Actualitati in managementul cancerului bronhopulmonar fara celula mica, stadii avansate

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Conflicte de interes (“Disclosures”)

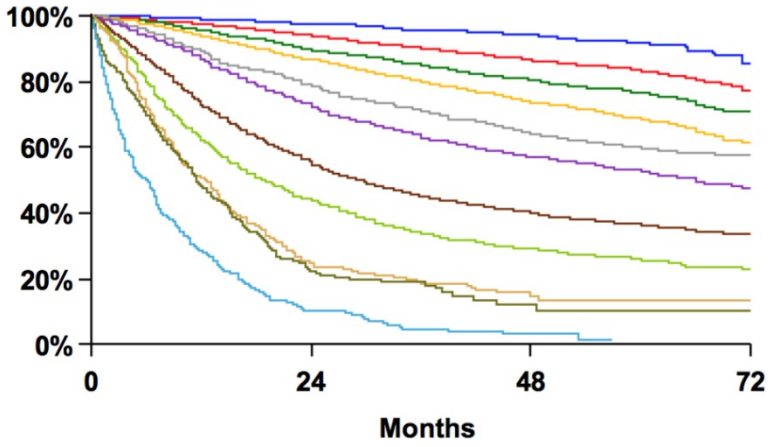
Plati pt activitati de cercectare clinica (trialuri clinice):

- BMS
- MSD
- Merck Serono
- Sanofi
- Roche
- Novartis
- Eli Lilly
- Gilead
- Pharma Mar
- Amgen
- Astellas
- Clovis
- Tesaro
- Mylan
- BeiGene
- Bayer Pharm

GOOD SCIENCE
BETTER MEDICINE
BEST PRACTICE

ESMO GUIDELINES:
METASTATIC NON-SMALL CELL LUNG CANCER

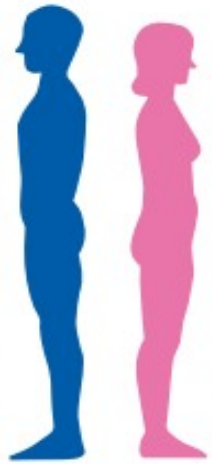
LUNG CANCER OUTCOME: 8TH TNM



Proposed	Events / N	MST	24 Month	60 Month
IA1	68 / 781	NR	97%	92%
IA2	505 / 3105	NR	94%	83%
IA3	546 / 2417	NR	90%	77%
IB	560 / 1928	NR	87%	68%
IIA	215 / 585	NR	79%	60%
IIB	605 / 1453	66.0	72%	53%
IIIA	2052 / 3200	29.3	55%	36%
IIIB	1551 / 2140	19.0	44%	26%
IIIC	831 / 986	12.6	24%	13%
IVA	336 / 484	11.5	23%	10%
IVB	328 / 398	6.0	10%	0%

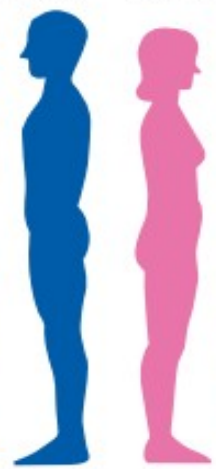
Estimated New Cases

Males			Females		
Prostate	191,930	21%	Breast	276,480	30%
Lung & bronchus	116,300	13%	Lung & bronchus	112,520	12%
Colon & rectum	78,300	9%	Colon & rectum	69,650	8%
Urinary bladder	62,100	7%	Uterine corpus	65,620	7%
Melanoma of the skin	60,190	7%	Thyroid	40,170	4%
Kidney & renal pelvis	45,520	5%	Melanoma of the skin	40,160	4%
Non-Hodgkin lymphoma	42,380	5%	Non-Hodgkin lymphoma	34,860	4%
Oral cavity & pharynx	38,380	4%	Kidney & renal pelvis	28,230	3%
Leukemia	35,470	4%	Pancreas	27,200	3%
Pancreas	30,400	3%	Leukemia	25,060	3%
All Sites	**893,660**	**100%**	**All Sites**	**912,930**	**100%**

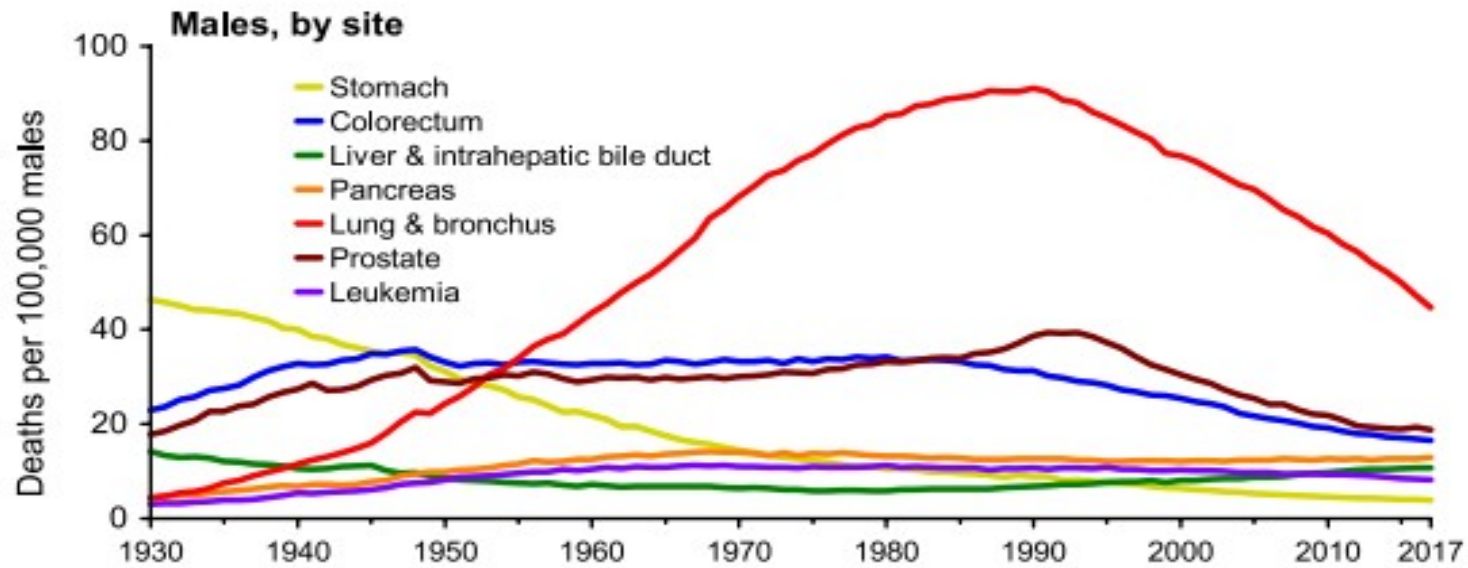


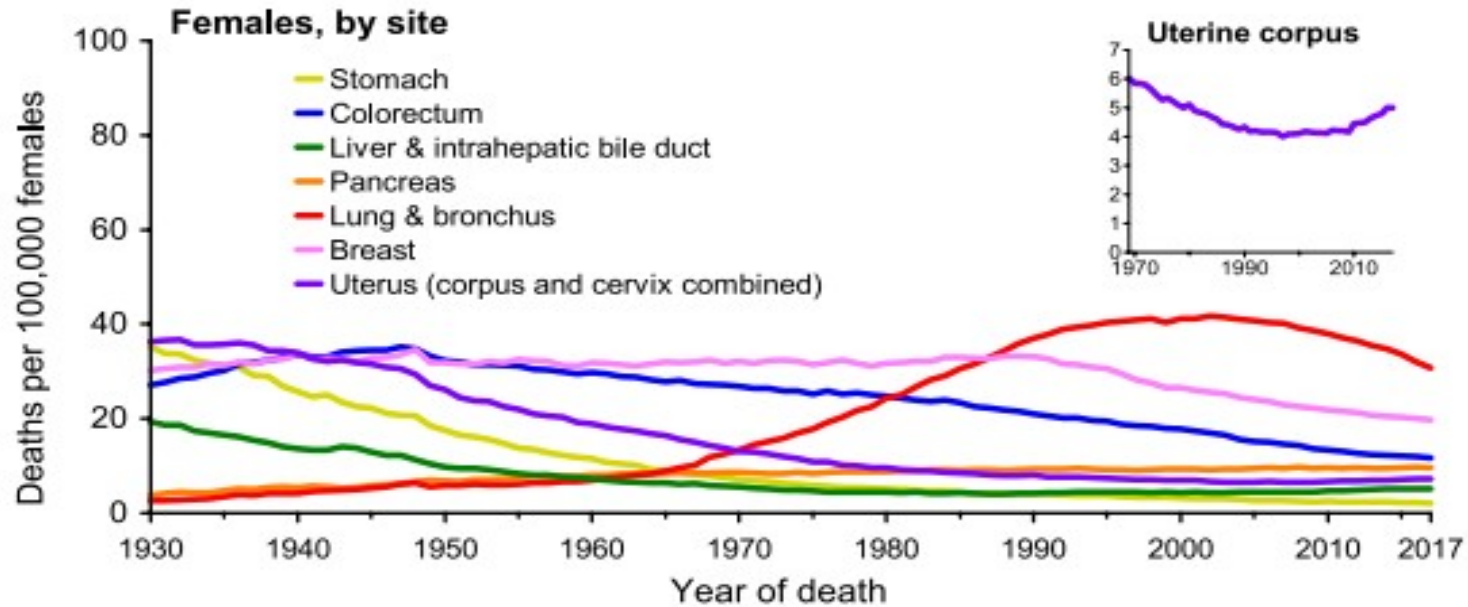
Estimated Deaths

Males			Females		
Lung & bronchus	72,500	23%	Lung & bronchus	63,220	22%
Prostate	33,330	10%	Breast	42,170	15%
Colon & rectum	28,630	9%	Colon & rectum	24,570	9%
Pancreas	24,640	8%	Pancreas	22,410	8%
Liver & intrahepatic bile duct	20,020	6%	Ovary	13,940	5%
Leukemia	13,420	4%	Uterine corpus	12,590	4%
Esophagus	13,100	4%	Liver & intrahepatic bile duct	10,140	4%
Urinary bladder	13,050	4%	Leukemia	9,680	3%
Non-Hodgkin lymphoma	11,460	4%	Non-Hodgkin lymphoma	8,480	3%
Brain & other nervous system	10,190	3%	Brain & other nervous system	7,830	3%
All Sites	**321,160**	**100%**	**All Sites**	**285,360**	**100%**



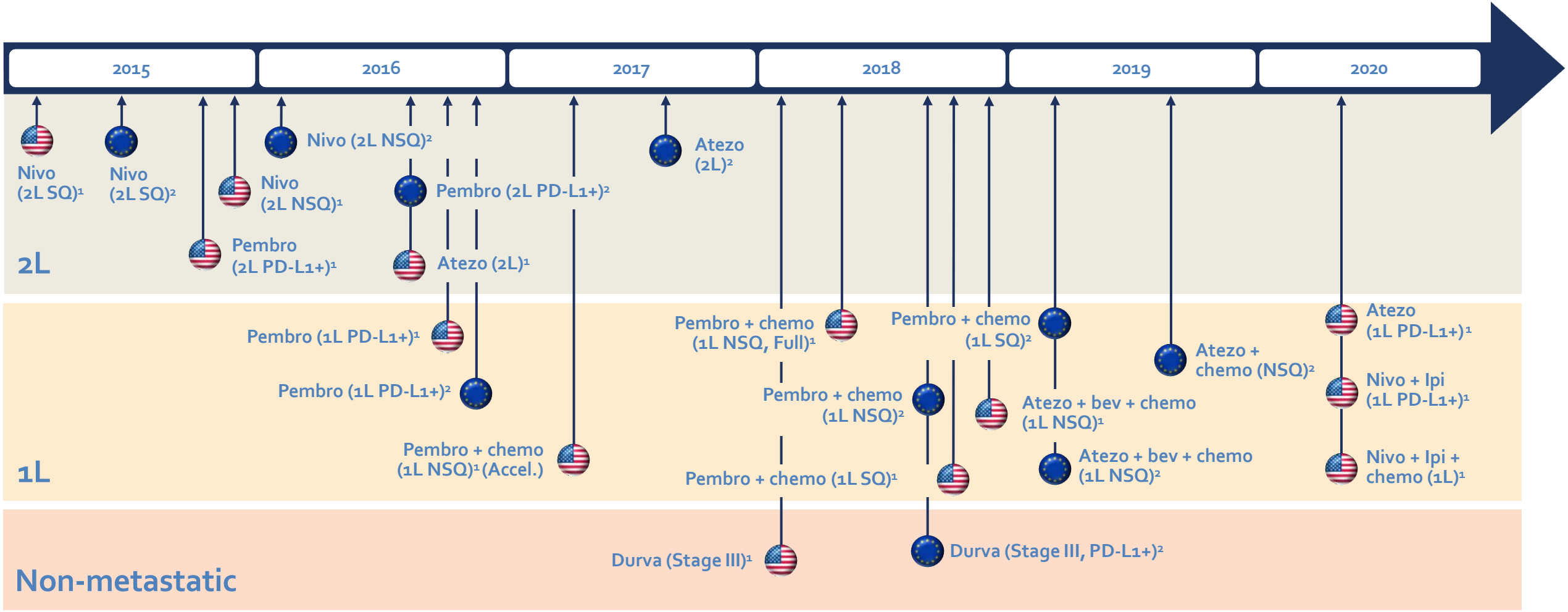
Siegel R et al. CA Cancer J Clin 2020; 70(1):7-30.





Siegel R et al. CA Cancer J Clin 2020; 70(1):7-30.

CHECKOINT INHIBITORS IN NSCLC : KEY MILESTONES



1. U.S. Food and Drug Administration. 2. European Medicines Agency.

BIOMARKERS ARE NEEDED FOR IO PATIENTS SELECTION

Not all patients respond to and benefit from these treatments

- Enrich the treatment population for benefit

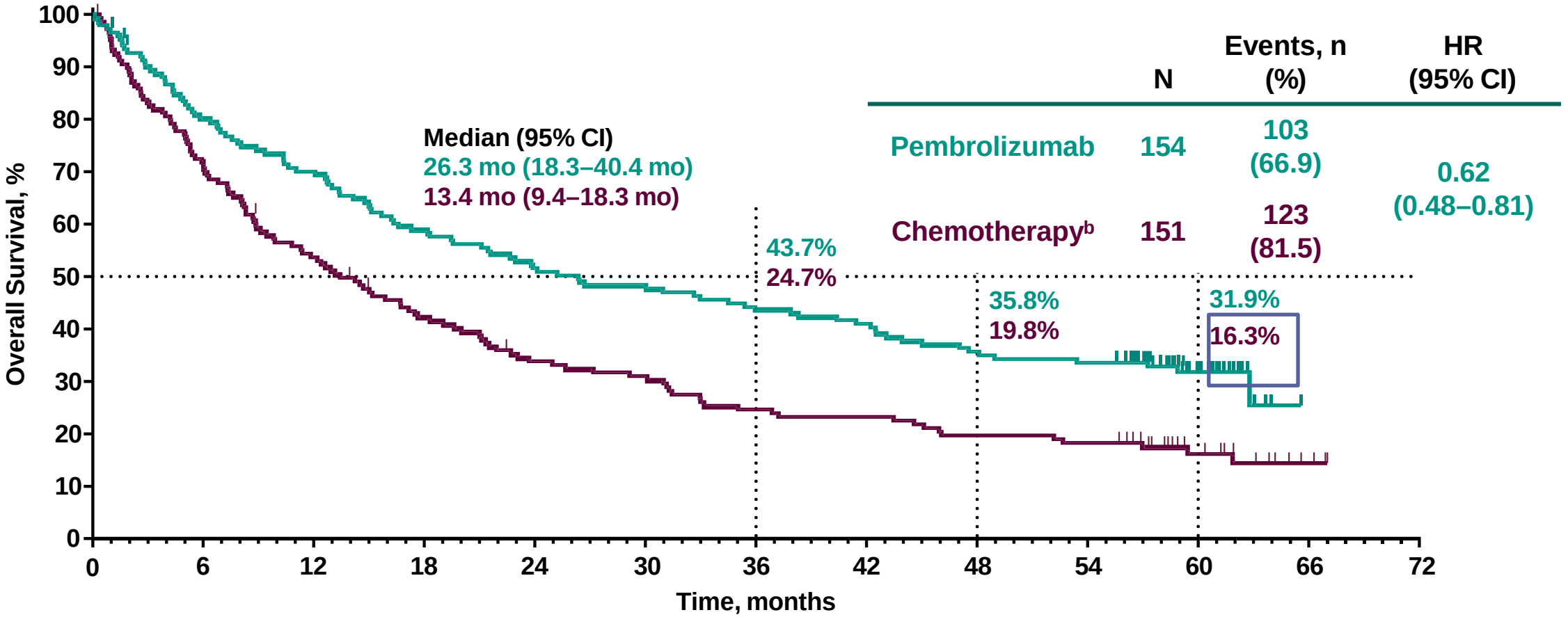
Avoidance of harm?

- There are toxicities from these drugs
- Alternative treatment would be better

Financial burden

Kerr, ELCC 2018; Tray, Cancer Immunology Res 2018

LONG-TERM BENEFIT: 5 YEARS OS PEMBROLIZUMAB MONOTHERAPY

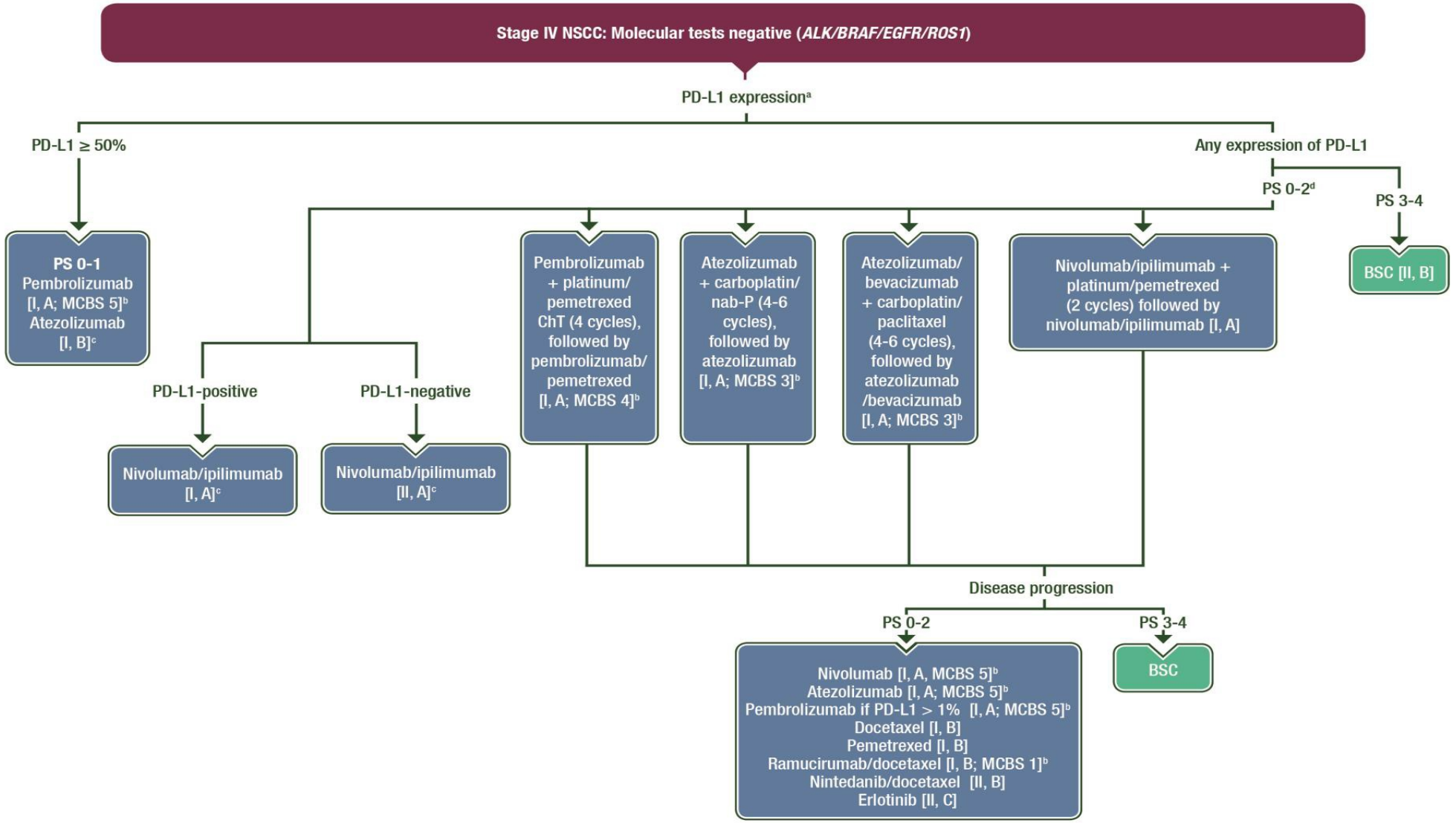


	N	Events, n (%)	HR (95% CI)
Pembrolizumab	154	103 (66.9)	0.62 (0.48–0.81)
Chemotherapy[b]	151	123 (81.5)	

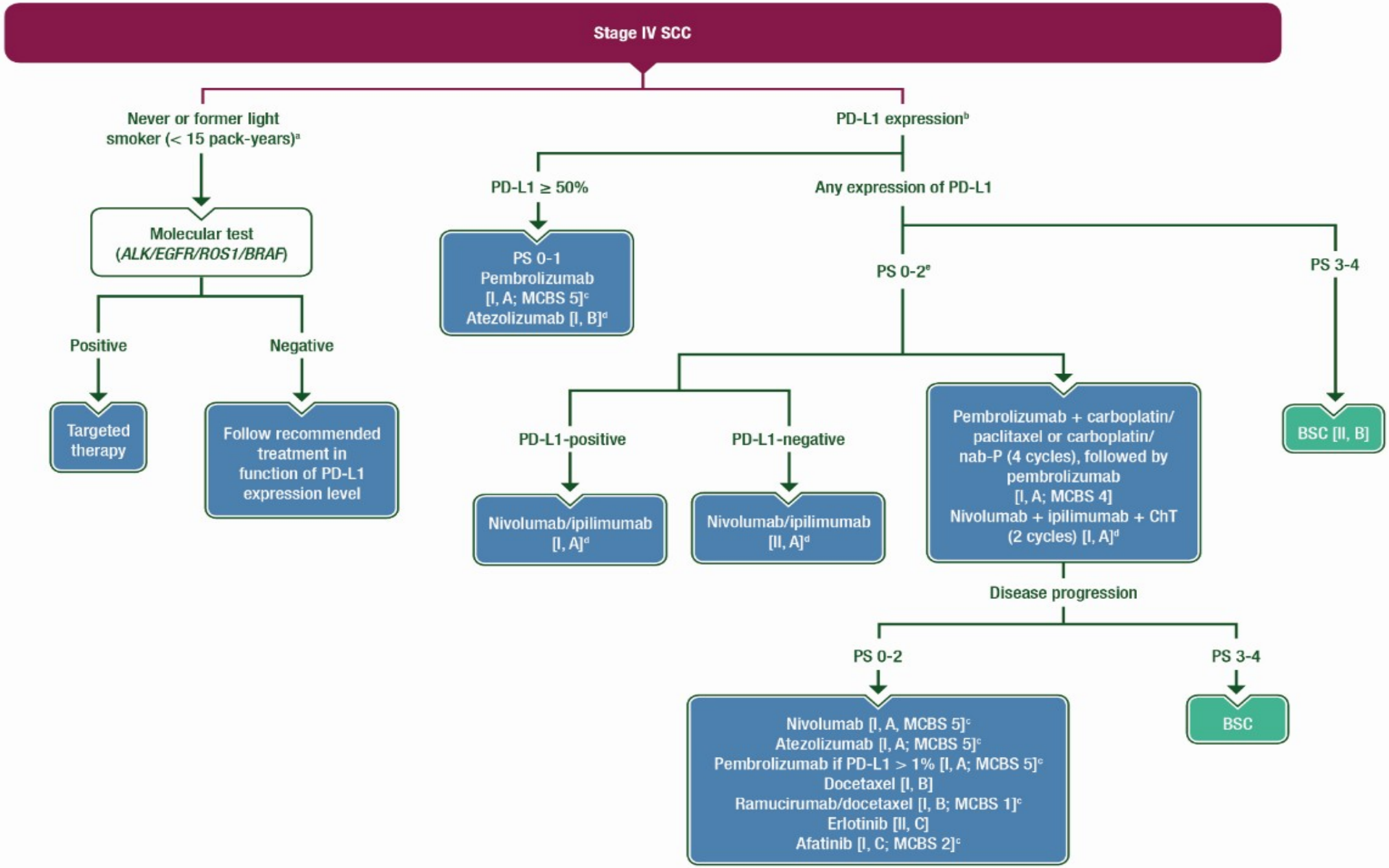
No. at risk												
Pembrolizumab	154	121	106	89	78	73	66	62	54	51	20	0	0
Chemotherapy	151	108	80	61	48	44	35	33	28	26	13	3	0

Effective crossover rate from chemotherapy to anti–PD-L1 therapy, 66.0%

Brahmer J. ESMO 2020, LBA51.



Planchard D et al. Ann Oncol (2018) 29 (suppl 4): iv192–iv237; updated 2020 https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer



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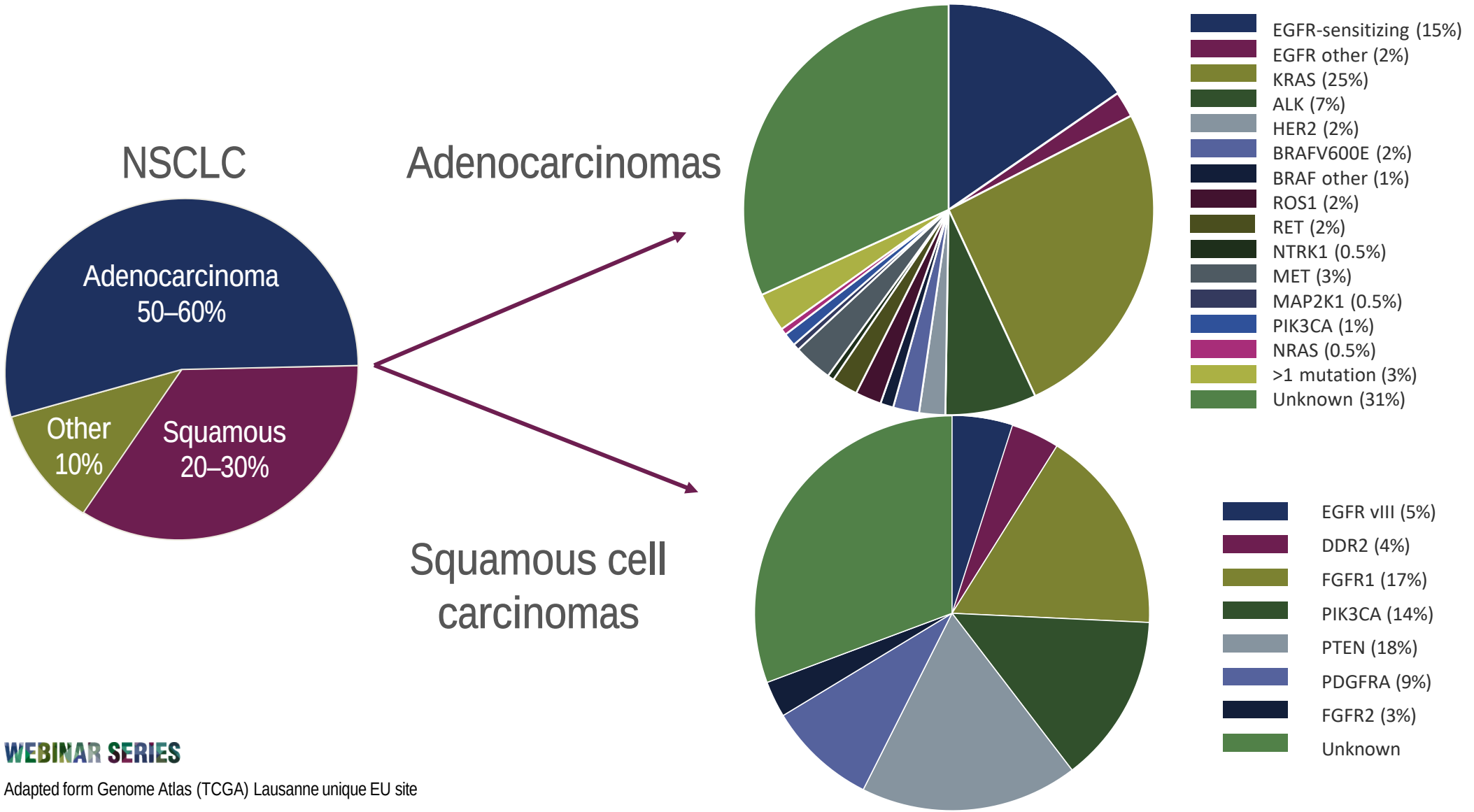
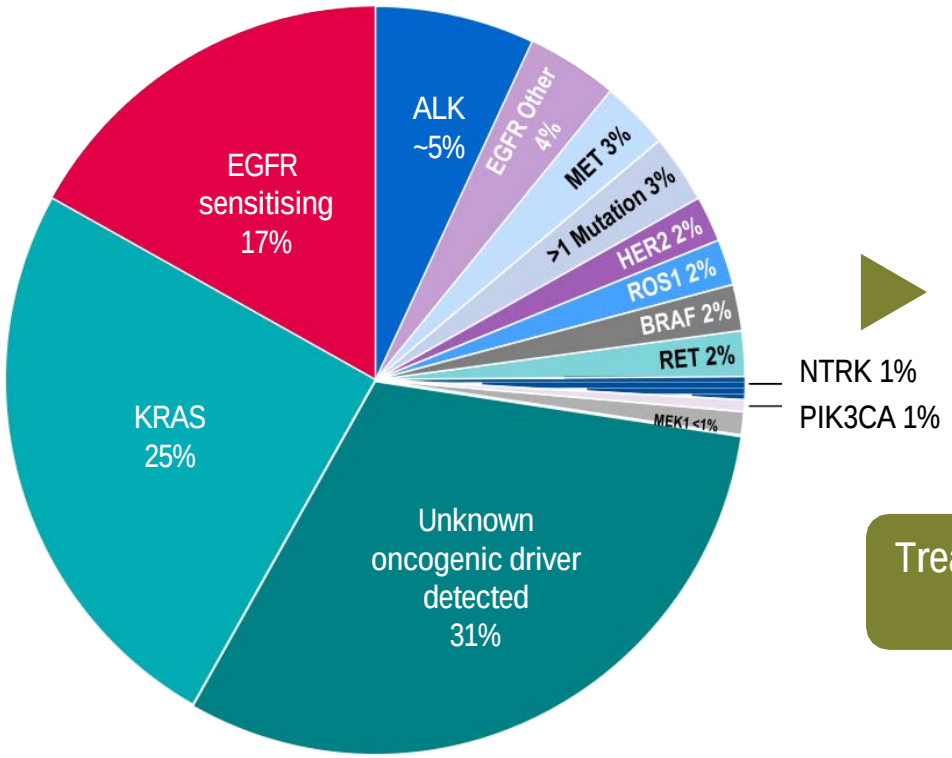
DRIVER ALTERATIONS IN NSCLC



Adapted form Genome Atlas (TCGA) Lausanne unique EU site

TARGETED THERAPIES FOR PRECISION MEDICINE

Common mutations in lung cancer



Treatment is selected by genomic profiling

EGFR sensitising
- Afatinib
- Erlotinib
- Erlotinib + bevacizumab
- Gefitinib
- Necitumumab
- Osimertinib
- Amivantanab JNJ-372
- U3-1402

BRAF
- Dabrafenib
- Dabra/Trametinib
- Vemurafenib

HER2
- Afatinib
- Dacomitinib
- Emtansine
- Pertuzumab
- Trastuzumab
- TAK-778
- Poziotinib
- Trastuzumab-deruxtecan

ALK
- Alectinib
- Brigatinib
- Ceritinib
- Crizotinib
- Ensartinib
- Lorlatinib

RET
- Apatinib
- Cabozantinib
- Lenvatinib
- Selpercatinib LOXO-292
- Ponatinib
- Vandetanib
- Pralsetinib BLU-667

ROS1
- Ceritinib
- Crizotinib
- DS-6051b
- Entrectinib
- Lorlatinib
- Repotrectinib

MET
- Cabozantinib
- Crizotinib
- Capmatinib
- Savolitinib
- Reprotrectnib
- Tepotinib

NTRK
- DS-6051b
- Entrectinib
- Larotrectinib
- Selitrectinib
- Cabozantinib
- LOXO-101

PIK3CA
- LY3023414

MEK1
- Cobimetinib
- Selumetinib
- Trametinib

KRAS
- Sotorasib AMG 510
- MRTX849

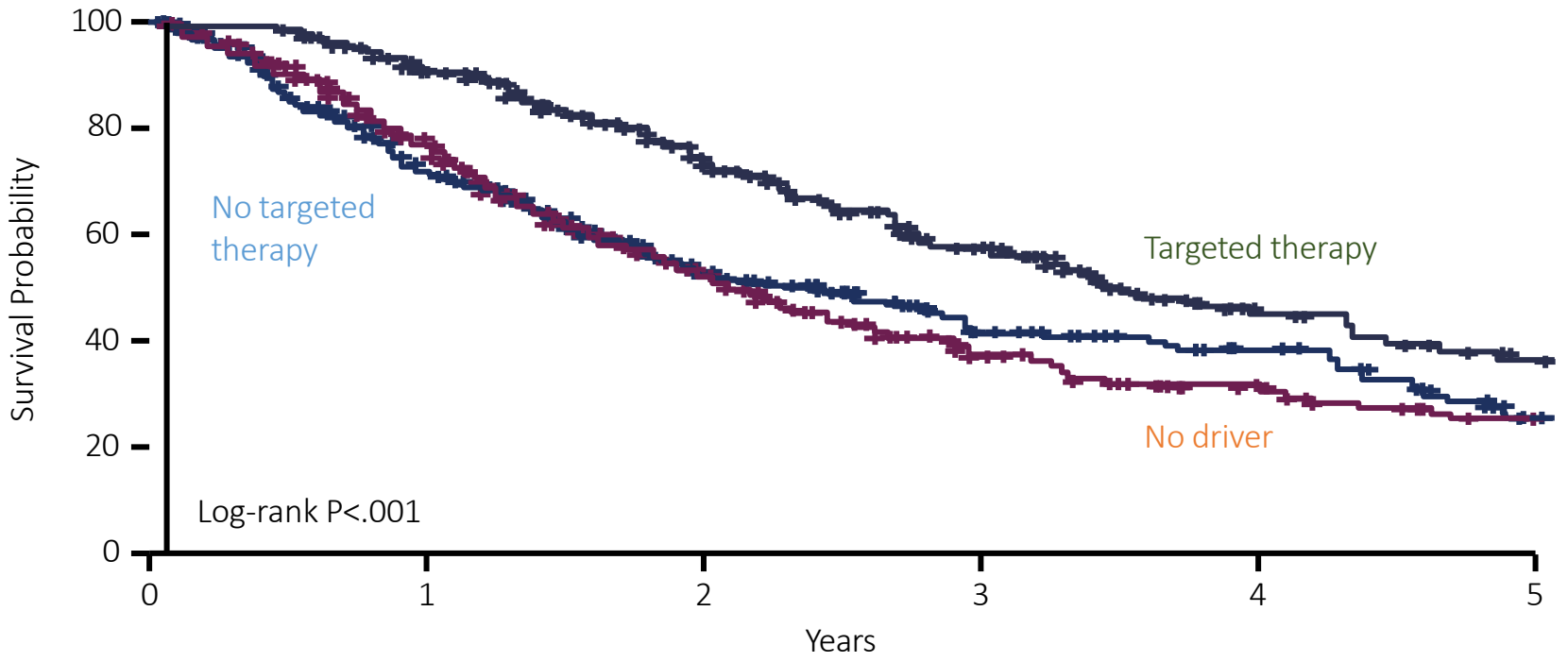
WEBINAR SERIES

ESMO

Adapted from Tsao AS, et al. J Thorac Oncol 2016; 11(5):613-638.

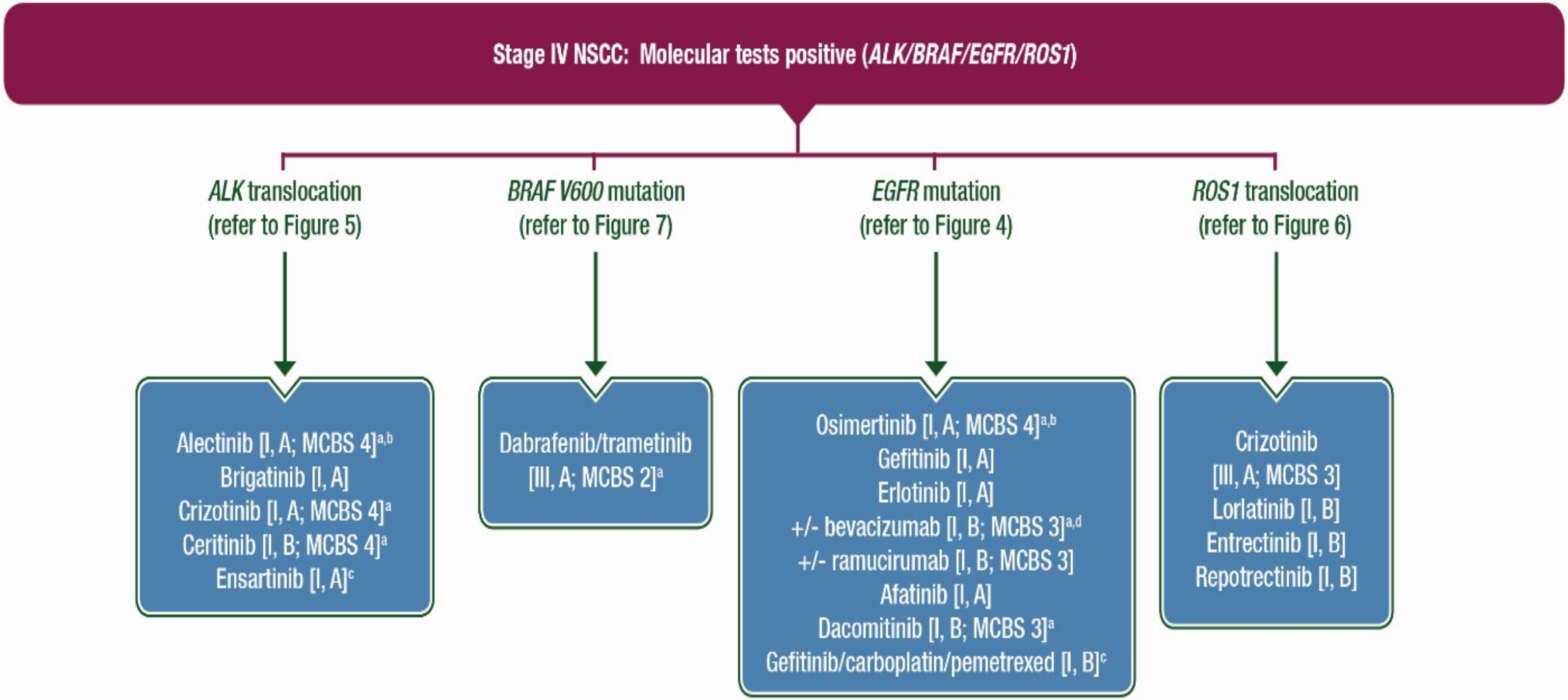
Dearden S, et al. Ann Oncol 2013; 24:2371-2376.

ONCOGENE ADDICTION DEFINES TARGETED OPPORTUNITIES



No. at risk						
Patients with oncogenic driver						
No targeted therapy	318	205	110	64	43	20
Targeted therapy	260	225	143	72	36	23
Patients with no driver	360	250	122	59	36	23

Kris M, et al. JAMA 2014 311:1998–2006



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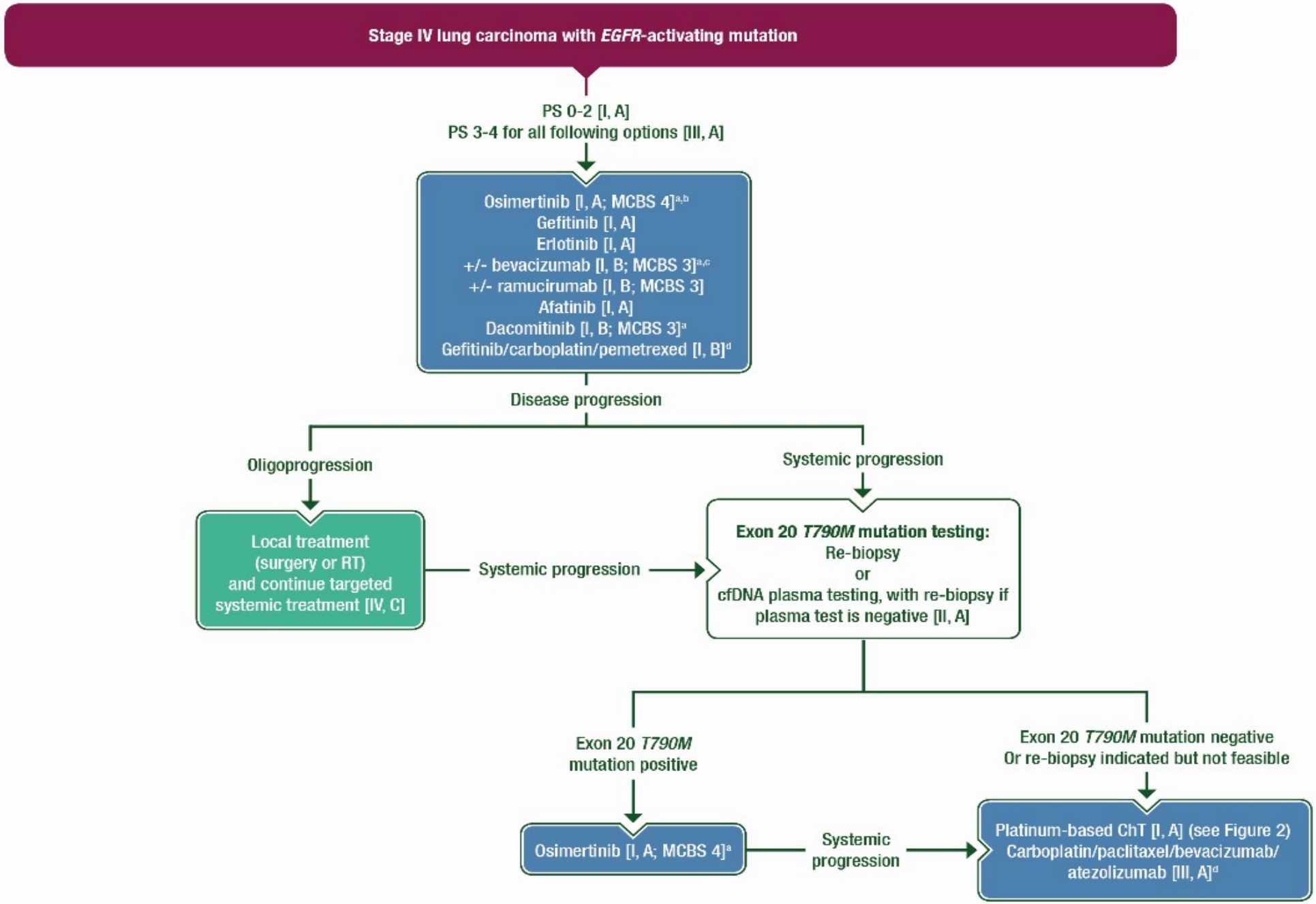

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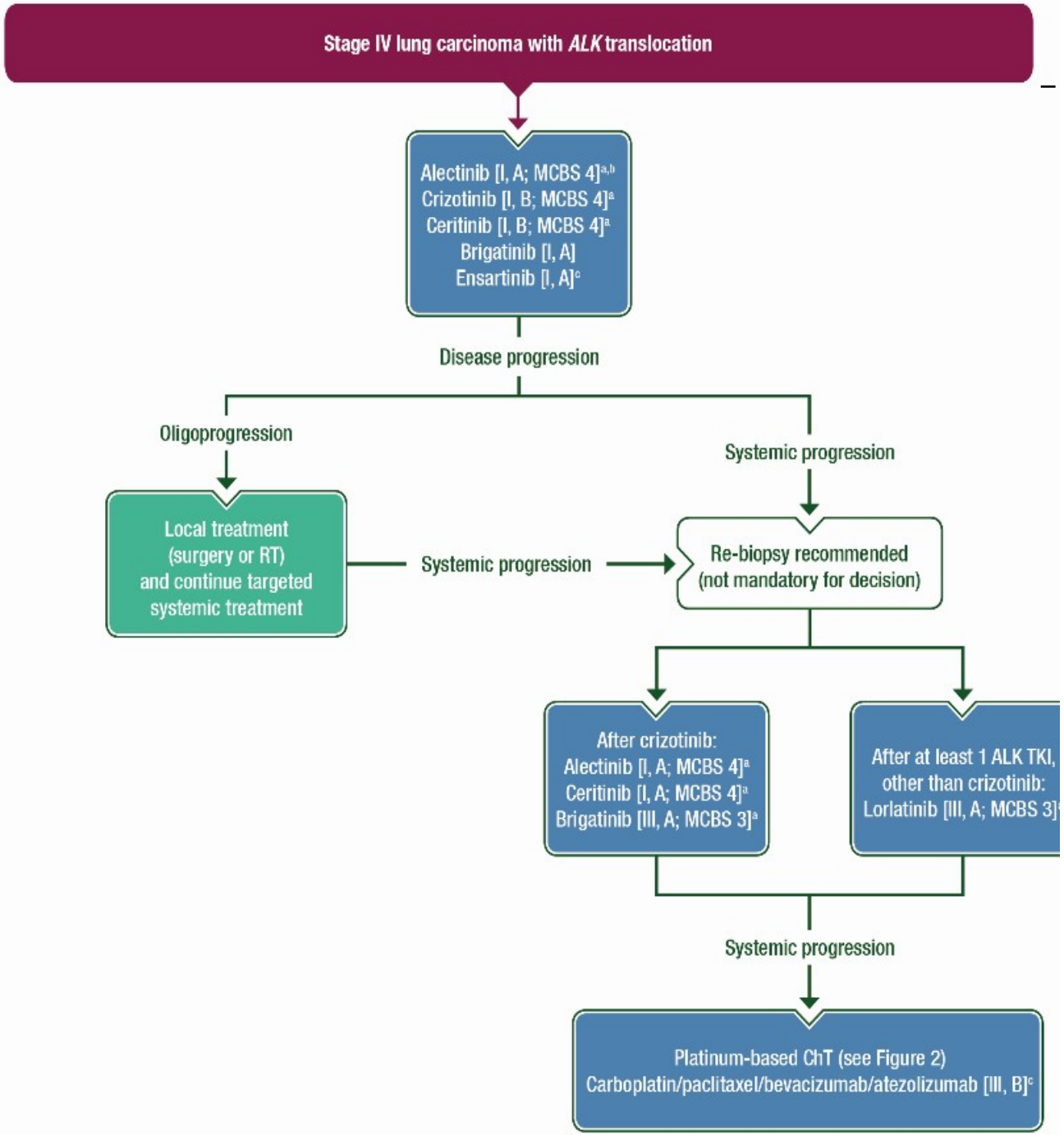

New ALK inhibitors
An illustration of drug design for precision oncology

1. More potent ALK inhibitor

2. Broader activity against mutated ALK proteins

3. Better CNS penetration

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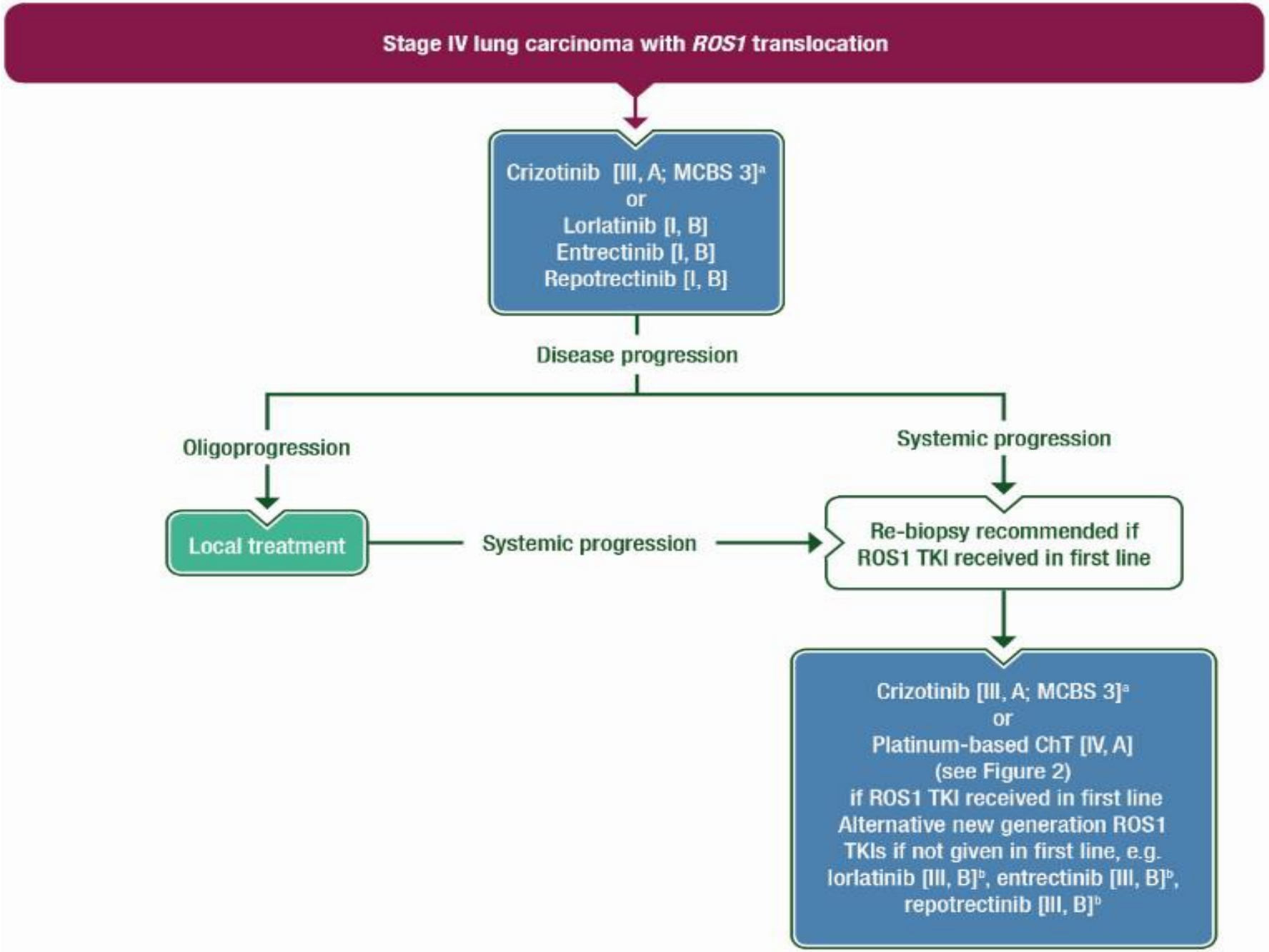

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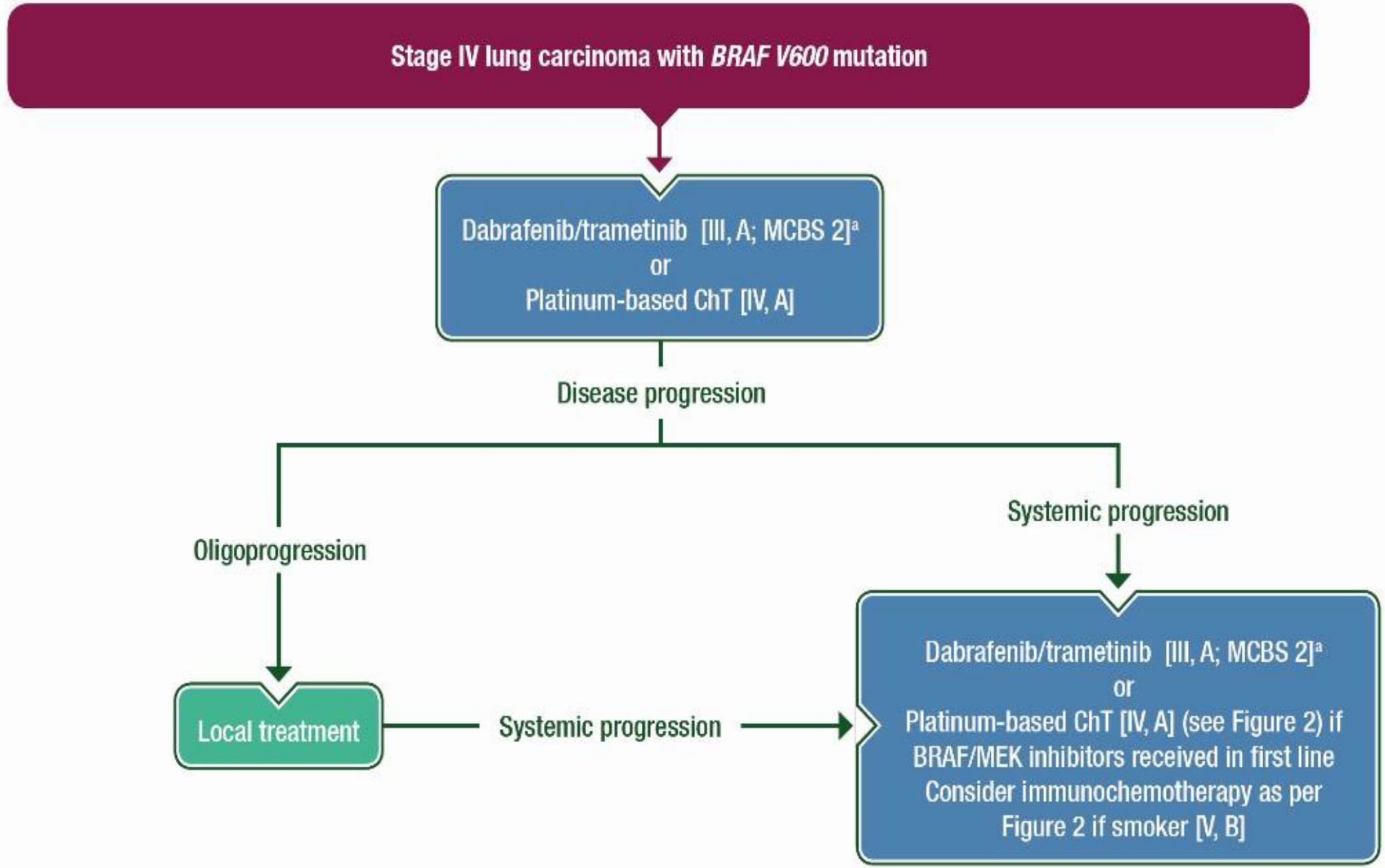

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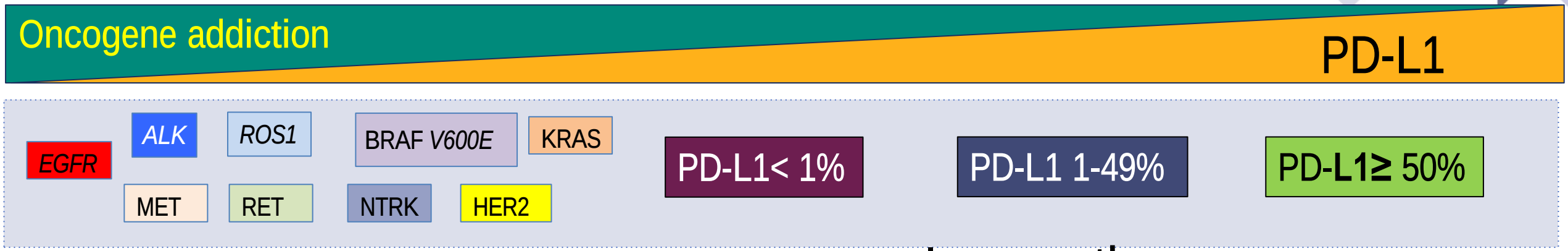
NEW TREATMENT PARADIGM IN NSCLC



Targeted therapies

Immunotherapy

Chemotherapy + Immunotherapy

Immunotherapy + Immunotherapy

PD-L1≥50%: Pembrolizumab monotherapy (or atezolizumab)

1-year OS similar (KEYNOTE-024 70.3%, KEYNOTE-189 69.2%, Impower 110 64.9% and KEYNOTE-407 65.2%)

for highly symptomatic pts (high tumor burden), reasonable to use pembrolizumab plus chemotherapy

For patients with PD-L1 TPS 1%–49% and negative PD-L1 expression,

in favor of combination of chemotherapy plus pembrolizumab or atezolizumab (+/- bevacizumab for non-squamous) OR nivolumab + ipilimumab +/- 2 cycle of chemo

Va multumesc pentru atentie!