Patient Name:	**Doe, Jane**	**Physician:**	**John Doe, MD**	**Accession #:**	**O16-00612**
Sex:	Female	**Specialty Group:**	John Doe, MD	**Collected:**	2/6/2017
DOB:	12/1/1960 (56)	**Phone / Fax:**	999-999-9999 / 999-999-9999	**Received:**	2/12/2017
Reference #:	O16-612	**CC:**		**Reported:**	2/13/2017

Consultation Report

DIAGNOSIS

A. **LUNG, RIGHT:**

- 95% of tumor cells positive for PD-L1 protein expression by immunohistochemistry; please see image and comment

Summary Notes / Comments :

PD-L1 is a programmed cell death ligand on tumor cell membrane and is capable of binding to PD1 receptor on activating T-cells. If such binding occurs, it can negatively affect the activating T-cells' ability to slow/neutralize tumor growth (1-3). Cancer patients who experience disease progression either during or after first-line therapy are offered anti-PD-L1 targeted therapy with Nivolumab, Pembrolizumab, Atezolizumab, or Durvalumab (4). Pembrolizumab targeted therapy can also be offered as a first-line treatment option (5). Semi-quantitative detection of PD-L1 protein by immunohistochemistry is performed to determine the percentage of PD-L1 positive tumor cells by IHC assays (6). Some package inserts state that "an" FDA-approved assay regardless of which assay is chosen is sufficient for patients' eligibility (7). In a collaborative study performed on this laboratory on a large cohort of NSCLC patients, the sensitivity of E1L3N monoclonal antibodies was superior to the FDA-approved antibodies 22c3 and 28-8 (to be presented at the 2017 USCAP meeting). Given current lack of consensus on scoring criteria of various FDA-cleared assays (8), the results in the table and diagnosis report the percentage of positive cells, along with stratification into the following three scoring categories: no expression (<1% of tumor cells positive), low expression (1-49%) and high expression (50-100%). **In this particular case, the percentage of positive tumor cell population is 95%, rendering the patient eligible for applicable anti PD1/PD-L1 targeted therapy agents.**

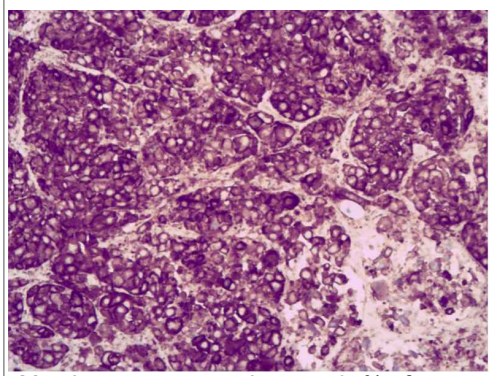
References:

1. Herbst RS, Baas P, Kim DW, et al. Pembrolizumab versus docetaxel for previously treated, PD-L1-positive, advanced non-small- cell lung cancer (KEYNOTE-010): a randomised controlled trial. *Lancet 2015* (**http://www.ncbi.nlm.nih.gov/pubmed/26712084**)
2. Phillips T, Simmons P, Inzunza HD, et al. Development of an Automated PD-L1 Immunohistochemistry (IHC) Assay for Non-Small Cell Lung Cancer. *Appl Immunohistochem Mol Morphol 2015;23:541- 549* (**http://www.ncbi.nlm.nih.gov/pubmed/26317305**)
3. Brahmer JR, Tykodi SS, Chow LQ, et al. Safety and activity of anti- PD-L1 antibody in patients with advanced cancer. *N Engl J Med 2012;366:2455-2465* (**http://www.ncbi.nlm.nih.gov/pubmed/22658128**)
4. NCCN NSCLC Guidelines Version 4.2016 (**http://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf**)
5. Pembrolizumab versus Chemotherapy for PD-L1-Positive Non-Small-Cell Lung Cancer. Reck, M, Rodríguez-Abreu, Robinson AG, et al. *N Engl J Med 2016; 375:1823-1833*
6. Roach C, Zhang N, Cortigiano E, et al. Development of a Companion Diagnostic Immunohistochemistry Assay for Pembrolizumab Therapy in Non-Small-Cell Lung Cancer. *Appl Immunohistochem Mol Morphol 2016;24(6):392-397* (**http://www.ncbi.nlm.nih.gov/pubmed/27333219**)
7. Keytruda Package Insert (**https://www.merck.com/product/usa/pi_circulars/k/keytruda/keytruda_pi.pdf**)
8. Kerr KM, Nicolson MC. Non-Small Cell Lung Cancer, PD-L1, and the Pathologist. *Arch Pathol Lab Med 2016;140:249-254* (**http://www.archivesofpathology.org/doi/pdf/10.5858/arpa.2015-0303-SA**)

Table of Immunohistochemistry Results

Block	Antibody Name(Clone)	Result(s)	% Positive Cells
O16-00612	PDL1 (E1L3N)	Positive	>95%

Images



Membranous expression on >95% of tumor cells

Pembrolizumab Package Insert Online QR Code

NCCN 2017 NSCLC QR Code

Patient Name:	**Doe, Jane**	**Physician:**	**John Doe, MD**	**Accession #:**	**O16-00612**
Sex:	Female	**Specialty Group:**	John Doe, MD	**Collected:**	2/6/2017
DOB:	12/1/1960 (56)	**Phone / Fax:**	999-999-9999 / 999-999-9999	**Received:**	2/12/2017
Reference #:	O16-612	**CC:**		**Reported:**	2/13/2017

Consultation Report

Procedure

Deparaffinized sections, destained sections, or unstained smears of patient, as well as appropriate positive control tissues, are incubated with the following panel of monoclonal and/or polyclonal antibodies listed in the table below. Localization is via a biotin-free, polymer-based immunoperoxidase technique, with pretreatments (heat induced epitope retrieval) according to protocols optimized for each antibody. Satisfactory positive and negative control reactivity is observed. Procedure and scoring were performed according to FDA-approved package insert (when applicable). For 22C3 antibody, results are considered positive when strong membranous expression is noted on >50% of tumor cells. For 28-8 antibody, results are considered positive when strong membranous expression is noted on 1-10% of tumor cells.

Gross Description

A. Received from "Facility Name" (Miami, FL) is 1 paraffin tissue block labeled O16-612 with accompanying report and requisition sheet. Specimen was submitted for PD-L1 testing by immunohistochemistry studies with interpretation.

Electronic Signature **Hadi Yaziji, M.D.**

CPT Code(s): 88360 (1)

***** END OF REPORT *****