

PD-L1 Testing and CPS Interpretation in Oesophageal Cancer

WHY MIGHT YOU RECEIVE REQUESTS FOR PROGRAMMED DEATH LIGAND-1 (PD-L1) COMBINED POSITIVE SCORE (CPS) IN OESOPHAGEAL CANCER?

Licence for KEYTRUDA® (pembrolizumab) in first-line oesophageal cancer:¹

- KEYTRUDA®, in combination with platinum and fluoropyrimidine based chemotherapy, is indicated for the first-line treatment of patients with locally advanced unresectable or metastatic carcinoma of the oesophagus or HER-2 negative gastroesophageal junction adenocarcinoma in adults whose tumours express PD-L1 with a CPS ≥ 10.

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 OESOPHAGEAL CANCER

CPS was developed as a means of assessing PD-L1 expression in both tumour cells and tumour-infiltrating immune cells.³ Oesophageal tumours are frequently infiltrated by immune cells including lymphocytes and macrophages.³ Expression of PD-L1 on tumour infiltrating immune cells has been linked to response to anti-PD-L1 therapy, including KEYTRUDA®.⁴ Of patients with locally advanced unresectable or metastatic oesophageal carcinoma or gastroesophageal junction carcinoma in **KEYNOTE-590**: 51% (n=383/749) had tumours that expressed PD-L1 with a CPS ≥10 based on the PD-L1 IHC 22C3 pharmDx assay.¹

Evaluating PD-L1 expression with CPS is important for patients with advanced oesophageal cancer, regardless of squamous cell carcinoma or adenocarcinoma histology.^{1,4}

HOW TO CALCULATE CPS⁴

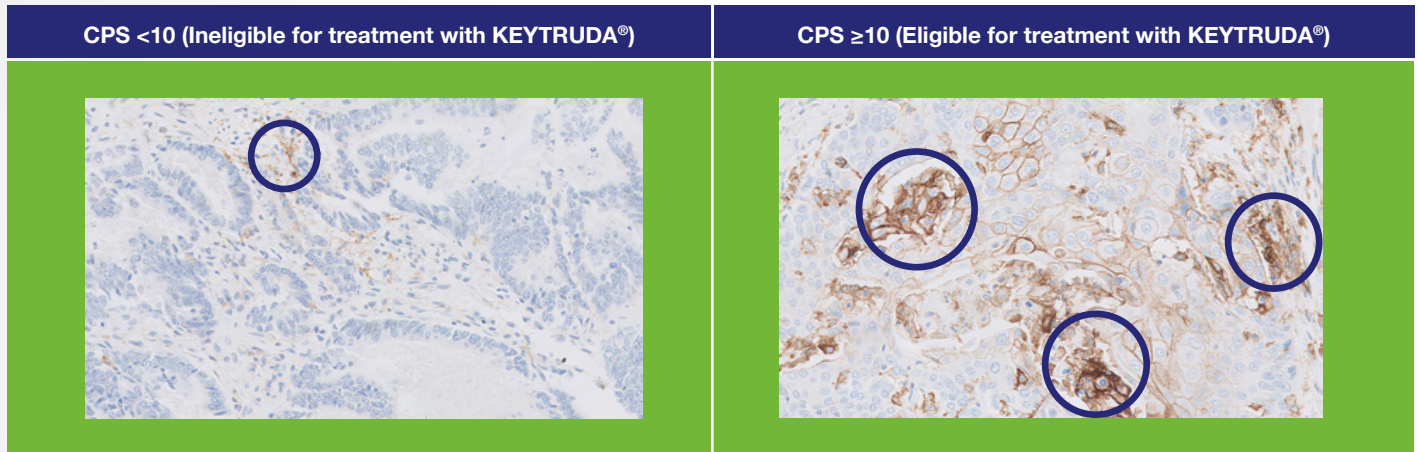
$$\text{CPS} = \frac{\text{Total number of PD-L1 stained cells (including tumour cells, lymphocytes and macrophages)}}{\text{Total number of viable tumour cells}} \times 100$$

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.⁴

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 and 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.⁴

EXAMPLE IMAGES OF CPS LEVEL* (20x)⁴



*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 oesophageal tumours on Dako ASL 48 platform⁴
- The PD-L1 IHC 22C3 PharmDx assay was employed in the Phase III KEYNOTE-590 study of patients with locally advanced unresectable or metastatic oesophageal carcinoma or gastroesophageal junction carcinoma⁴

There is insufficient data available on concordance of PD-L1 IHC 22C3 PharmDx assay and any other commercially available PD-L1 IHC assay in oesophageal tumour samples.

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 and the assay manual before prescribing or recommending.

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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Abbreviations: 5 FU, 5 fluorouracil; CPS, combined positive score; FFPE, formalin fixed paraffin embedded; FNA, fine needle aspiration; IHC, immunohistochemistry; LDT, laboratory developed test; 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. Power R, et al. Front Oncol. 2020; 10:891;
4. PD-L1 IHC 22C3 pharmDx Interpretation Manual – Esophageal Cancer.



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