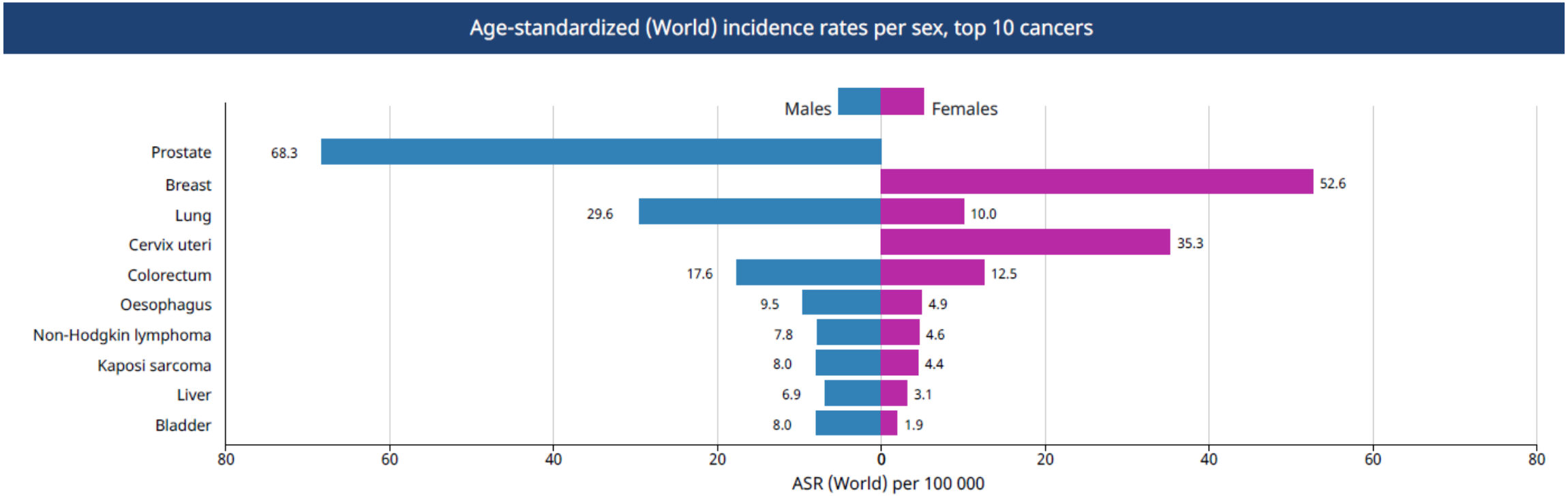
Number of new cases in 2020, females, all ages



Incidence, Mortality and Prevalence by cancer site										
	New cases				Deaths				5-year prevalence (all ages)	
Cancer	Number	Rank	(%)	Cum.risk	Number	Rank	(%)	Cum.risk	Number	Prop. (per 100 000)
Breast	15 491	1	14.3	5.60	4 664	3	8.2	1.74	47 818	158.90
Prostate	13 152	2	12.2	7.87	3 896	4	6.9	2.27	39 863	136.44
Cervix uteri	10 702	3	9.9	3.58	5 870	2	10.3	2.10	26 486	88.01
Lung	8 950	4	8.3	2.21	7 730	1	13.6	1.94	9 709	16.37
Kaposi sarcoma	3 984	5	3.7	0.50	723	17	1.3	0.09	11 010	18.56
Colon	3 657	6	3.4	0.86	2 053	7	3.6	0.47	8 293	13.98
Non-Hodgkin lymphoma	3 500	7	3.2	0.58	1 797	9	3.2	0.32	9 630	16.24

Incidence and mortality rate

Age standardised rates



Management principles

physical exam

biopsy

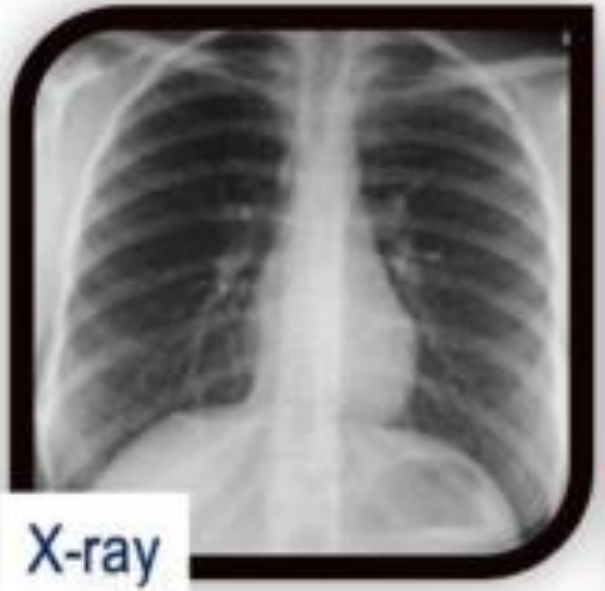
x-ray

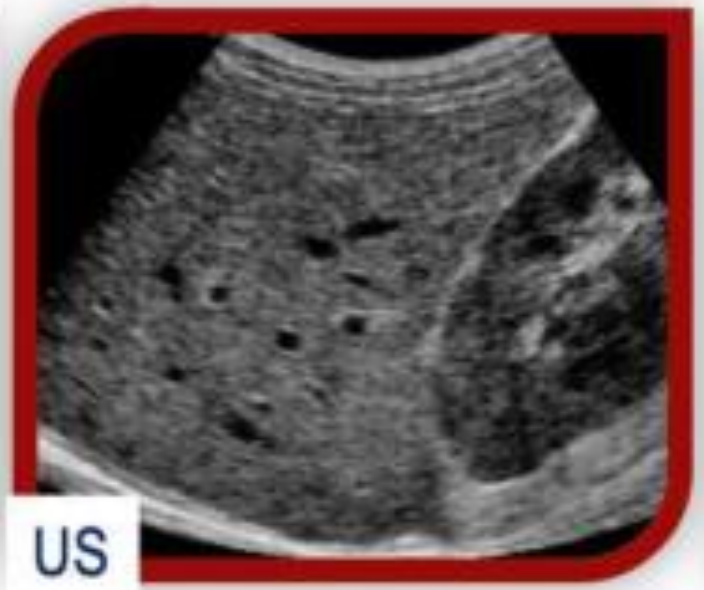
CT and MRI

radionuclide bone scan

PET scan

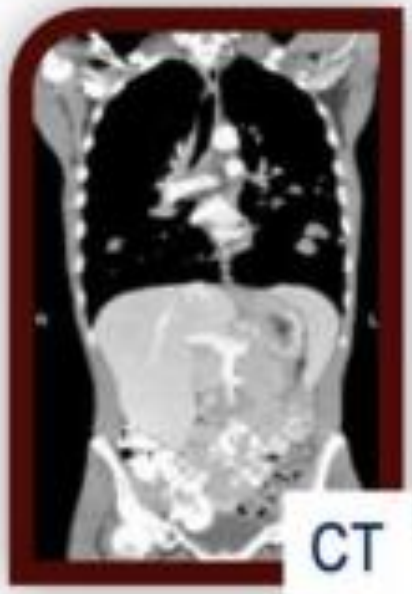
Anatomy Function

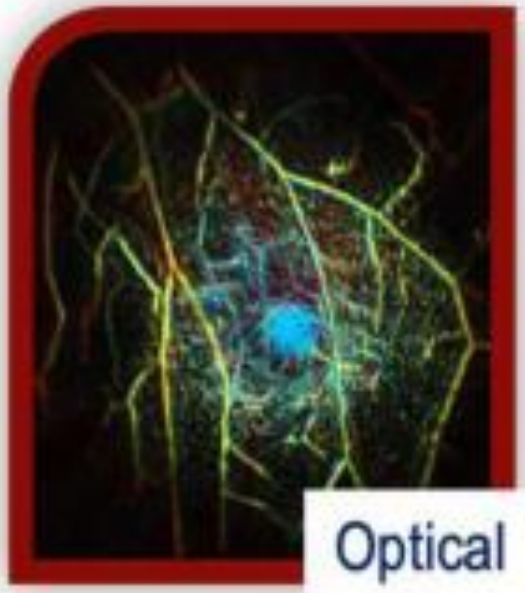

X-ray

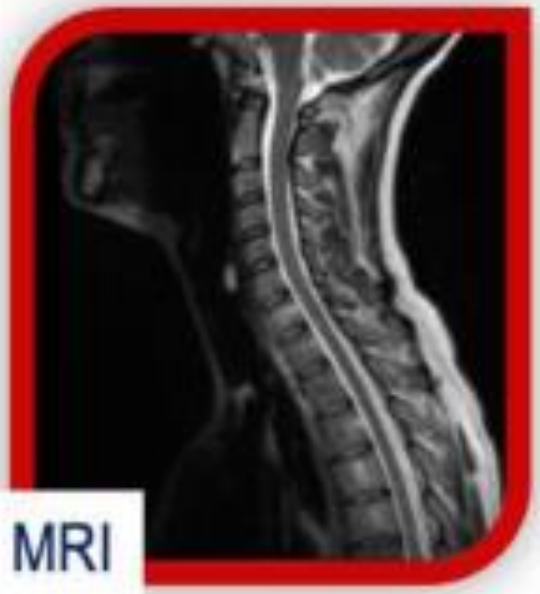

US


Scinti

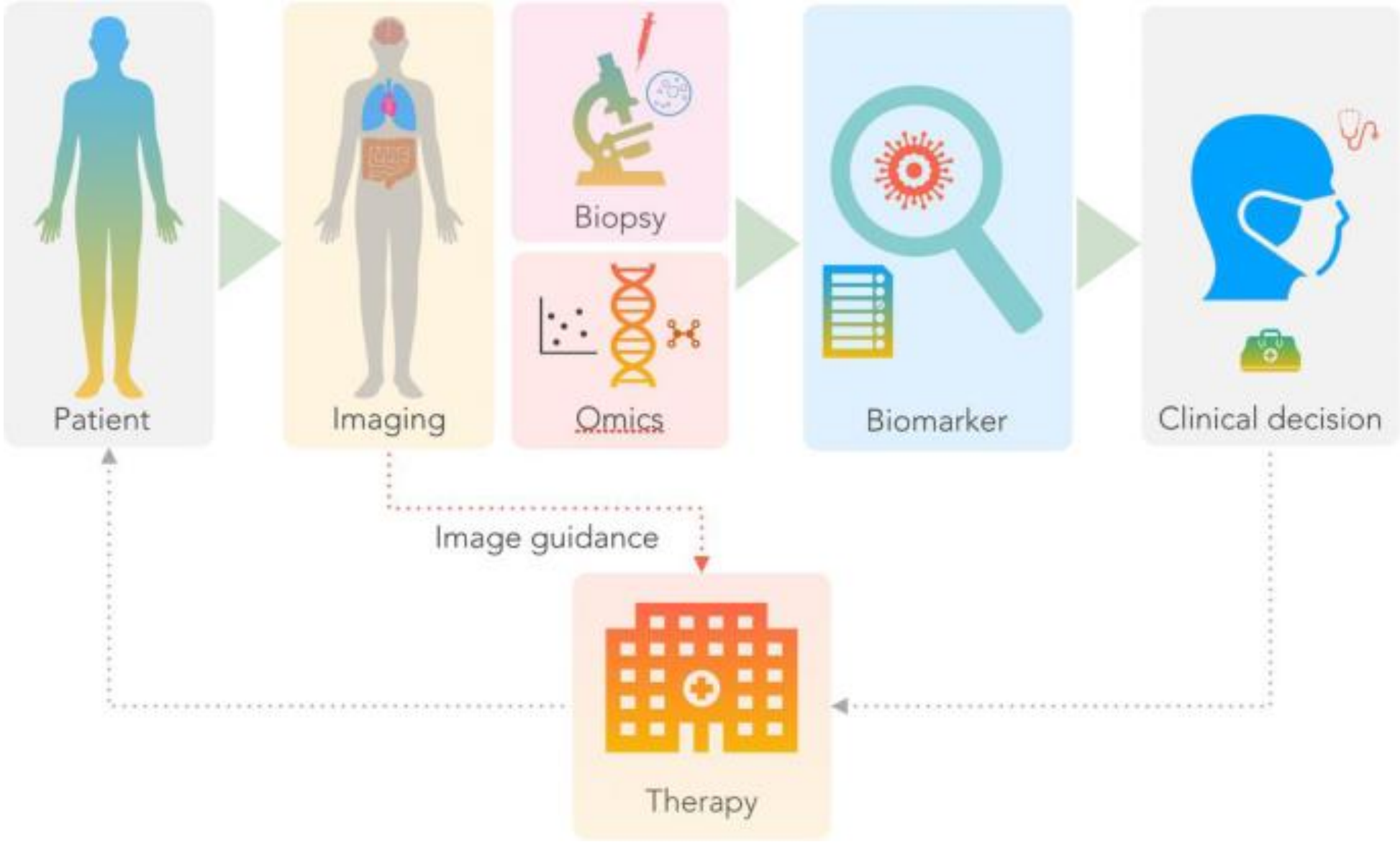

PET

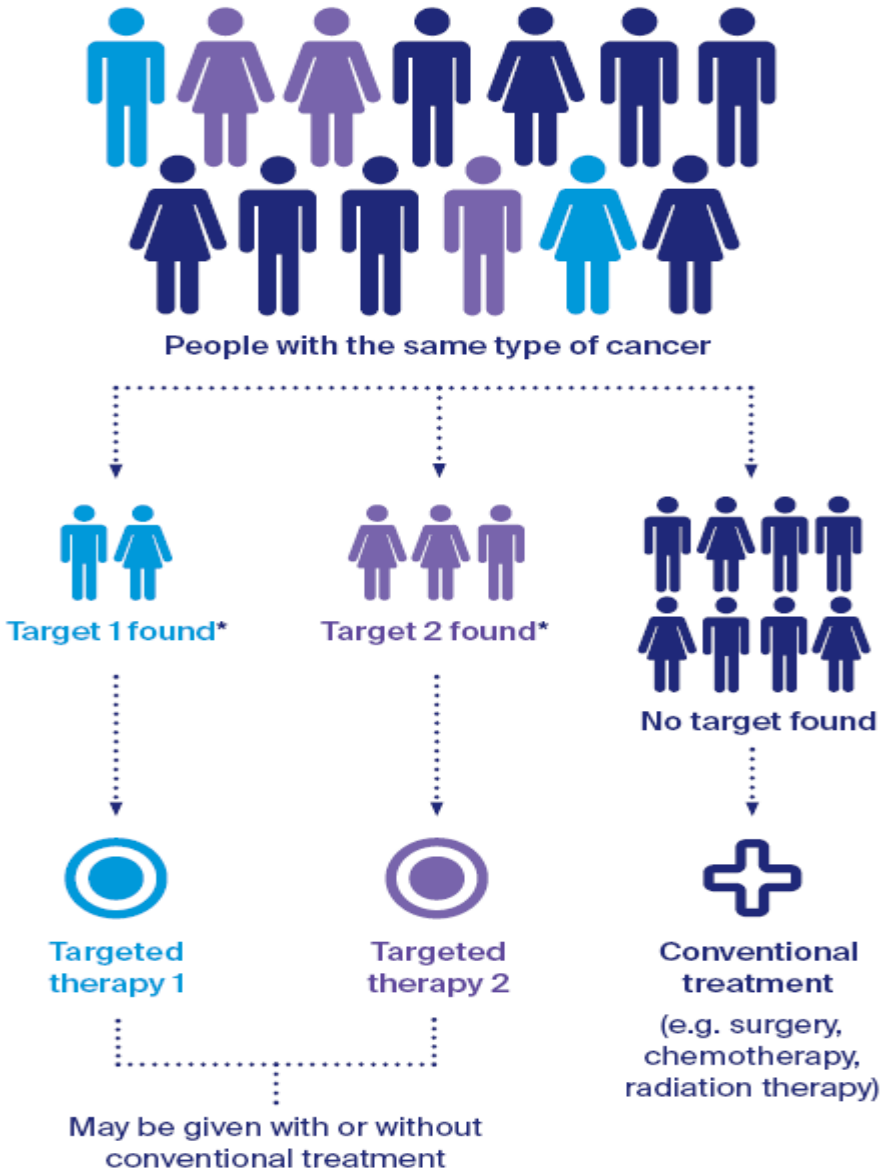

CT

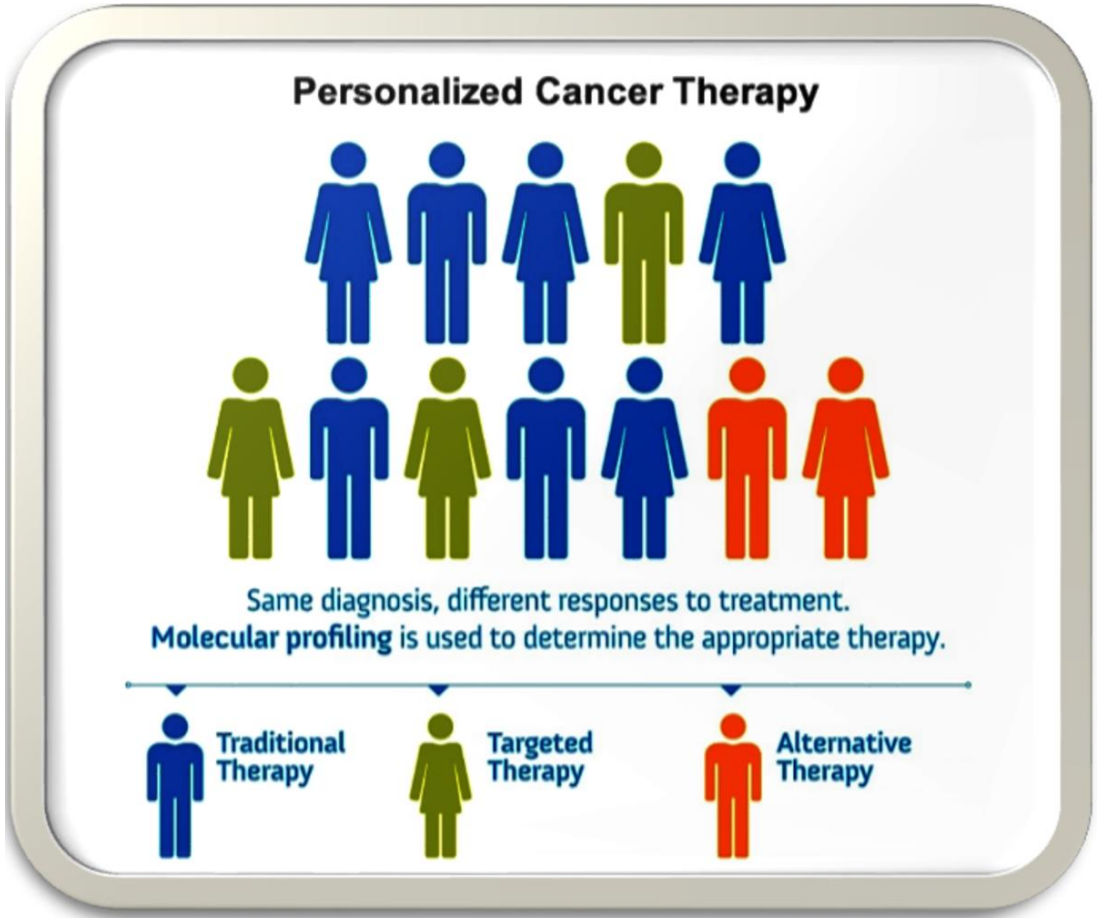

Optical

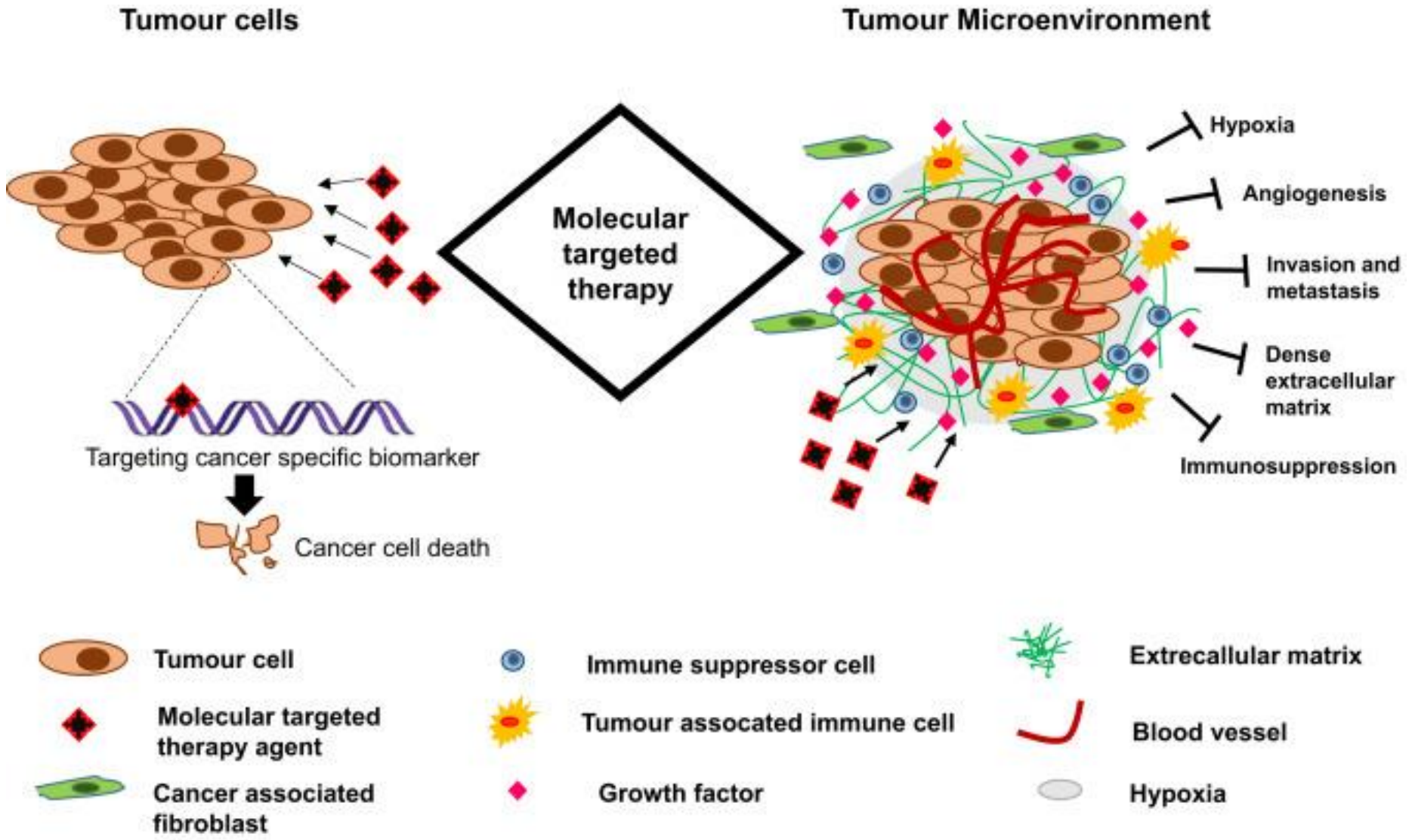

MRI

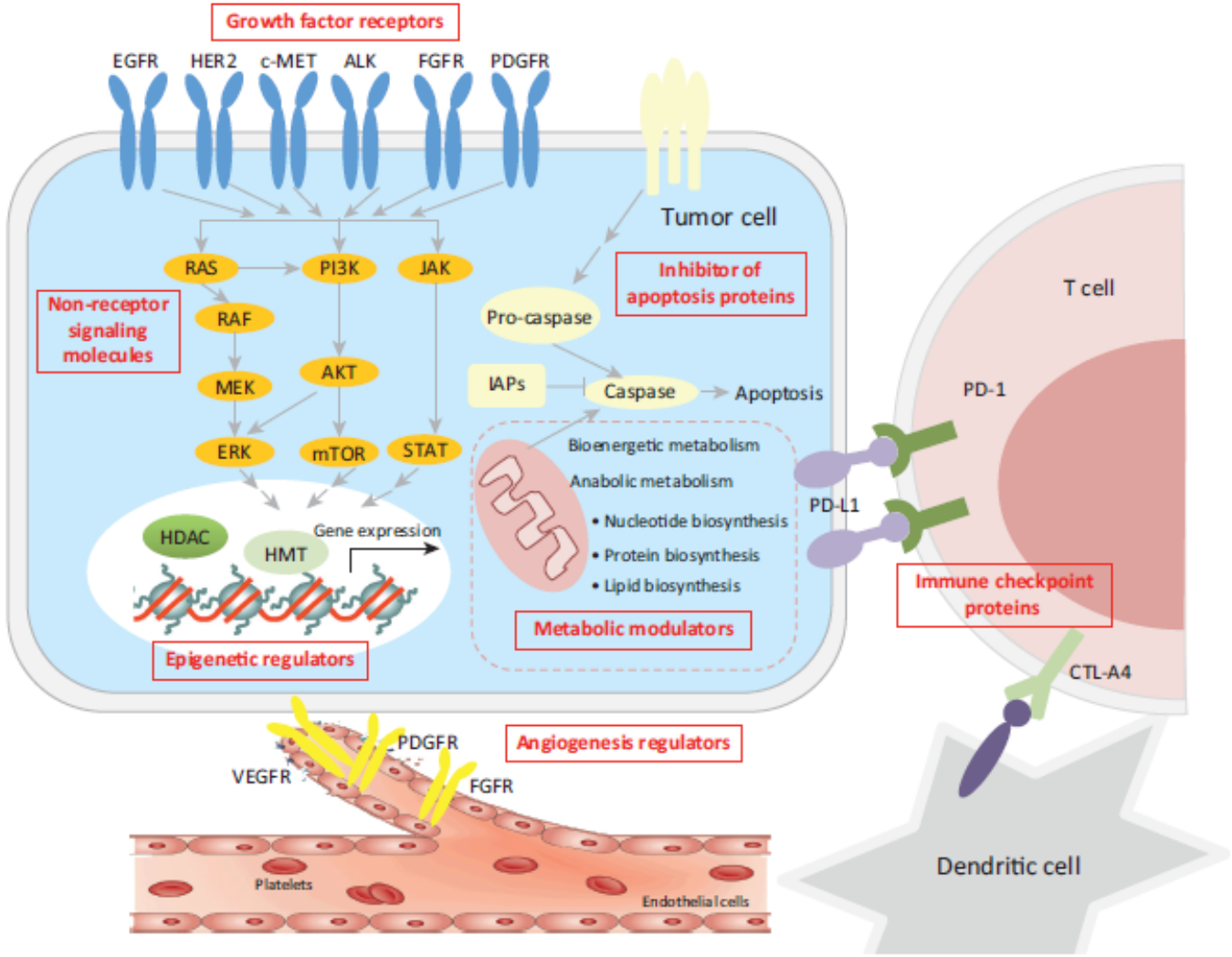

SPECT

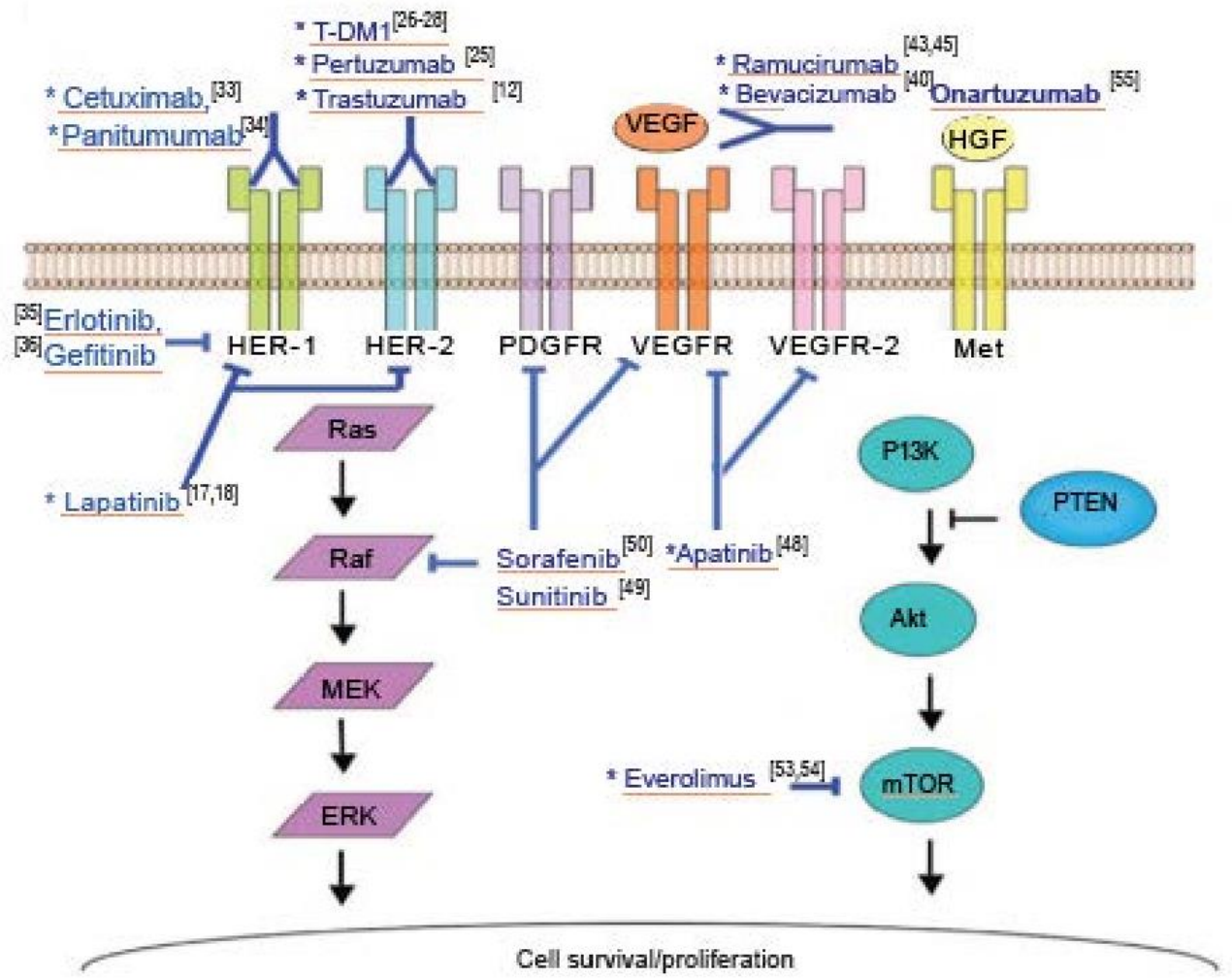

Patient
Imaging
Biopsy
Omics
Biomarker
Clinical decision
Image guidance
Therapy

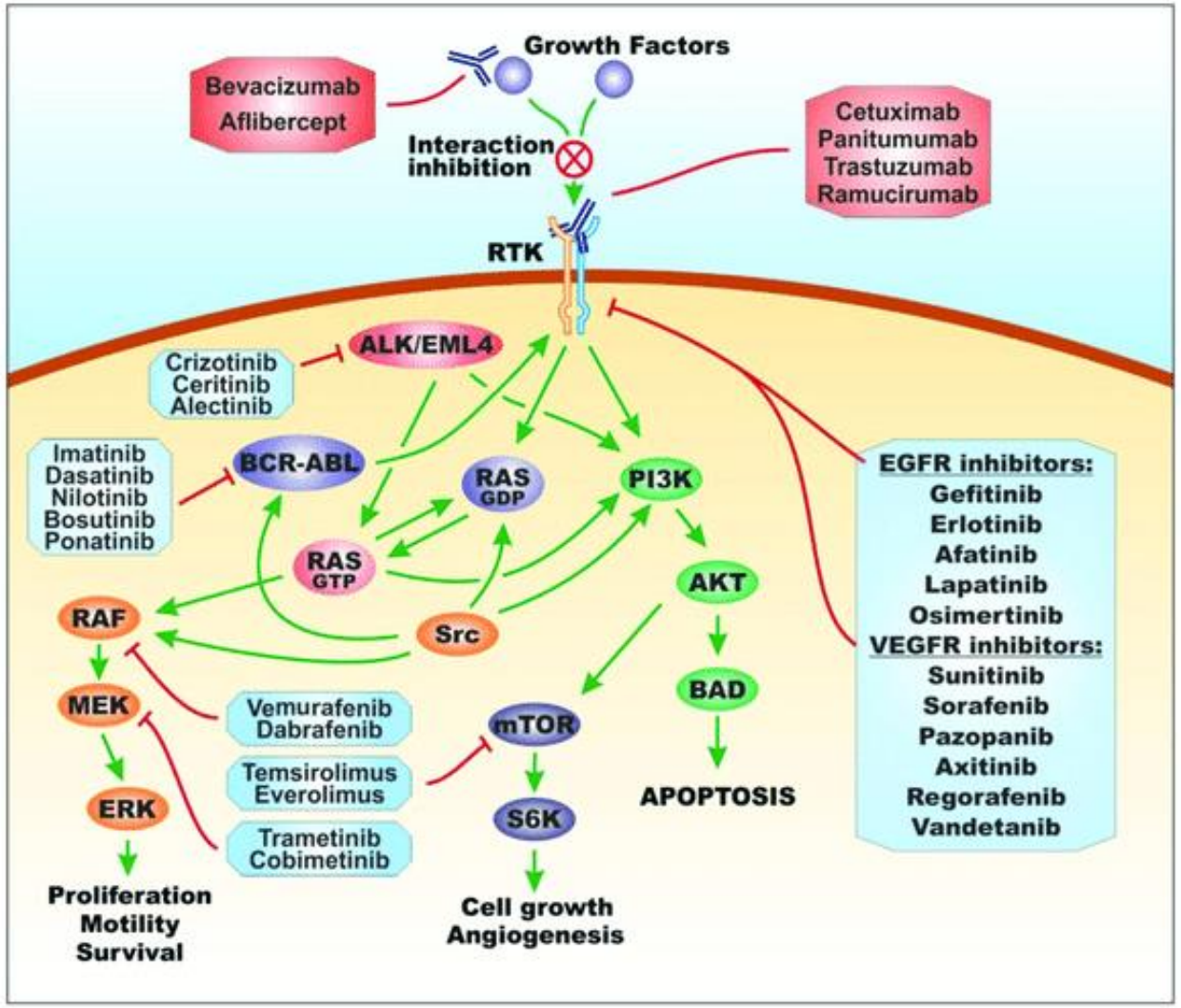

People with the same type of cancer
Target 1 found*
Target 2 found*
No target found
Targeted therapy 1
Targeted therapy 2
Conventional treatment
(e.g. surgery, chemotherapy, radiation therapy)
May be given with or without conventional treatment


Personalized Cancer Therapy
Same diagnosis, different responses to treatment.
Molecular profiling is used to determine the appropriate therapy.
Traditional Therapy
Targeted Therapy
Alternative Therapy


Tumour cells
Tumour Microenvironment
Molecular targeted therapy
Hypoxia
Angiogenesis
Invasion and metastasis
Dense extracellular matrix
Immunosuppression
Targeting cancer specific biomarker
Cancer cell death
Tumour cell
Molecular targeted therapy agent
Cancer associated fibroblast
Immune suppressor cell
Tumour assocated immune cell
Growth factor
Extrecallular matrix
Blood vessel
Hypoxia


Growth factor receptors
EGFR
HER2
c-MET
ALK
FGFR
PDGFR
Tumor cell
RAS
PI3K
JAK
RAF
MEK
AKT
ERK
mTOR
STAT
Non-receptor signaling molecules
Inhibitor of apoptosis proteins
Pro-caspase
IAPs
Caspase
Apoptosis
Bioenergetic metabolism
Anabolic metabolism
• Nucleotide biosynthesis
• Protein biosynthesis
• Lipid biosynthesis
Metabolic modulators
HDAC
HMT
Gene expression
Epigenetic regulators
T cell
PD-1
PD-L1
Immune checkpoint proteins
CTL-A4
Dendritic cell
PDGFR
VEGFR
FGFR
Angiogenesis regulators
Platelets
Endothelial cells
TRENDS in Pharmacological Sciences


* T-DM1[26-28]
* Pertuzumab [25]
* Trastuzumab [12]
* Cetuximab, [33]
*Panitumumab[34]
* Ramucirumab [43,45]
* Bevacizumab [40]
Onartuzumab [55]
VEGF
HGF
[35]Erlotinib,
[36]Gefitinib
HER-1
HER-2
PDGFR
VEGFR
VEGFR-2
Met
Ras
P13K
PTEN
* Lapatinib [17,18]
Raf
Sorafenib[50]
Sunitinib [49]
*Apatinib[48]
Akt
MEK
* Everolimus [53,54]
mTOR
ERK
Cell survival/proliferation


Growth Factors
Bevacizumab
Aflibercept
Interaction inhibition
Cetuximab
Panitumumab
Trastuzumab
Ramucirumab
RTK
ALK/EML4
Crizotinib
Ceritinib
Alectinib
Imatinib
Dasatinib
Nilotinib
Bosutinib
Ponatinib
BCR-ABL
RAS GDP
PI3K
RAS GTP
AKT
RAF
Src
BAD
MEK
Vemurafenib
Dabrafenib
mTOR
Temsirolimus
Everolimus
APOPTOSIS
ERK
S6K
Trametinib
Cobimetinib
Proliferation
Motility
Survival
Cell growth
Angiogenesis
EGFR inhibitors:
Gefitinib
Erlotinib
Afatinib
Lapatinib
Osimertinib
VEGFR inhibitors:
Sunitinib
Sorafenib
Pazopanib
Axitinib
Regorafenib
Vandetanib

MOLECULAR DIAGNOSTICS IN ONCOLOGY

HEREDITARY CANCER SYNDROMES

ASSAYS

- RECURRENT MUTATIONS (PCR)
- SINGLE-GENE ANALYSIS (SANGER SEQUENCING, MLPA)
- MULTIGENE PANELS (NGS)
- WHOLE EXOME SEQUENCING

CANCER PATIENTS

- RISK OF 2ND MALIGNANCY
- CHOICE OF TREATMENT

HEALTHY PEOPLE

- IDENTIFICATION OF SUBJECTS AT-RISK

PREDICTIVE MARKERS

ASSAYS

- DNA
- RNA
- PROTEINS
- CELLS
- TISSUE SLICES
- PDXs

MOLECULAR TARGETS

- HER2
- EGFR-MUT
- BRAF-MUT
- ALK
- ROS

TUMOR PHENOTYPES

- MSI-H
- BRCAness
- MUTATION BURDEN

CIRCULATING TUMOR FRAGMENTS

ASSAYS

- CTCs
- ctDNA
- RNA
- PROTEINS

CANCER PATIENTS

- CONTROL OF TUMOR ERADICATION
- MONITORING OF TUMOR BURDEN
- CHOICE OF THERAPY

HEALTHY PEOPLE

- EARLY DIAGNOSIS

CARCINOMAS OF UNKNOWN PRIMARY

ASSAYS

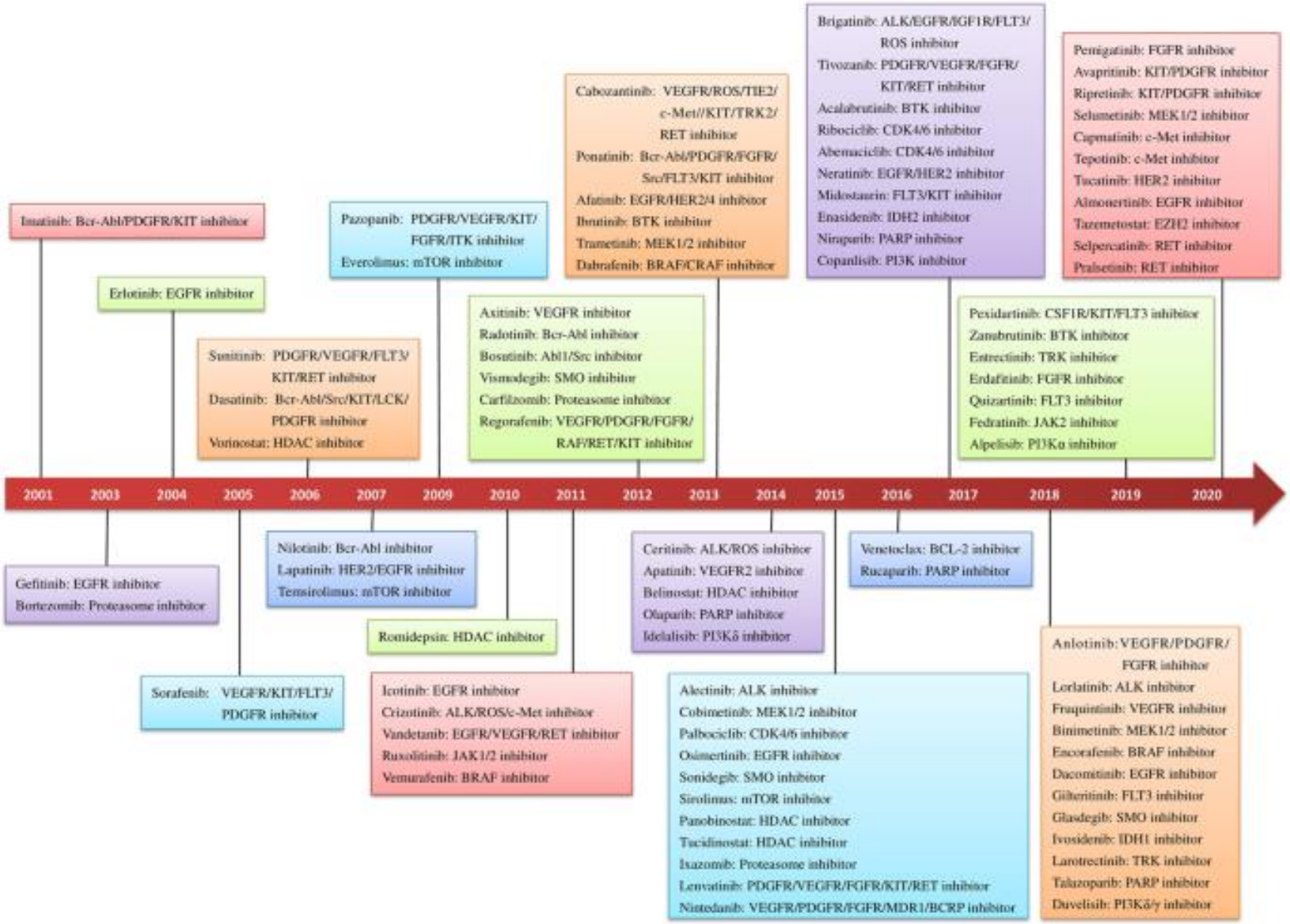
- SINGLE MARKERS
- INTEGRATIVE ASSAYS

TISSUE-SPECIFIC MARKERS

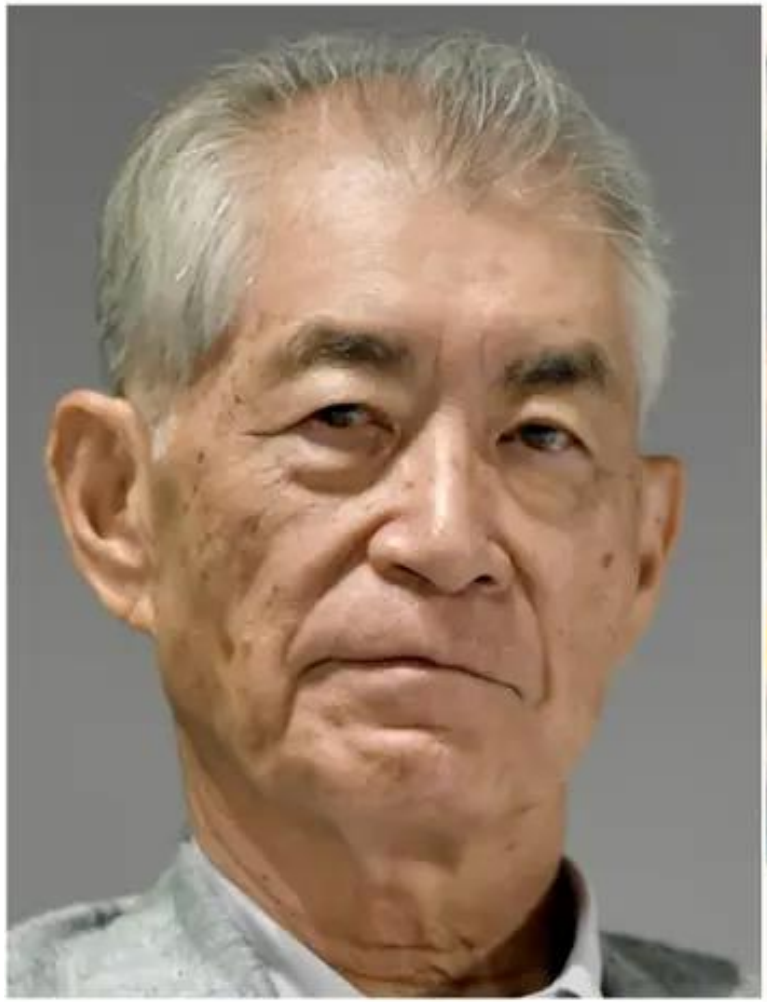
- RNA
- PROTEINS

TUMOR-SPECIFIC MARKERS

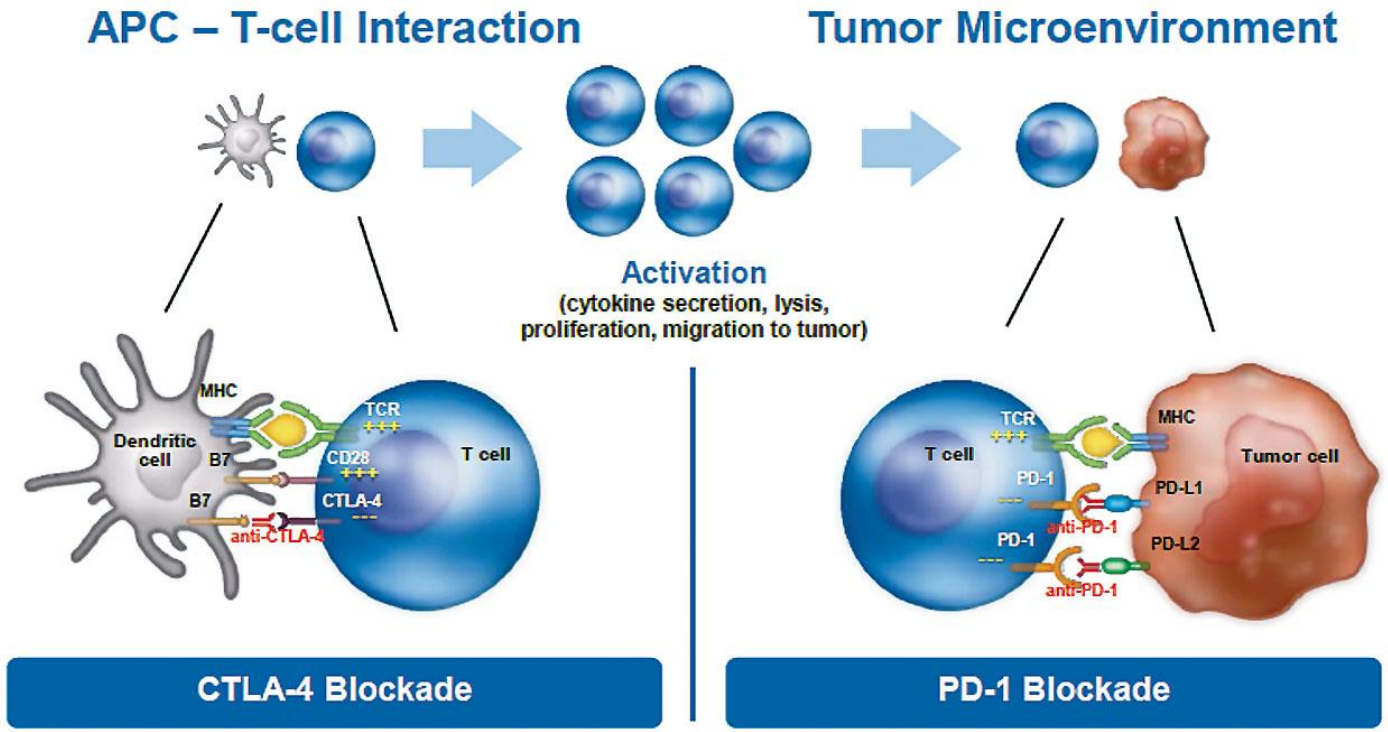
- POINT MUTATIONS
- GENE REARRANGEMENTS
- COPY NUMBER VARIATIONS


Imatinib: Bcr-Abl/PDGFR/KIT inhibitor
Erlotinib: EGFR inhibitor
Sunitinib: PDGFR/VEGFR/FLT3/ KIT/RET inhibitor
Dasatinib: Bcr-Abl/Src/KIT/LCK/ PDGFR inhibitor
Vorinostat: HDAC inhibitor
Pazopanib: PDGFR/VEGFR/KIT/ FGFR/ITK inhibitor
Everolimus: mTOR inhibitor
Axitinib: VEGFR inhibitor
Radotinib: Bcr-Abl inhibitor
Bosutinib: Abl1/Src inhibitor
Vismodegib: SMO inhibitor
Carfilzomib: Proteasome inhibitor
Regorafenib: VEGFR/PDGFR/FGFR/ RAF/RET/KIT inhibitor
Cabozantinib: VEGFR/ROS/TIE2/ c-Met//KIT/TRK2/ RET inhibitor
Ponatinib: Bcr-Abl/PDGFR/FGFR/ Src/FLT3/KIT inhibitor
Afatinib: EGFR/HER2/4 inhibitor
Ibrutinib: BTK inhibitor
Trametinib: MEK1/2 inhibitor
Dabrafenib: BRAF/CRAF inhibitor
Brigatinib: ALK/EGFR/IGF1R/FLT3/ ROS inhibitor
Tivozanib: PDGFR/VEGFR/FGFR/ KIT/RET inhibitor
Acalabrutinib: BTK inhibitor
Ribociclib: CDK4/6 inhibitor
Abemaciclib: CDK4/6 inhibitor
Neratinib: EGFR/HER2 inhibitor
Midostaurin: FLT3/KIT inhibitor
Enasidenib: IDH2 inhibitor
Niraparib: PARP inhibitor
Copanlisib: PI3K inhibitor
Pemigatinib: FGFR inhibitor
Avapritinib: KIT/PDGFR inhibitor
Ripretinib: KIT/PDGFR inhibitor
Selumetinib: MEK1/2 inhibitor
Capmatinib: c-Met inhibitor
Tepotinib: c-Met inhibitor
Tucatinib: HER2 inhibitor
Almonertinib: EGFR inhibitor
Tazemetostat: EZH2 inhibitor
Selpercatinib: RET inhibitor
Pralsetinib: RET inhibitor
Pexidartinib: CSF1R/KIT/FLT3 inhibitor
Zanubrutinib: BTK inhibitor
Entrectinib: TRK inhibitor
Erdafitinib: FGFR inhibitor
Quizartinib: FLT3 inhibitor
Fedratinib: JAK2 inhibitor
Alpelisib: PI3Kα inhibitor
2001
2003
2004
2005
2006
2007
2009
2010
2011
2012
2013
2014
2015
2016
2017
2018
2019
2020
Gefitinib: EGFR inhibitor
Bortezomib: Proteasome inhibitor
Sorafenib: VEGFR/KIT/FLT3/ PDGFR inhibitor
Nilotinib: Bcr-Abl inhibitor
Lapatinib: HER2/EGFR inhibitor
Temsirolimus: mTOR inhibitor
Romidepsin: HDAC inhibitor
Icotinib: EGFR inhibitor
Crizotinib: ALK/ROS/c-Met inhibitor
Vandetanib: EGFR/VEGFR/RET inhibitor
Ruxolitinib: JAK1/2 inhibitor
Vemurafenib: BRAF inhibitor
Ceritinib: ALK/ROS inhibitor
Apatinib: VEGFR2 inhibitor
Belinostat: HDAC inhibitor
Olaparib: PARP inhibitor
Idelalisib: PI3Kδ inhibitor
Alectinib: ALK inhibitor
Cobimetinib: MEK1/2 inhibitor
Palbociclib: CDK4/6 inhibitor
Osimertinib: EGFR inhibitor
Sonidegib: SMO inhibitor
Sirolimus: mTOR inhibitor
Panobinostat: HDAC inhibitor
Tucidinostat: HDAC inhibitor
Ixazomib: Proteasome inhibitor
Lenvatinib: PDGFR/VEGFR/FGFR/KIT/RET inhibitor
Nintedanib: VEGFR/PDGFR/FGFR/MDR1/BCRP inhibitor
Venetoclax: BCL-2 inhibitor
Rucaparib: PARP inhibitor
Anlotinib: VEGFR/PDGFR/ FGFR inhibitor
Lorlatinib: ALK inhibitor
Fruquintinib: VEGFR inhibitor
Binimetinib: MEK1/2 inhibitor
Encorafenib: BRAF inhibitor
Dacomitinib: EGFR inhibitor
Gilteritinib: FLT3 inhibitor
Glasdegib: SMO inhibitor
Ivosidenib: IDH1 inhibitor
Larotrectinib: TRK inhibitor
Talazoparib: PARP inhibitor
Duvelisib: PI3Kδ/γ inhibitor

Tasuku Honjo & James Allison



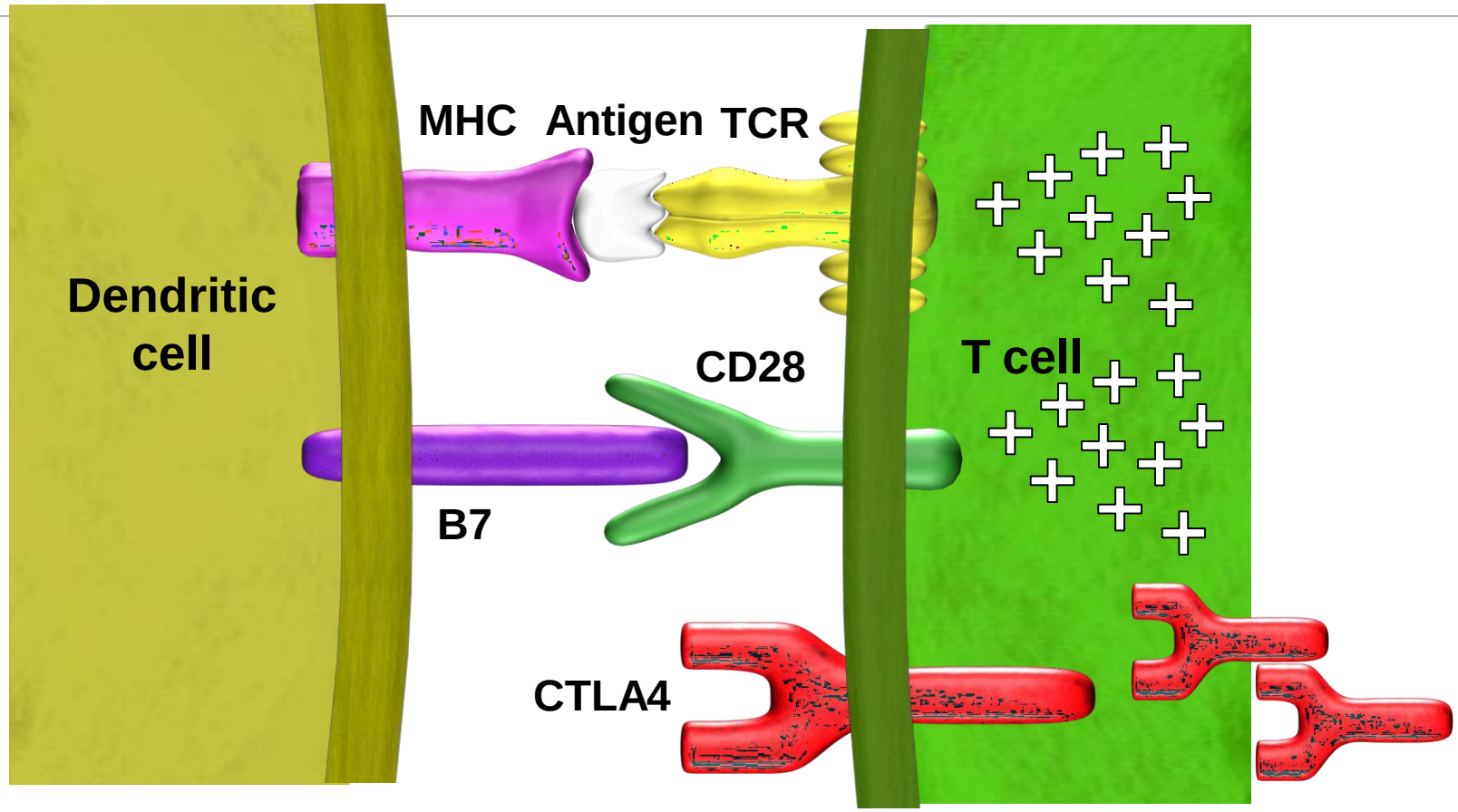
Immunotherapy



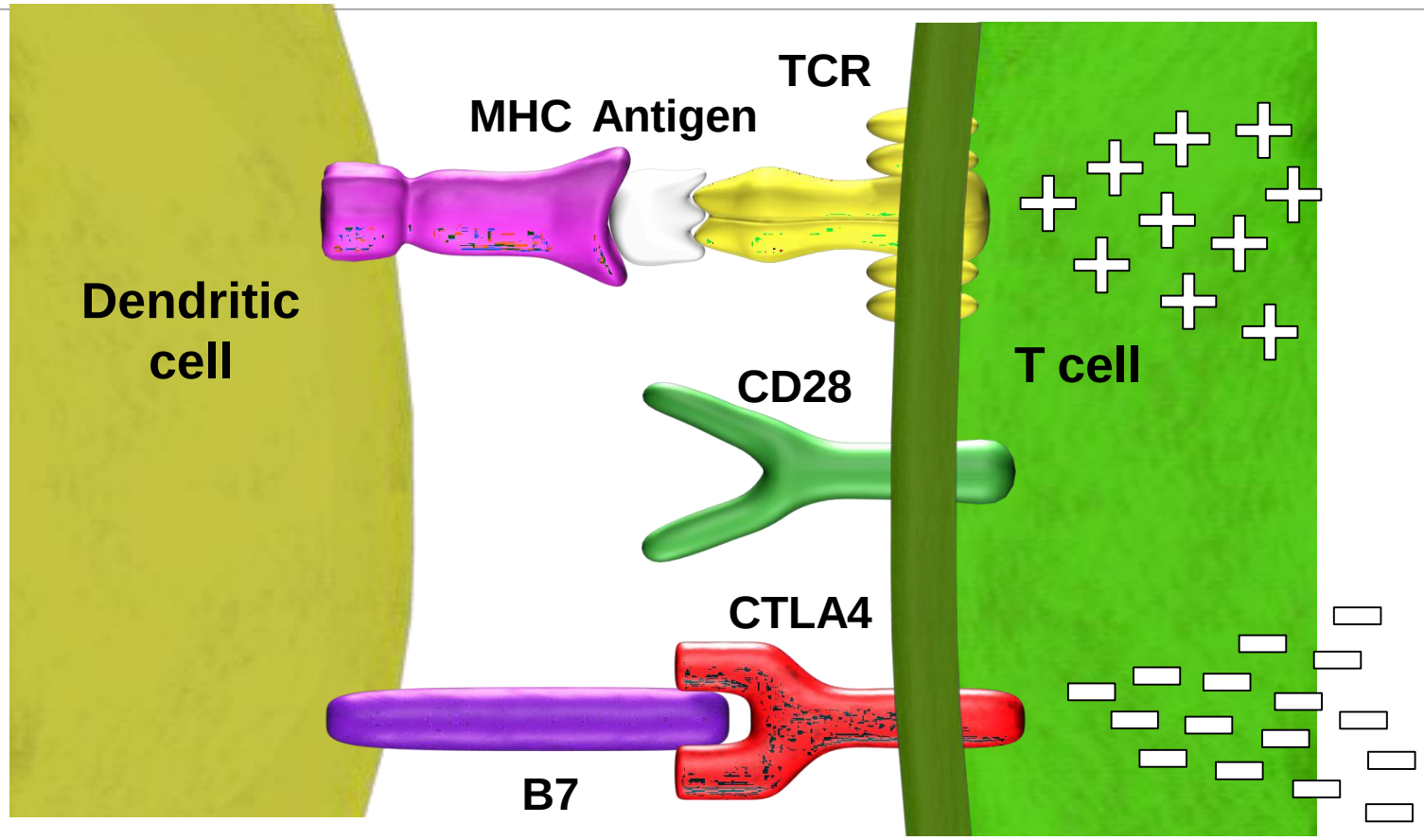
Immunotherapy

INTERFERON ALPHA 2B
1996
adjuvant treatment of melanoma
cytokine
effects on immune modulation, anti-proliferation as well as anti-angiogenesis.
significant toxicity which resulted in many patients not completing the full course of treatment.
INTERLEUKIN 2
metastatic disease
There has been considerable progress since then.

CTLA4 Receptors Are Up-Regulated Following T-Cell Activation



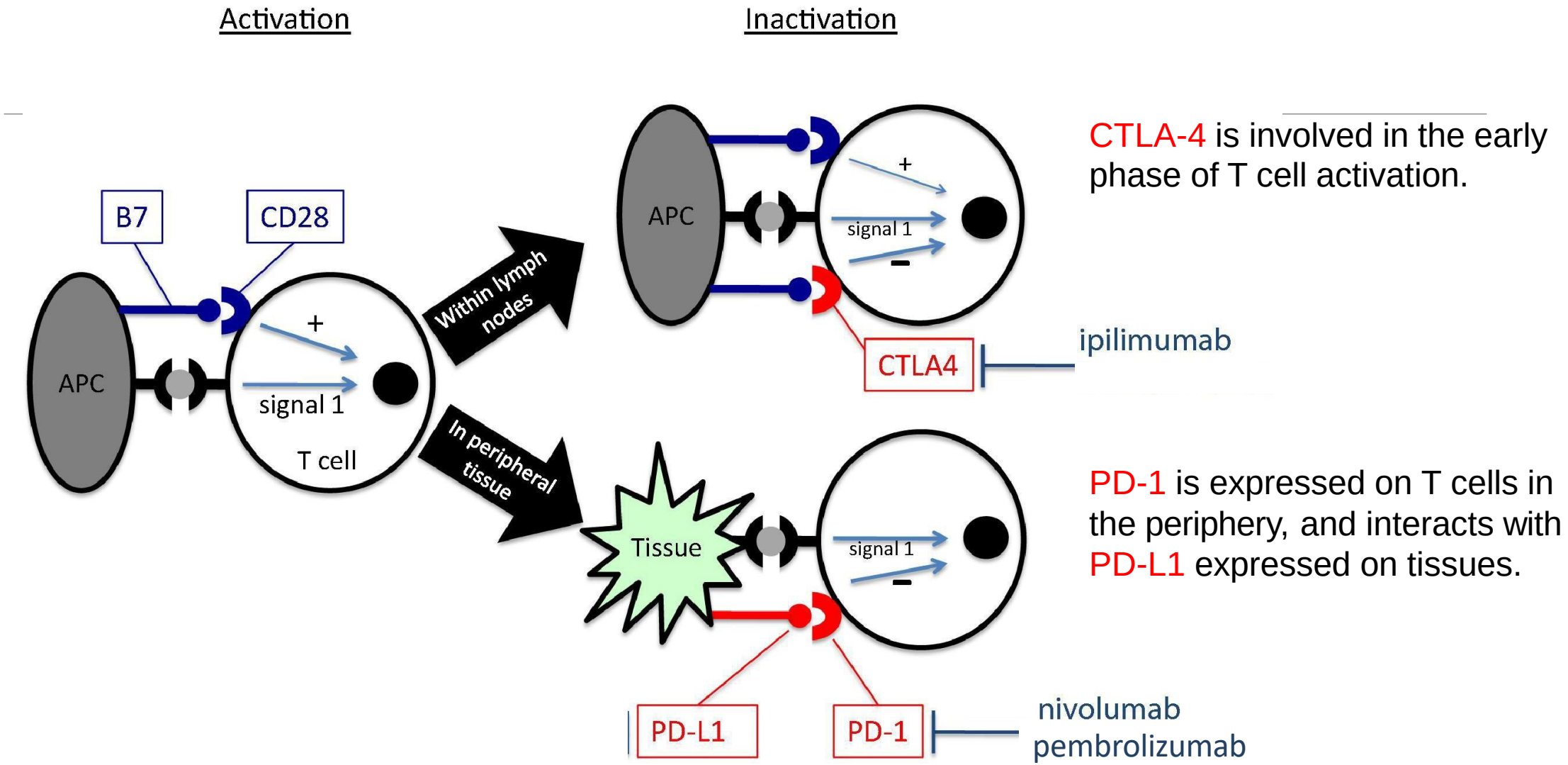
CTLA4 Negatively ModulatesT-Cell Activation



CTLA4 binds B7 with greater affinity than does CD28 and sends a negative signal to the T cell.

T cell regulation

T cell activation and inhibition relies upon co-stimulatory (+) or inhibitory signals (−) to prevent widespread autoimmunity



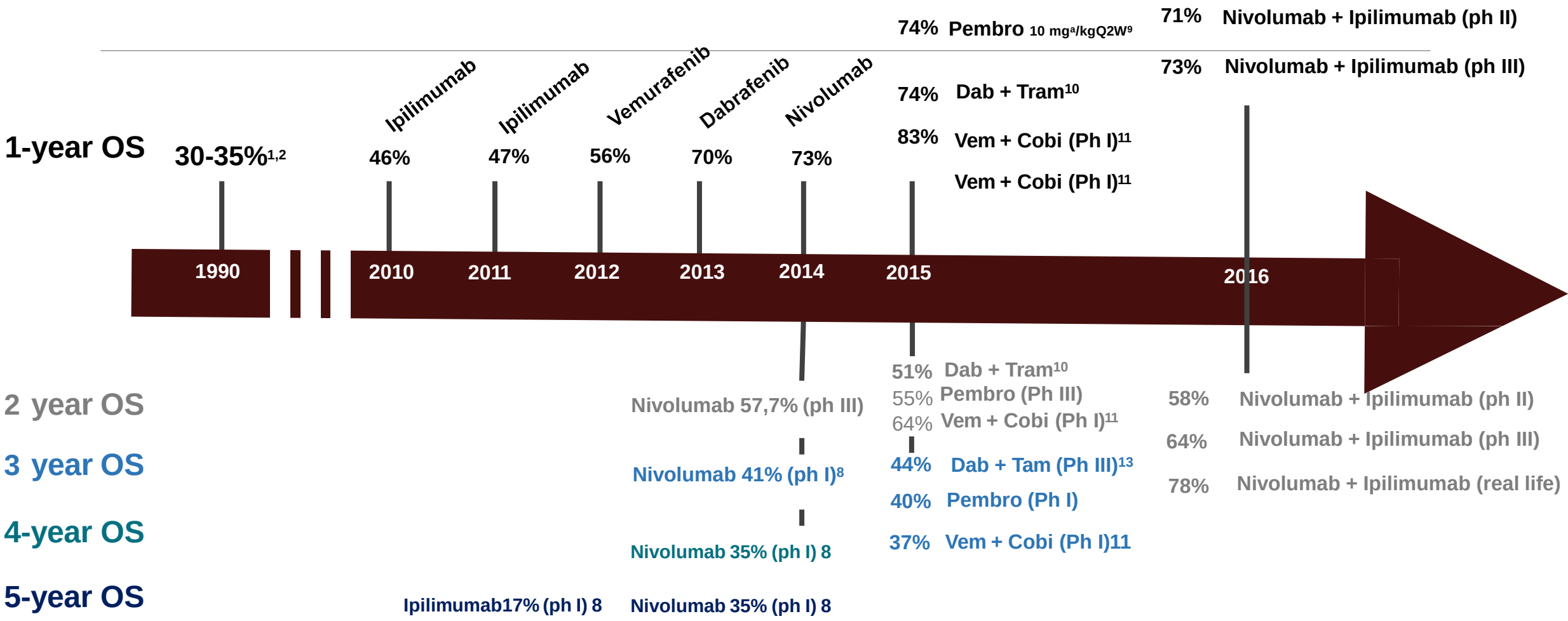
CTLA-4 is involved in the early phase of T cell activation.

PD-1 is expressed on T cells in the periphery, and interacts with PD-L1 expressed on tissues.

Modified from Alexander M. Menzies, Georgina V. Long. **Recent advances in melanoma systemic therapy. BRAF inhibitors, CTLA4 antibodies and beyond**

European Journal of Cancer, Volume 49, Issue 15, 2013, 3229–3241

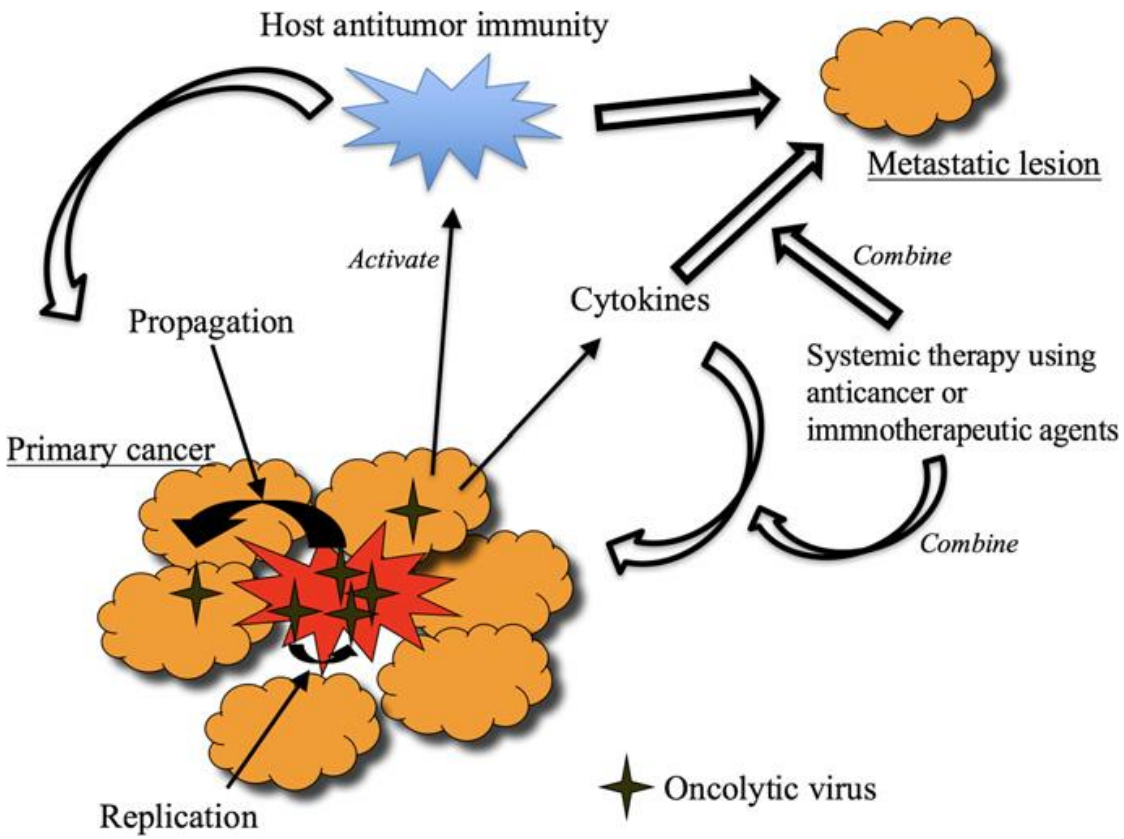
OS in Melanoma



1. SmPC COTELLIC Cobimetinib EMA. 2. SmPC MEKINIST Trametinib EMA. 3. SmPC OPDIVO Nivolumab EMA. 4. SmPC TAFINLAR Dabrafenib EMA. 5. SmPC YERVOY Ipilimumab EMA. 6. SmPC ZELBORAF Vemurafenib EMA.

Oncolytic viruses

Oncolytic viruses



- Preferential infection and replication in tumour cells, the initiation of tumour cell lysis
- Induction of innate and adaptive anti-tumour immunity.
- Genetically engineered to reduce pathogenicity and increase immunogenicity resulting in minimally toxic therapeutic agents: neurotropic gene, immunogenic gene, integrates GM-CSF gene

Oncolytic Virus Therapy

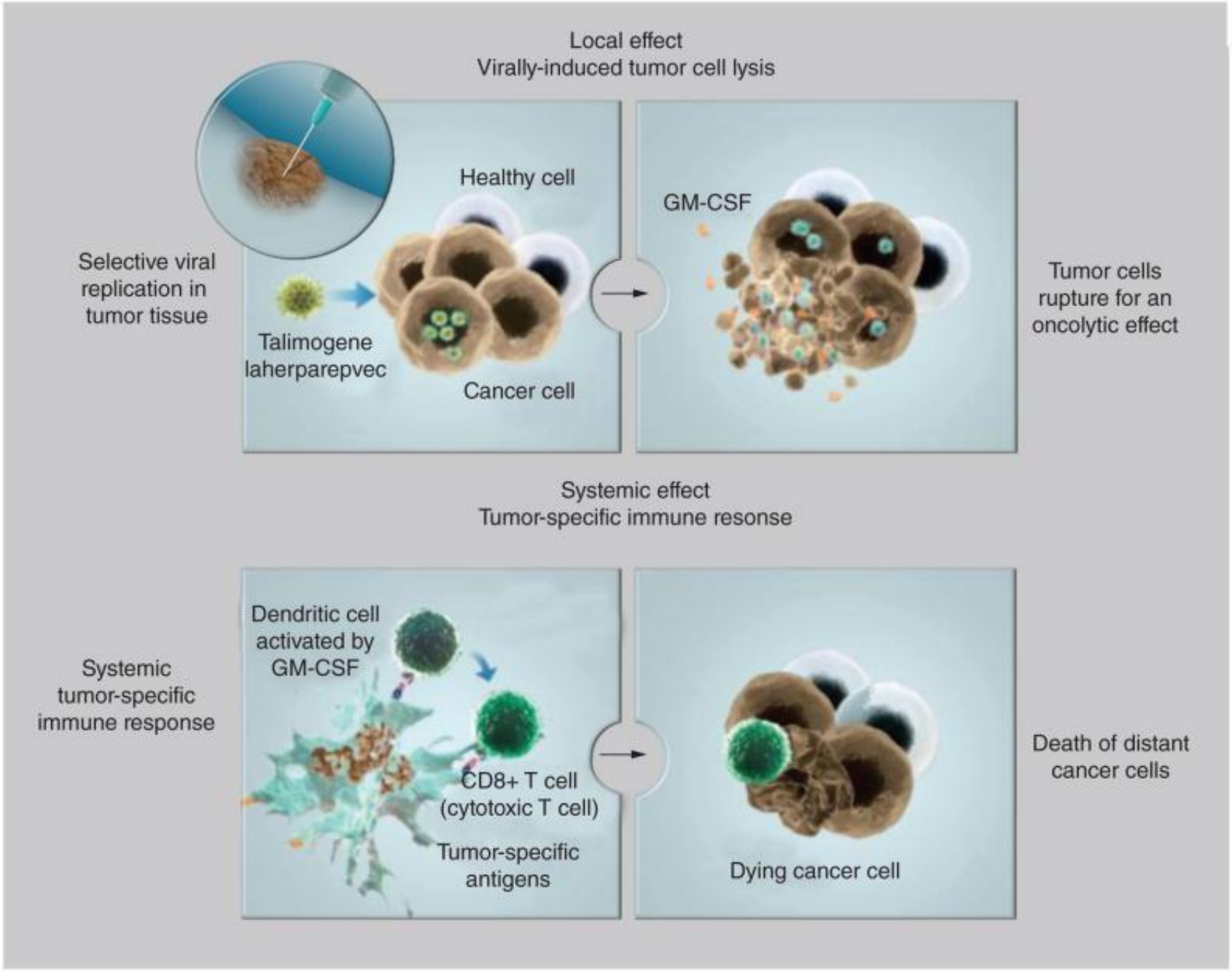
- **Talimogene laherparepvec** is the **first approved oncolytic virus therapy** (US, EU, and Australia)
- Indicated (as monotherapy) for the treatment of adults with **unresectable melanoma** that is regionally or distantly metastatic (Stage **IIIB**, **IIIC** and **IV M1a**) with no bone, brain, lung or other visceral disease[1]

1. Amgen. Imlygic® Summary of Product Characteristics. Section 4.1.

Talimogene laherparepvec

- is a herpes simplex virus type-1–derived oncolytic immunotherapy designed to selectively replicate in tumors, produce GM-CSF, and enhance local and systemic antitumor immune responses[1]

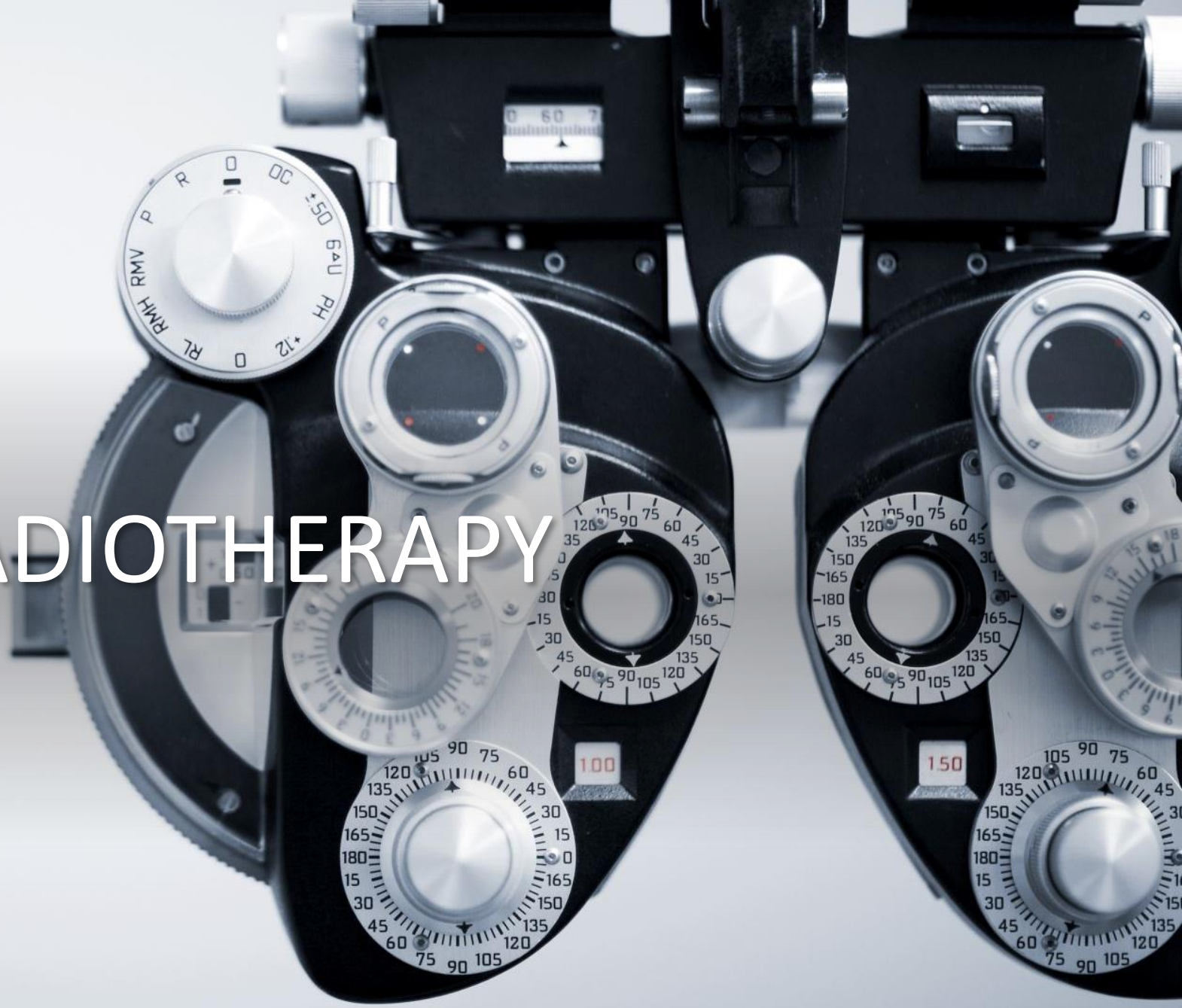
Amgen. Imlygic® Summary of Product Characteristics. Section 4.1.

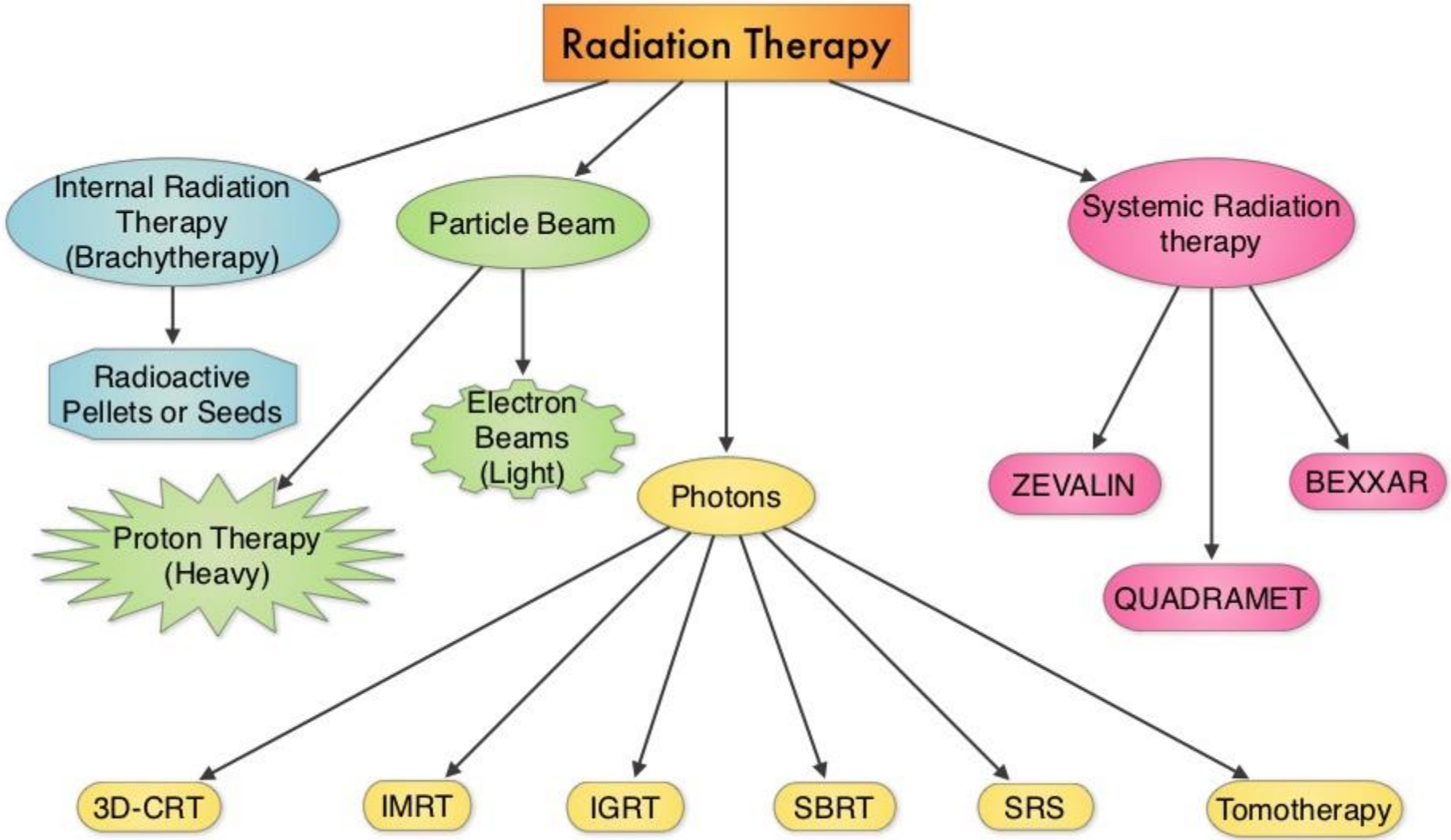


Proposed mechanism of action for talimogene laherparepvec

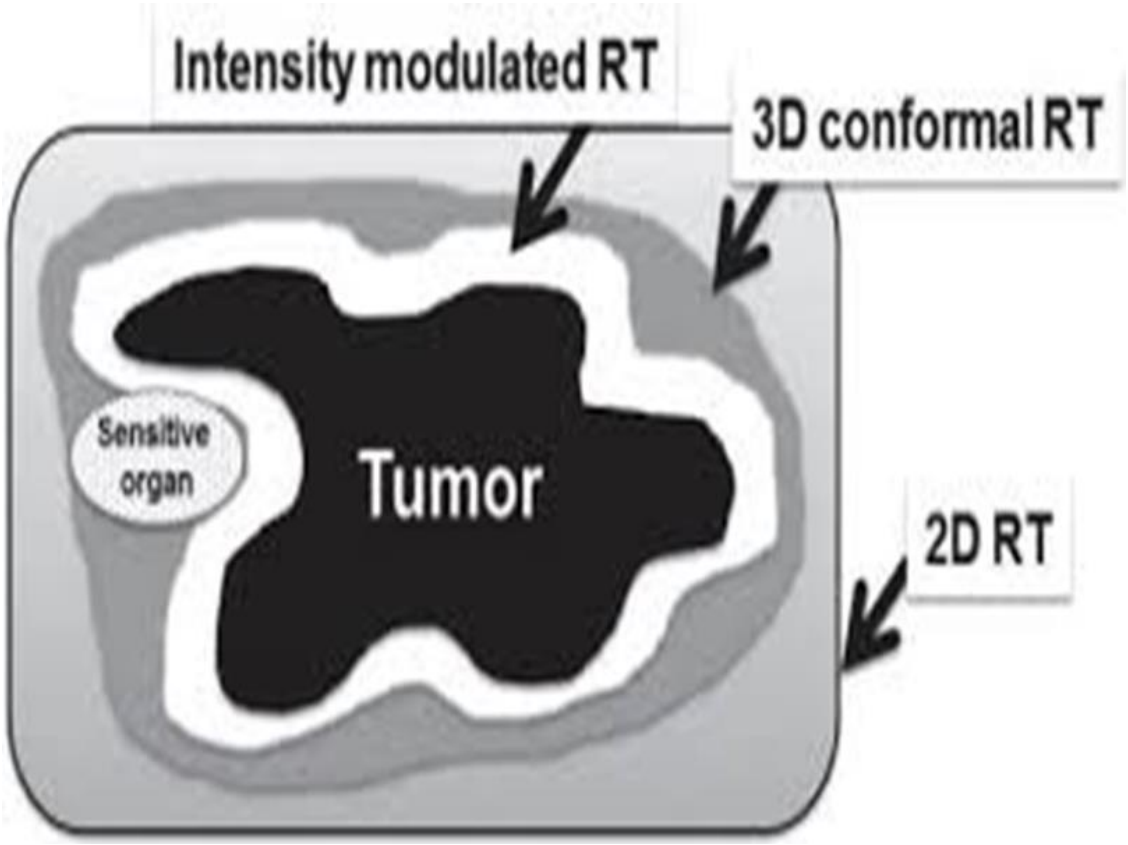
- Johnson DB, Puzanov I, Kelley C. Talimogene laherparepvec (T-VEC) for the treatment of advanced melanoma. Immunotherapy. 2015 Jul; 7(6): 611–619.

RADIOTHERAPY




Radiation Therapy
Internal Radiation Therapy (Brachytherapy)
Particle Beam
Systemic Radiation therapy
Radioactive Pellets or Seeds
Electron Beams (Light)
Photons
Proton Therapy (Heavy)
ZEVALIN
BEXXAR
QUADRAMET
3D-CRT
IMRT
IGRT
SBRT
SRS
Tomotherapy

Techniques


Intensity modulated RT
3D conformal RT
2D RT
Sensitive organ
Tumor

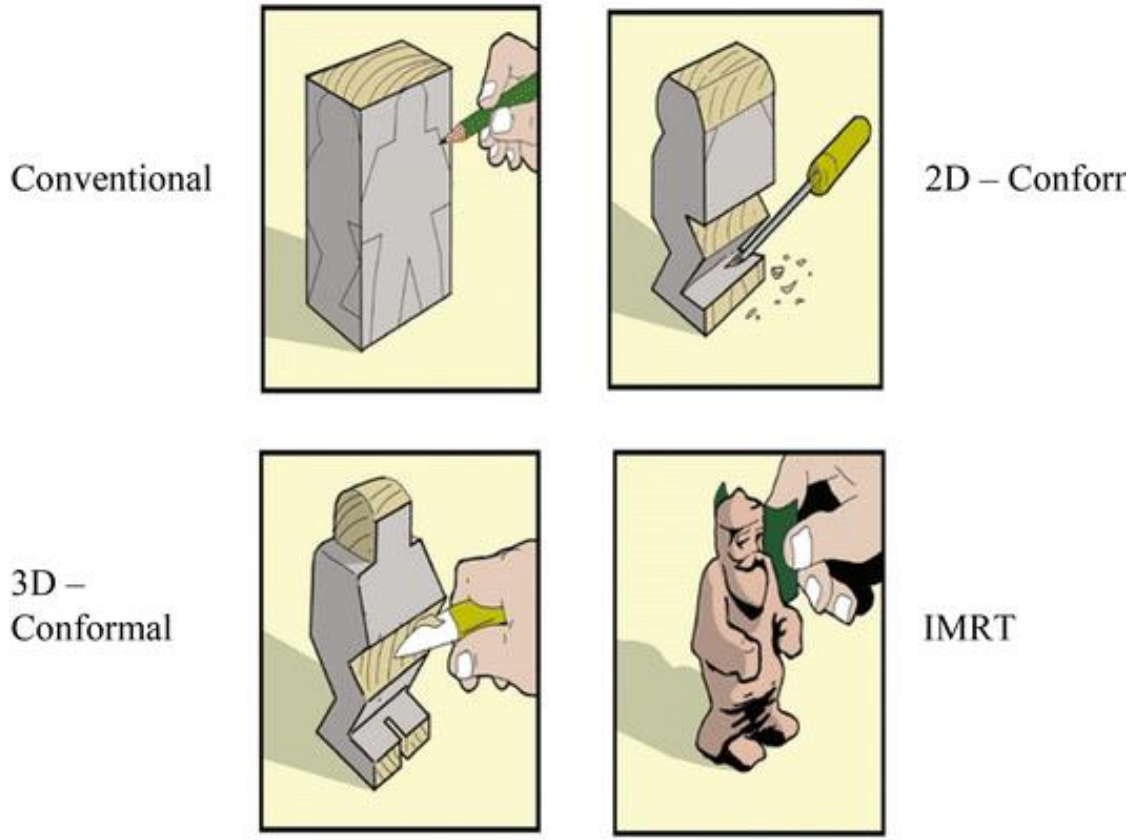
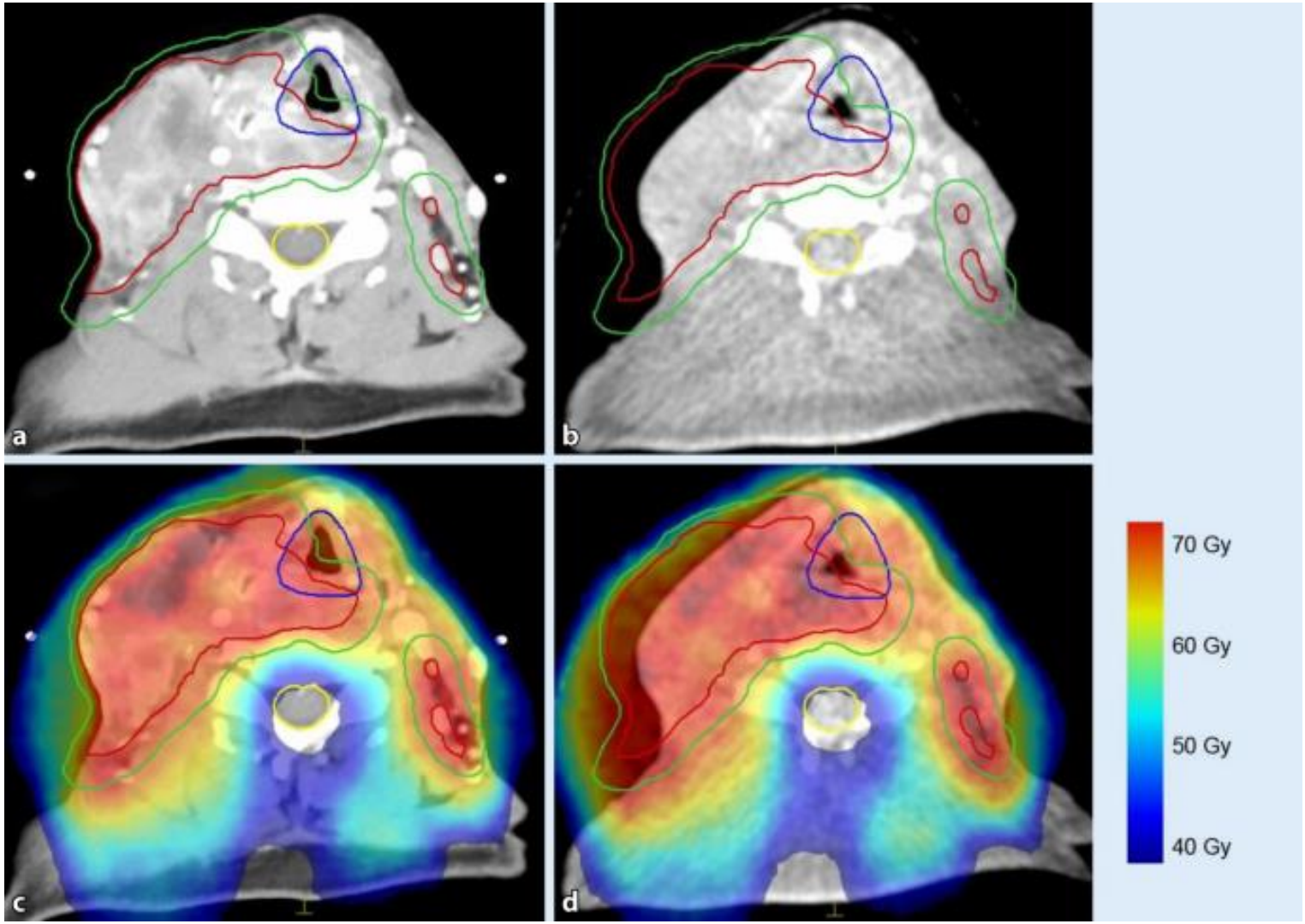
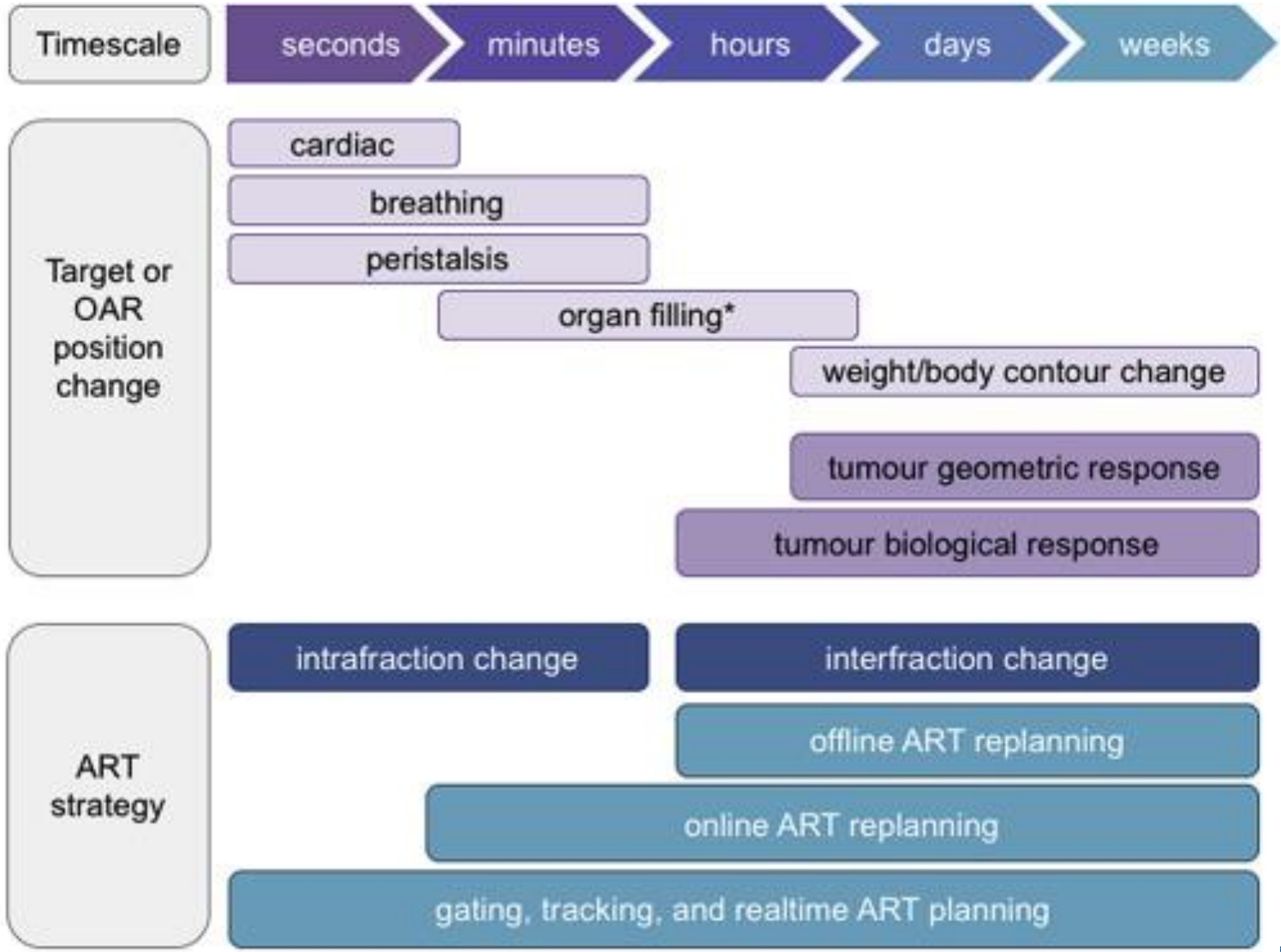

Conventional
2D – Conforr
3D –
Conformal
IMRT

Image guided RT





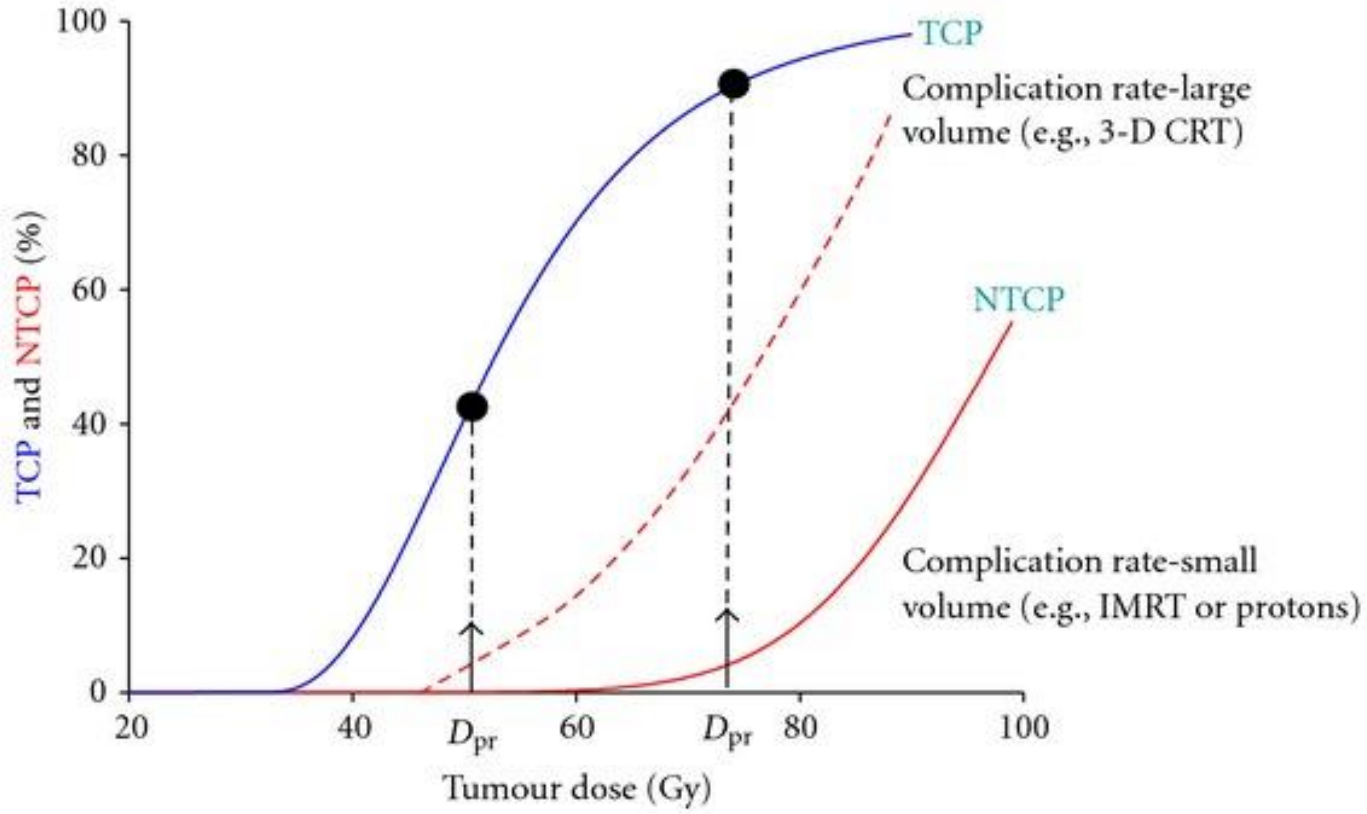
* Organs subject to filling and deformation including bladder, rectum, cervix, and stomach etc

AIM

Escalate dose of radiotherapy

Reduce dose to healthy tissues

Decreased toxicity increase tumor control



Radiotherapy

Cure of localised disease

- Definitive
- Adjuvant
- Salvage

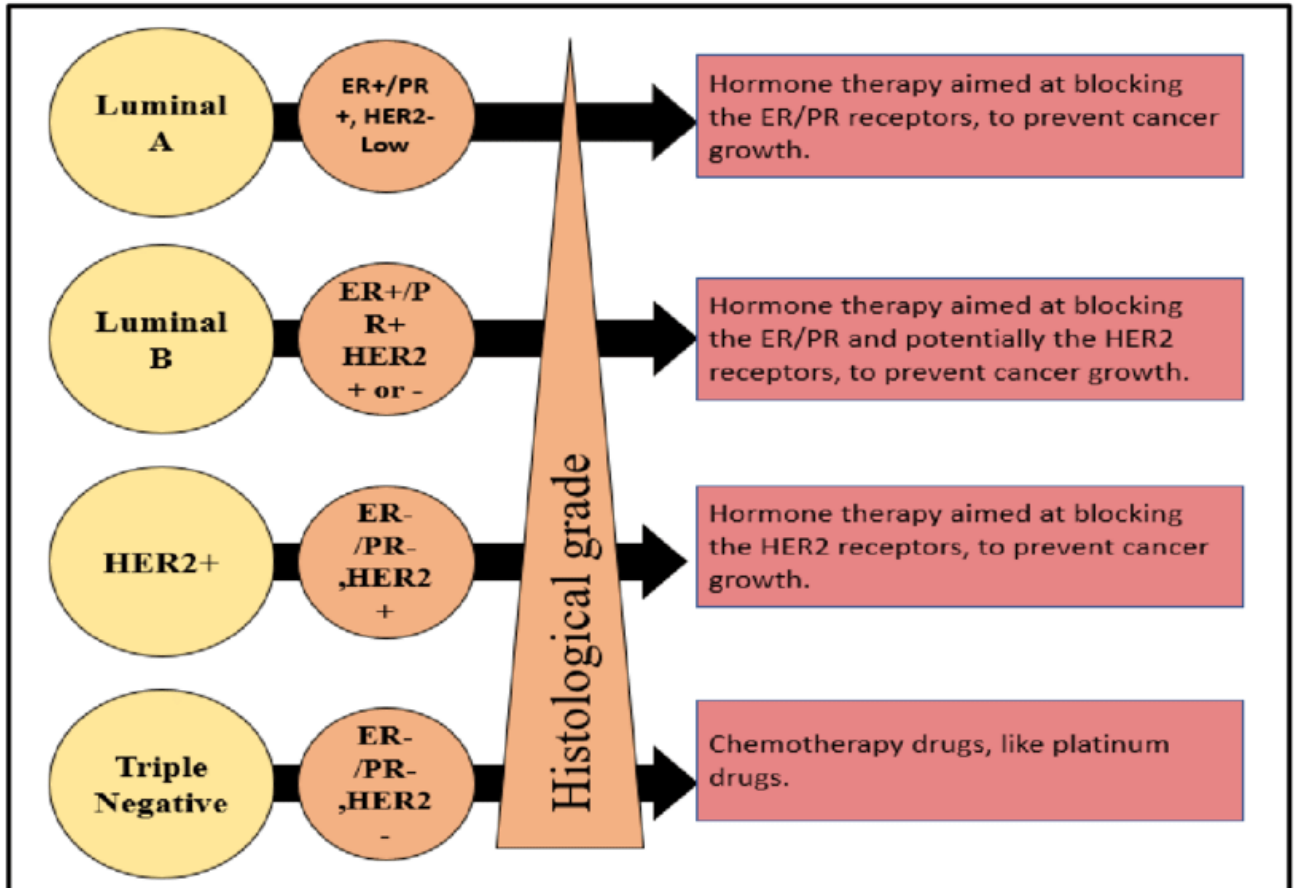
Palliation of extensive disease

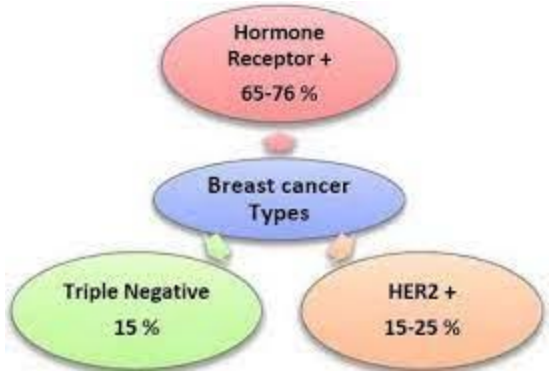
Limited metastatic disease: Metastases directed therapies

Brachytherapy: close to or within the tumor

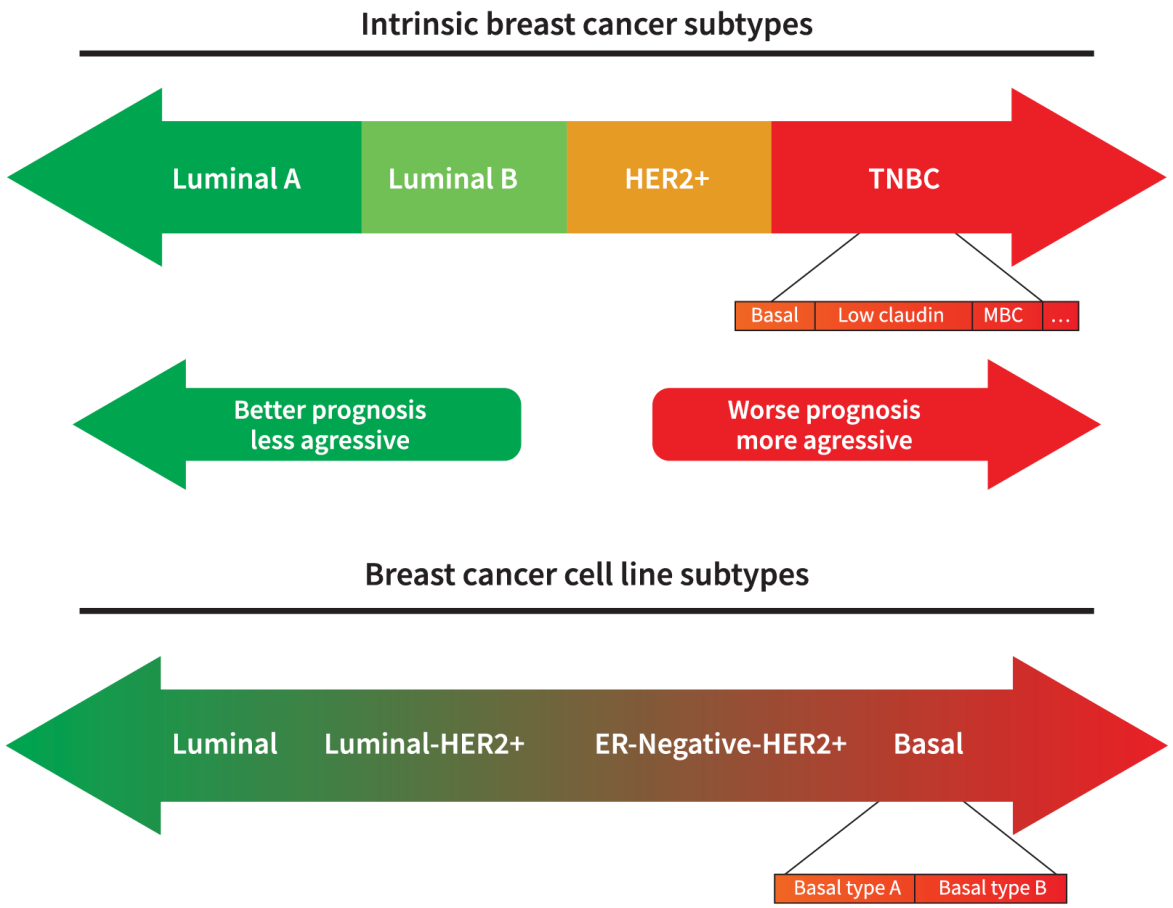
Breast cancer

Breast cancer

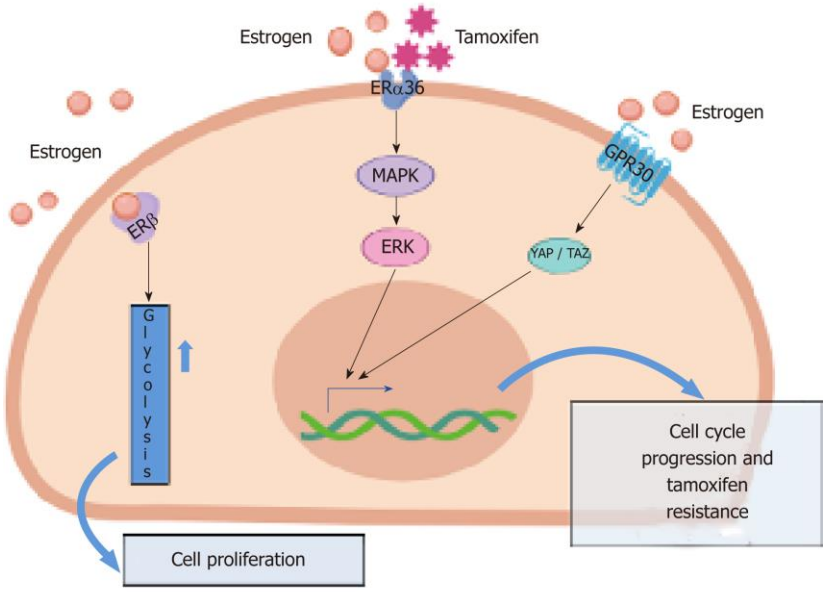




Subtypes



Estrogen positive, Endocrine sensitive



Tamoxifen

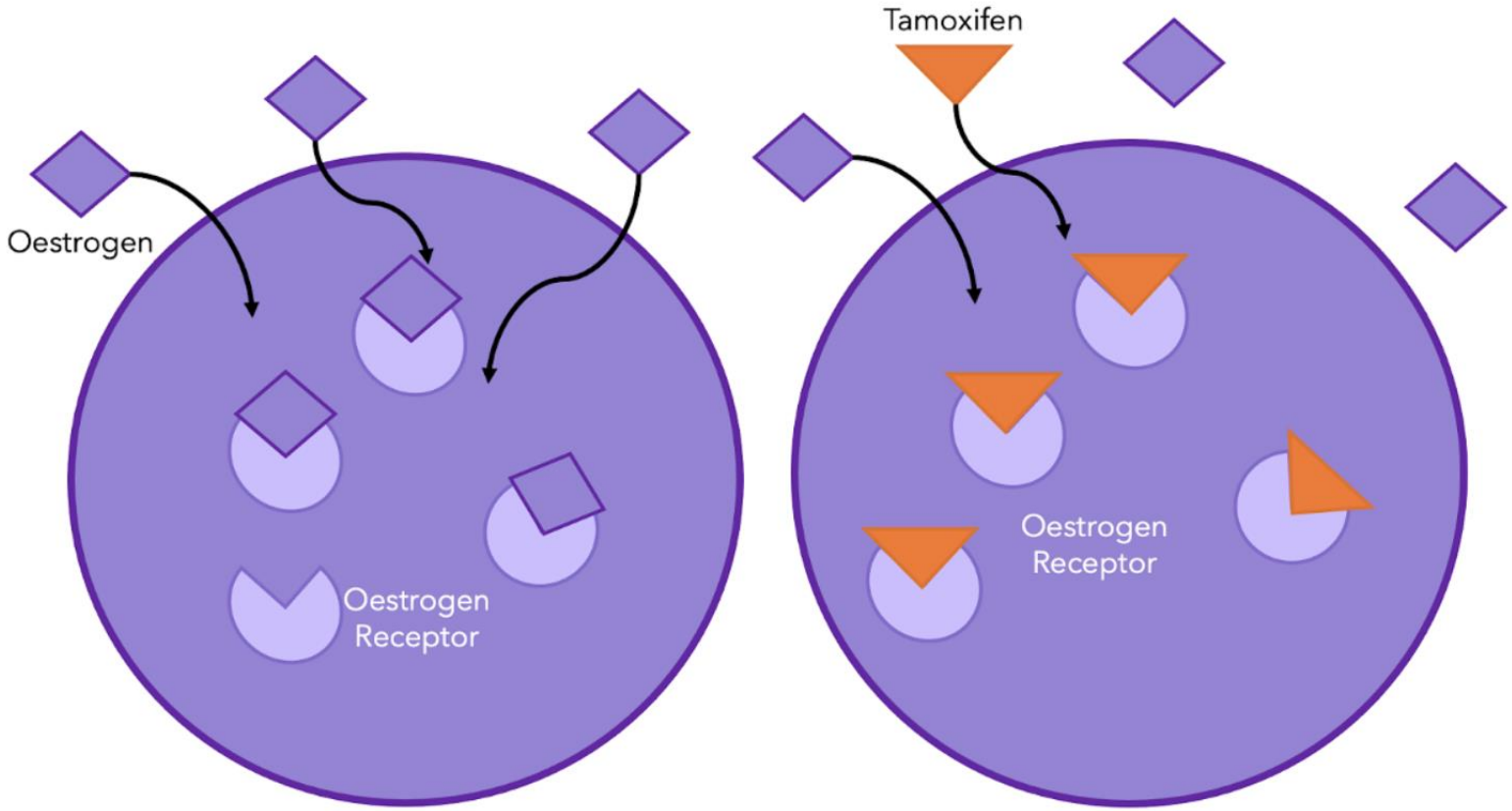


Figure 1: Tamoxifen binds to the oestrogen receptors, preventing oestrogen from binding to them. This blocks oestrogen from being able to promote cell growth.

Aromatase Inhibitor

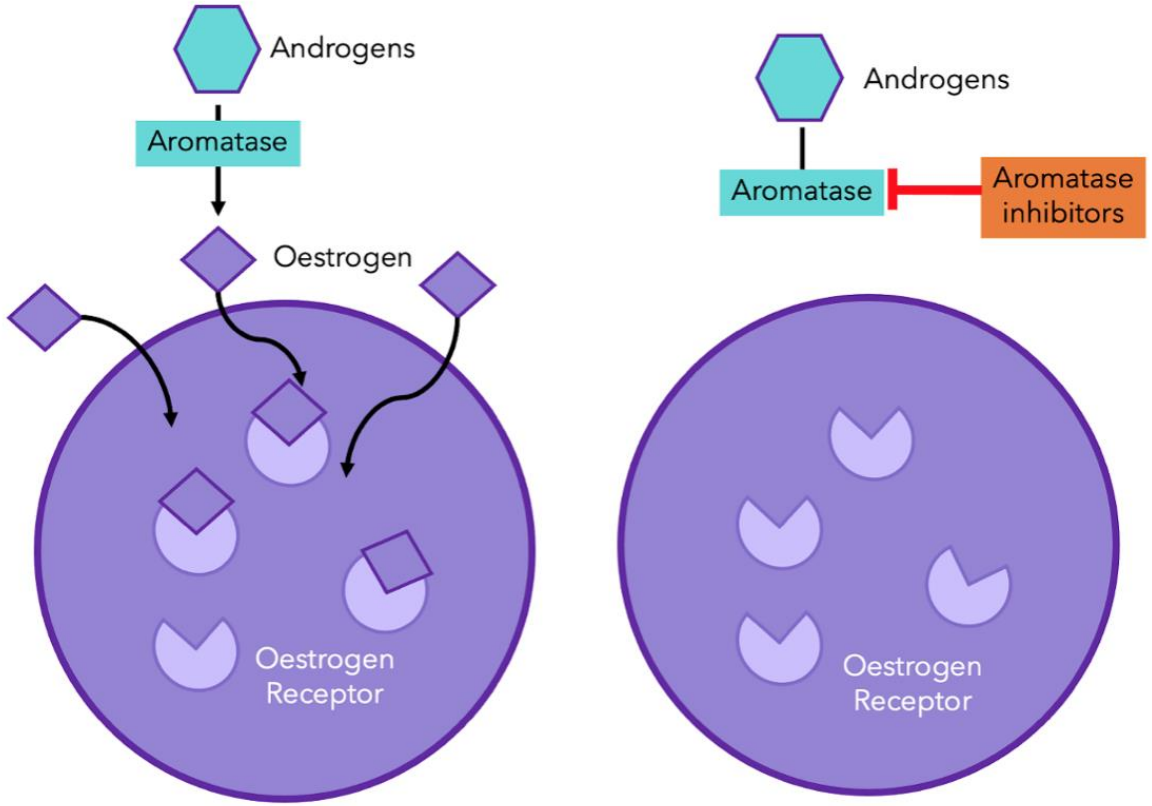
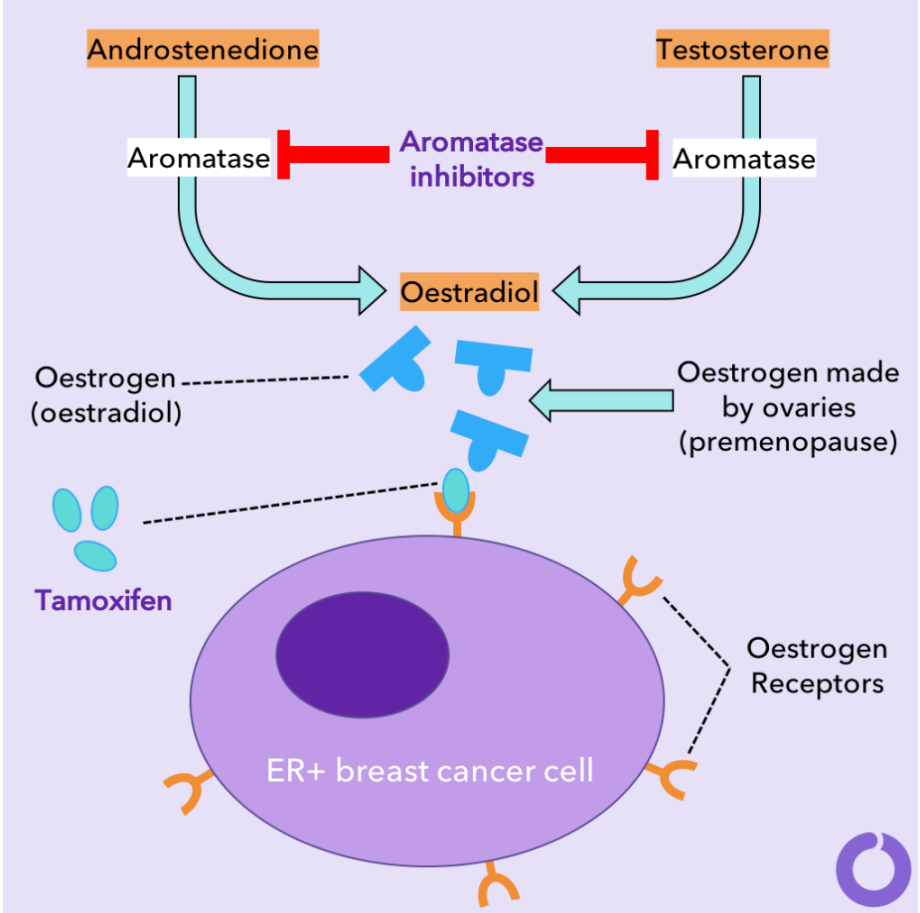
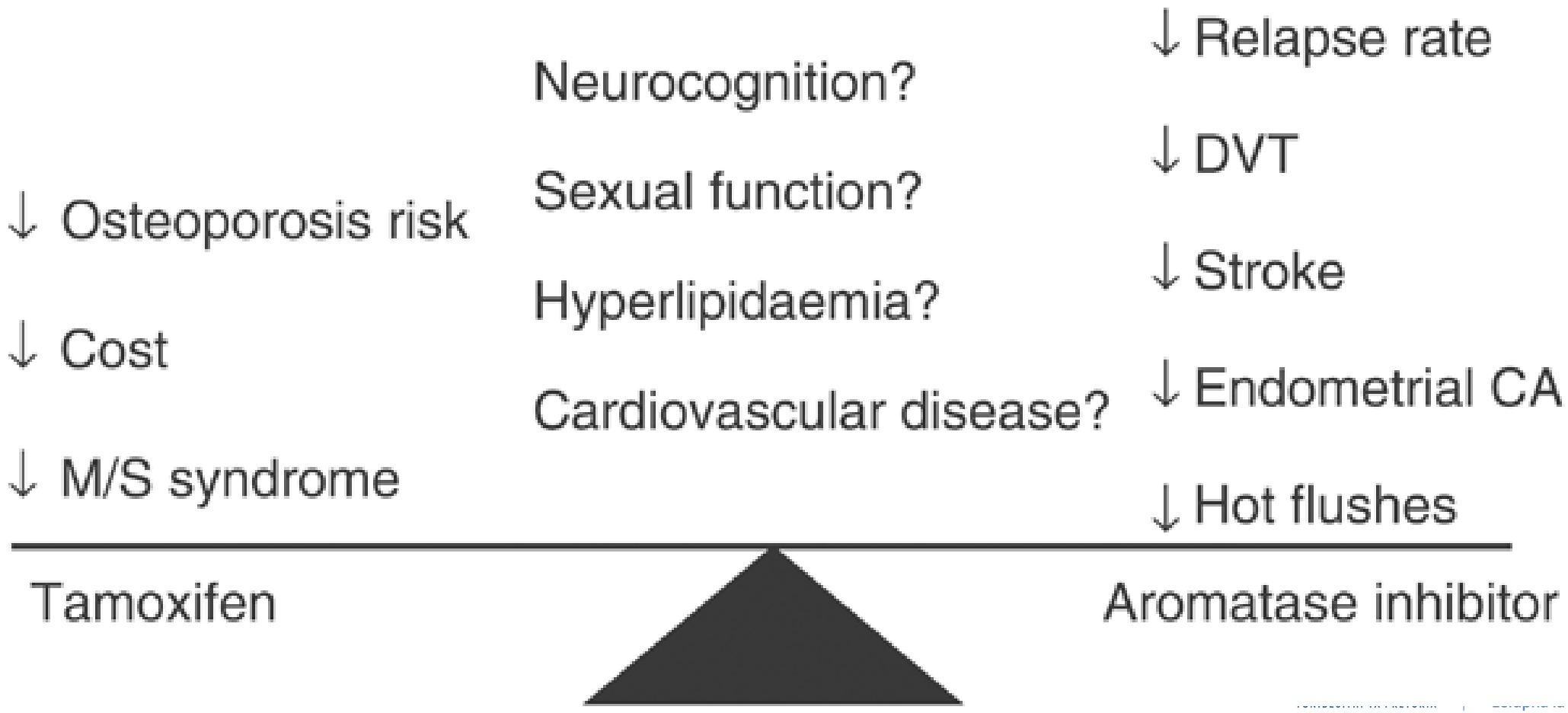


Figure 2: Aromatase inhibitors prevent the enzyme aromatase from working. This stops oestrogen production in the body and therefore there is no oestrogen available to promote cancer cell growth.

Aromatase Inhibitors



Tamoxifen vs AI



Outcomes

Clinical Outcomes	5 vs 10 years Tamoxifen	5 Tamoxifen + 5 A I *
Return of cancer at 10 years	~ 20% (5-yr tamoxifen) ~ 18% (10-yr tamoxifen)	~ 23% (5-yr tamoxifen) ~ 19% (5 tamoxifen+5 AI)
Difference 10 yr vs 5 yr	~ 2 %	~ 4 %
Serious side-effects	~ 2% **	~ 5% ***

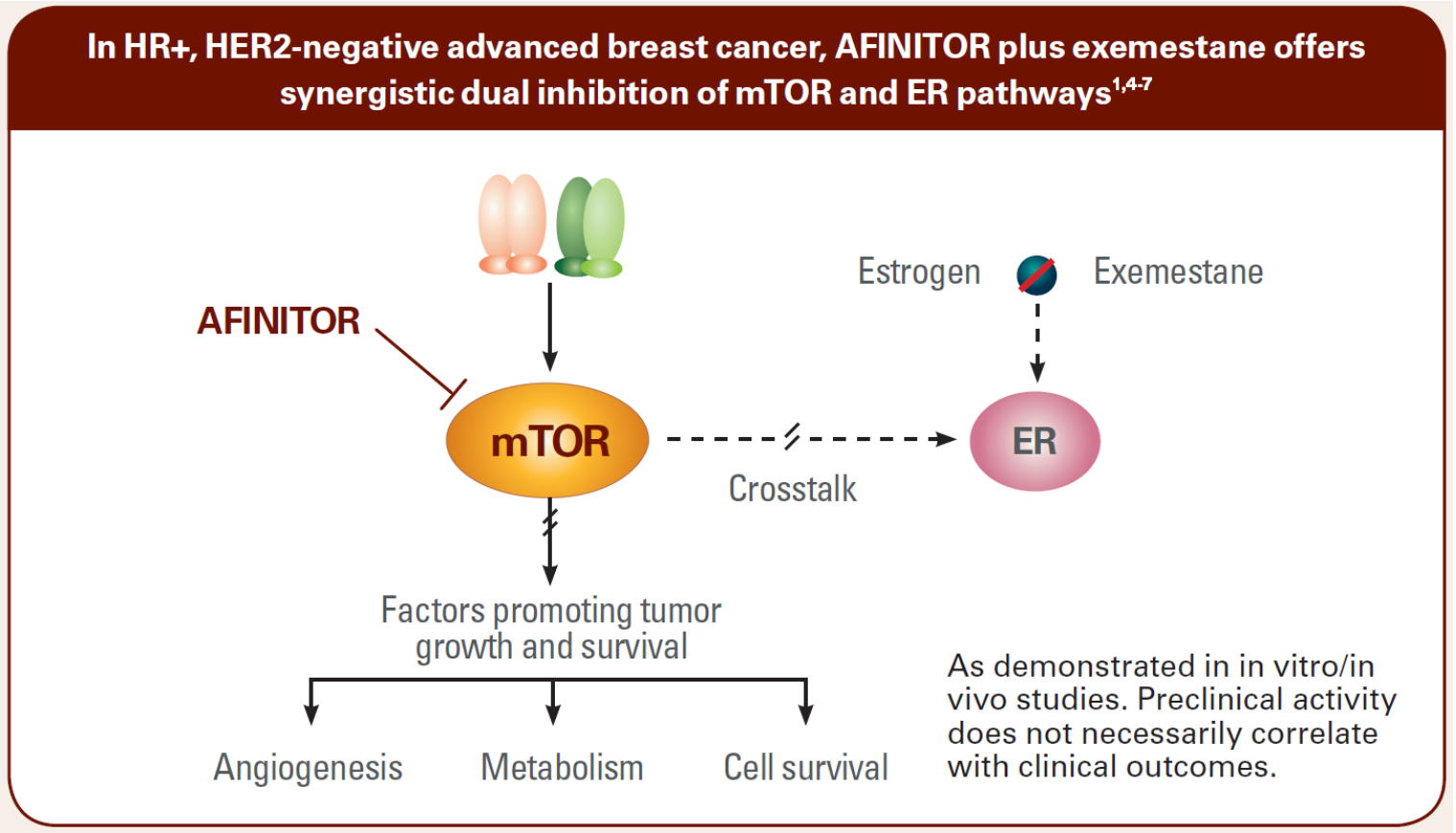
* AI = aromatase inhibitor
** For added 5-yr of tamoxifen; endometrial cancer 1.5% more (3%-1.5%), embolism, 1% more.
*** For added 5-years of AI, 5% more fracture (14%-9%).

Clinical Outcomes	Aromatase (switch) (A)	Tamoxifen (B)	Difference (A-B)
Die within 10 years	9% (9/100)	10% (10/100)	*~1% (1/100 less)*
Endometrial cancer within 10 years	0.4%	1%	*~1% (less)*
Bone fracture within 10 years	16% **	12%	*~4% (more)*

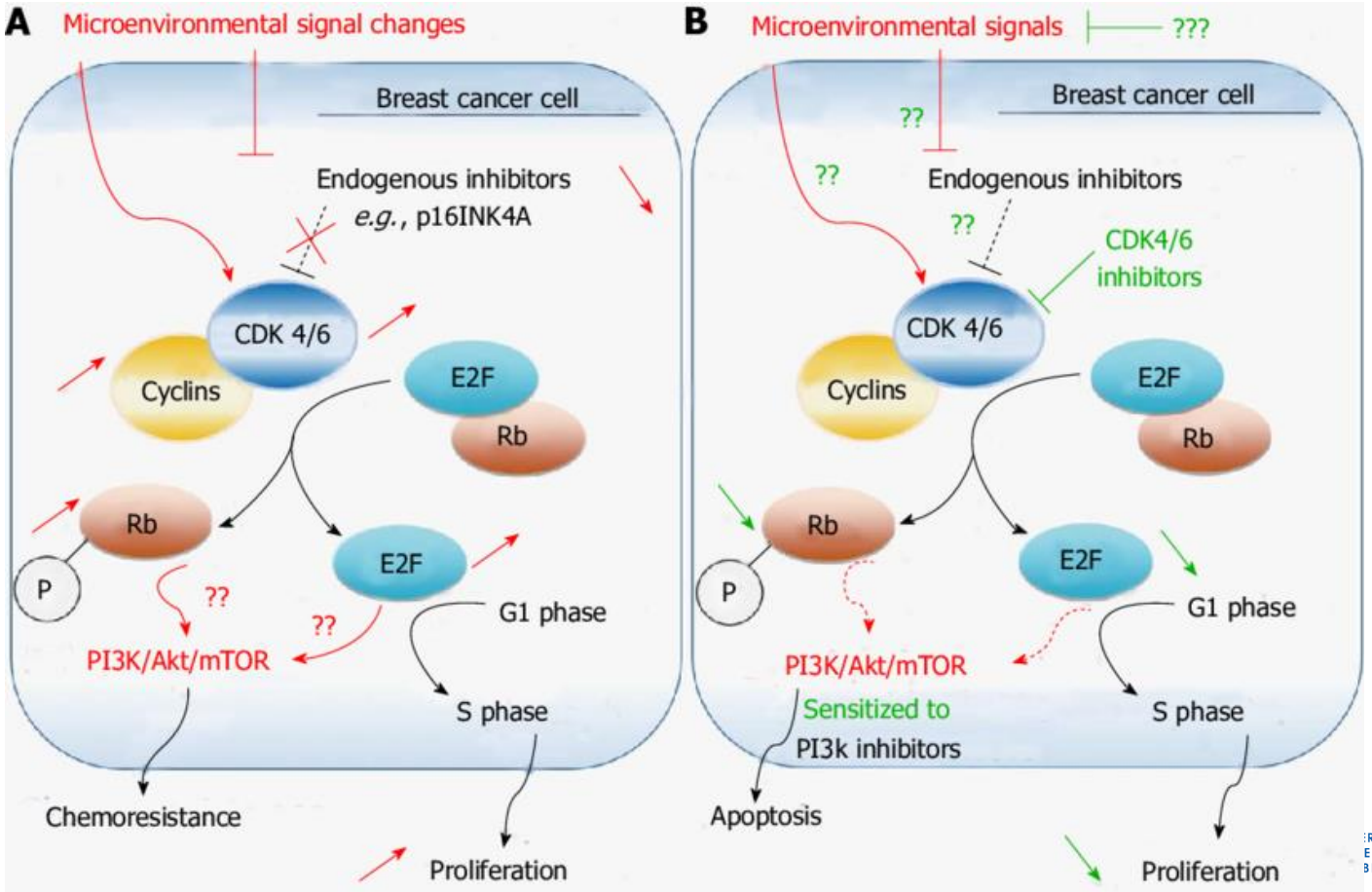
**Other side effects: 40-50% have bone/muscle pain, and menopausal symptoms may worsen.

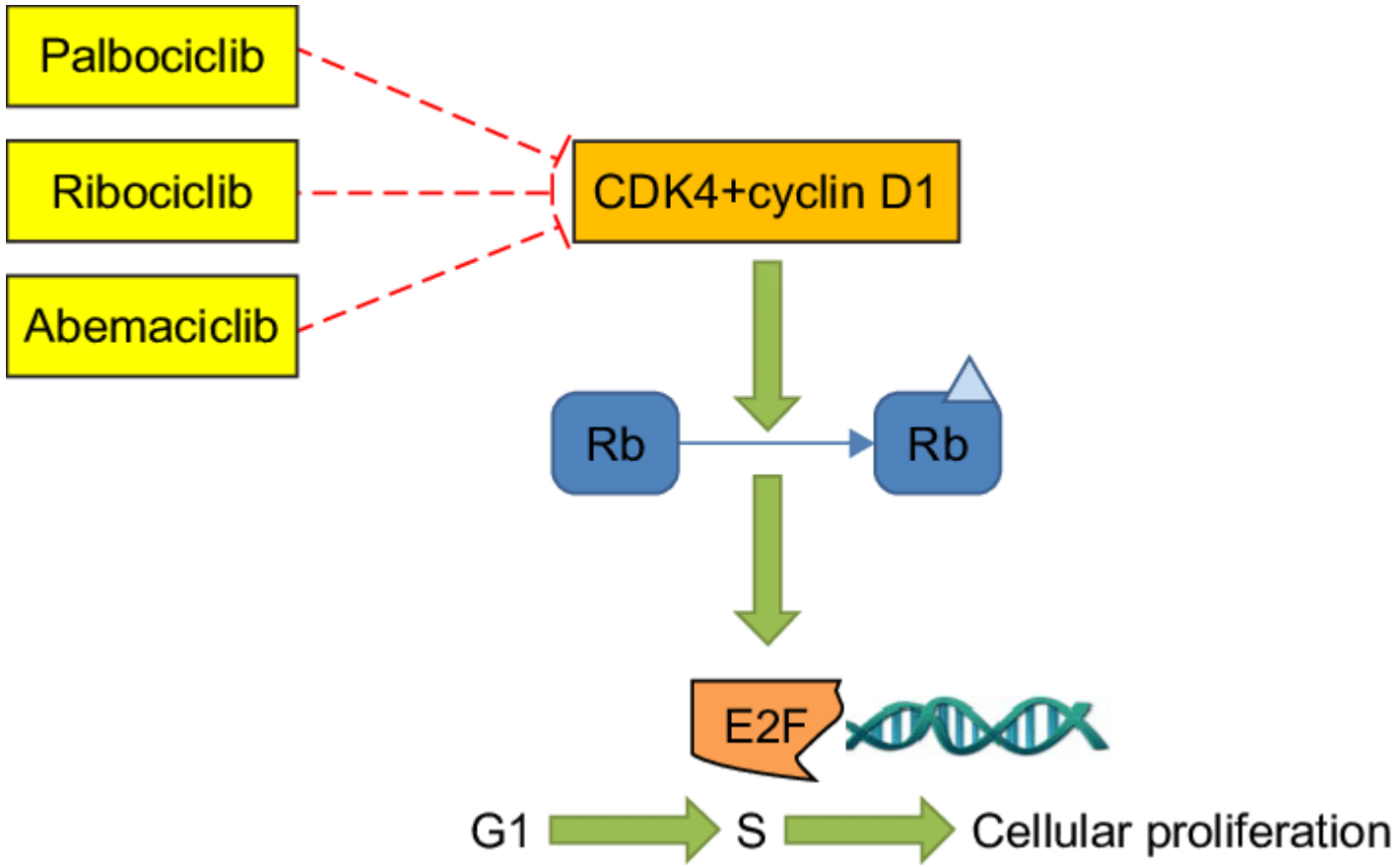
appe
lo

Targeted agents for ER + disease

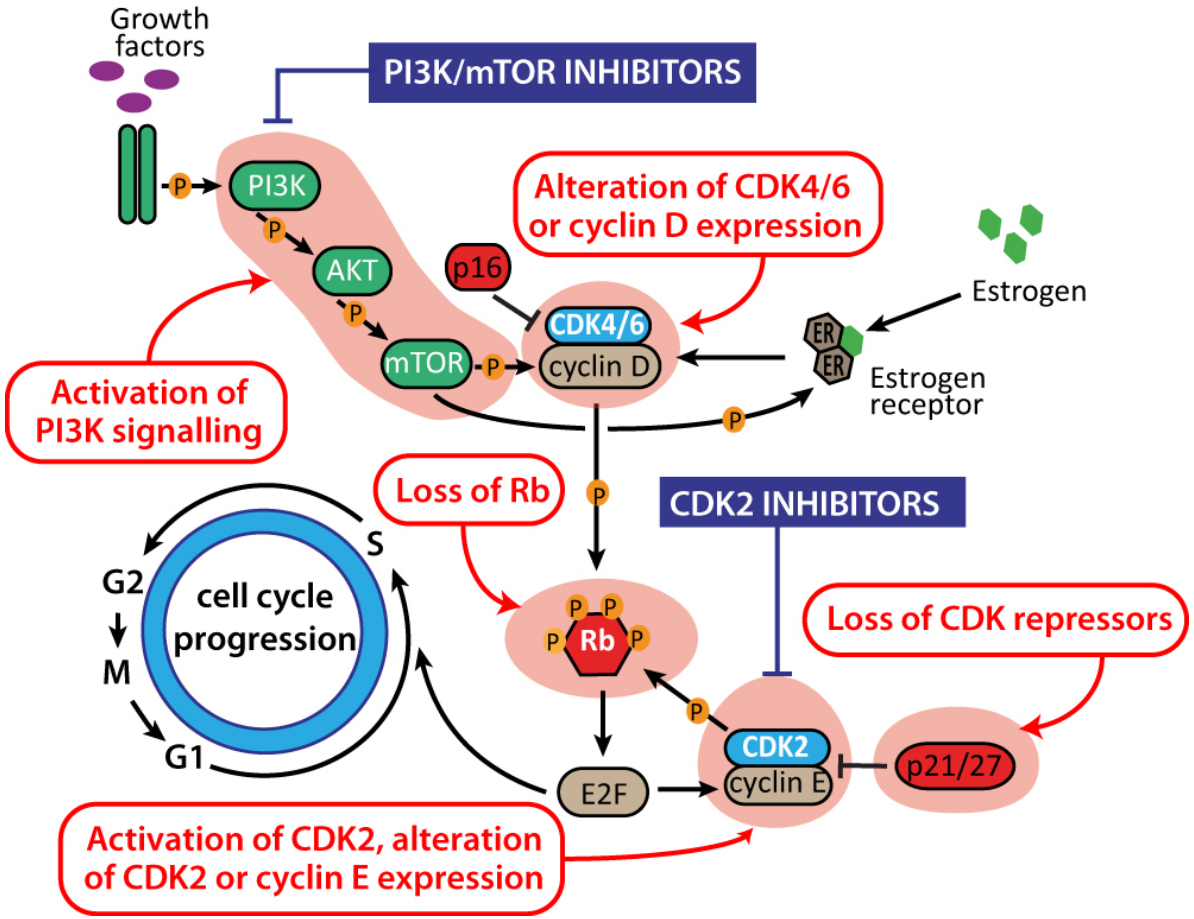


CDK4/6 inhibitors





PI3K inhibitors



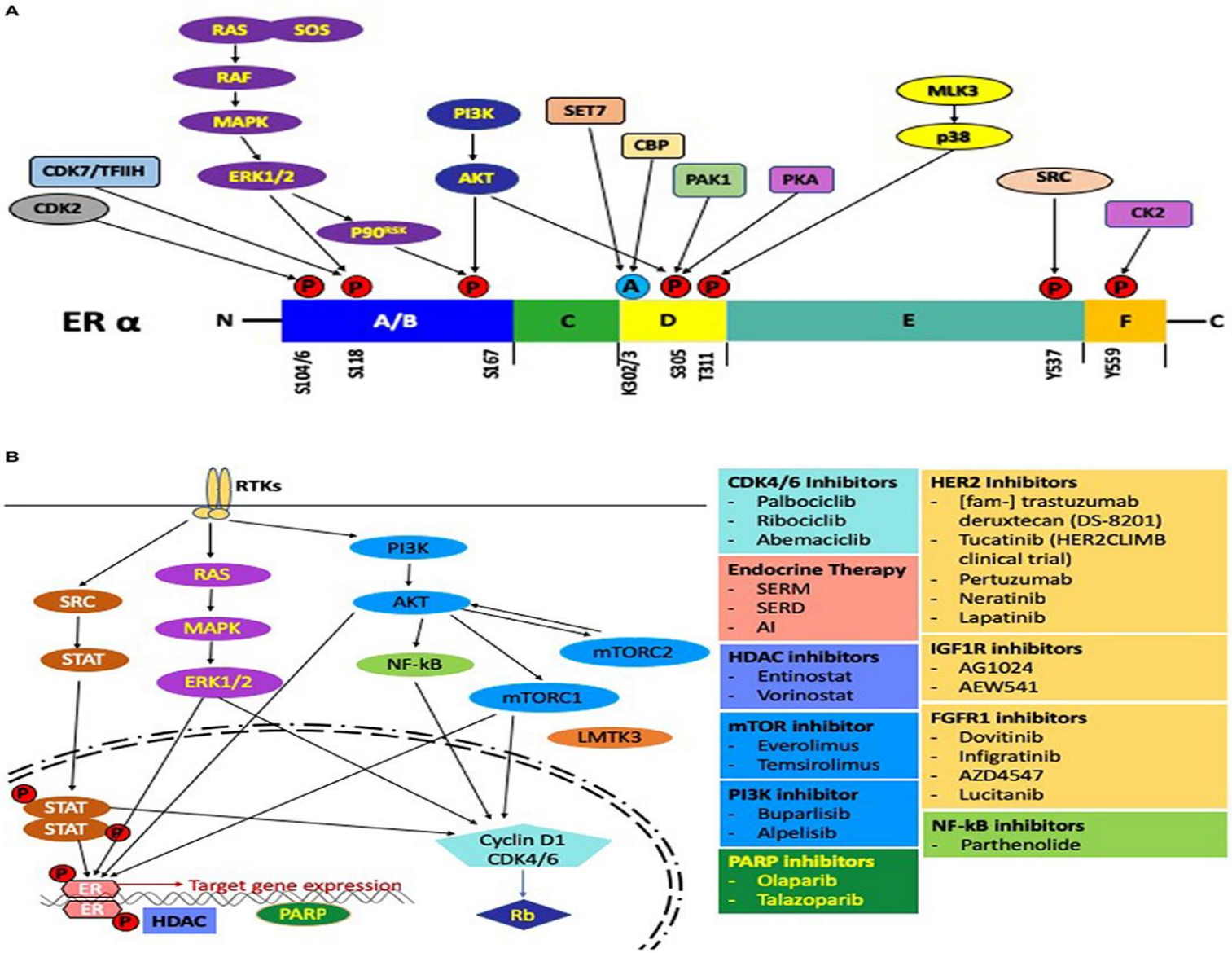
Review Article | Published: 14 June 2021

PI3K inhibitors are finally coming of age

Bart Vanhaesebroeck ✉, Matthew W. D. Perry, Jennifer R. Brown, Fabrice André & Klaus Okkenhaug

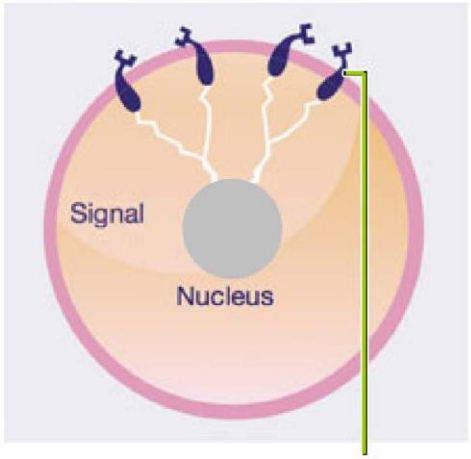
Nature Reviews Drug Discovery **20**, 741–769 (2021) | Cite this article

CDK4/6 inhibitors



HER 2+

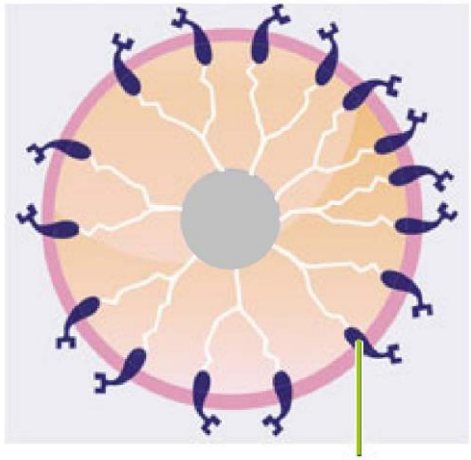
Normal Breast Cell



Normal amount of HER2 receptors

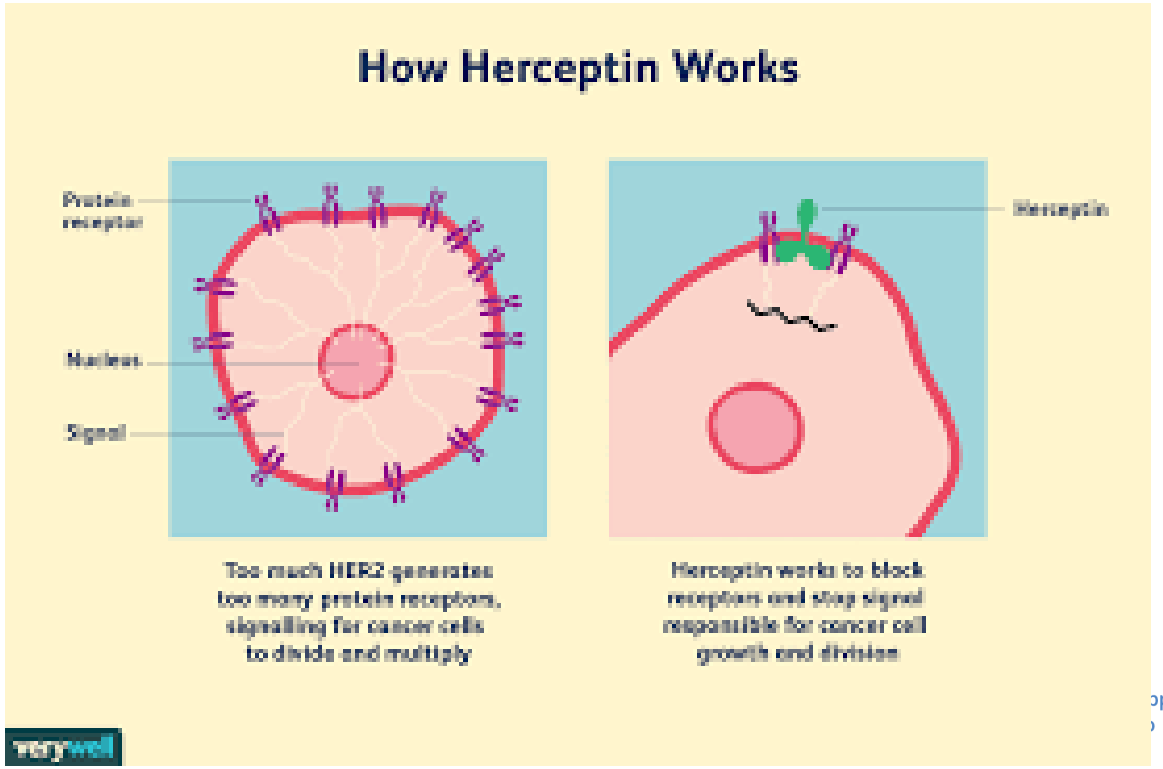
tells cells to grow and divide

Abnormal Breast Cancer Cell

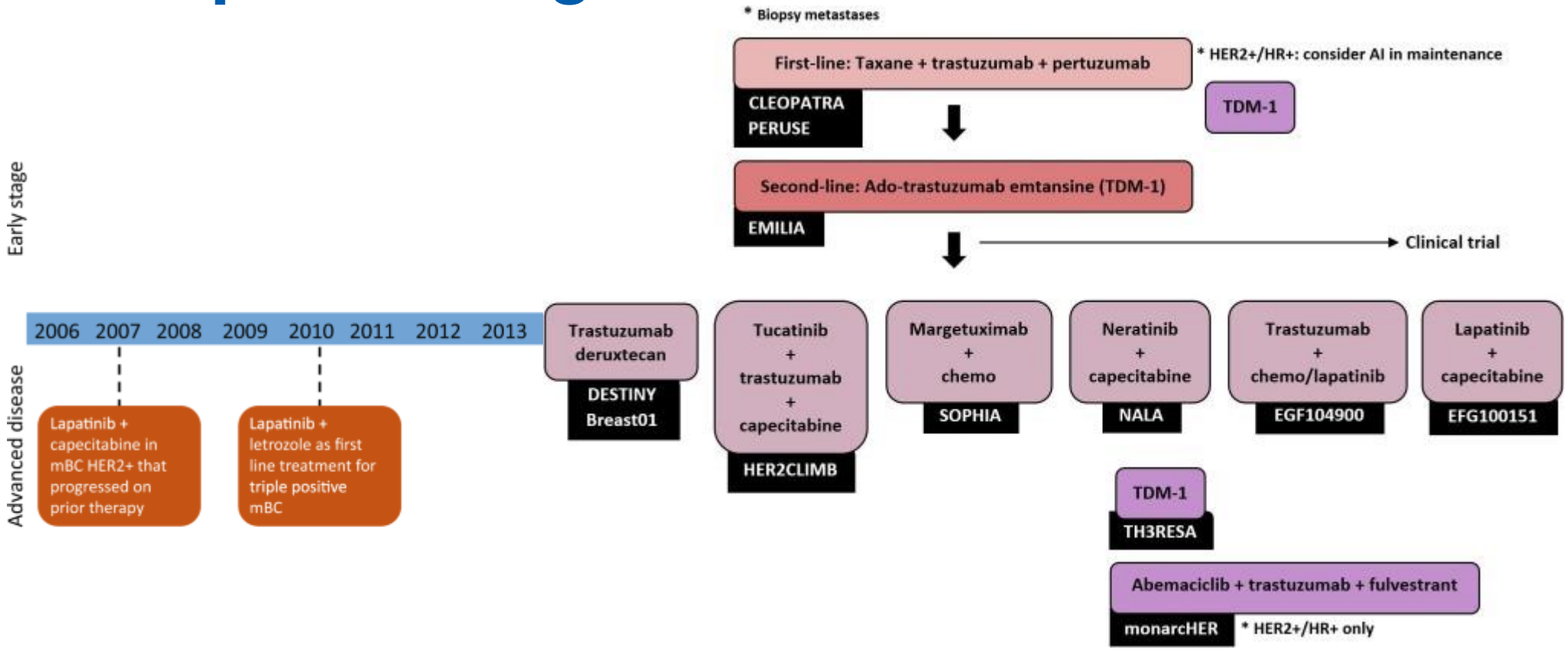


Overproduction of HER2 receptors

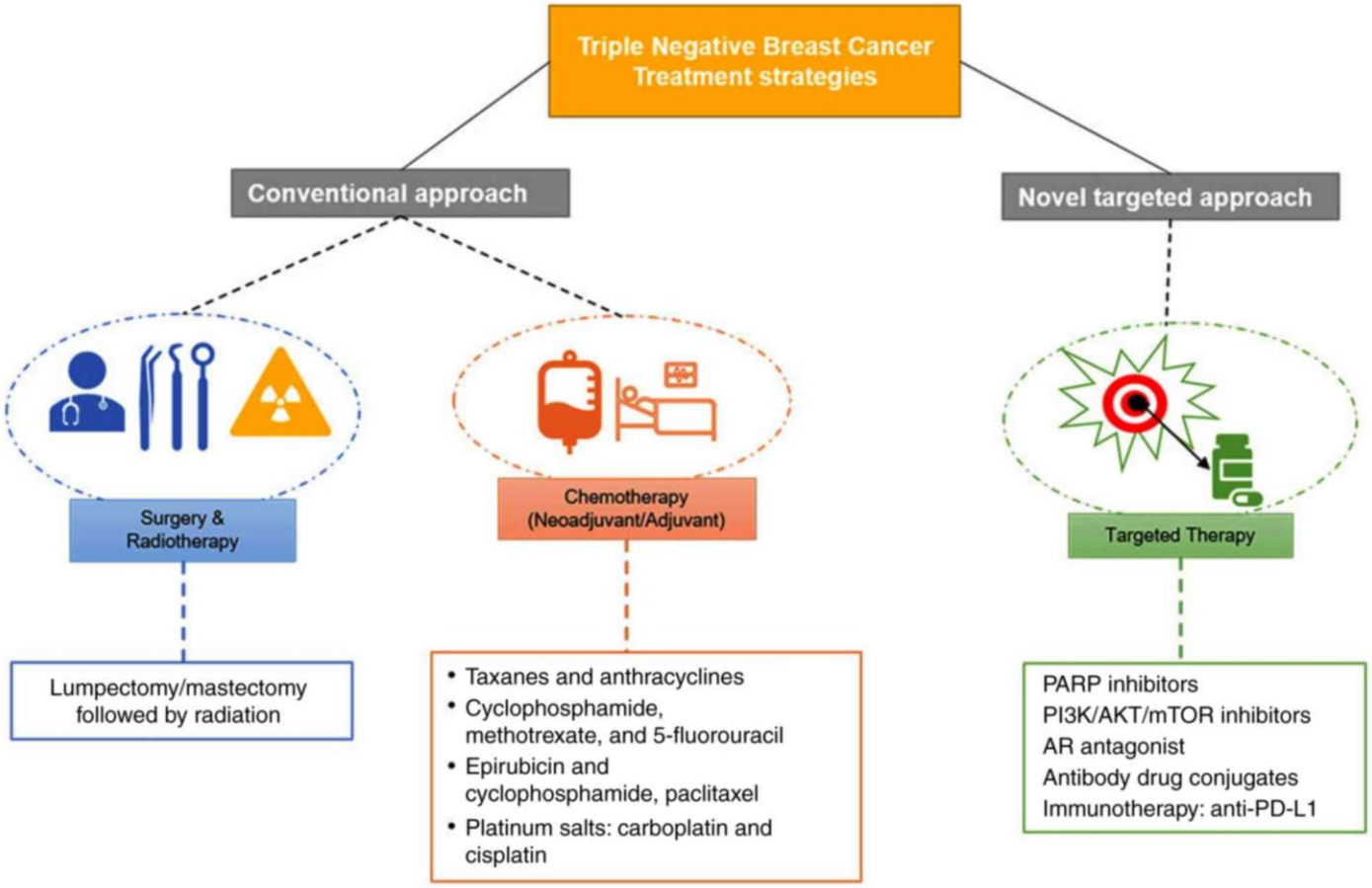
tells cells to grow and divide to quickly eventually least to cancer.



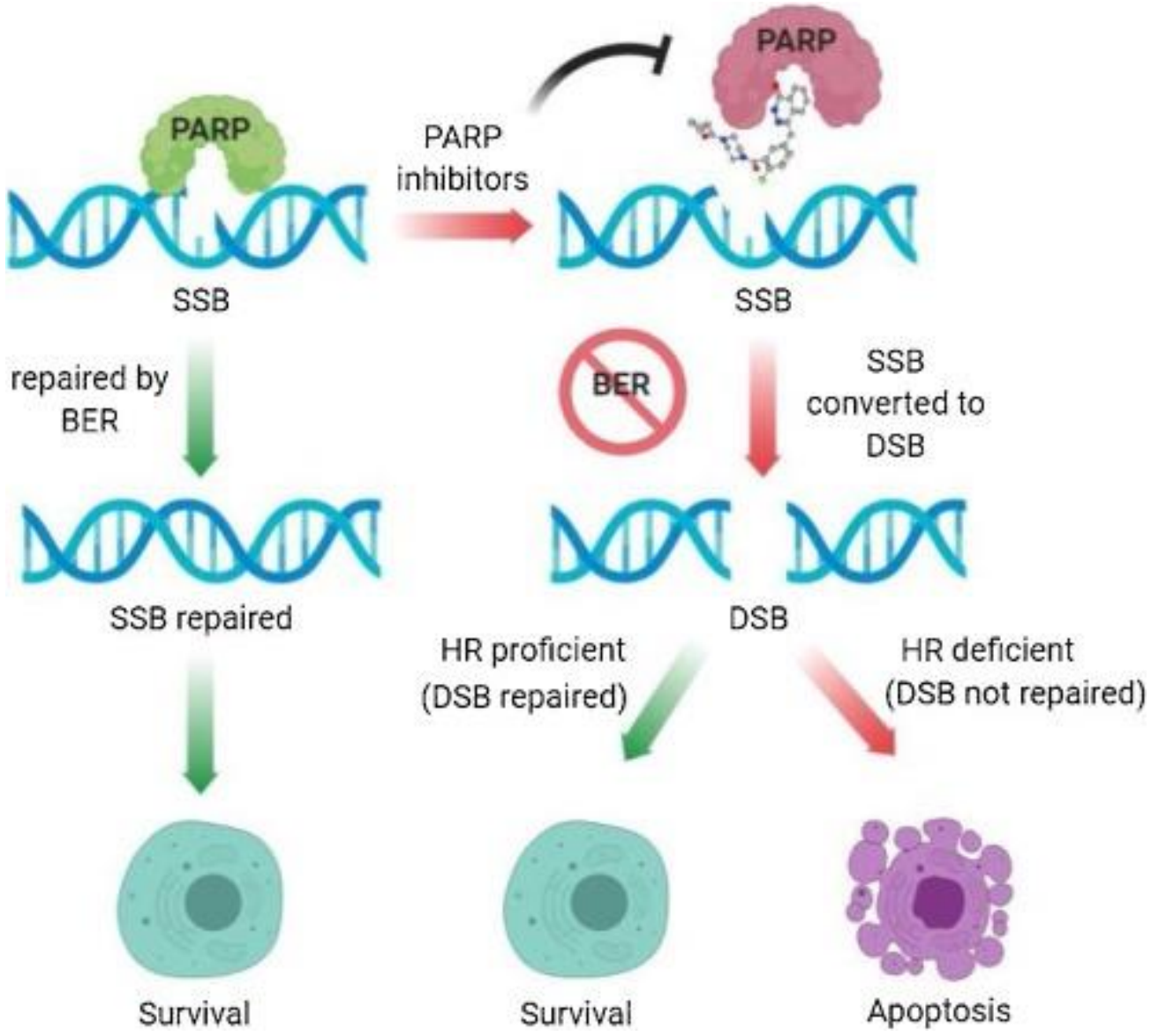
HER 2 positive agents

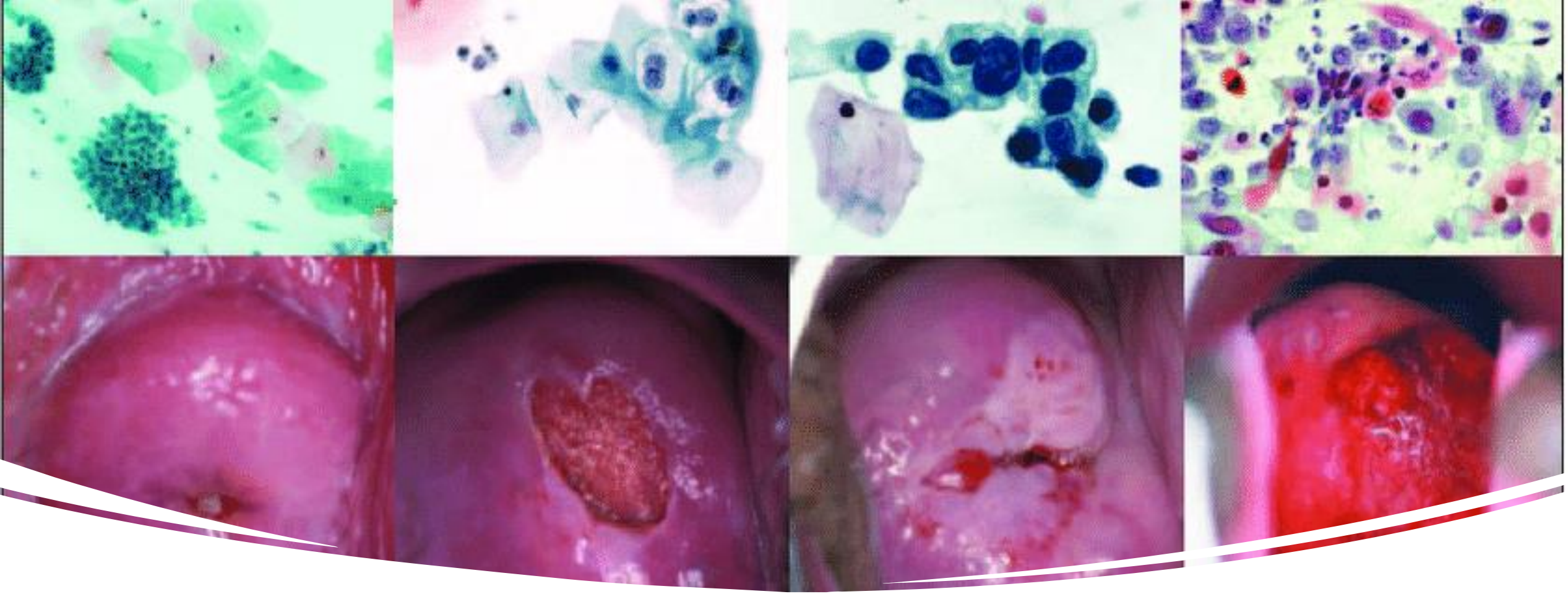


Triple negative breast cancer



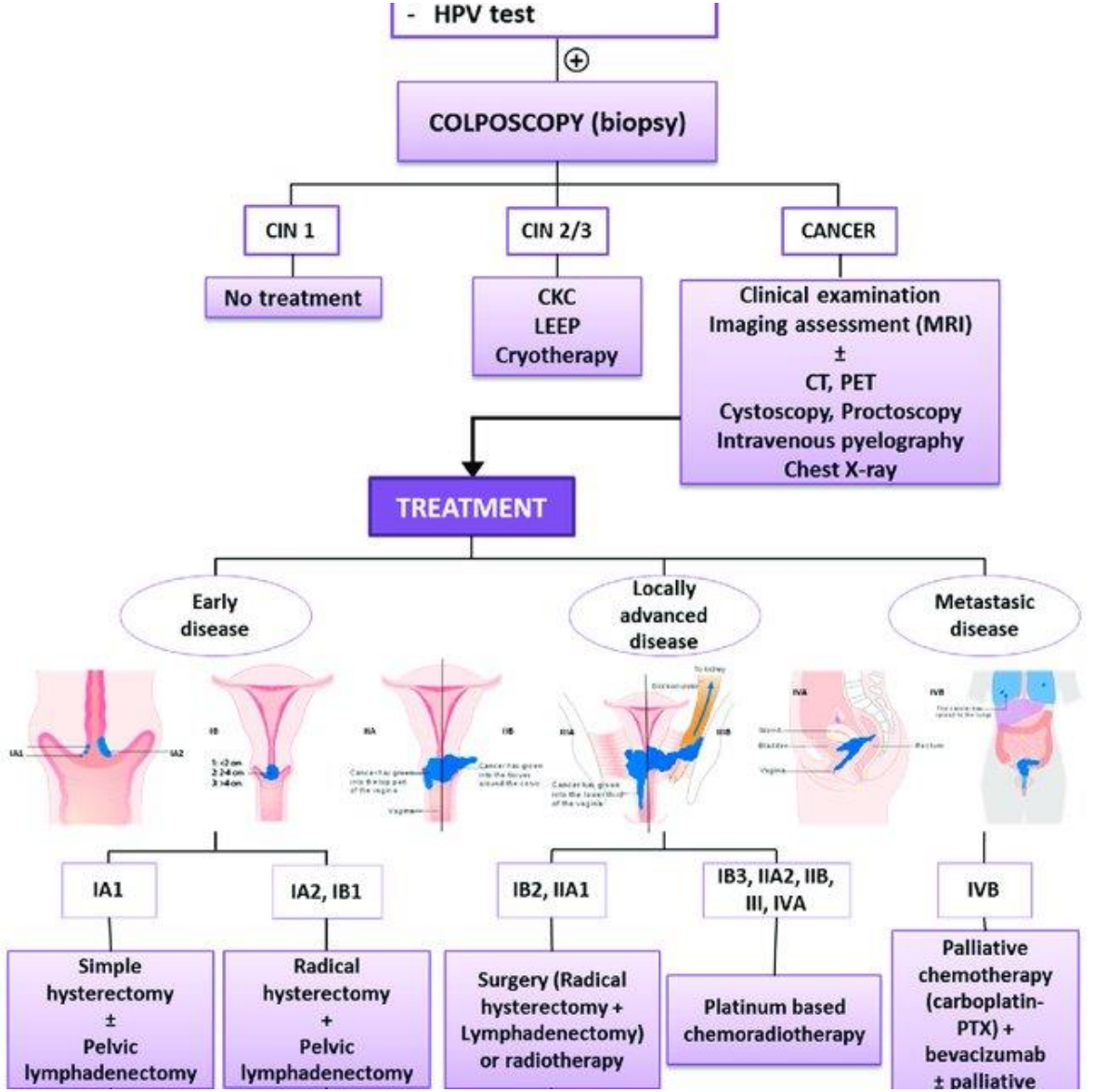
PARP inhibitors





Cervical cancer

Cervical cancer



Prostate cancer

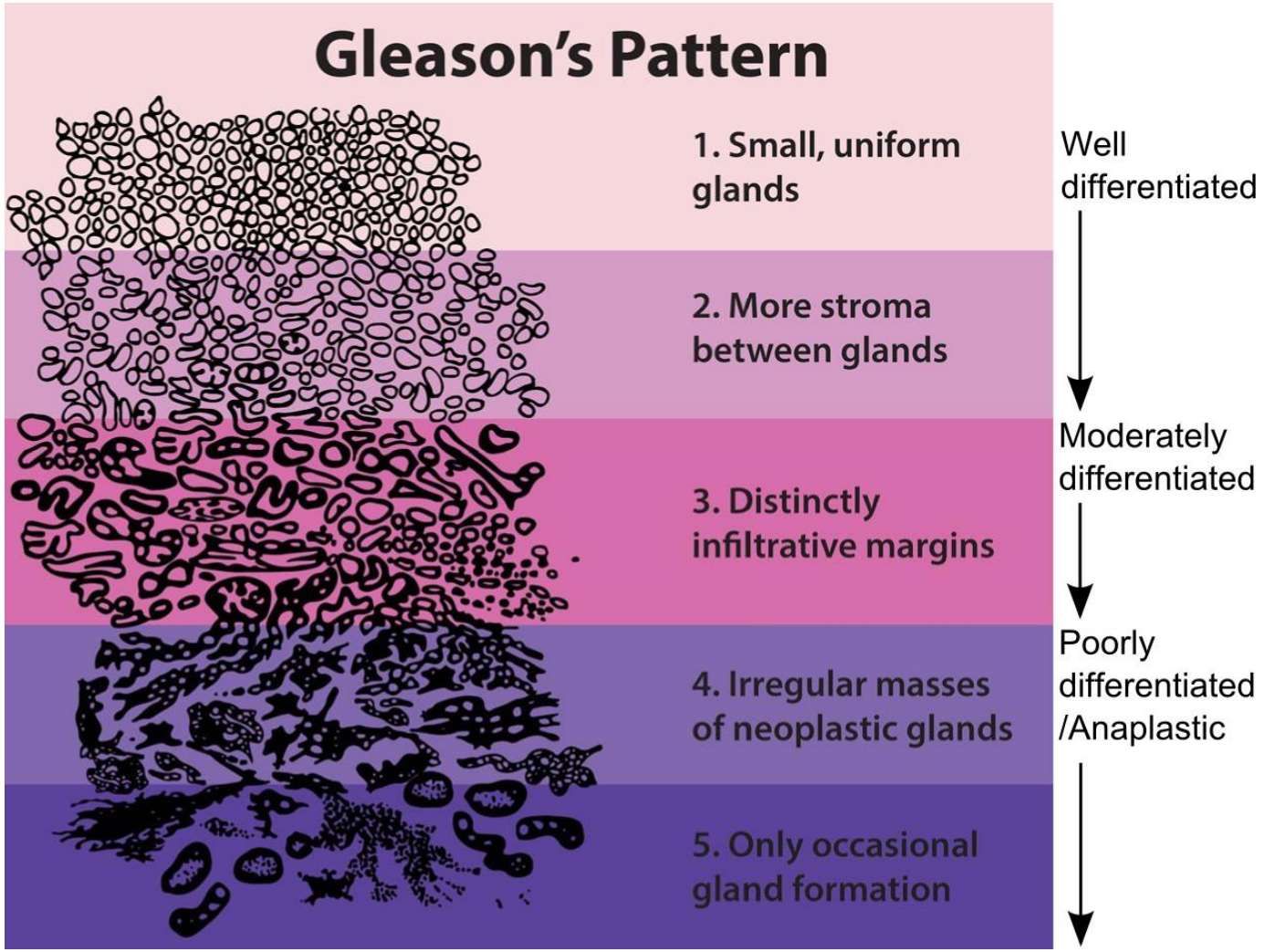
LOCALISED

METASTATIC

D'Amico 1998 Risk Stratification

Risk Group	Biopsy	PSA	Stage (1992 AJCC)	Estimated 5 year recurrence risk
Low	≤ Gleason 6	≤10	T1c, T2a	<25%
Intermediate	Gleason 7	>10, ≤20	T2b	25-50%
High	≥ Gleason 8	>20	T2c	>50%

GS


Gleason's Pattern
1. Small, uniform glands
2. More stroma between glands
3. Distinctly infiltrative margins
4. Irregular masses of neoplastic glands
5. Only occasional gland formation
Well differentiated
Moderately differentiated
Poorly differentiated /Anaplastic

- Accurate
- Simpler
- Grade 1

ISUP Prostate Cancer Grade Groups

Grade group	Gleason score	Gleason pattern
1	≤6	≤3+3
2	7	3+4
3	7	4+3
4	8	4+4, 3+5, 5+3
5	9 or 10	4+5, 5+4, or 5+5

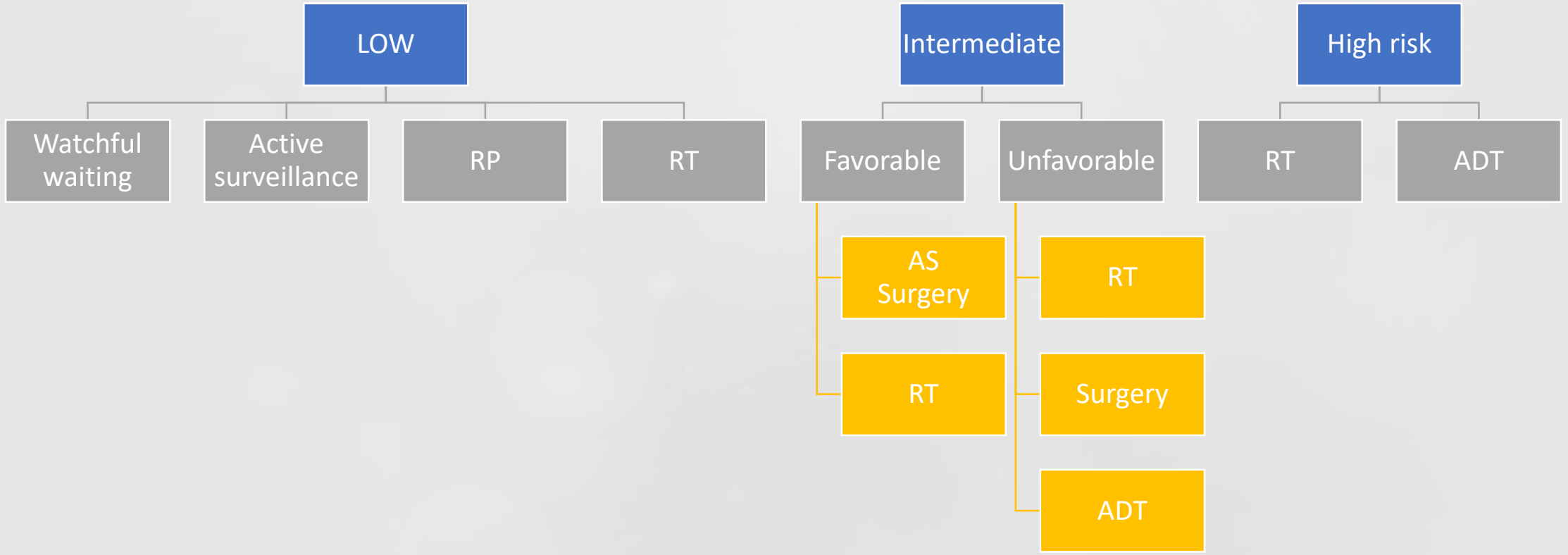
Localised disease

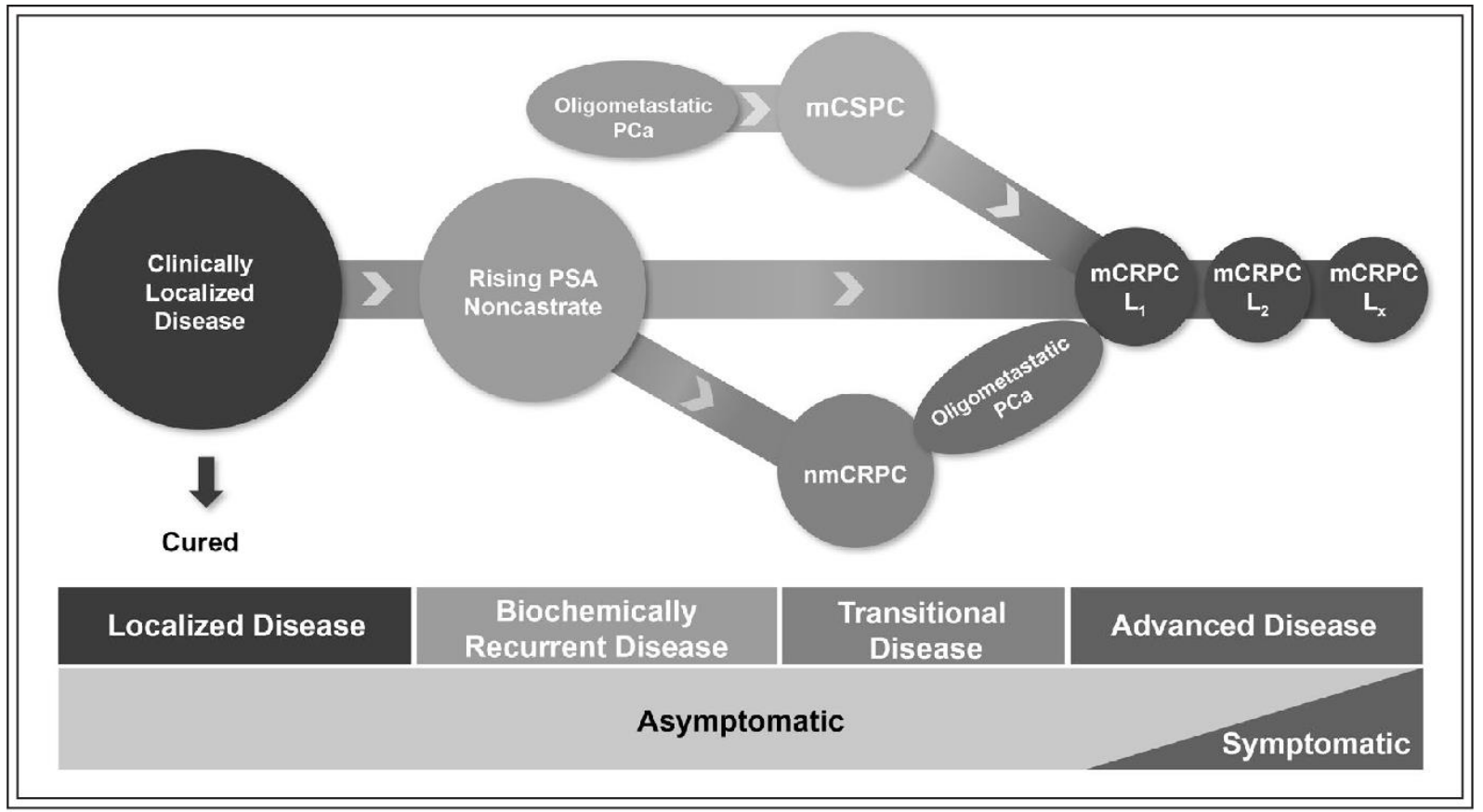
Table 1: National Comprehensive Cancer Network Risk Stratification of Prostate Cancer

Clinical and Pathologic Features	Very Low or Low Risk	Intermediate Risk	High or Very High Risk
T stage	T1-T2a	T2b-T2c	T3a-T4
PSA (ng/mL)	<10	10–20	>20
Biopsy GS (GG)	≤6 (GG1)	7 (GG2 or 3)	8–10 (GG4 or 5)

Note.—GG = grade group, GS = Gleason score, PSA = prostate-specific antigen.

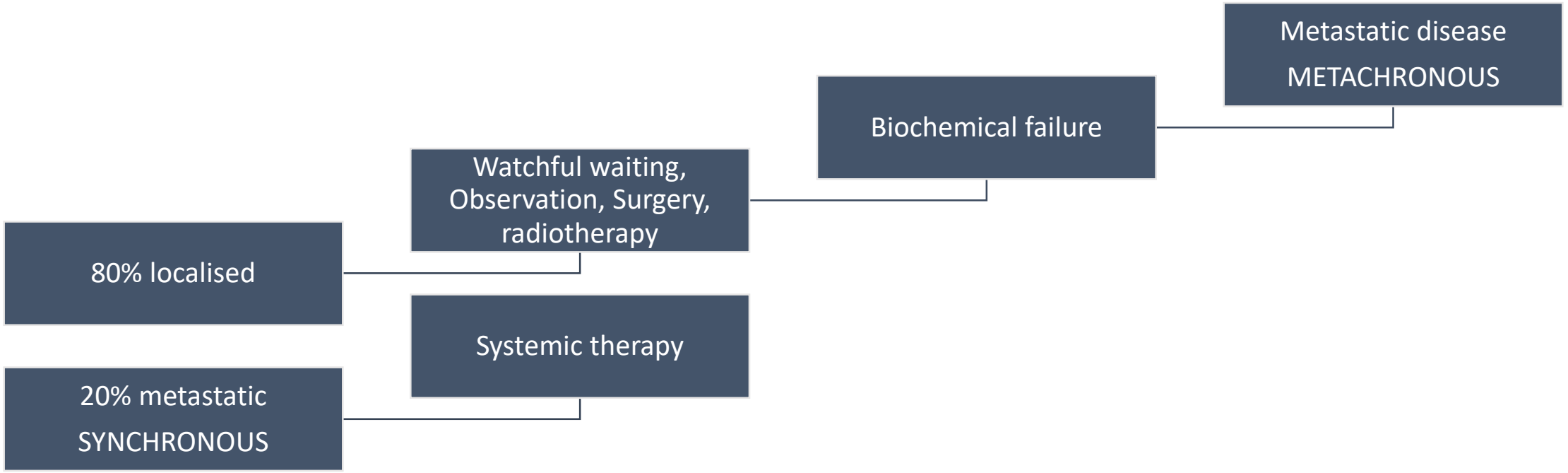
Management localised disease





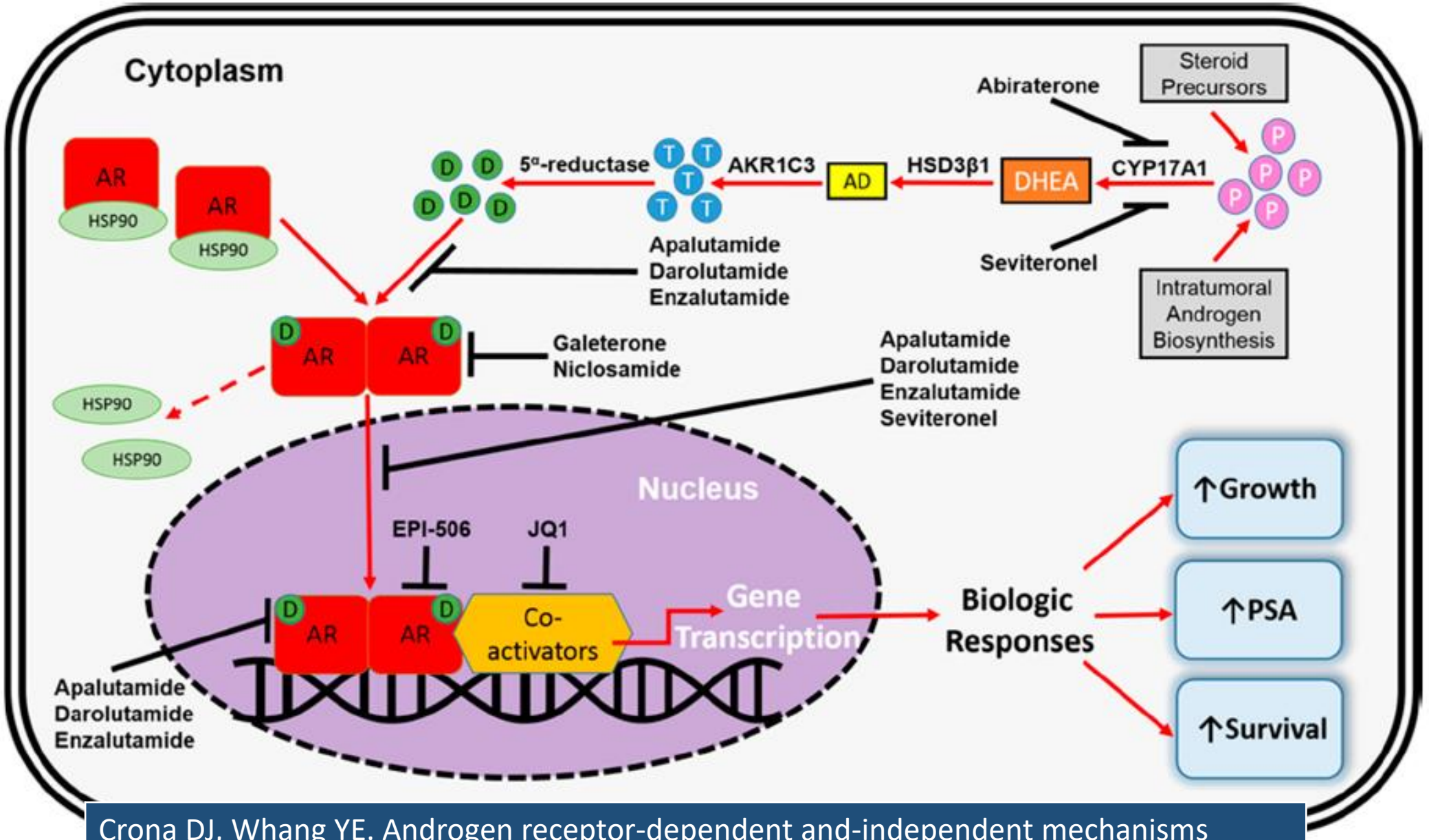
RADAR IV. Can J Urol. 2020 Oct;27(5):10352-10362.

Synchronous vs Metanchronous



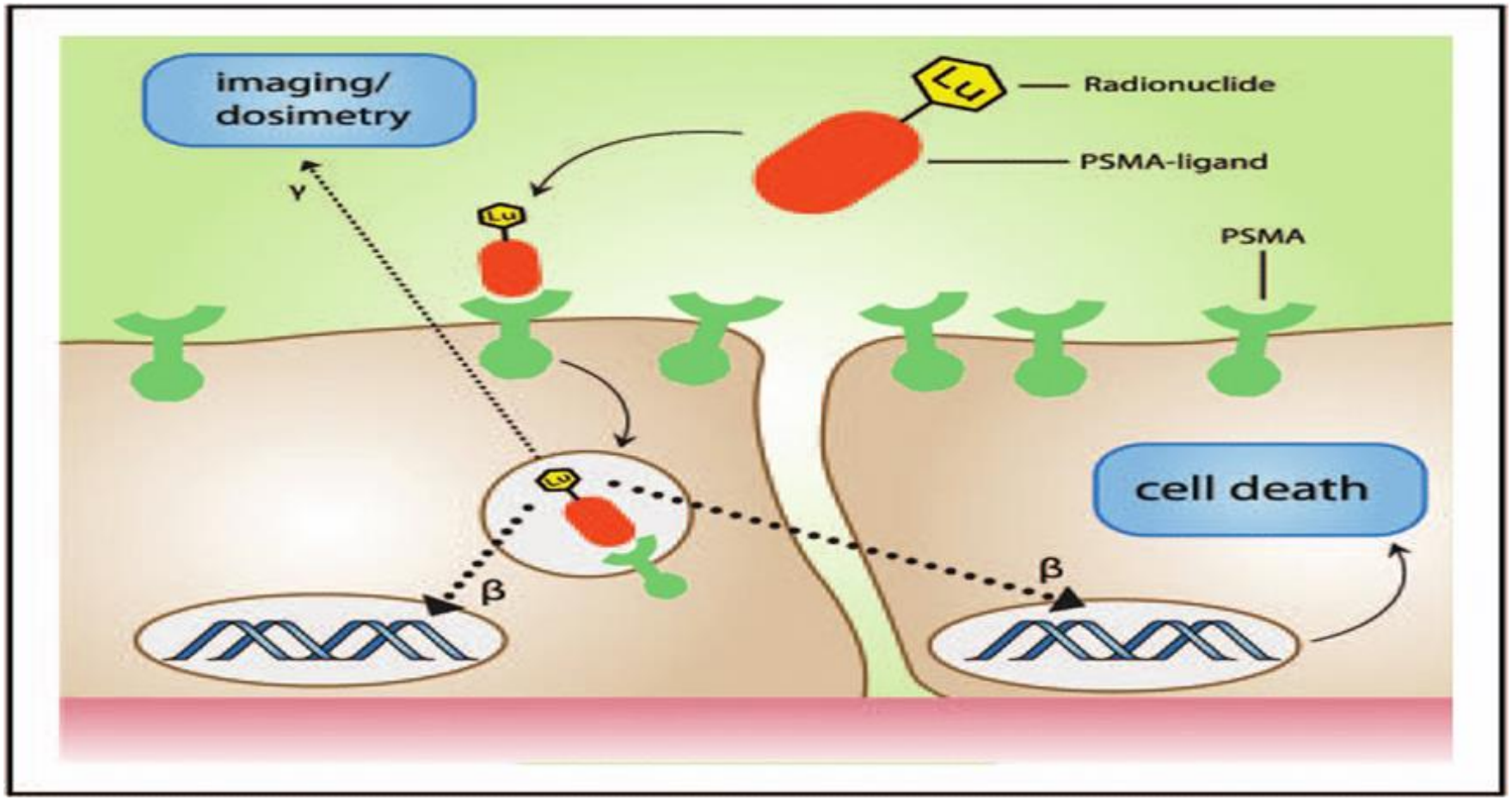
Principles

- ADT
- Early introduction of systemic therapy
- Chemotherapy
- Androgen receptor targeted therapies

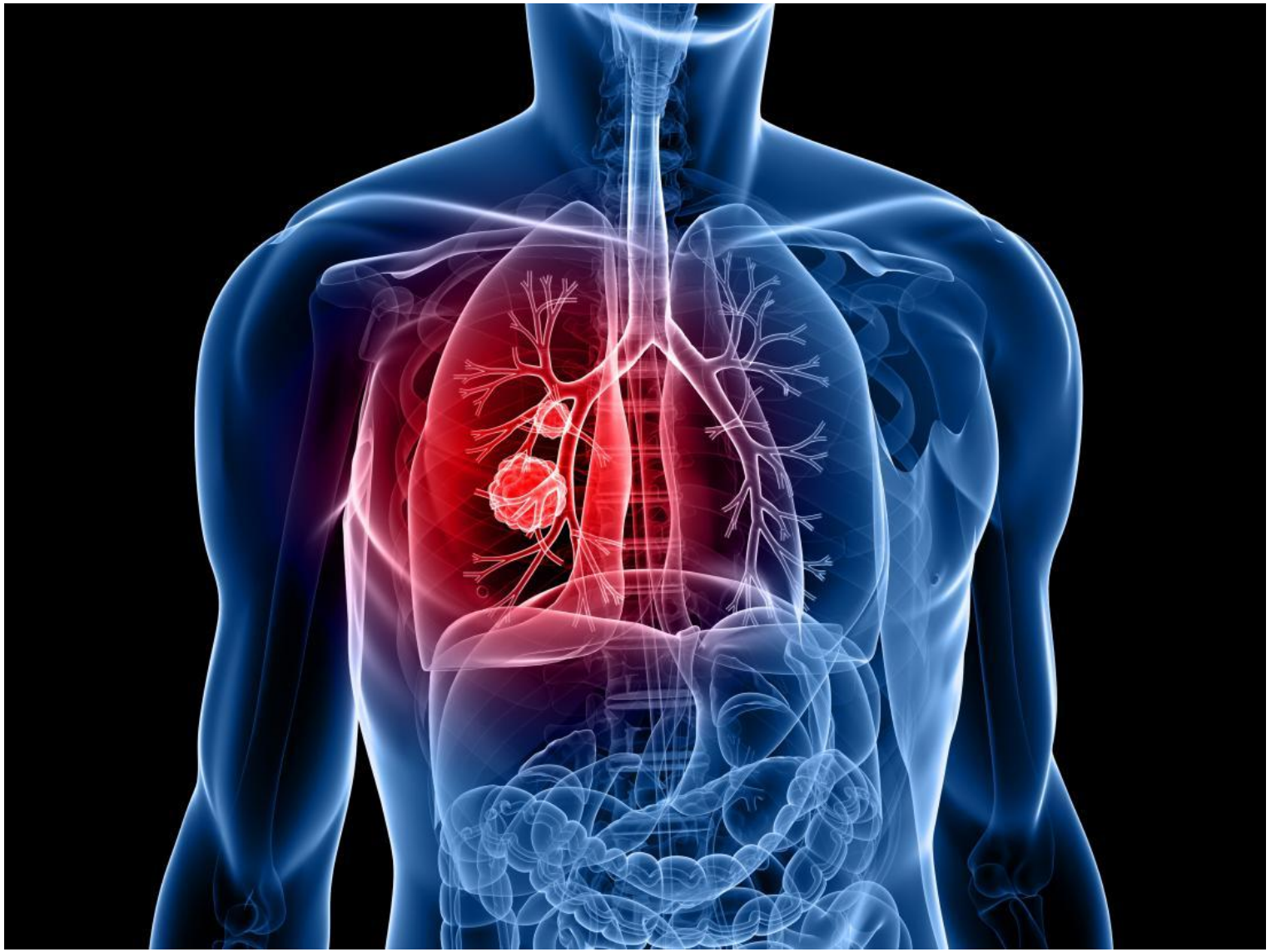


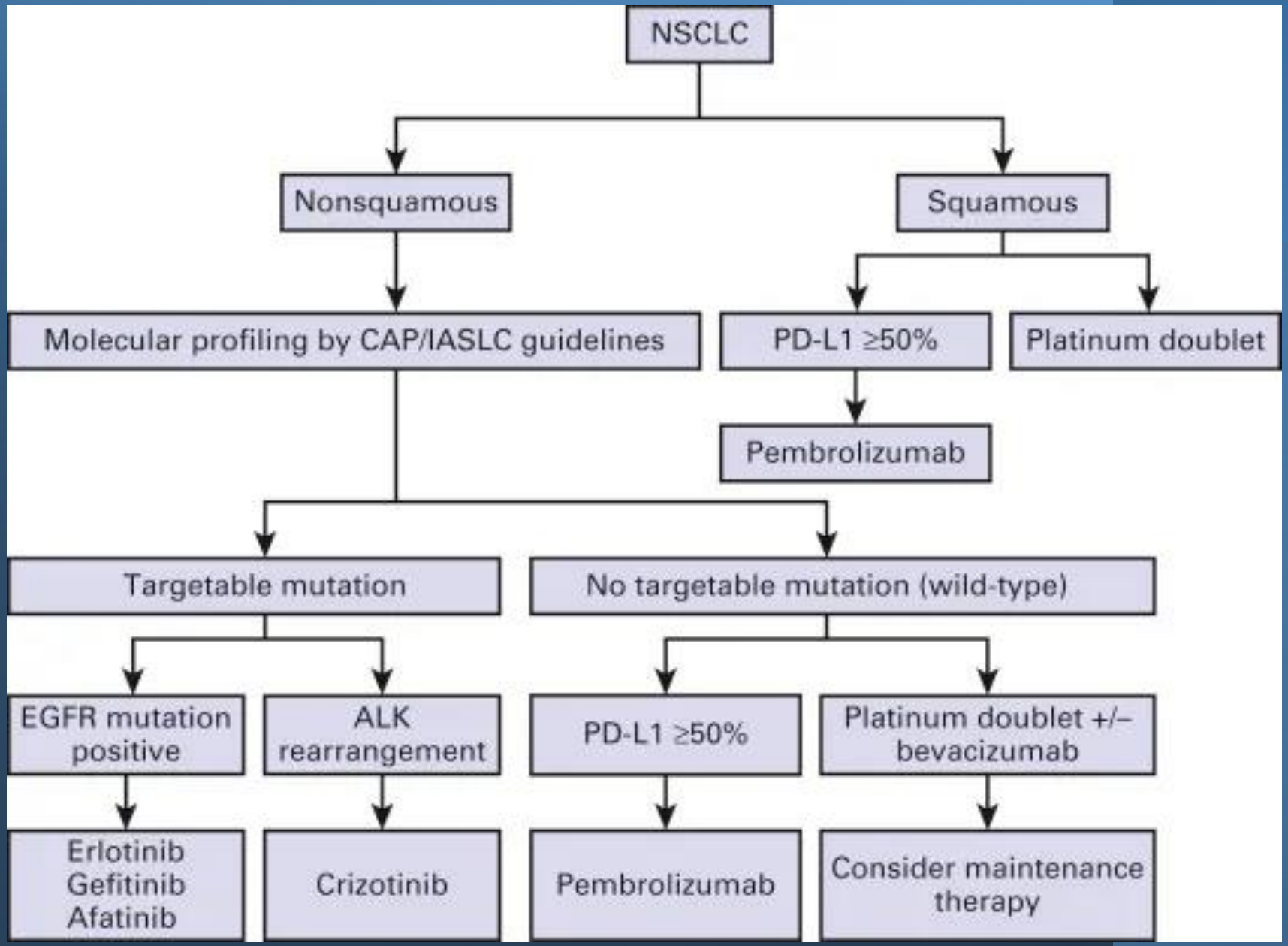
Crona DJ, Whang YE. Androgen receptor-dependent and-independent mechanisms involved in prostate cancer therapy resistance. Cancers. 2017 Jun;9(6):67.

Theranostics

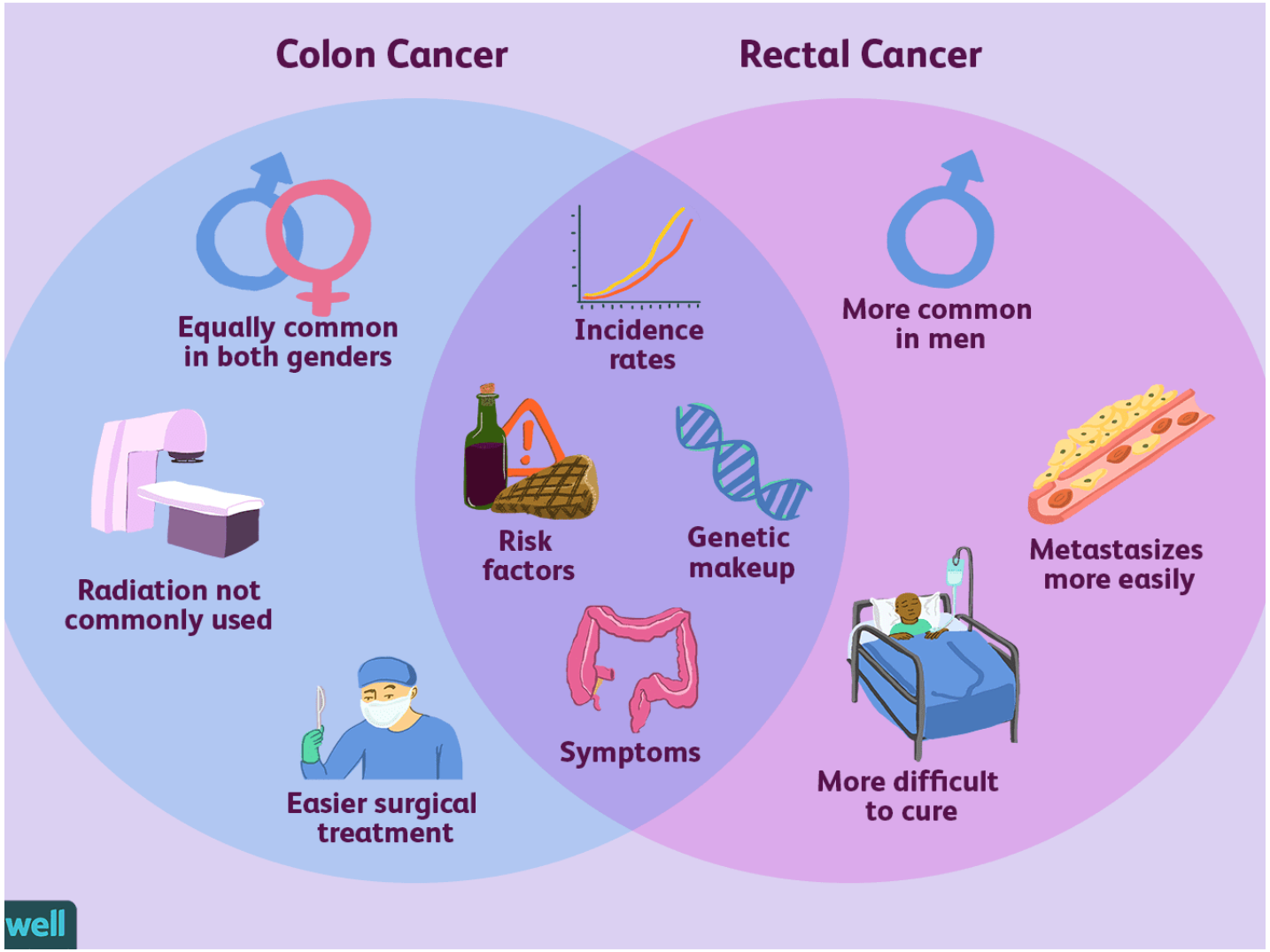


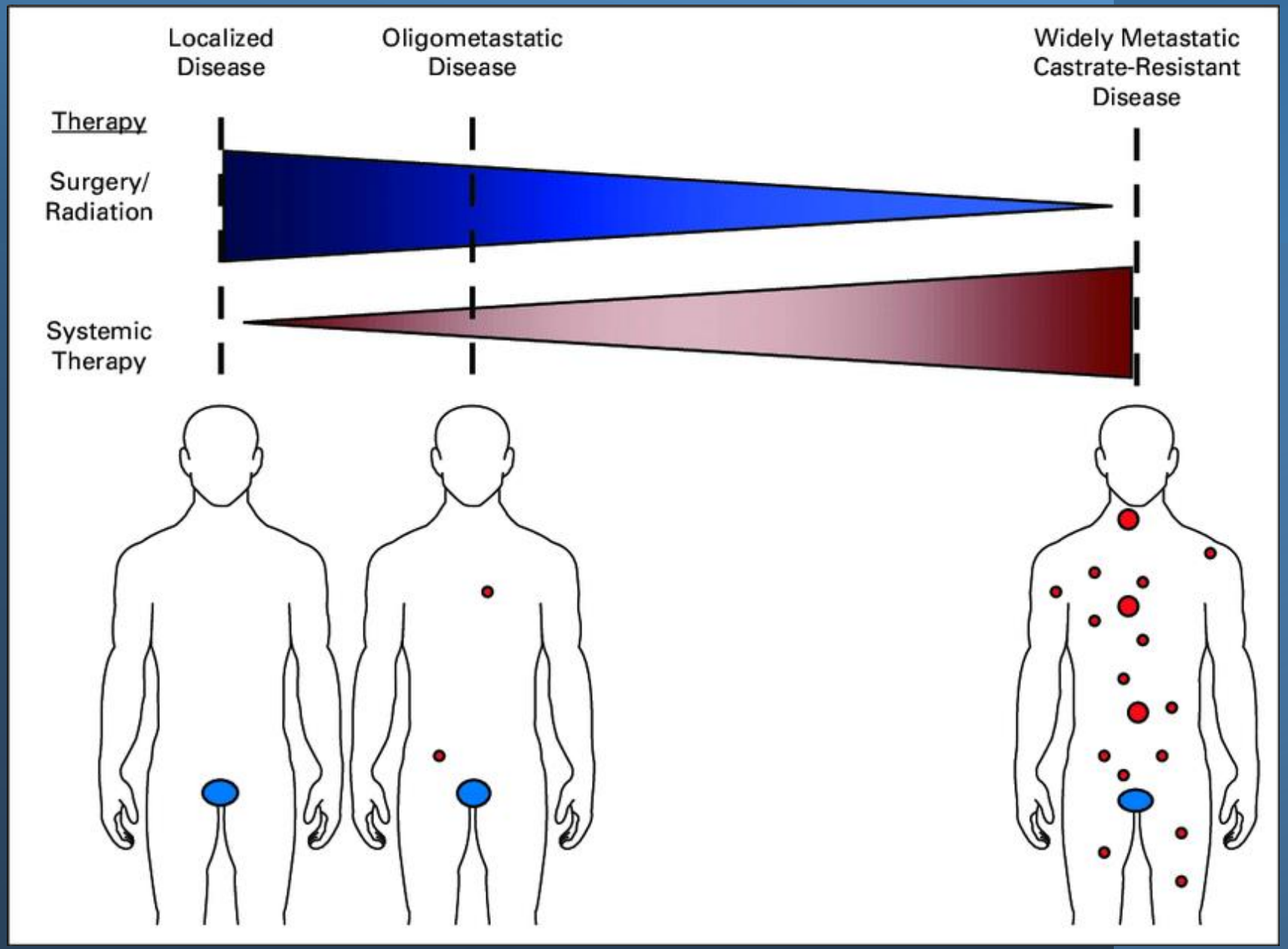
Lung cancer



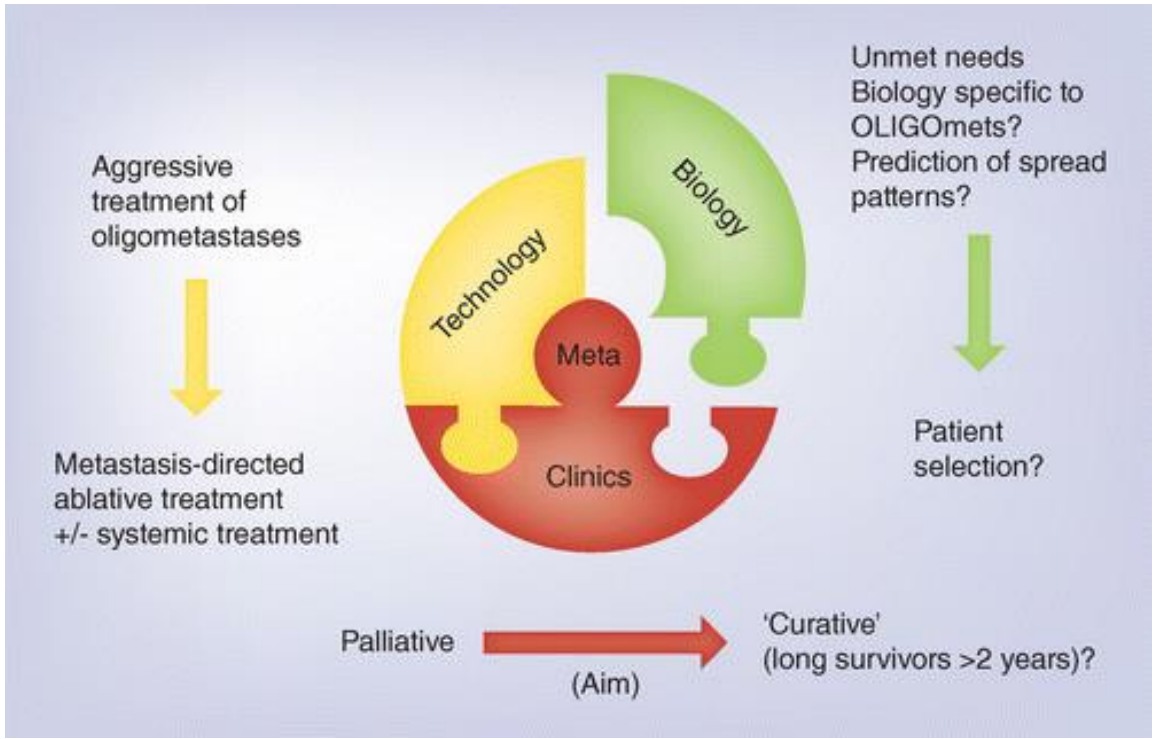

NSCLC
Nonsquamous
Squamous
Molecular profiling by CAP/IASLC guidelines
PD-L1 ≥50%
Platinum doublet
Pembrolizumab
Targetable mutation
No targetable mutation (wild-type)
EGFR mutation positive
ALK rearrangement
PD-L1 ≥50%
Platinum doublet +/– bevacizumab
Erlotinib
Gefitinib
Afatinib
Crizotinib
Pembrolizumab
Consider maintenance therapy

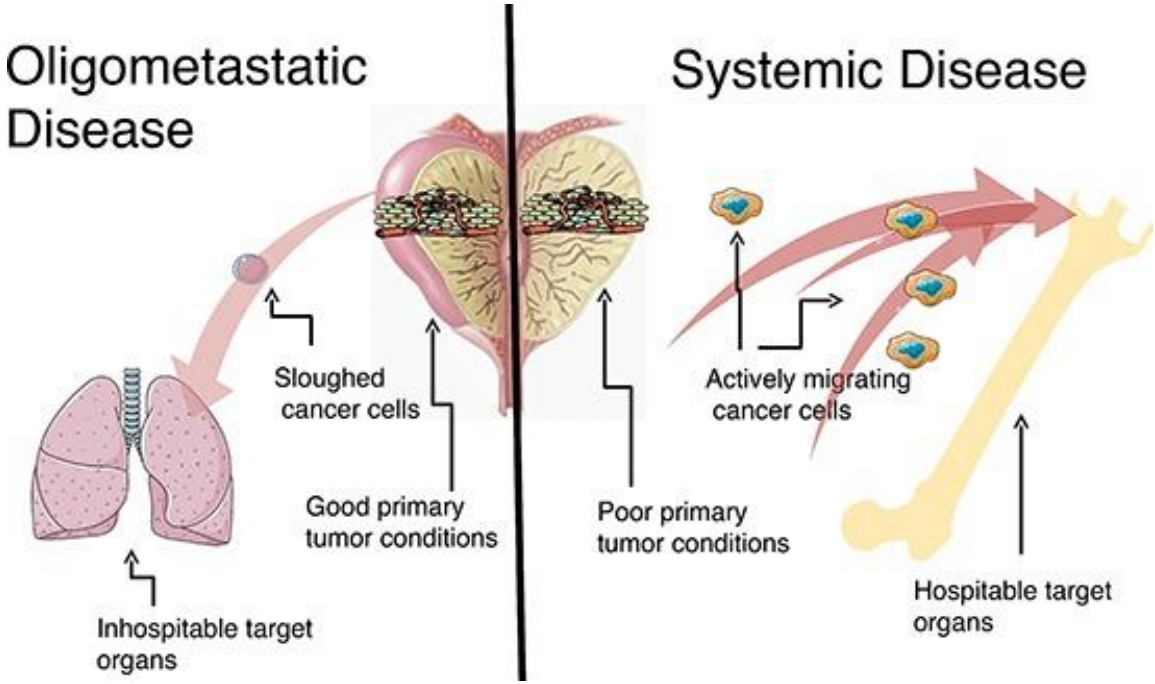
COLORECTAL Cancer




Localized Disease
Oligometastatic Disease
Widely Metastatic Castrate-Resistant Disease
Therapy
Surgery/ Radiation
Systemic Therapy

Oligometastatic disease





Oncological emergencies

Metabolic: Tumor Lysis syndrome, Hypercalcaemia

Haematolgical: Neutropaenia, Thrombosis

Structural: SVC syndrome, malignant spinal cord compression

Treatment related: Chemotherapy, Radiotherapy

Metabolic: Tumor lysis

Diagnosis and management: ACKD 2021

Risk factors

- Large tumor burden
- High lysis potential;
- Intesntiy of CT
- Inc LDH
- Pre existing kidney disease
- ↓ BP
- Volume depletion
- Nephrotoxin exposure
- Decreased urine pH

Lab diagnosis within 2-24hrs

Cairo Bishop definition

↑Phosphorous >1.45mmol/L

↑Potassium >6mmol/L

↓Calcium <1.75mmol/L or <25% dec from baseline

↑Uric acid >476umol/L or >25% inc from baseline

Clinical diagnosis

- At least one of the following
- ↑Cr ≥ 1.5ULN
- Arrythmia
- Seizures

Management

- Aggressive IV hydration
- Maintain urine outflow
- Medical management of metabolic abn
- Uric acid therapy: Allopurinol, rasburicase
- HD for refractory hyperkalaemia or symptomatic hypocalcaemia

Hypercalcaemia of malignancy

10-30%

Breast, myeloma, lung, head and neck, cervical cancer

Causes: Humoral, bone invasion

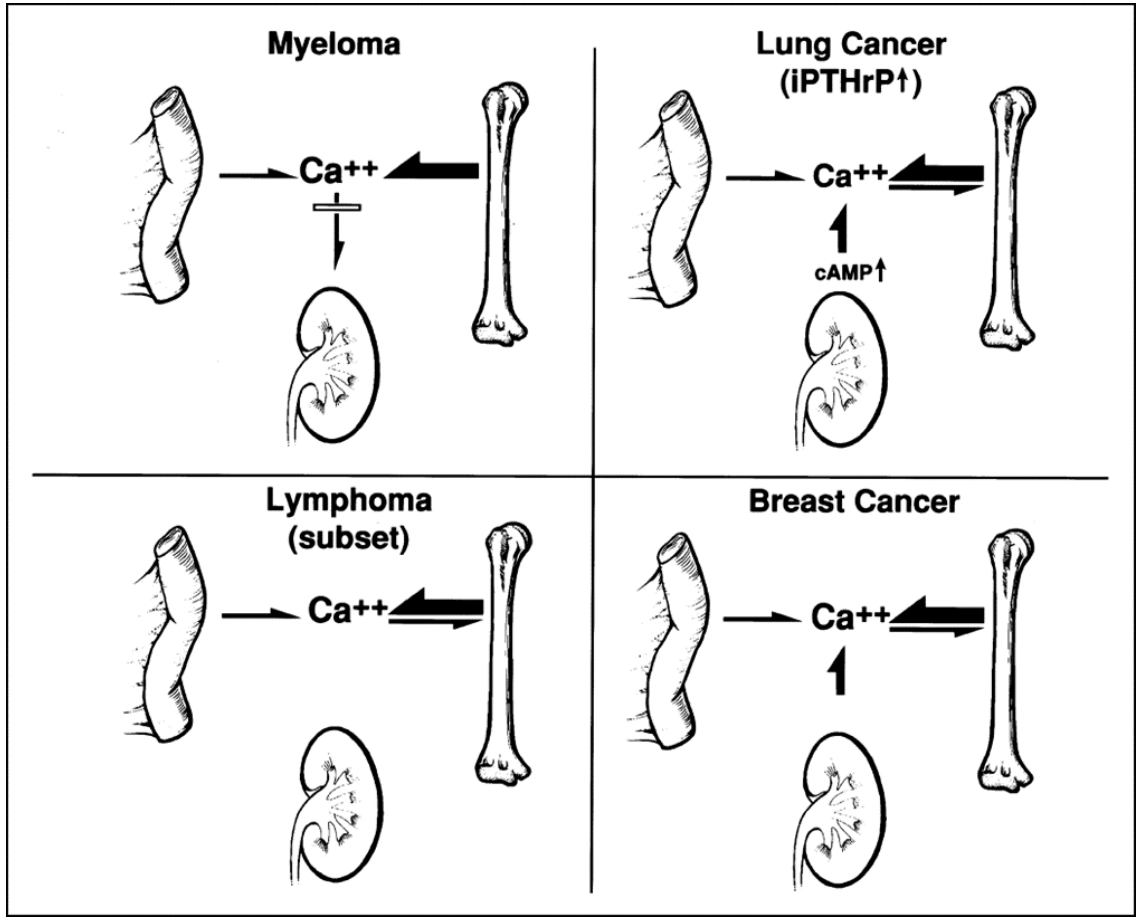
Humoral: 80%: PTH Related hormone, increase D3 (80%)

Lytic bone lesions: 20%

Rare: Immobilisation, medication

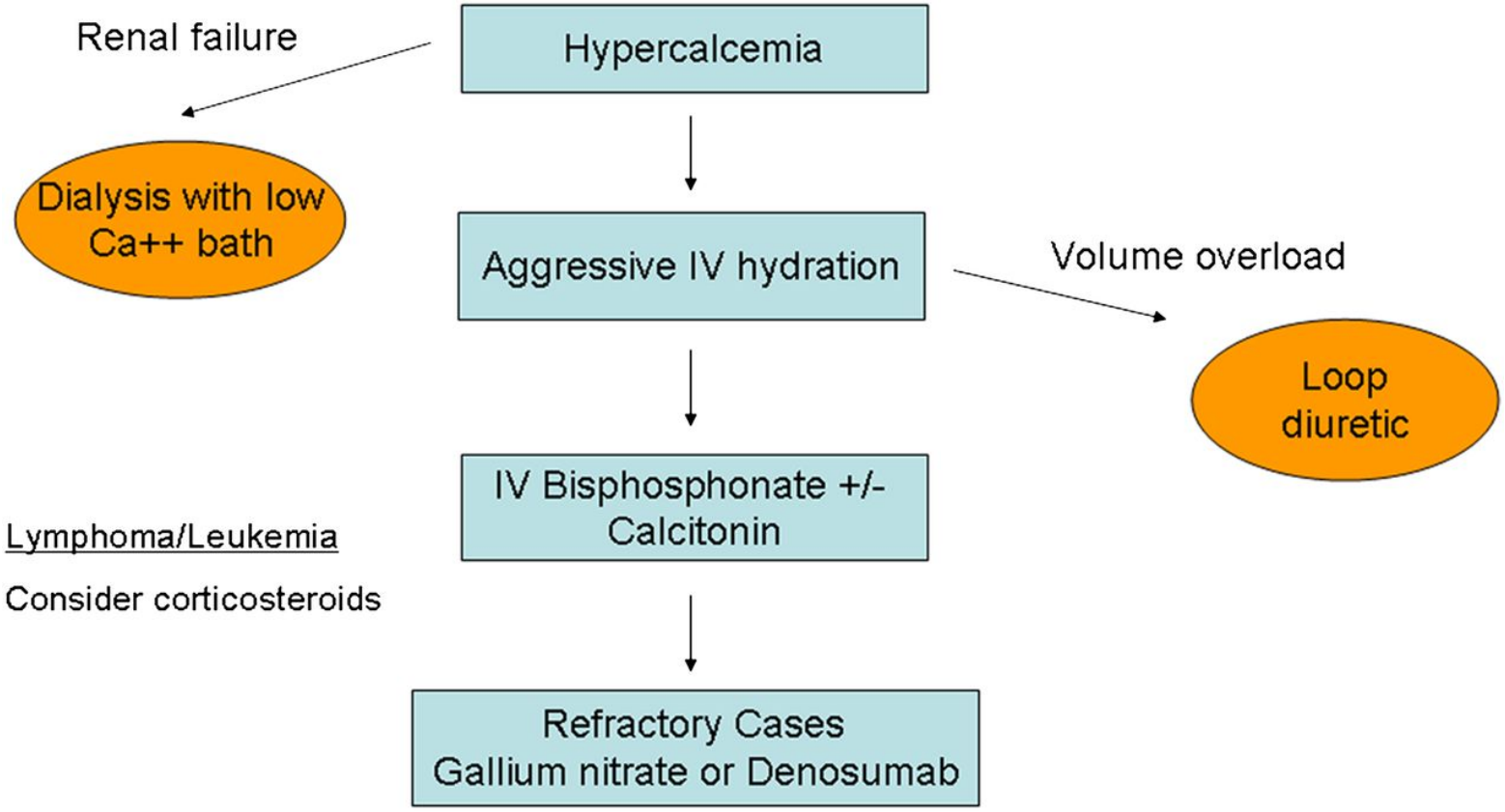
Presentation

Pathophysiology of hypercalcaemia



Symptoms

Treatment



Febrile neutropaenia

- One of the common oncological emergencies
- Single axillary/oral temperature of 38.5°C **or**
- Higher or a sustained temperature of 38°C or higher for one hour
- **And** an absolute neutrophil count (ANC) less than 500 cells per mm3 or an expected decrease of ANC to less than 500 cells per mm3 in the next 48 hours
- Early intervention is beneficial
- Prompt referral is required
- *In absence of neutropaenia: consider UTI, soft tissue infections*
- *Beware of opportunistic infections*

Thrombosis

- Trousseau in 1865
- Virchows triad: stasis, increased coagulability, endothelial damage
- Mechanism may be direct or indirect
  - Venous
  - Arterial
  - DIC

Aetiology

Arterial

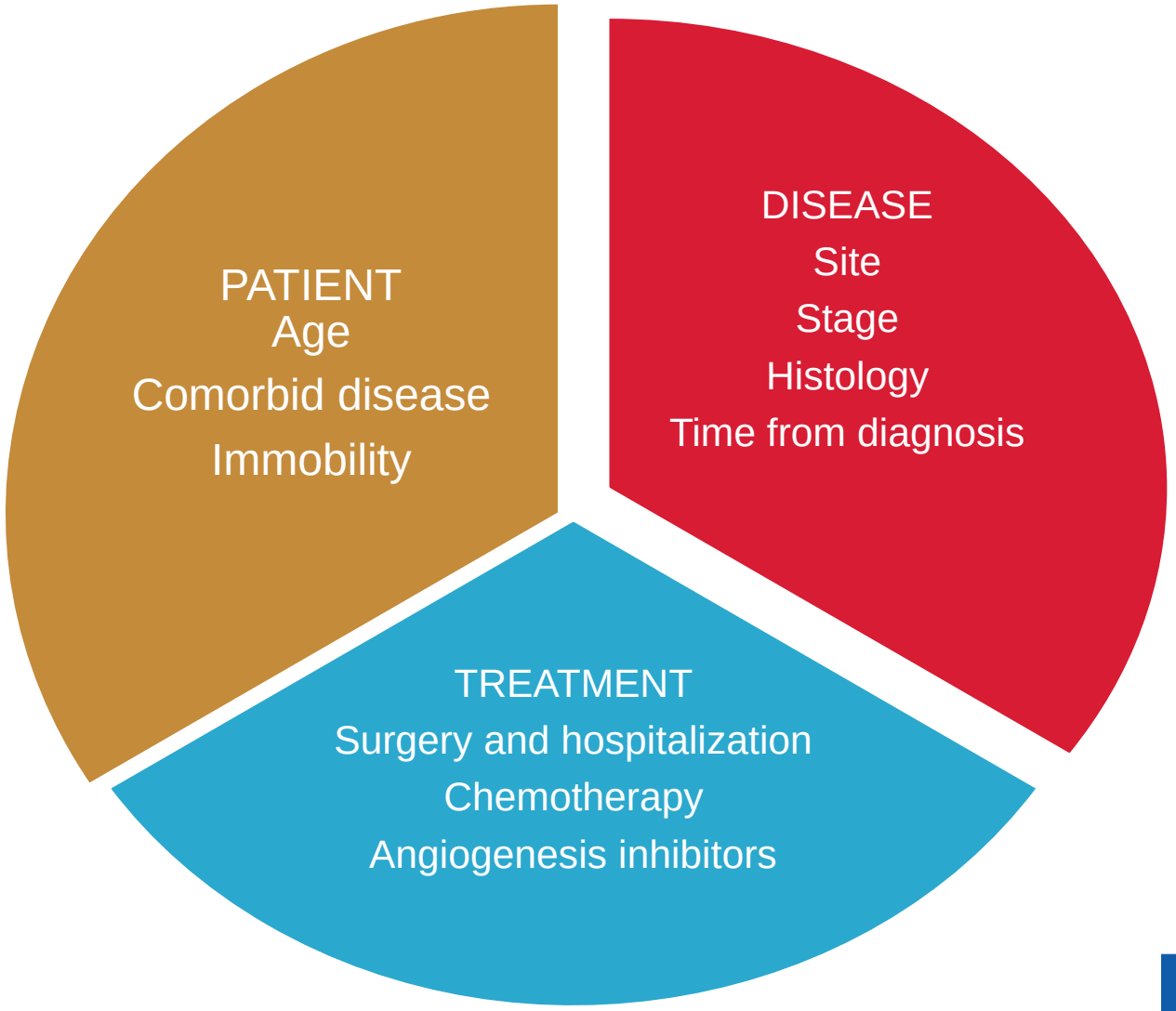
- Typically endothelial damage
- Drugs
  - Platinum-based agents(cisplatin),
  - Vascular endothelial growth factor (VEGF) inhibitors (bevacizumab)
  - VEGF tyrosine kinase receptor inhibitors (sorafenib/sunitinib/pazopanib)
- Hypertension, vascular abnormalities, atherosclerosis

VTE

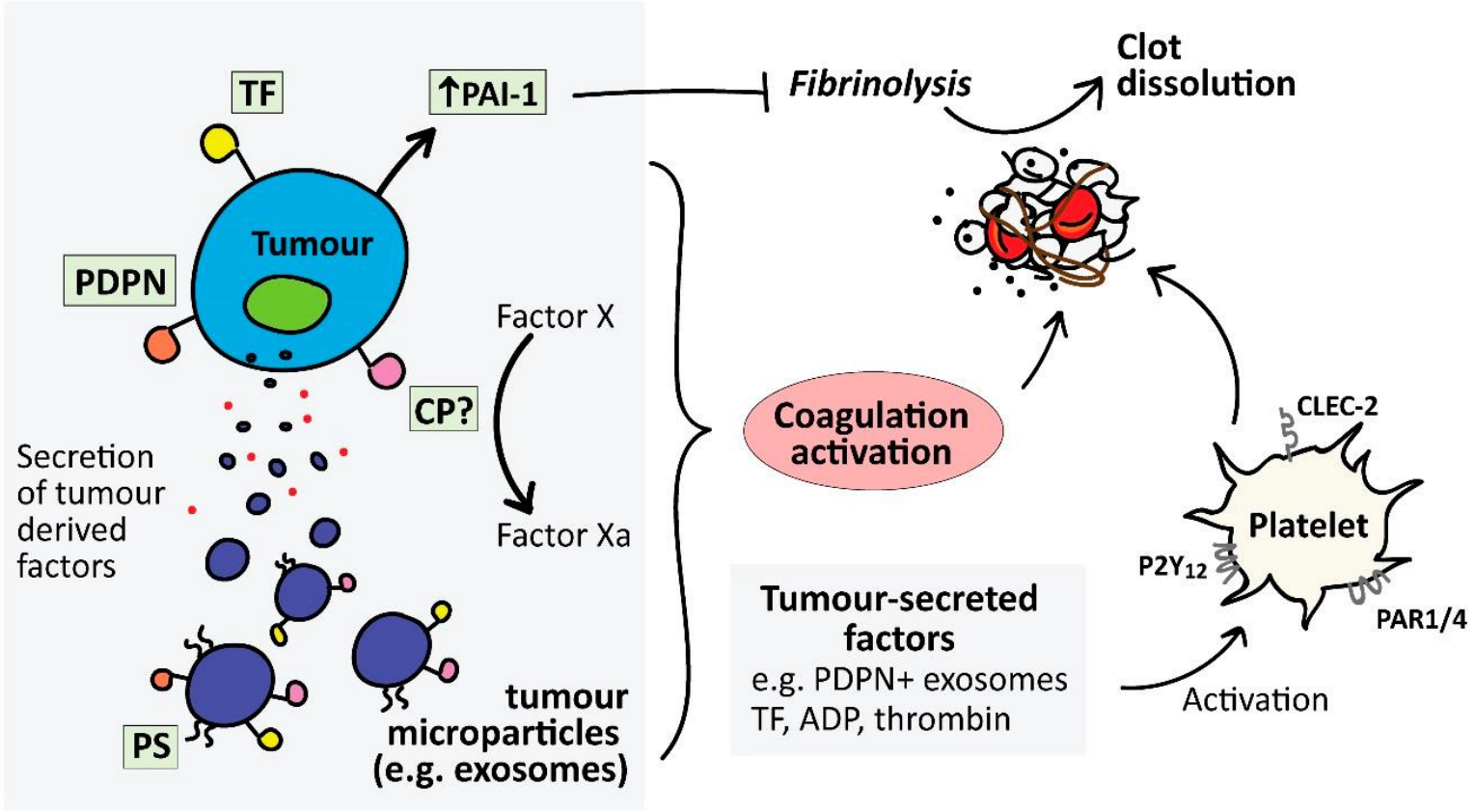
VTE

- 5-7 x more common in cancer patient
- DVT and pulmonary emboli
- 3X more fatal
- Presence at diagnosis(most often) associated with worse prognosis
- 0.5% per annum

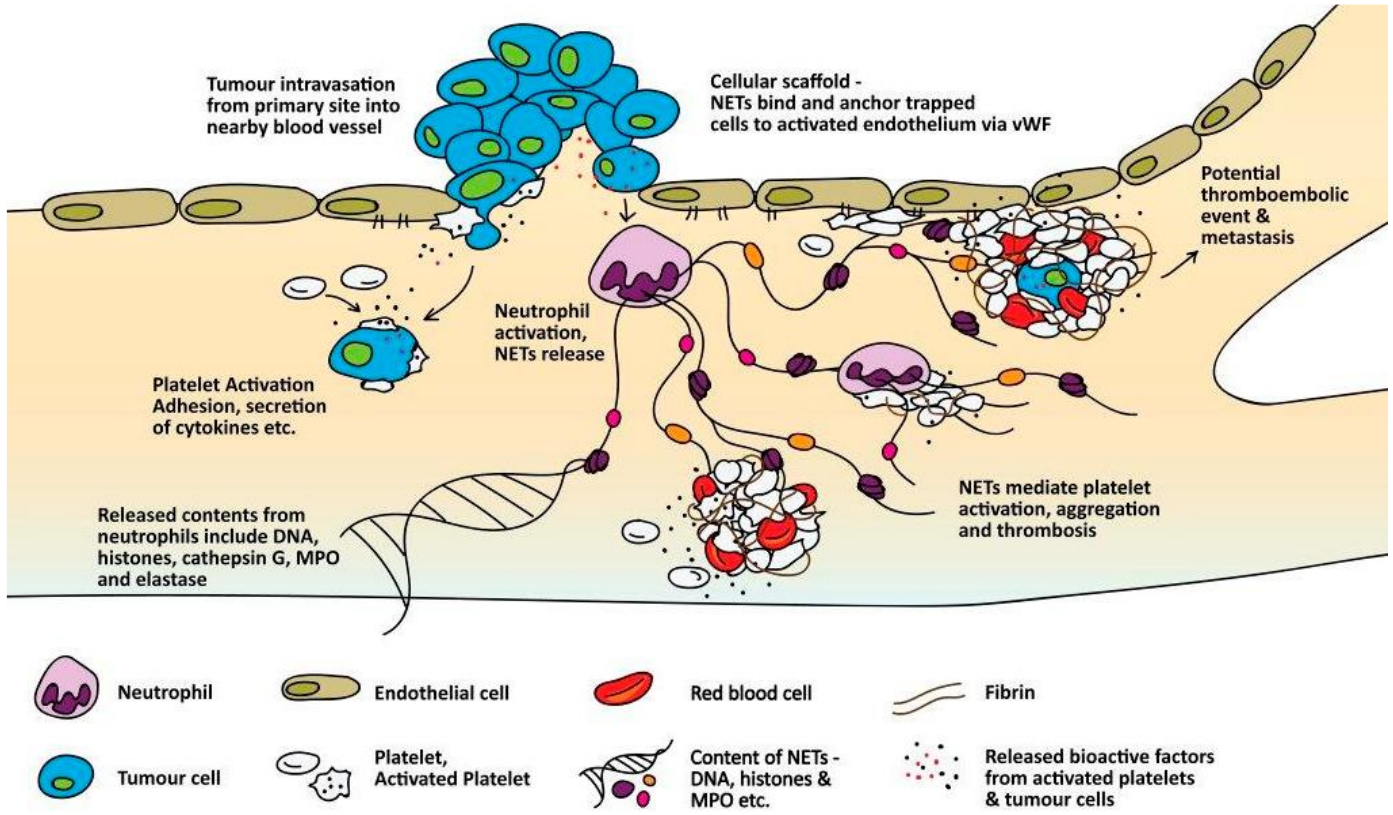
Risk factors



Mechanism: direct



Mechanism: Indirect



Management

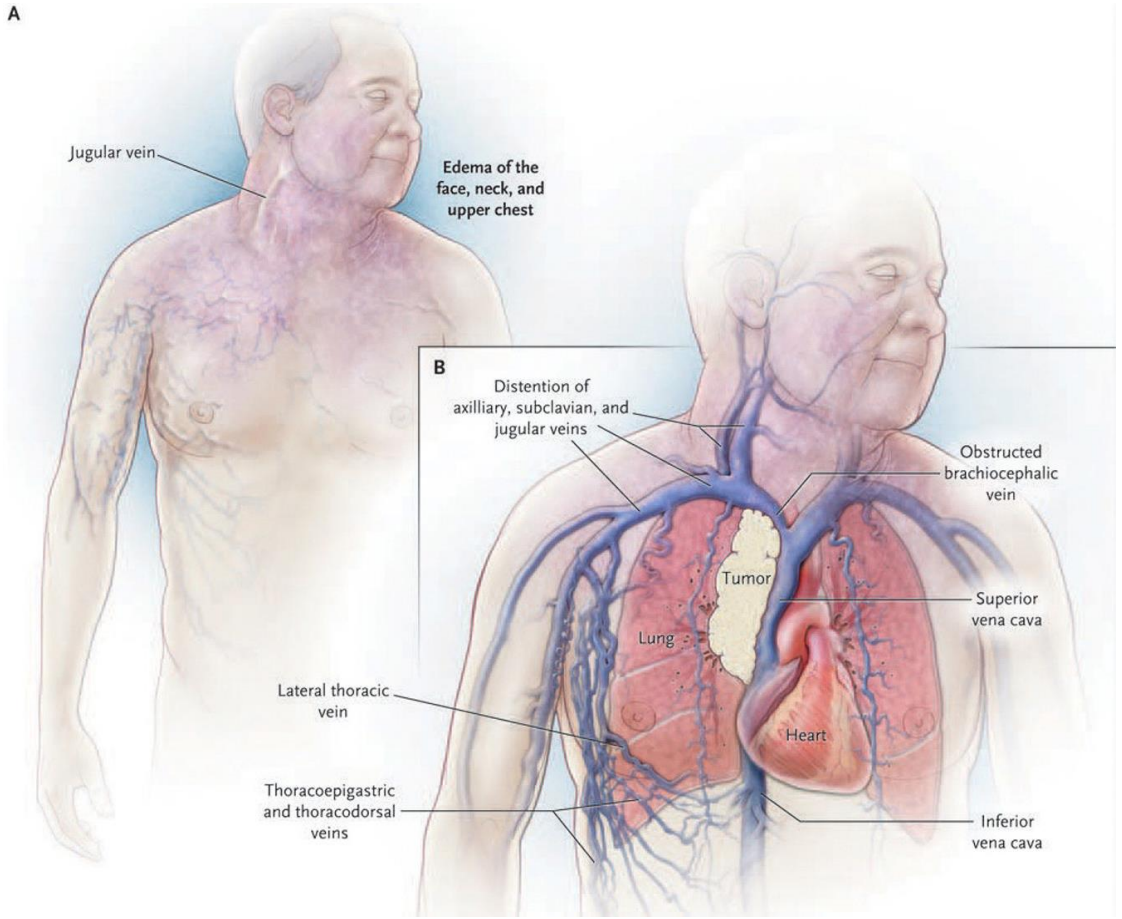
Patient education
Assess risk, surveillance
Prophylaxis for 4 weeks if undergoing major abdominal surgery: LMWH superior to warfarin
Edoxaban (Lixiana)was non-inferior to subcutaneous dalteparin
Rivaroxaban (Xarelto) was associated with low VTE recurrence but higher clinically relevant non major bleeding
Beware drug i

Structural: SVC syndrome

- Gradual compression of the superior vena cava where it enters the right atrium, leading to edema and retrograde flow.
- Lung cancer, lymphoma, breast cancer

Symptoms

N Engl J Med. *2007; 356(18): 1863.*



Facial odemea
Cough
Dyspnoea
Pain
Plethora
Swelling of arm
Collateral veins

Treatment SVC

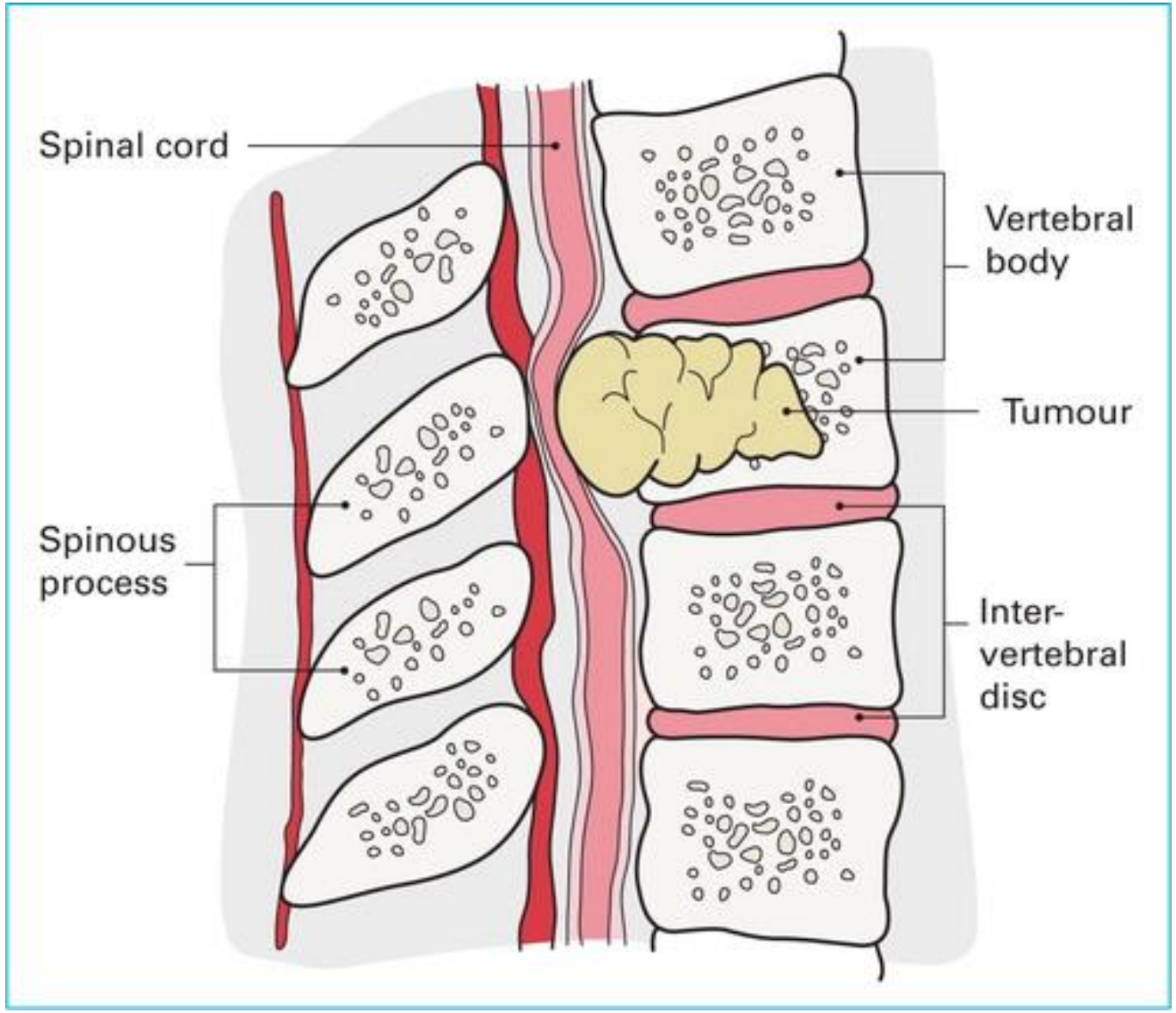
- Oxygen, elevate bed, Lasix
- Steroids
- Radiotherapy
- Chemotherapy
- Stenting
- Outcome and prognosis

Malignant spinal cord compression

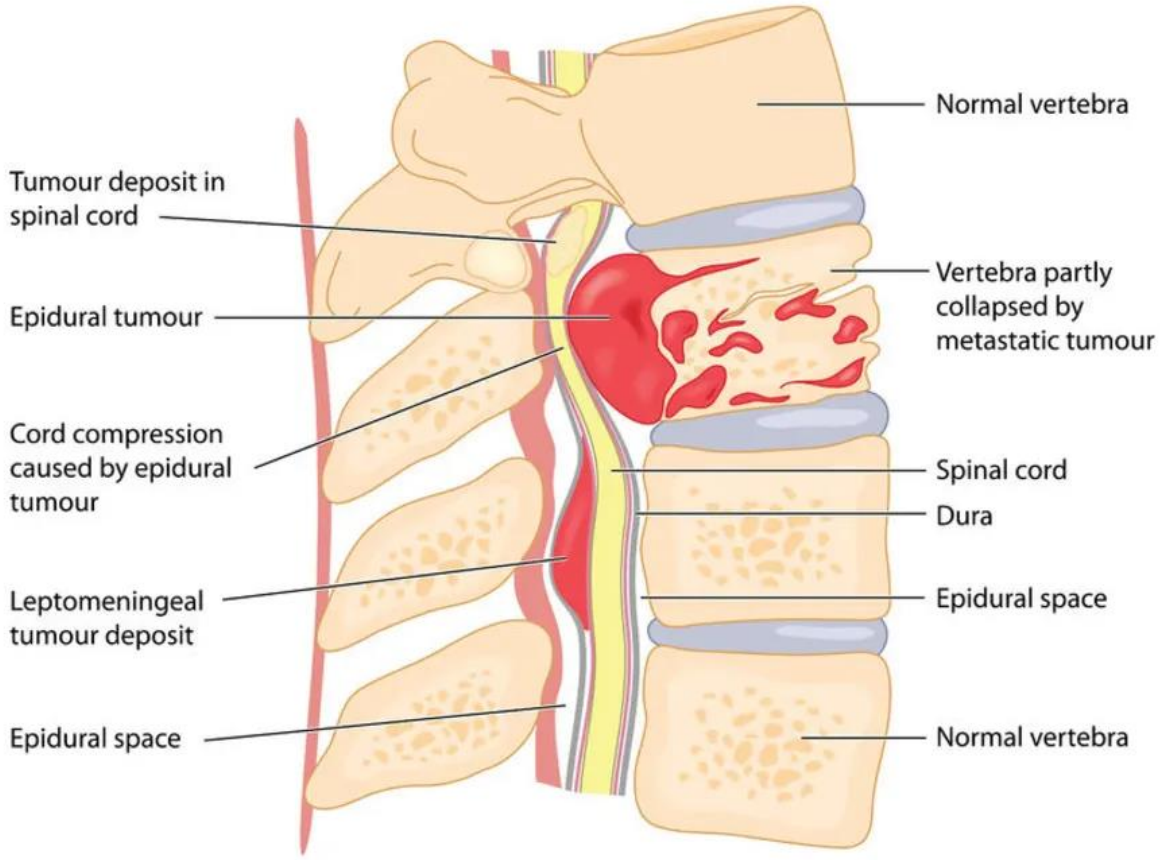
- Emergency
- Pain, progressive neurological decline
- Treatment within 24 hrs of onset better chance of reversal
- 2.5% to 5%
- Usually lung, prostate, or breast cancer
- First manifestation of systemic cancer in 20% to

34%

- Myeloma 10%



Mechanism



https://www.spineuniverse.com/resource-center/spinal-fractures/cancer-spinal-fractures

Presentation

- Thoracic spine----lumbosacral ---cervical
- Back pain: 85-90%, worse at nite, vasalva
- Motor weakness: 35% to 75%
- Sensory deficits: sensory level
- Bowel or bladder dysfunction: late

Management

MRI

- Gold standard
- Sensitivity 93% specificity 97%
- Whole spine: 20% to 35%
- CT myelogram

Management: Steroids

- Dexamethasone
- Duration
- Wean off
- Caution

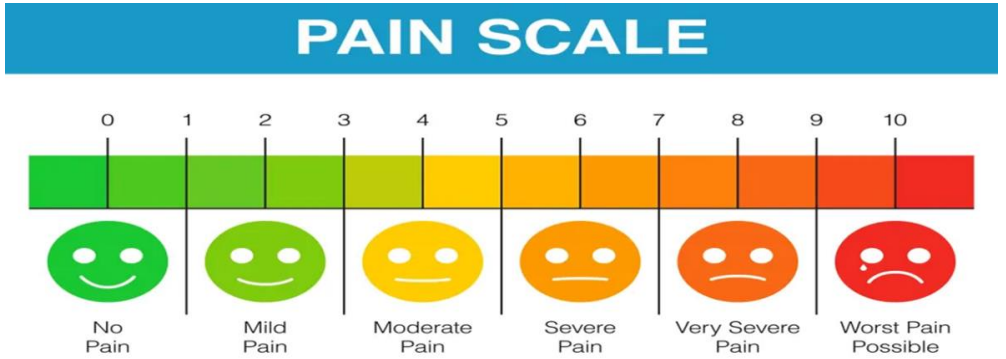
Management: Pain control

Journal of Clinical Oncology®
Volume 37, Issue 1 61

Opioids	
Morphine*	
Immediate release	7.5-15 mg orally every 3 hours as needed or 2-4 mg intravenously every 2 hours as needed
Sustained release†	15 mg orally every 8-12 hours
Oxycodone*	
Immediate release	5-10 mg orally every 3 hours as needed
Sustained release†	10 mg orally every 8-12 hours
Hydromorphone*	
Immediate release	2-4 mg orally every 3 hours as needed or 0.4-0.8 mg intravenously every 2 hours as needed
Fentanyl*	
Sustained release†	12 μg/h transdermally every 72 hours

Neuropathic pain adjuvants	
Dexamethasone	10 mg orally or intravenous load, then 4-6 mg orally or intravenously every 6 hours
Gabapentin*	100 mg orally twice daily; 300 mg at bedtime
Pregabalin*	75 mg orally twice daily
Amitriptyline	10-25 mg orally at bedtime
Nortriptyline	10-25 mg orally at bedtime

Bone pain adjuvants	
Zoledronic acid‡	4 mg intravenously every 3-4 weeks
Pamidronate‡	90 mg intravenously every 3-4 weeks
Acetaminophen§	1,000 mg orally every 8 hours
Bowel regimen medications	
Senna	1-2 tablets twice daily
Polyethylene glycol	17 g one to two times daily
Bisacodyl suppository	Daily as needed



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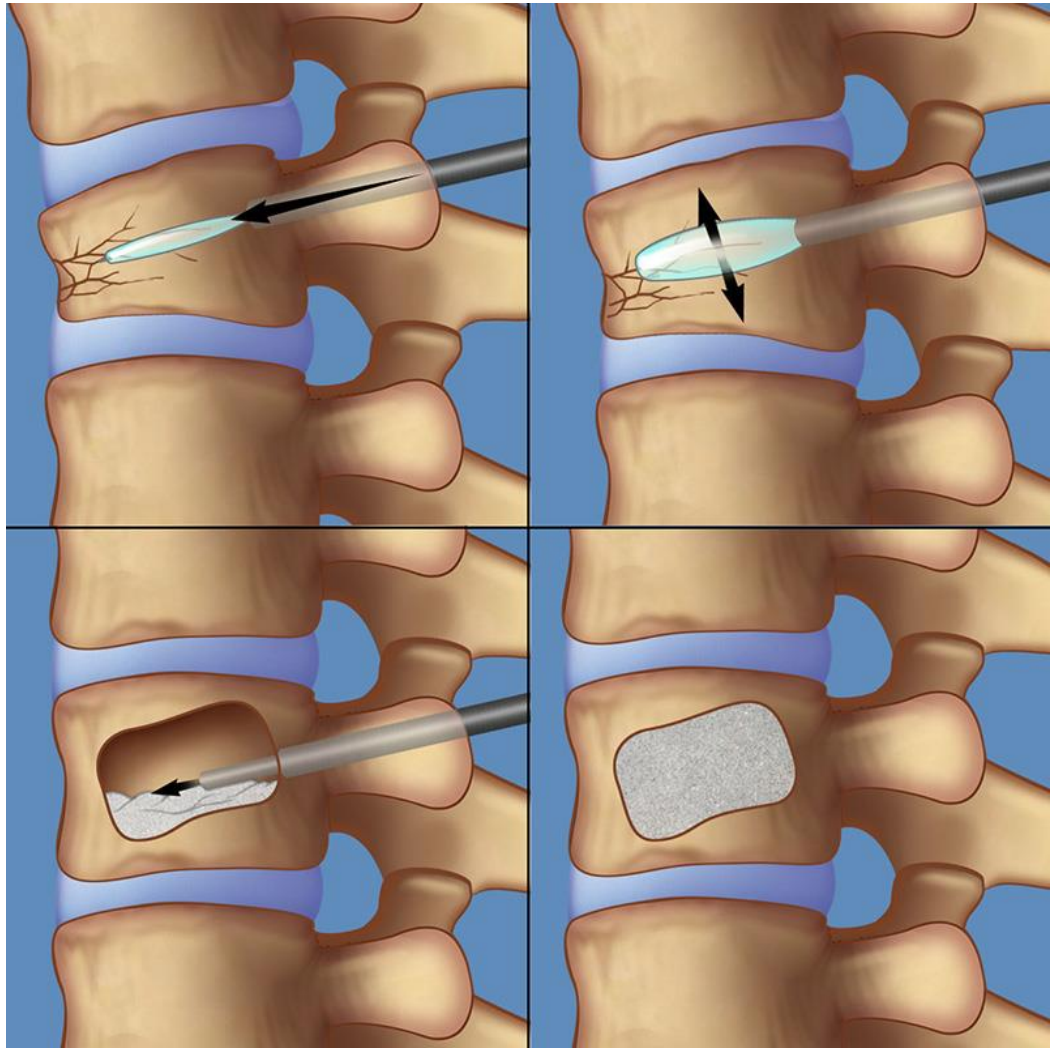
Faculty of Health Sciences
Fakulteit Gesondheidswetenskappe
Lefapha la Disaense tša Maphelo

Surgery

- Spinal stability, presence of neurologic deficits, and patient prognosis.
- Immediate and sustained pain relief and improved quality of life
- Minimally invasive decompressions to highly sophisticated, individualized techniques that consider the location and extent
- Surgical decompression with instrumented fusion
- Vertebroplasty and kyphoplasty
- The Spine Instability Neoplastic Score, with 95.7% sensitivity and 79.5% specificity for predicting spinal stability, can help to determine the need for surgical intervention



SINS score and Modified Bauer score

Spine Instability Neoplastic Score (SINS)

SINS Component	Description	Score
Location	Junctional (Occ-C2, C7-T2, T11-L1, L5-S1) Mobile (C3-6, L2-4) Semirigid (T3-10) Rigid (S2-5)	3 2 1 0
Pain	Yes* Occasional non-mechanical pain No	3 1 0
Bone Lesion	Lytic Mixed Blastic	2 1 0
Alignment	Subluxation / translation De novo deformity Normal	4 2 0
Vertebral Body	>50% collapse <50% collapse No collapse with >50% VB involved None of above	3 2 1 0
Posterolateral Involvement	Bilateral Unilateral	3 1

Tallied Score from 6 components

Stable	Potentially Unstable	Unstable
0-6	7-12	13-18

Fisher CG, et al. A novel classification system for spinal instability in neoplastic disease: an evidence-based approach and expert consensus from the Spine Oncology Study Group. Spine 35(22):E1221-9, 2010

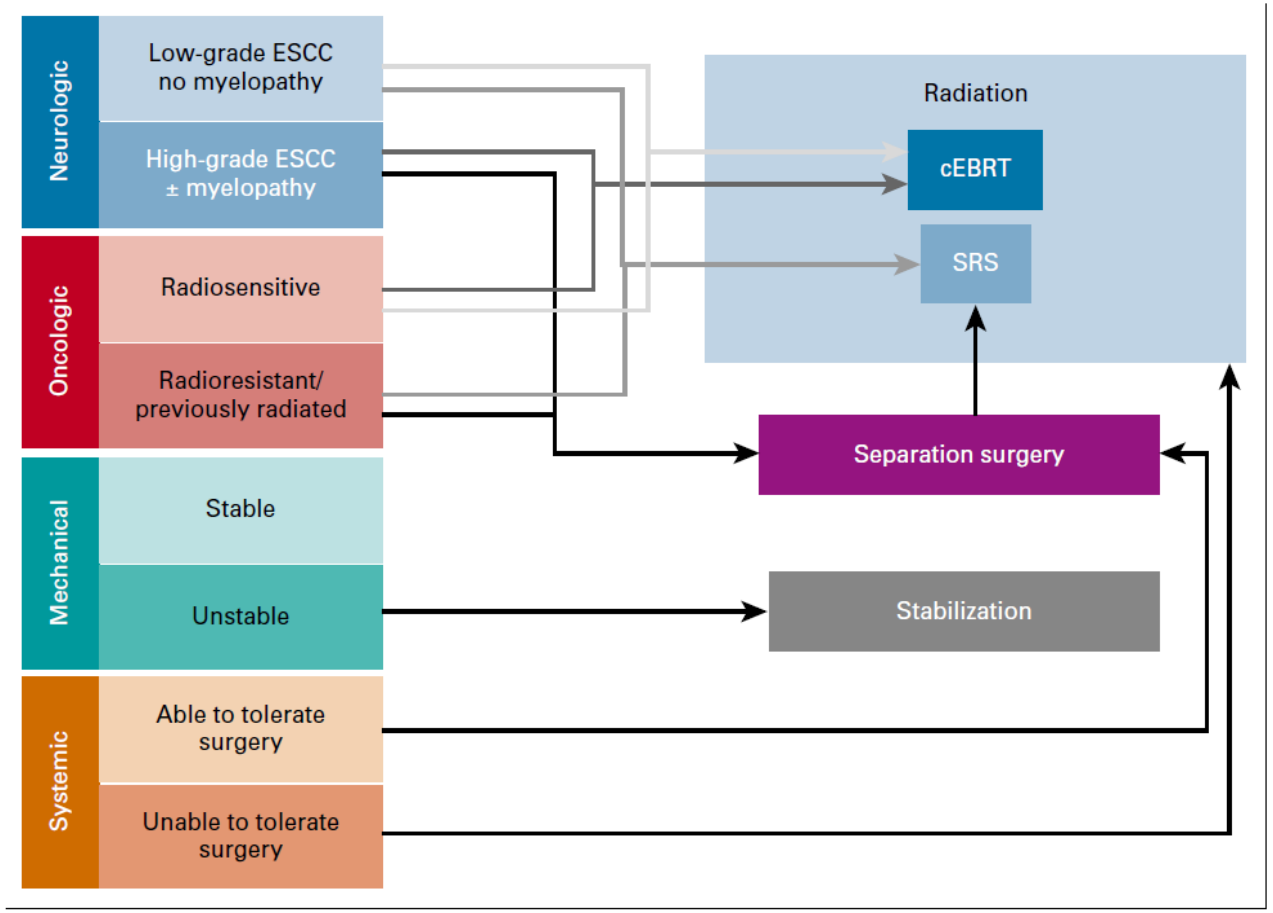
Modified Bauer scoring system

		Total score	Median OS (months)
(1) no visceral metastases	+0		
(2) solitary skeletal metastasis	+1	0-1	4.8
(3) no lung cancer	+1	2	18.2
(4) primary tumor: breast, kidney	+1	3-4	28.4

(1) – (4): one point each if applicable

RT vs Surgery and RT

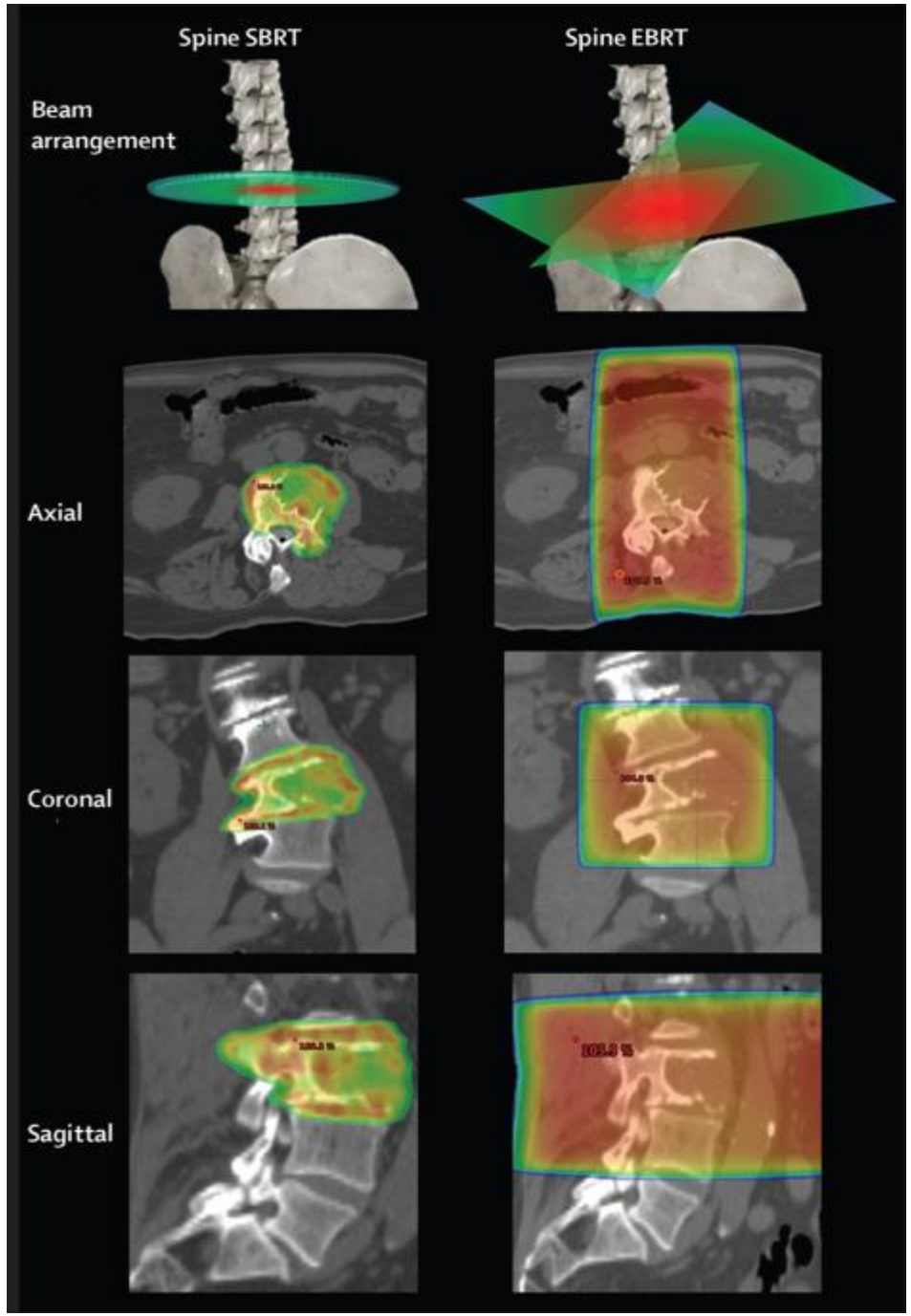
Treatment



J Clin Oncol 35:2419-2427, 2017

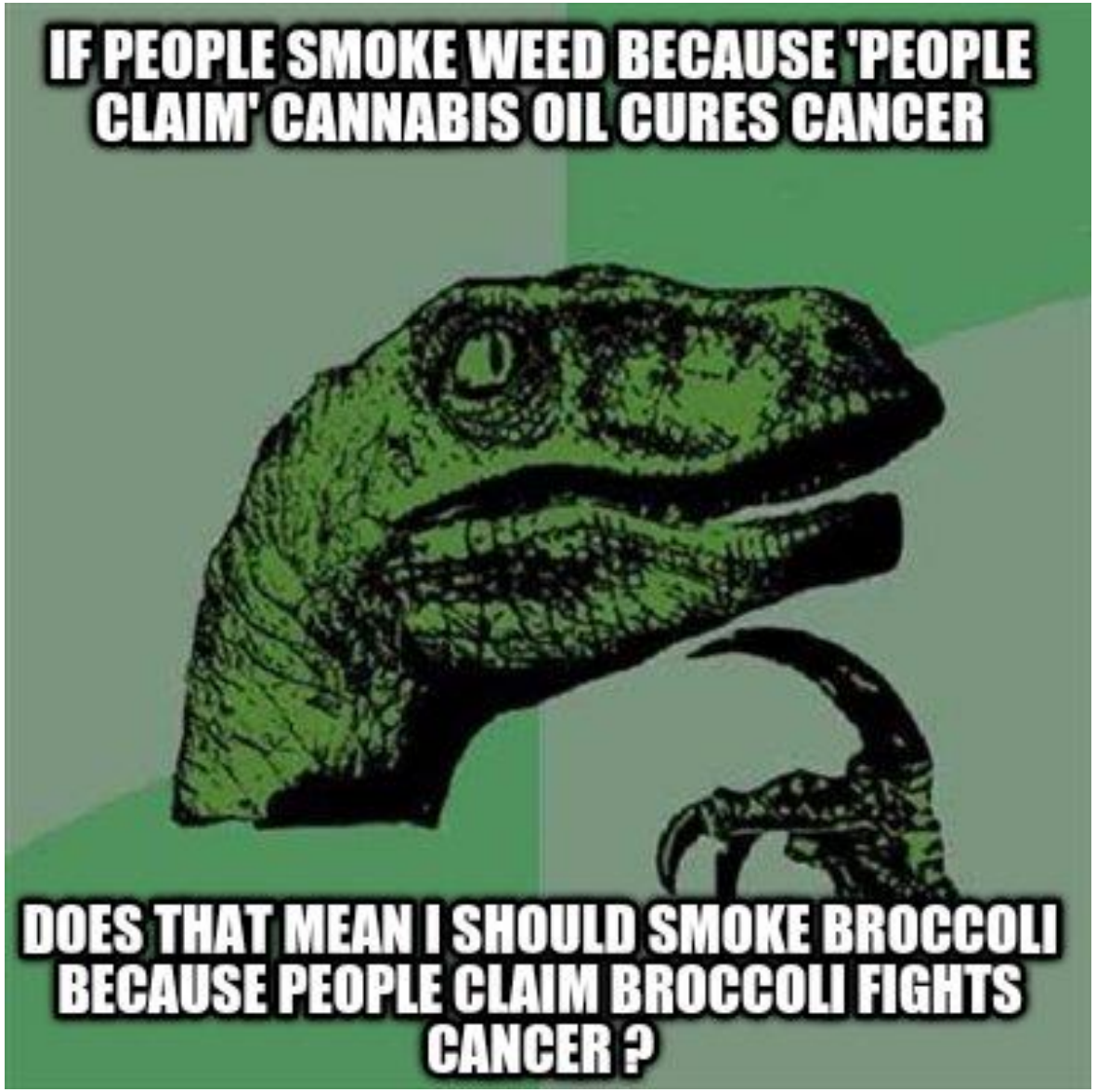
Radiotherapy

- External beam RT
- SBRT



Rehabilitation

- During acute hospitalization
- Bowel and bladder dysfunction
- Pressure sores
- Transition from acute environment
- Psychosocial factors


IF PEOPLE SMOKE WEED BECAUSE 'PEOPLE CLAIM' CANNABIS OIL CURES CANCER
DOES THAT MEAN I SHOULD SMOKE BROCCOLI BECAUSE PEOPLE CLAIM BROCCOLI FIGHTS CANCER ?

CBD oil

What is CBD oil, and how does it differ from marijuana and hemp?

Less THC than a typical, CBD is not a psychoactive agent

Is there any truth to the claims that CBD oil can cure cancer?

Right now, no. There is no evidence that CBD oil can cure cancer.

What, if anything, can CBD oil do to alleviate the symptoms of cancer or the side effects of cancer treatment?

It's hard to say if CBD oil can alleviate cancer symptoms or cancer treatment side effects, because the studies are pretty mixed and even fewer are standardized.

There have been reports that cannabinoids like THC and CBD may be helpful for nausea and vomiting and anorexia, as well as neuropathy, anxiety, depression and insomnia.

Have any CBD-oil derived products been approved by the U.S. Food and Drug Administration (FDA) to treat cancer, its symptoms, or the side effects caused by its treatment?

No.

Have any products using CBD-oil been approved by the FDA to treat anything?

Yes. Epidiolex.

What are the dangers of using CBD oil?

Quality, cleanliness and regulation are the biggest concerns.

There have been some reports of people getting infections after using CBD and cannabis products. This is especially concerning for immunocompromised patients, who are already susceptible to bacterial and fungal infections.

Does CBD oil have any side effects?

CBD oil can adversely affect liver function. In fact, this is on the warning label for Epidiolex.

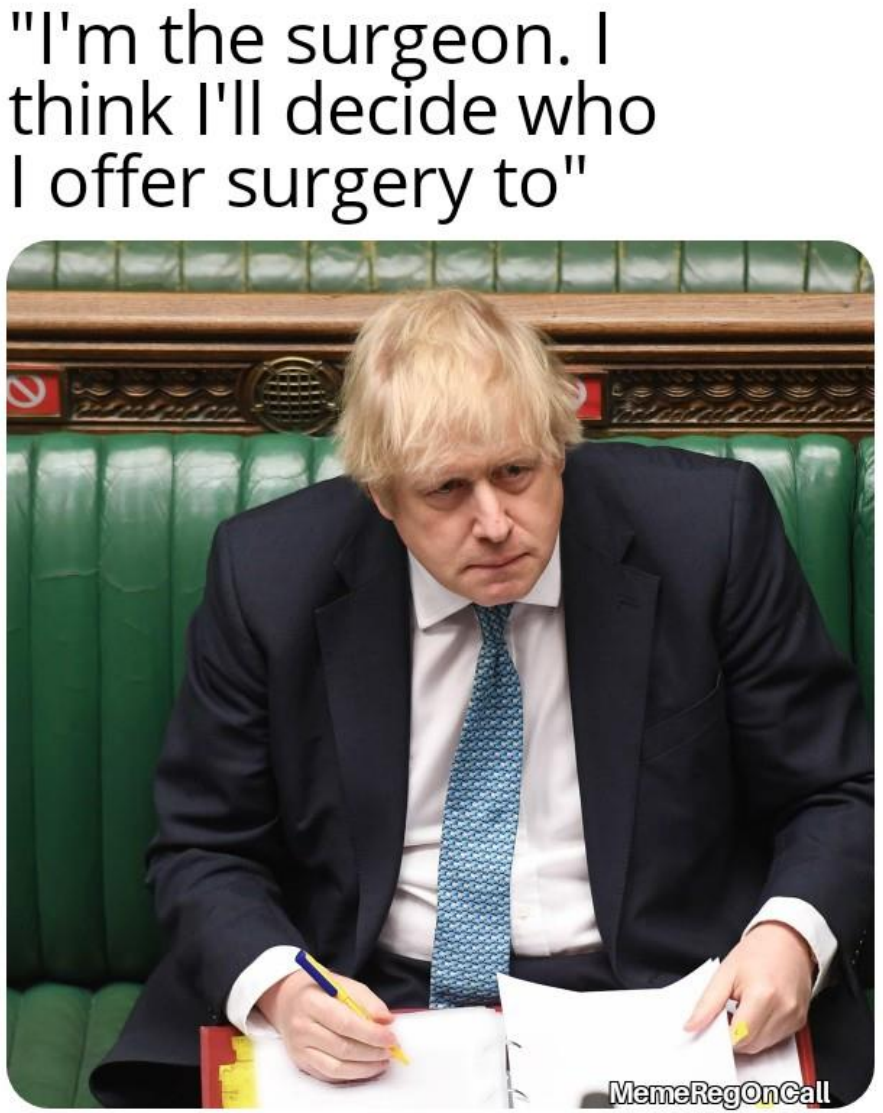
And in lab studies, CBD has been shown to inhibit certain enzymes responsible for the metabolism of drugs, such as CYP2D6 and CYP3A4. This can affect how drugs work and affect our bodies, either by reducing their efficiency or making them more dangerous. This includes chemotherapy and other medications.

What's the most important thing cancer patients should know about CBD oil?

There's still a lot to learn.

Conclusion

- Cancer treatment is very complex
- GP has an important role to play
- MDT management is important



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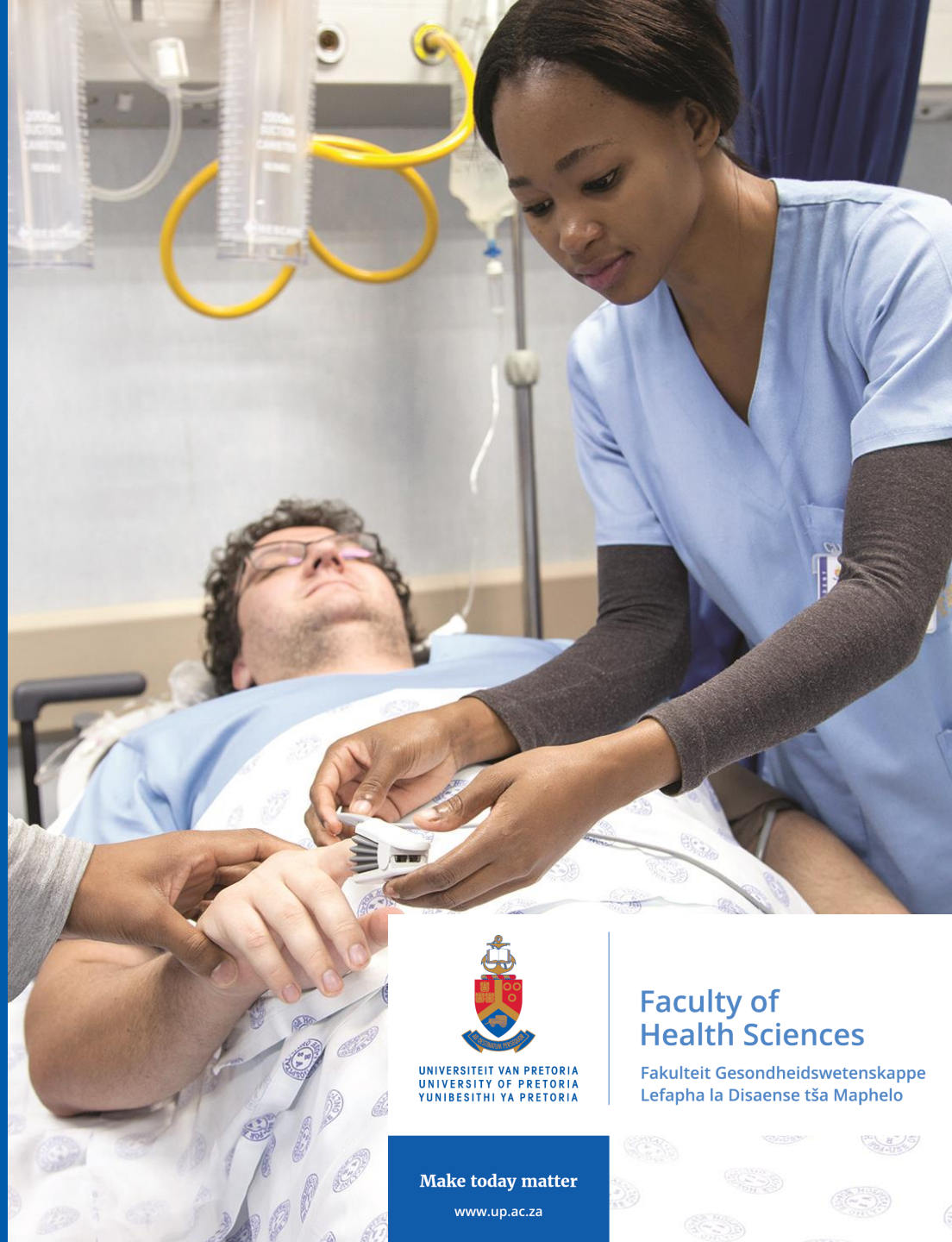

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