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THIS IS INTENDED FOR PATHOLOGISTS ONLY

PD-L1 Testing and CPS Interpretation in Head and Neck Squamous Cell Carcinoma (HNSCC)

WHY ARE YOU LIKELY TO RECEIVE REQUESTS FOR PROGRAMMED DEATH LIGAND-1 (PD-L1) COMBINED POSITIVE SCORE (CPS) IN HNSCC?

Licence for KEYTRUDA® (pembrolizumab) in first-line HNSCC:^{1*}

- KEYTRUDA, as monotherapy or in combination with platinum and 5-fluorouracil (5-FU) chemotherapy, is indicated for the first-line treatment of metastatic or unresectable recurrent head and neck squamous cell carcinoma (HNSCC) in adults whose tumours express PD-L1 with a CPS ≥ 1

VISIT MSD CONNECT TO FIND OUT MORE ABOUT KEYNOTE-048 STUDY DESIGN AND OUTCOMES



This link will direct you to a MSD promotional website

THE IMPORTANCE OF PD-L1 EXPRESSION

PD-L1 is a transmembrane protein that binds to the programmed death-1 (PD-1) receptor on to cytotoxic T cells and other immune cells.² The PD-1/PD-L1 interaction inactivates T cells and normally serves to protect against immune recognition of self; however, many tumours have been shown to upregulate PD-L1 expression to evade the immune system.² Blocking the PD-1/PD-L1 interaction ensures T cells remain active and helps the immune system to recognise tumour cells.²

CPS SCORING IN R/M HNSCC

CPS was developed as a means of assessing PD-L1 expression in both tumour cells and tumour-infiltrating immune cells.³ HNSCC tumours are frequently infiltrated by immune cells including lymphocytes and macrophages. Expression of PD-L1 on tumour infiltrating immune cells has been linked to response to anti-PD-L1 therapy, including KEYTRUDA. In the KEYNOTE-048 study, 85% (754/882) of treatment-naïve patients with M/uR HNSCC had tumours that expressed PD-L1 (CPS ≥ 1).^{3,4}

HOW TO CALCULATE CPS

$$\text{CPS} = \frac{\text{Total number of PD-L1 stained cells (including tumour cells, lymphocytes and macrophages)}}{\text{Total number of viable tumour cells}} \times 100$$

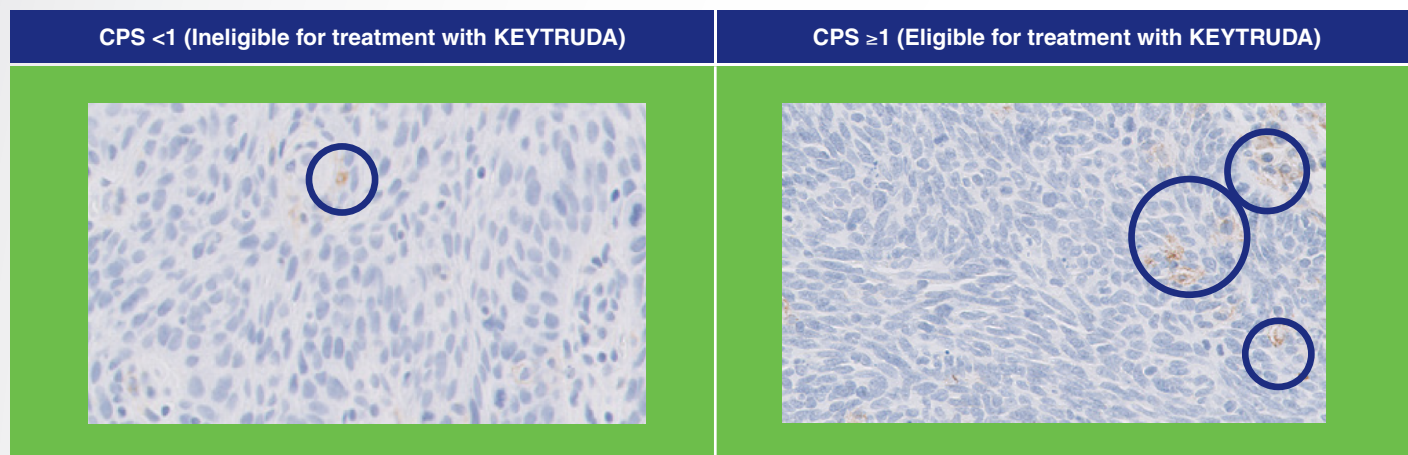
PLEASE NOTE: TPS is an alternative method of determining PD-L1 expression in tumour cells which is not applicable for first-line M/uR HNSCC, as it does not include infiltrating immune cells in the calculation of the score.

INTERPRETING AND REPORTING CPS

To calculate the CPS, samples are visually divided into regions with equal numbers of tumour cells. An estimate of the total number of viable tumour cells and PD-L1 stained cells is then calculated for each region and averaged to calculate the CPS.³

CPS scoring ranges from 0–100, representing the level of PD-L1 expression in all cells (both tumour and immune infiltrating) divided by the number of tumour cells. Note that CPS is not reported as a percentage but rather as a score between 0–100. Results over 100 are reported as 100. When reporting results, you may be asked to report the results of a control cell line slide staining.³

EXAMPLE IMAGES OF CPS LEVEL[†] (20x)³



[†]Circles highlight PD-L1 stained cells

CHOOSING AN APPROPRIATE PD-L1 ASSAY

A number of PD-L1 immunohistochemistry (IHC) assays are currently commercially available:

- The PD-L1 IHC 22C3 PharmDx assay is an IHC test designed by Dako. It is specifically designed to detect PD-L1 expression in formalin fixed paraffin embedded (FFPE) tumour samples, including HNSCC on Dako ASL 48 platform³
- The PD-L1 IHC 22C3 PharmDx assay was employed in the Phase III KEYNOTE-048 study of patients with M/uR HNSCC^{3,4}
- Data demonstrate that the 22C3 antibody laboratory developed test (LDT) on the BenchMark XT platform has high concordance with the PD-L1 IHC 22C3 PharmDx assay in HNSCC tumour samples⁵
- Moderate concordance has been shown between the 22C3 PharmDx assay (Dako ASL 48 platform) and SP263 (Ventana Benchmark Ultra platform)⁶

Pooled safety data of KEYTRUDA across all indications and full AE management can be found in the Summary of Product Characteristics (SmPC).

Refer to SmPC before prescribing

If you have any questions or would like to request any further materials please contact: MSD medical information (0208 154 8000, medicalinformationuk@msd.com)

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*KEYTRUDA as monotherapy is also indicated for the treatment of recurrent or metastatic head and neck squamous cell carcinoma in adults whose tumours express PD-L1 with a ≥ 50% Tumour Proportion Score (TPS) and progressing on or after platinum-containing chemotherapy (Note: KEYTRUDA is not reimbursed for this indication in the UK)

Abbreviations: 5 FU, 5 fluorouracil; CPS, combined positive score; FFPE, formalin fixed paraffin embedded; FNA, fine needle aspiration; HNSCC, head and neck squamous cell carcinoma; IHC, immunohistochemistry; LDT, laboratory developed test; M/uR, metastatic or unresectable recurrent; PD-1, programmed death-1; PD-L1, Programmed death ligand-1; TPS, tumour proportion score.

References:

1. KEYTRUDA 50 mg powder for concentrate for solution for infusion. Summary of Product Characteristics. (December 2020);
2. Forster MD and Devlin M-J, *Front.Oncol.* 2018; 8:310;
3. Agilent. PD-L1 IHC 22C3 pharmDx Interpretation Manual – Head and Neck Squamous Cell Carcinoma (HNSCC);
4. Burtneiss B et al. *Lancet.* 2019;394:1915–28;
5. Vainer G.W et al. Poster presented at IASLC WCLC 2019. Poster PS-03-023;
6. De Ruiter EJ et al. *European Journal of Cancer.* 2019; 110, S20 (P3.05)



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