OPINION ON MEDICINAL PRODUCTS

nivolumab
OPDIVO 10 mg/ml,

solution for dilution for infusion

New indication

Adopted by the Transparency Committee on 12 October 2022

SUMMARY

The legally binding text is the original French opinion version

- **Oesophageal cancer**
- **Sector: Hospital**

Key points

Approval of reimbursement for the first-line treatment of adult patients with unresectable, recurrent or metastatic oesophageal squamous cell carcinoma, with PD-L1 tumour cell expression ≥1%, in combination with fluoropyrimidine- and platinum-based combination chemotherapy.

Therapeutic improvement?

OPDIVO (nivolumab) provides therapeutic improvement with respect to chemotherapy (fluoropyrimidine- and platinum-based), as a first-line treatment for adult patients with unresectable, recurrent or metastatic oesophageal squamous cell carcinoma, with PD-L1 tumour cell expression ≥1%.

Role in therapeutic strategy?

For patients with unresectable (if radiotherapy is contraindicated) locally advanced or metastatic oesophageal squamous cell carcinoma or adenocarcinoma, referral for systemic treatment (palliative chemotherapy) is the conventional treatment. The main chemotherapy drugs used are a fluoropyrimidine associated with a platinum derivative. Other regimens such as FOLFOX associating fluorouracil-oxaliplatin-folinic acid are sometimes used as a treatment option.

Since 2021, KEYTRUDA (pembrolizumab) in association with a chemotherapy regimen based on platinum salts and fluoropyrimidine is a first-line treatment for adult patients with unresectable locally advanced or metastatic, type I only (Siewert classification) HER-2-negative gastro-oesophageal junction adenocarcinoma or oesophageal cancer, with PD-L1 tumour expression where CPS ≥ 10 based on the findings of the KEYNOTE 590 study (including approximately 70% squamous cancer patients).

Role of OPDIVO (nivolumab) in the therapeutic strategy:

OPDIVO (nivolumab) in combination with fluoropyrimidine- and platinum-based combination chemotherapyis a first-line treatment option for the treatment of adult patients with unresectable, recurrent or metastatic oesophageal squamous cell carcinoma, with PD-L1 tumour cell expression ≥1%. Given the lack of comparative data, it is not possible to determine its role in the therapeutic strategy with respect to KEYTRUDA (pembrolizumab).

Committee's conclusions

Clinical Benefit

- Oesophageal cancer is a serious life-threatening disease.
- The proprietary medicinal product OPDIVO (nivolumab) is a curative medicinal product.
- Its efficacy/adverse effect ratio is significant.
- Therapeutic alternatives are available (see clinically relevant comparators).
- OPDIVO (nivolumab) in combination with fluoropyrimidine- and platinum-based combination chemotherapy is a first-line treatment of adult patients with unresectable, recurrent or metastatic oesophageal squamous cell carcinoma, with PD-L1 tumour cell expression ≥1%.

Public health benefit

Considering:

- the severity of the disease and its prevalence,
- the partially met medical need,
- the partial response to the identified need, with evidence of improvement in progression-free survival and overall survival, of OPDIVO (nivolumab) in combination with fluoropyrimidine- and platinum-based combination chemotherapy versus chemotherapy alone, among patients with PD-L1 tumour cell expression ≥1%,
- the lack of data enabling formal conclusions to be drawn in term of quality of life,
- the lack of expected additional impact on the care and/or life pathway;

OPDIVO (nivolumab), in combination with chemotherapy, is not likely to have an additional public health benefit.

Considering all of these elements, the Committee deems that the clinical benefit of OPDIVO (nivolumab) when associated with a chemotherapy regimen is significant in the marketing authorisation indication.

The Committee approves inclusion in the list of proprietary medicinal products qualifying for reimbursement for the indication "OPDIVO is indicated in combination with fluoropyrimidine- and platinum-based combination chemotherapy, as a first-line treatment of adult patients with unresectable, recurrent or metastatic oesophageal squamous cell carcinoma, with PD-L1 tumour cell expression ≥1% at the dosages of the marketing authorisation.

Clinical Added Value

Considering:

the evidence in a phase III, randomised, open-label study of the superiority of OPDIVO (nivolumab) in combination with fluoropyrimidine- and platinum-based combination chemotherapy versus chemotherapy alone among patients with PD-L1 tumour cell expression ≥1% in terms of:

- **overall survival, with an overall median survival of 15.4 months for the nivolumab + chemotherapy group, and 9.1 months for the chemotherapy group, representing an absolute gain of 6.3 months in favour of the nivolumab + chemotherapy group (HR=0.54, 99.5%CI [0.37; 0.80]; p<0.0001).**
- **progression-free survival, with an overall progression-free survival of 6.9 months for the nivolumab + chemotherapy group, and 4.4 months for the chemotherapy group, representing an absolute gain of 2.5 months in favour of the nivolumab + chemotherapy group (HR=0.65, 98.5%CI [0.46; 0.92]; p=0.0023).**

despite:

- **increased toxicity reported with the onset of adverse events (AEs) of immunological origin in particular. The proportion of patients having grade 3-4 AEs is higher in the chemotherapy + nivolumab group versus chemotherapy alone (72.9% vs. 55.9%); the same is true for serious AEs (60% vs. 42.8%), and AEs leading to treatment discontinuation (41.9% vs. 26.6%).**
- **the lack of formal conclusion that can be drawn from the quality-of-life findings,**

the Transparency Committee deems that OPDIVO (nivolumab) in combination with fluoropyrimidine- and platinum-based combination chemotherapy provides moderate clinical added value (CAV III) versus chemotherapy alone, as a first-line treatment, for the treatment of adult patients with unresectable, recurrent or metastatic oesophageal squamous cell carcinoma, with PD-L1 tumour cell expression ≥1%.

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