Review of NEO Testing Platforms

Lawrence M. Weiss, MD
Medical Director, Aliso Viejo

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Dr. Weiss currently serves as NeoGenomics' Medical Director, Aliso Viejo and served as the Medical Director at Clarient Diagnostic Services, Inc. prior to the NeoGenomics acquisition in 2015. Dr. Weiss received his BS summa cum laude and MD summa cum laude from the University of Maryland. He completed a residency in Anatomic Pathology at the Brigham and Women's Hospital in Boston, MA and a fellowship in surgical pathology at Stanford University Medical Center. He was previously an Assistant Professor at Stanford and Director of Surgical Pathology, President of the Medical Staff, and Chairman of Pathology at the City of Hope. He is the author of over 500 papers and book chapters, as well as over a dozen books, including an *AFIP Lymph Node Fascicle, Applied Immunohistochemistry, Lymph Nodes*, and the recently published Knowles' *Hematopathology*. His laboratory discovered the first molecular evidence linking the Epstein-Barr virus with Hodgkin Lymphoma. He has won numerous awards, including the Benjamin Castleman, Arthur Purdy Stout, and the United States-Canadian Academy of Pathology Young Investigator Award, and has delivered over 250 national and international talks in pathology, including several named lectureships. He has been on the editorial board of ten scientific journals, and is a past President of the Los Angeles Society of Pathologists. He has been listed in the book *The Best Doctors in America* since 1994. Dr. Weiss's diagnostic interests lie in lymph node pathology, adrenal pathology, tumor pathology, and immunohistochemistry.

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Testing Modalities Offered by NeoGenomics

- Morphologic interpretation/consultation
- Immunohistochemistry
  - Diagnostic
  - Prognostic
- Flow cytometry
- Cytogenetics
- FISH
- Molecular studies
  - Single gene
  - Large NGS profiles

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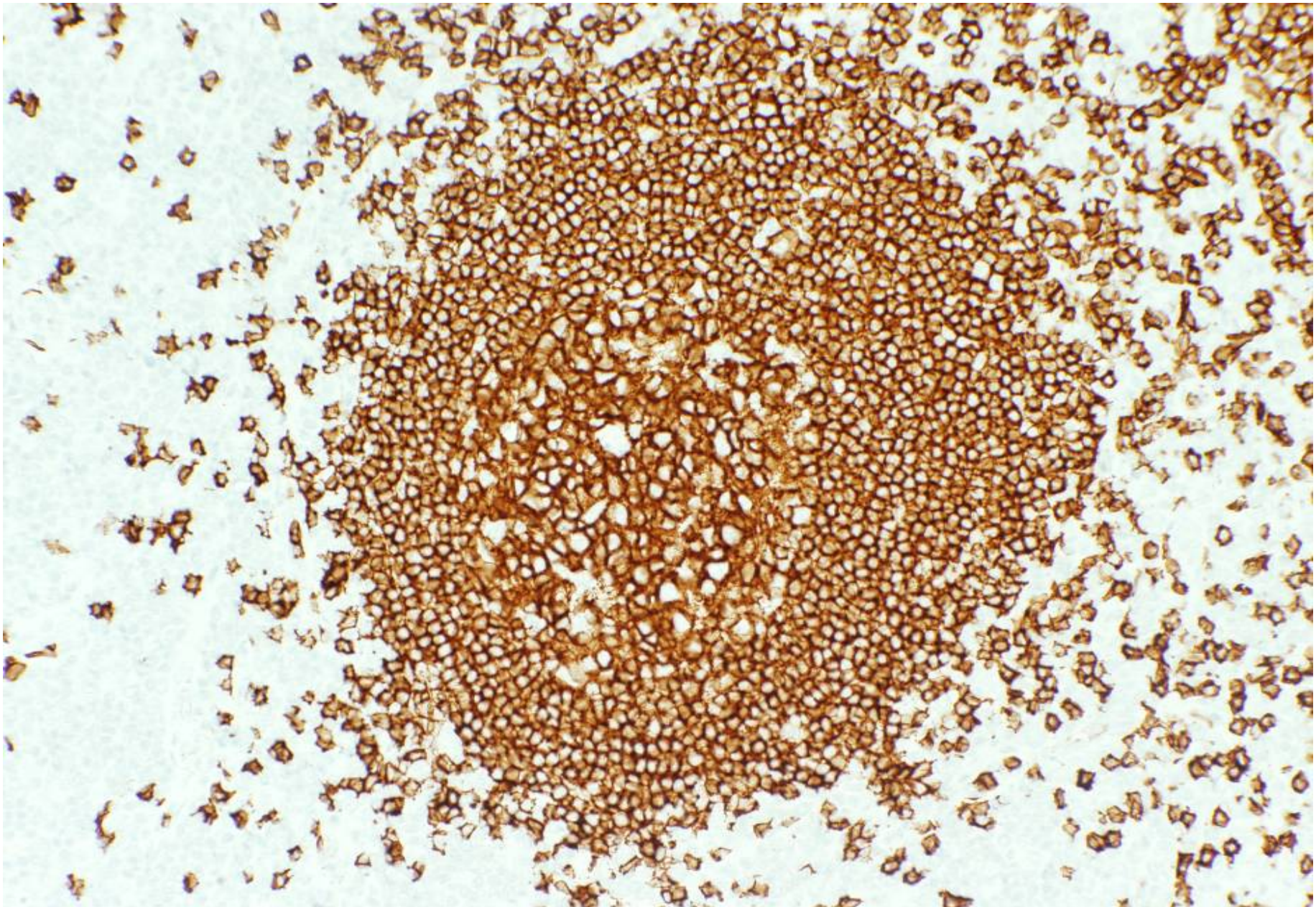
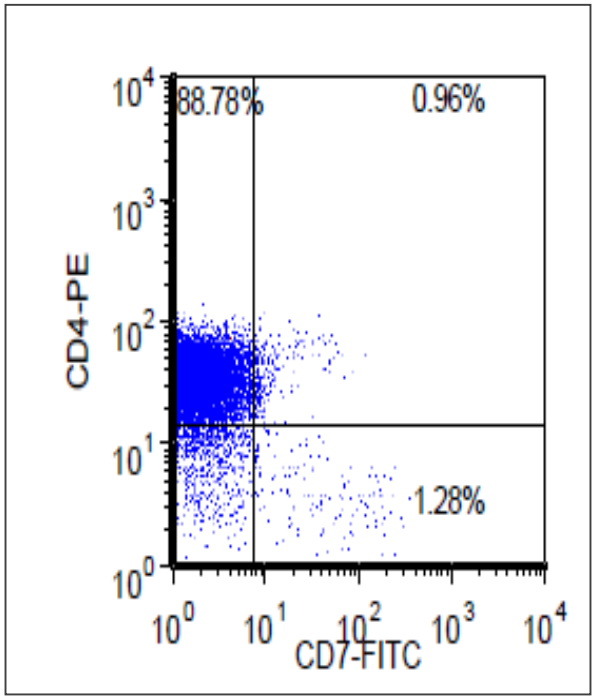
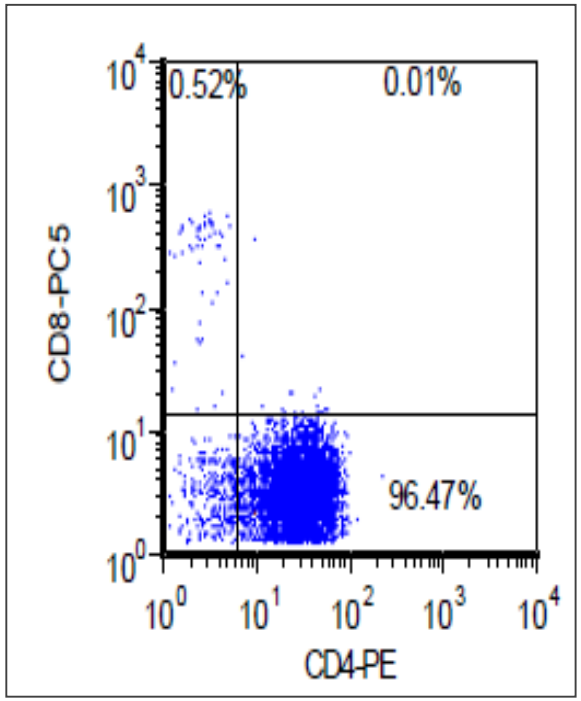
Reactive follicular hyperplasia in a lymph node: CD20



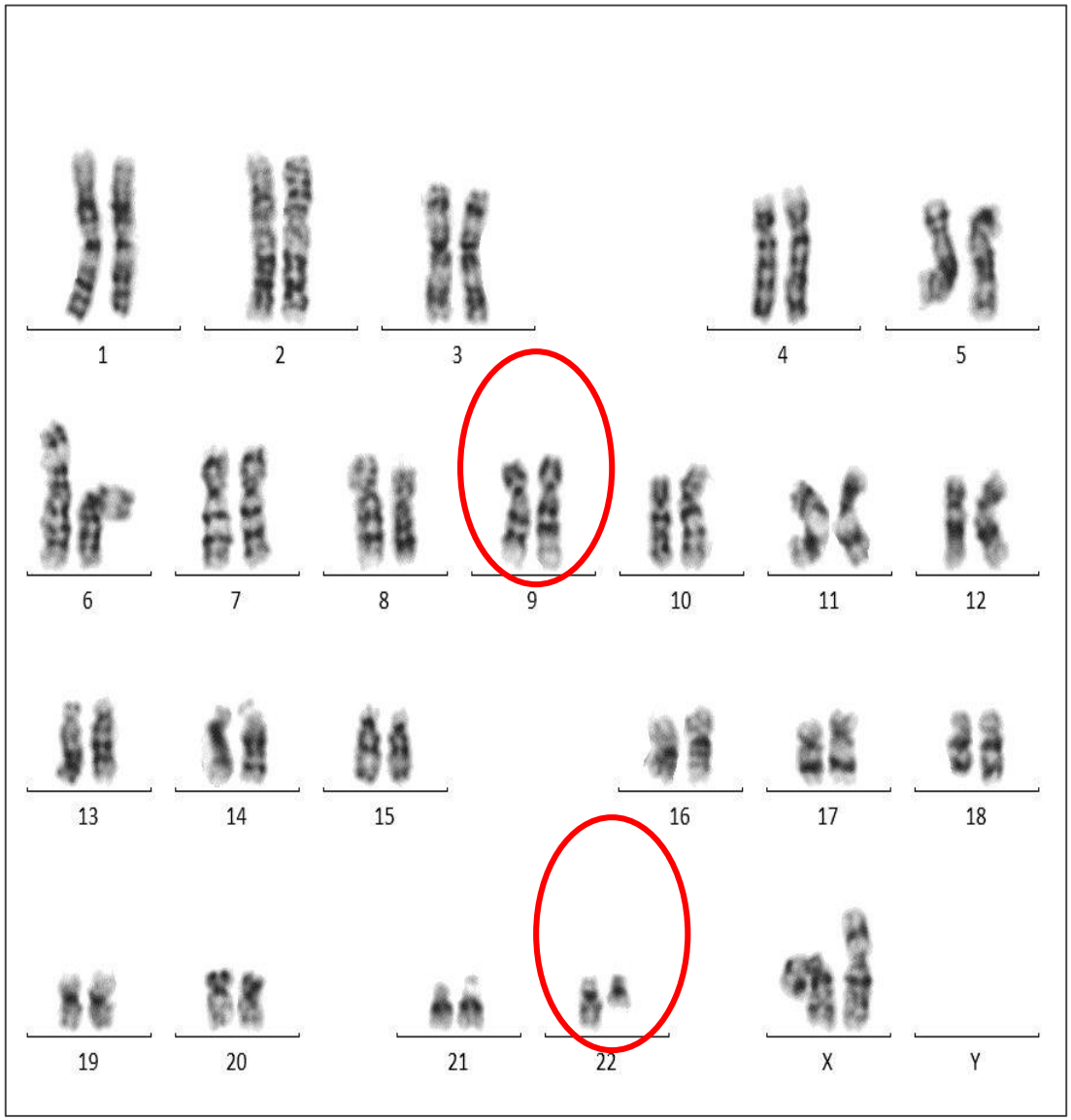
Flow Cytometry

Lymphocyte Gate 69.00 %			Lymphocyte and Activation Related Antigens					
T-Cells/NK			**B-Cells**			**Others**		
CD2	98	D	Kappa	0.0	N	HLA-DR	25	M
CD3	84	D	Lambda	0.0	N	CD10	0	N
CD4	96	M	CD19	0	N	CD11c	1	N
CD5	96	D	CD20	0	N	CD38	1	N
CD7	2	N	CD4/CD8 RATIO= 96.00 increased			CD45	100	B
CD8	1	N				Kappa/Lambda Ratio=NA		
NK-Cells			Coexpression %			NA Low or no B cells		
CD16	1	N	CD19/CD5 0.00			Lambda/Kappa Ratio=NA		
CD56	1	N	CD19/CD10 0.00			NA Low or no Bcells		





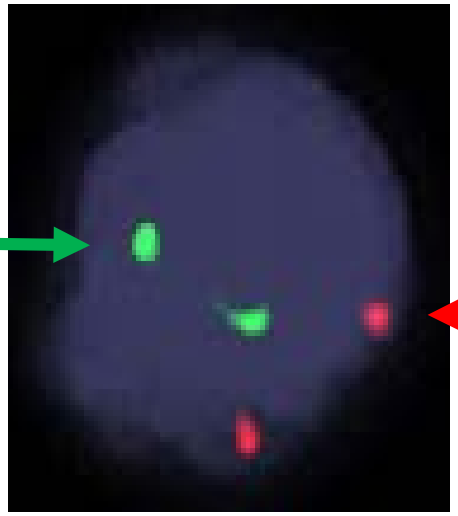
Cytogenetics



Fluorescent in-Situ Hybridization (FISH)

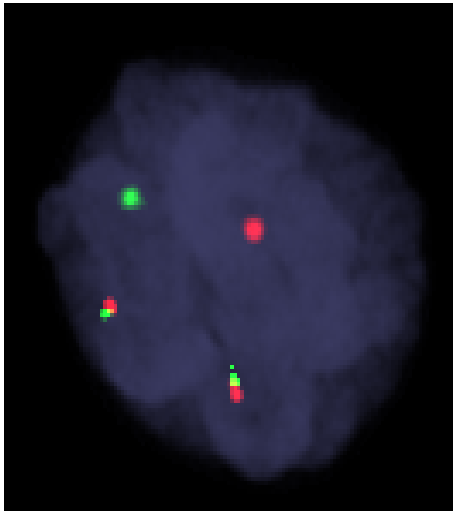
Normal

Chromosome 9



Chromosome 22

Abnormal



Why Pathologists Choose NeoGenomics?

- Full service lab with most comprehensive menu.
- Highly experienced technical staff able to perform complex studies with high accuracy
- Flexible business models allows clients to perform professional interpretations
- Expert medical staff able to interpret any studies and answer any questions
- Superior turn-around times
- Culture of compliance

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PD-L1 Testing

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Dual Role of Immune System in Cancer

- Suppress neoplastic growth by recognizing cells with neoantigens and eliminating them
- Promote neoplastic growth by inadvertently selecting for cancer clones that evade immune surveillance

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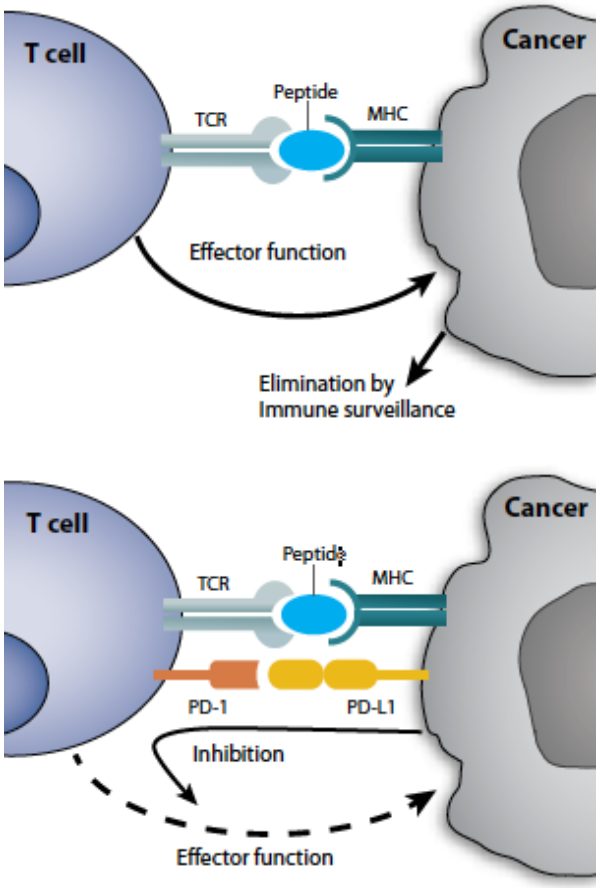
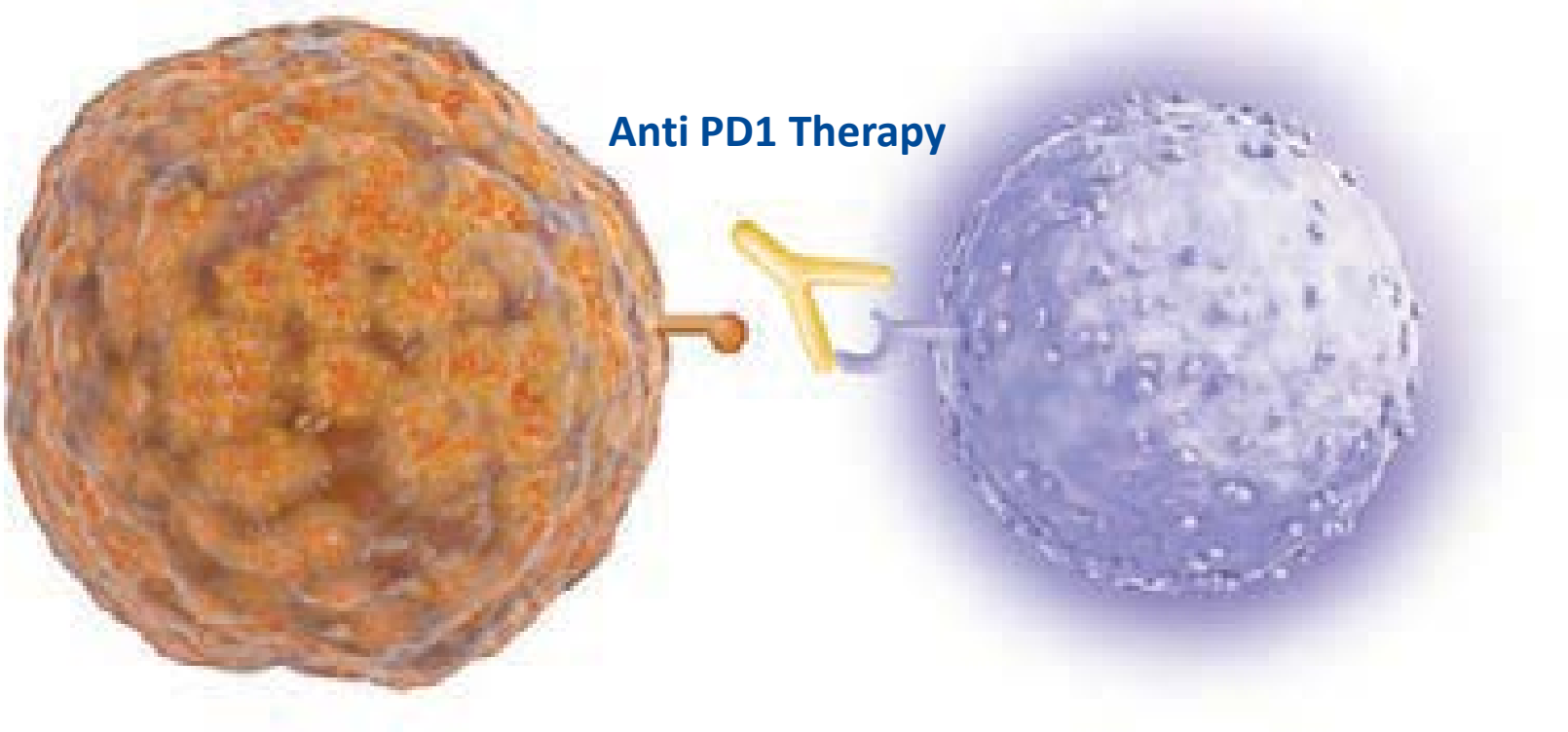
Interaction Between Immune Cell and Cancer (IASLC Atlas of PD-L1 Immunohistochemistry Testing in Lung Cancer Lung)



Anti–PD-L1 Therapy

PD-L1 Expressing Carcinoma Cell

PD1 Expressing Active Cytotoxic T-Cell



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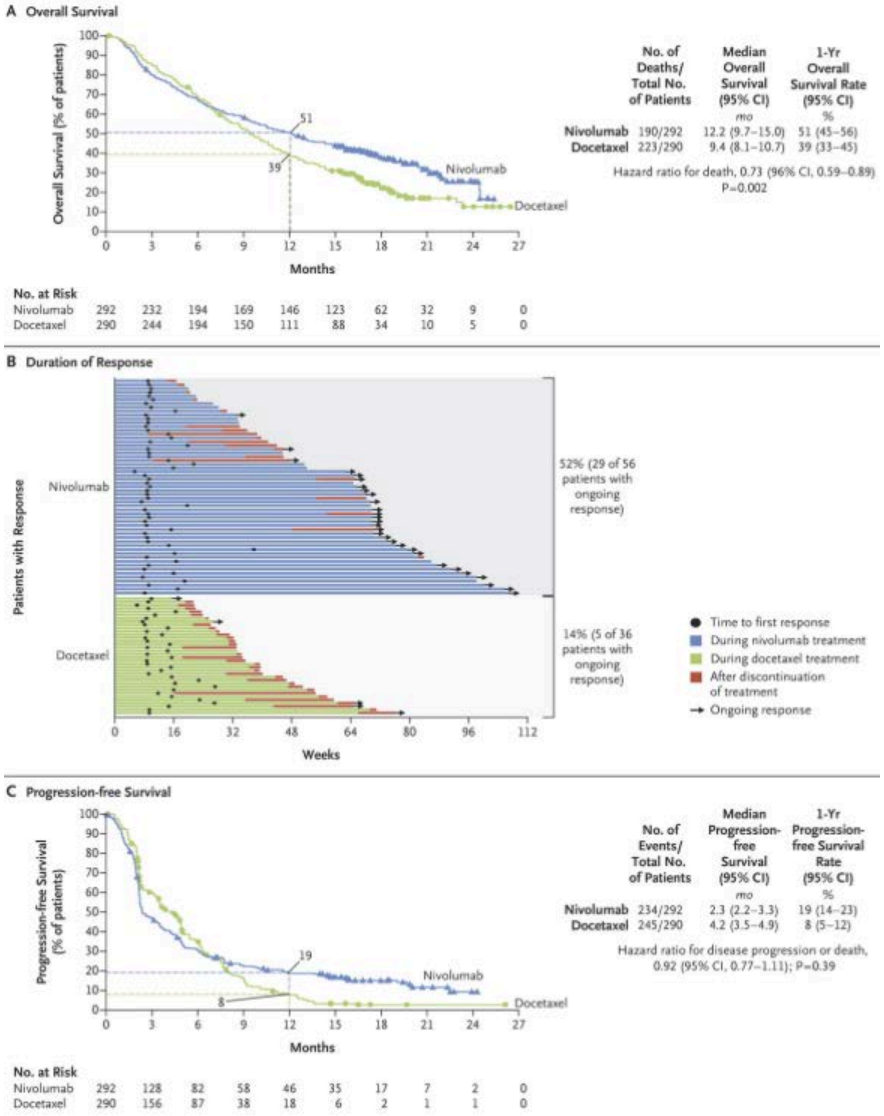
Imunno-Oncology vs. Targeted Therapy

Nivolumab (PD-1 Inhibitor) vs. Docetaxel in Advanced Non-Squamous Non-Small Cell Lung Cancer

(N Engl J Med 2015;373:1627-1639)



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Treatment Results in NSCLC Clinical Trials Applying PD-L1 IHC 22C3 (IASLC Atlas of PD-L1 Immunohistochemistry Testing in Lung Cancer)

Trial Name	Rx Line 2	Drug	PD-L1 TPS	No. of Patients	ORR, %	OS (median), months	PFS (median), months	PD-L1 Predict Trmt Resp?	Reference
KEYNOTE 010	Treated	Pembrolizumab vs docetaxel (Doc)	1-24%	471	8.6 (Pem) vs 10.9 (Doc)	9.7 (Pem) vs 8.5 (Doc)	2.6 (Pem) vs 4.0 (Doc)	Yes	(Herbst 2016)
			25-49%	120	15.8 (Pem) vs 9.1 (Doc)	9.8 (Pem) vs 9.9 (Doc)	2.9 (Pem) vs 3.8 (Doc)		
			50-74%	158	22.6 (Pem) vs 9.6 (Doc)	15.8 (Pem) vs 8.2 (Doc)	4.3 (Pem) vs 4.3 (Doc)		
			≥75%	284	33.7 (Pem) vs 7 (Doc)	16.6 (Pem) vs 8.2 (Doc)	6.2 (Pem) vs 4.0 (Doc)		
KEYNOTE 001	Treated and Naive	Pembrolizumab	<1%	28	10.7			Yes	(Garon 2015)
			1-49%	103	16.5				
			≥50%	73	45.2				
KEYNOTE 001	Naive	Pembrolizumab	<1%	12	8.3	14.7	3.5	Yes	(Hui 2016; Hui 2017)
			1-49%	52	17.3	19.5	4.2		
			≥50%	27	51.9	Not reached	12.5		
KEYNOTE 001	Treated	Pembrolizumab	<1%	90	9.9	8.6		Yes	(Hui 2016)
			1-49%	168	12.9	8.2			
			≥50%	138	38.3	15.4			

Companion vs. Complementary Testing

- Companion diagnostic test
  - Typically linked to a specific drug within its approved label
  - Identifies patient who have a significant benefit from the drug
- Complementary diagnostic test
  - Not required for use of drug
  - May provide additional information for physicians regarding the use of the drug in which patient may benefit from therapy (prognosis)

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PD-L1 Testing

- Companies develop an IHC kit to be used as a companion or complementary diagnostic test for each drug
- Different kits, with different antibodies and different scoring systems
  - Different manufacturers (DAKO vs. Ventana)
  - Different machine platforms
  - Count tumor cells, inflammatory cells, or both

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Different PD-L1 Antibodies

PD-L1 Diagnostic Antibody Clone	PD-L1 Binding Domain	Platform
28-8 (rabbit)	Extracellular	Link 48 Autostainer
22C3 (mouse)	Extracellular	Link 48 Autostainer
SP142 (rabbit)	Cytoplasmic	BenchMark ULTRA
SP263 (rabbit)	Extracellular	BenchMark

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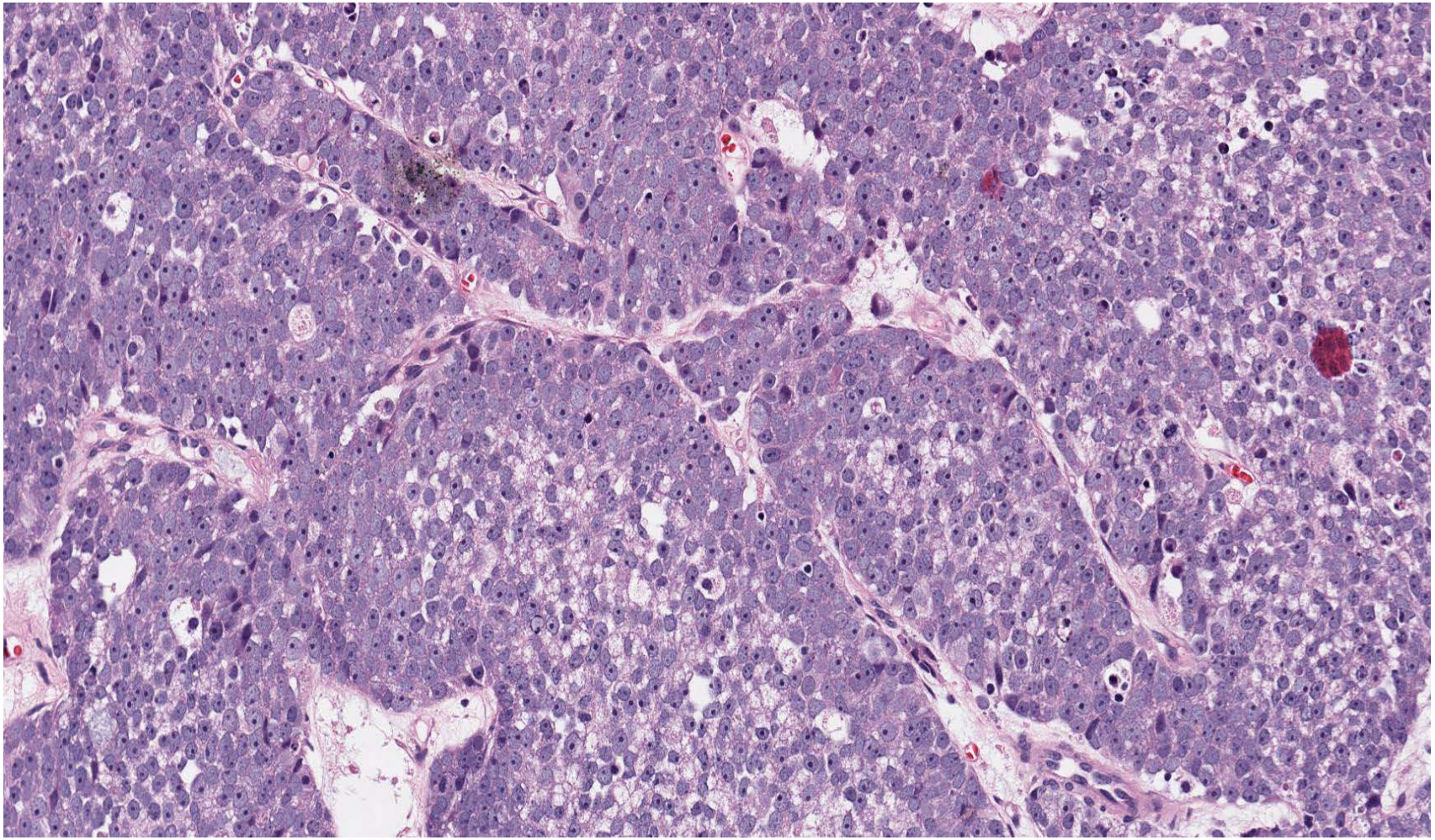
Name	Target	FDA-Companion PD-L1	FDA-Complimentary	Approved Indications
Ipilimumab (Yervoy®)	CTLA-4	None	None	Inoperable or Metastatic Melanoma
		None	None	Adjuvant Treatment of Stage IIIa Melanoma
Nivolumab (Opdivo®)	PD-1		≥1% (28-8)	Inoperable or Metastatic Melanoma
			≥1% (28-8)	Metastatic Non-Small Cell Lung Cancer
		None	None	Advanced Renal Cell Carcinoma
		None	None	Classical Hodgkin Lymphoma
		None	None	Recurrent or Metastatic Head and Neck Squamous Cell Carcinoma
		None	None	Locally Advanced or Metastatic Urothelial Carcinoma
Pembrolizumab (Keytruda®)	PD-1	None	None	Inoperable or Metastatic Melanoma
		≥1% (22C3)		Metastatic Non-Small Cell Lung Cancer with PD-L1 Expression
		≥50% (22C3)		Metastatic Non-Small Cell Lung Cancer with high PD-L1 Expression
		None	None	Recurrent or Metastatic Head and Neck Squamous Cell Carcinoma
		None	None	Refractory Classical Hodgkin Lymphoma
Atezolizumab (Tecentriq®)	PD-L1		≥5% IC (SP142)	Locally Advanced or Metastatic Urothelial Carcinoma
			≥50% TC or ≥10% IC (SP142)	Metastatic Non-Small Cell Lung Cancer
Avelumab (Bavencio®)	PD-L1	None	None	Metastatic Merkel Cell Carcinoma (MCC)

Science 331:1565–1570. doi:10.1126/science.1203486

Pulmonary Adenocarcinoma



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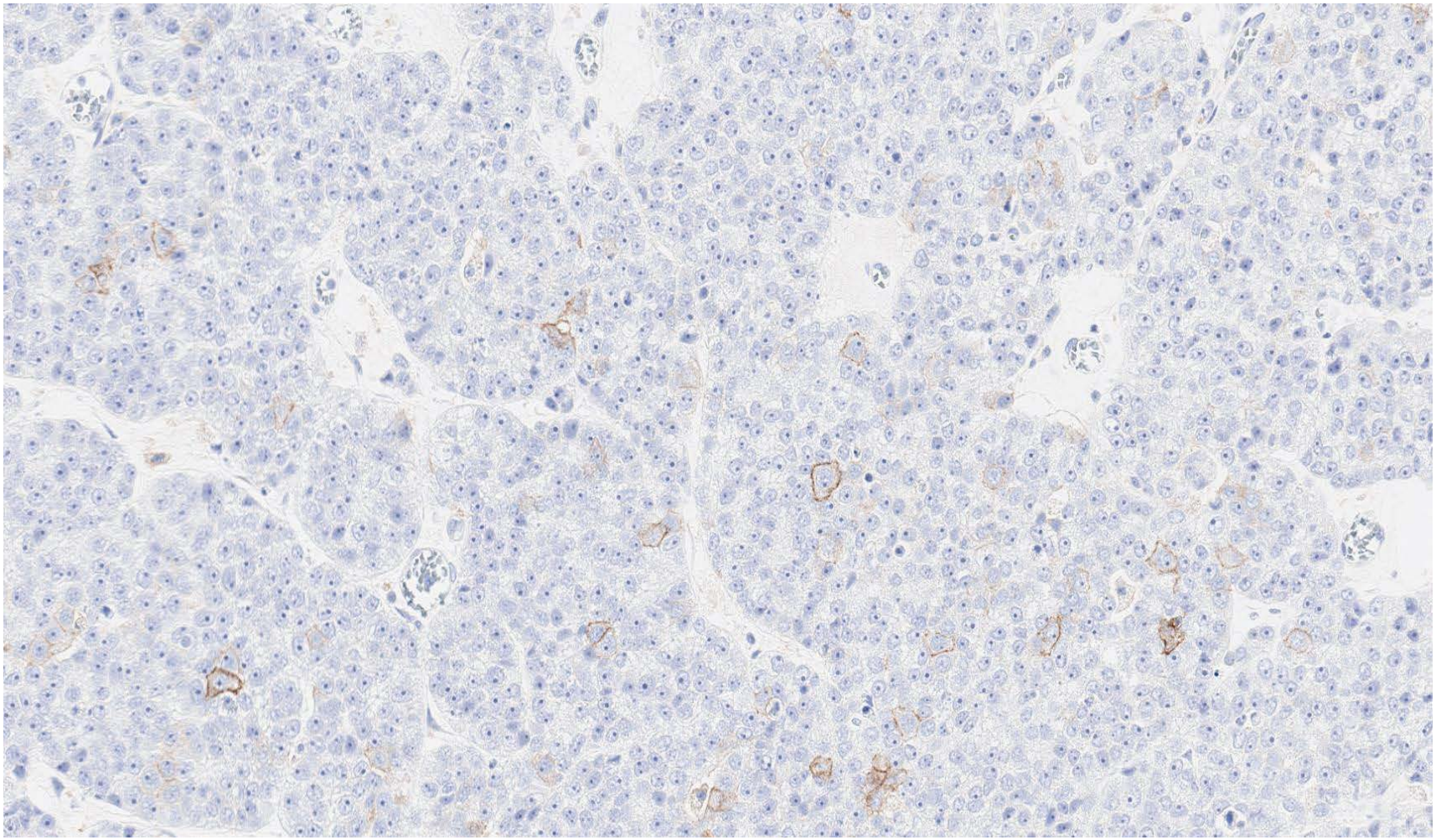
Pulmonary adenocarcinoma/PD-L1: 1.5% staining seen



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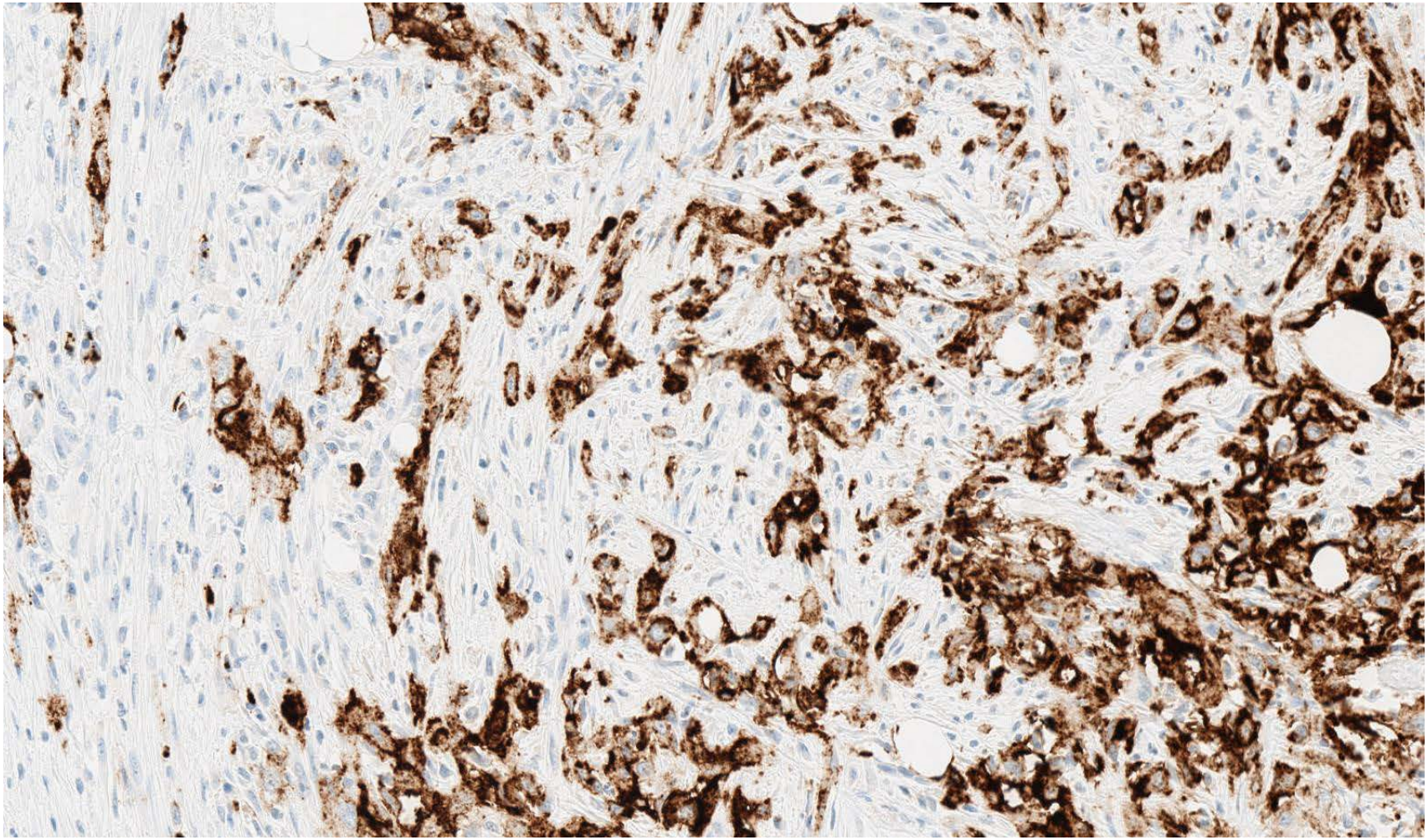
Bladder carcinoma



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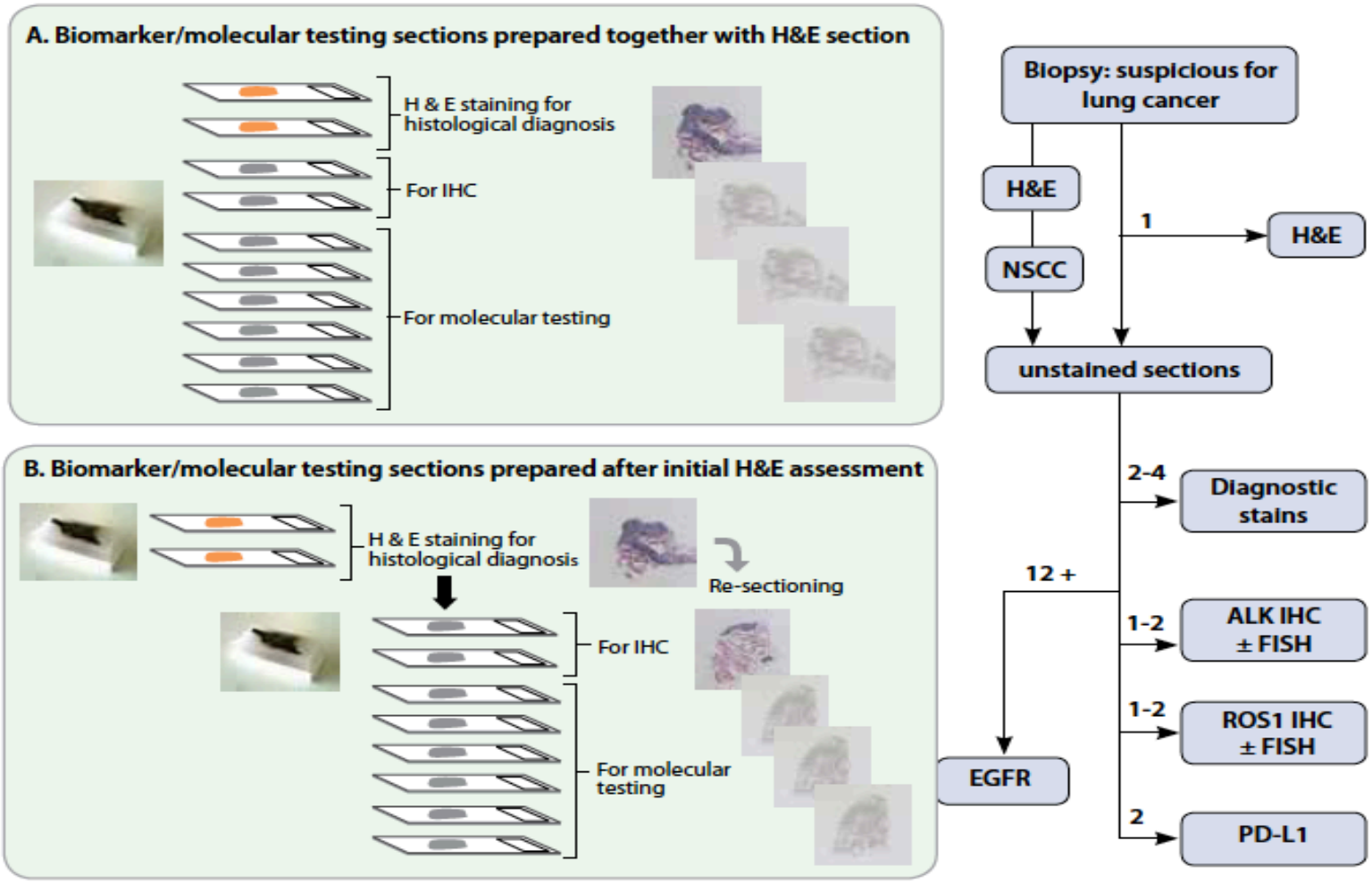
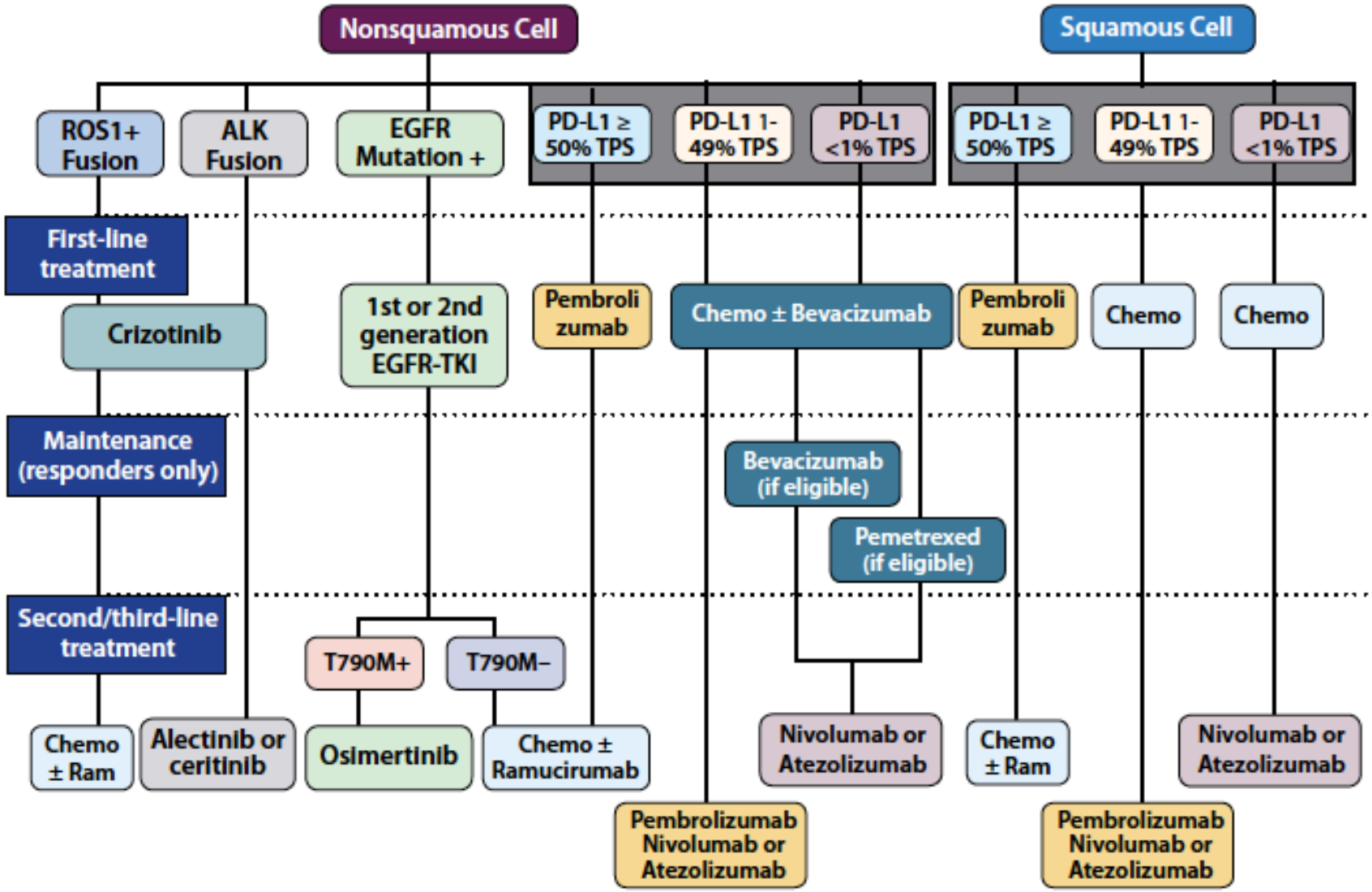
PD-L1 Testing is a Part of Overall Testing Strategy (IASLC Atlas of PD-L1 Immunohistochemistry Testing in Lung Cancer)



Role of PD-L1 In Treatment Plan for Lung Cancer (IASLC Atlas of PD-L1 IHC Testing in Lung Cancer Lung)



PD-1 Therapy Companion Testing: Rapidly Changing Landscape

- Keytruda approved on May 23, 2017 for use in unresectable or metastatic solid tumors that have been identified as having microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR)
- We already do routine testing for MSI/MMR in colon and endometrial carcinoma
- This new indication will open up MSI/MMR testing for other major cancers, including other gastrointestinal tumors , breast, prostate, bladder, thyroid, etc.

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Key Takeaways

- ☑ Full-service Lab with complete range of testing in all major testing modalities - “one-stop” shop
- ☑ High level of technical and professional expertise in all cancer testing areas
- ☑ PD-L1 and related testing is an important new area and will continue to grow in the foreseeable future
- ☑ Well positioned to address rapidly evolving cancer landscape

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Questions and Answers

15 Minute Break

The Webcast will resume at approximately 10:15 AM PST

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