

41 EXTERNAL REPRODUCIBILITY OF PD-L1 IHC 22C3 PHARMDX FOR CERVICAL CANCER AT CPS \geq 1 AND CPS \geq 10

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Background Despite advancements in cervical cancer care, women with persistent, recurrent, or metastatic cervical cancer face difficult prognoses with limited treatment options. Recent results from clinical trials KEYNOTE-158 (NCT02628067) and KEYNOTE-826 (NCT03635567) have demonstrated clinically meaningful results in patients with recurrent or metastatic cervical cancer whose tumors express PD-L1 with a Combined Positive Score (CPS) \geq 1. Here we give evidence of the reproducibility of PD-L1 expression determination in cervical cancer utilizing PD-L1 IHC 22C3 pharmDx at the CPS \geq 1 and CPS \geq 10 cutoffs.

Methods External reproducibility studies tested the inter-site, intra-site, inter-observer, and intra-observer assay reproducibility for cervical cancer at CPS \geq 1 and CPS \geq 10. To test inter- and intra-site reproducibility, five replicate sets of a blinded and randomized cervical cancer specimen set were tested at each of the three external sites. For inter- and intra-observer reproducibility, three external sites evaluated one pre-stained set of cervical cancer specimens. Percent agreement was calculated using Negative Percent Agreement (NPA), Positive Percent Agreement (PPA), and Overall Percent Agreement (OA). Pre-specified acceptance criteria (AC) for all components of the analyses were \geq 85.0% for the lower bound value of a 95% two-tailed percentile bootstrap confidence interval (CI) of each percent agreement point.

Results At the CPS \geq 1 cutoff: (i) inter-and intra-site NPA/PPA/OA met AC with point estimates (PE) \geq 97.5% and CI lower bounds \geq 94.7%, and (ii) inter- and intra-observer NPA/PPA/OA met AC with PE \geq 98.1% and CI lower bounds \geq 94.9%. At the CPS \geq 10 cutoff: (i) inter-and intra-site NPA/PPA/OA met AC, with PE \geq 92.8% and CI lower bounds \geq 86.7%, and (ii) inter- and intra-observer NPA/PPA/OA met AC, with PE \geq 98.4% and CI lower bounds \geq 95.9%.

Conclusions This study demonstrates high external lab reproducibility of PD-L1 IHC 22C3 pharmDx with respect to expression determination in cervical cancer at CPS \geq 1 and CPS \geq 10 cutoffs.

Ethics Approval The external reproducibility study was approved by WCG IRB, study numbers 1284639, 1284652, and 1284653.

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