Key Considerations when Evaluating Whether to Establish a PD-L1 Laboratory Developed Test (LDT)

Kim, Joseph[1]; Hung, Yin P. (Rex)[2]; Liu, Xiaoying[3]; Nam, Myong "Lucy"[4]; Rosa, Marilin[5]; Saeed, Lamees[5]; Schulte, Jefree J[6]; Zhang, Huina[7]; Zhang, Wei[8]; Chivukula, Mamatha[9]; Beumer, Kellie[10]; Kelly, Melissa[10]; Lazure, Patrice[11]; Murray, Suzanne[11]

[1]Q Synthesis LLC, Newtown, Pennsylvania; [2]Massachusetts General Hospital, Boston, Massachusetts; [3]Dartmouth Hitchcock Medical Center, Lebanon, New Hampshire; [4]Inova, Fairfax, Virginia; [5]Moffitt Cancer Center, Tampa, Florida; [6]University of Wisconsin–Madison, Madison, Wisconsin; [7]University of Rochester Medical Center, Rochester, New York; [8]University of Kansas Medical Center, Kansas City, Kansas; [9]Sutter Health, Burlingame, California; [10]American Society for Clinical Pathology, Chicago, Illinois; [11]AXDEV Group Inc., Brossard, QC, Canada

ASCP STRONGERTOGETHER

BACKGROUND

- PD-L1 IHC testing is often used to identify patients with cancer who may be eligible for immune checkpoint inhibitor therapy.
- The complexity around using different assays and platforms has caused confusion and reluctance to perform in-house PD-L1 testing.
- Some labs have established a laboratory developed test (LDT) that may be used across multiple types of tumors.

METHODS

In early 2023, 28 pathologists and 15 laboratory professionals joined the ASCP PD-L1 Learning Collaborative and explored ways to improve PD-L1 testing processes.

Among those performing PD-L1 testing:

Perform in-house	49%
Send out	31%
Combination of in-house and send out	20%

The Learning Collaborative met over four months (March – June 2023) and discussed clinical and operational issues that affect PD-L1 testing. Within the Learning Collaborative, an ad-hoc working group was formed to explore the topic of LDT. This group reviewed the literature, spoke with other pathologists using LDTs, and developed key guidance questions for laboratories.

REFERENCES

Hurwitz JT, Vaffis S, Grizzle AJ, et al. *Oncol Ther*. 2022;10(2):391-409.
Koomen BM, Badrising SK, van den Heuvel MM, Willems SM. *Histopathology*. 2020;76(6):793-802.
Nambirajan A, Husain N, Shukla S, et al. *Indian J Med Res*. 2019;150(4):376-384.
Munari E, Zamboni G, Lunardi G, et al. *Hum Pathol*. 2019;90:54-59.
Naso JR, Wang G, Banyi N, et al. *Ann Diagn Pathol*. 2021;50:151590.
Torlakovic E, Lim HJ, Adam J, et al. *Mod Pathol*. 2020;33(1):4-17.

SUMMARY

- PD-L1 is a routine biomarker test for certain types of cancers (eg, NSCLC, head and neck squamous cell, cervical, gastric, esophageal, triple negative breast cancer, etc.)
- Several different PD-L1 companion diagnostics are available they use different antibody clones, different platforms, and different scoring and interpretation requirements based on the type of cancer that is tested
- Many organizations have successfully established the use of a PD-L1 Laboratory Developed Test (LDT)
- A PD-L1 LDT may be the right approach for labs that aim to simplify PD-L1 testing

ACKNOWLEDGMENTS

The ASCP PD-L1 Learning Collaborative was a part of a larger education initiative led by ASCP, Q Synthesis LLC, and AXDEV Group. This program was called “Engaging the Cancer Care Team: Streamlining Biomarker Testing for Optimal Patient Outcomes” and was supported by an educational grant from Merck.

RESULTS

The working group identified the following topics and questions to guide those who may be considering whether to establish a PD-L1 LDT:

Testing volume and types of cancers: How many tests are performed each month to justify an in-house PD-L1 test? Which types of cancers are tested? Do we have (or do we plan to develop) reflex PD-L1 testing protocols for certain types of tumors?

Buy-in from oncologists: Do our medical oncologists feel that a PD-L1 LDT provides the results they need to make treatment decisions across different types of cancers?

Assay selection and testing platforms: Which IHC platform (eg, Ventana, Dako, Leica, etc.) do we currently use and which assay (eg, 22C3, 28-8, SP263, E1L3N, etc.) should we use? How well do these assays stain tumor cells vs. immune cells?

Examples of companion diagnostics: 22C3 on Dako, 28-8 on Dako, SP263 on Ventana

Examples of LDTs: E1L3N on Leica, 22C3 on Leica

IHC testing processes: What is our volume of IHC testing and how would adding PD-L1 impact our workflow for all IHC tests? How often do we encounter technical issues? How much staff time will it take to add PD-L1? What are the maintenance costs?

Interpretation and scoring: Which pathologists are trained to interpret PD-L1 tests? Are they trained to interpret tumor cells, immune cells, or both? Are we a training program? Which scoring systems will we use and how will we report results?

Validation: How many cases are needed for validation? Should validation samples include tumor cell and immune cell staining?

Reimbursement: How will the lab be reimbursed for performing PD-L1 testing and interpretation?

CONCLUSIONS

Before establishing a PD-L1 LDT, the medical laboratory must review these questions against the backdrop of an evolving PD-L1 testing landscape. An LDT may be the right approach for labs that aim to simplify PD-L1 testing based on the IHC platform(s) they are using.