Immunothérapie et cancers ORL

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Pembrolizumab (PD-1 Antibody)

indiqué en monothérapie dans le traitement des patients adultes atteints d’un mélanome avancé (non résécable ou métastatique)

METHODS:
This study was an open-label, multicentre, phase 1b trial of patients with recurrent or metastatic squamous cell carcinoma of the head and neck. Patients had any level of PD-L1 expression (i.e., at least 1% of tumour cells or stroma that were PD-L1-positive by immunohistochemistry). Patients received pembrolizumab 10 mg/kg intravenously every 2 weeks.

FINDINGS:
Of the 104 patients screened, 82 (78%) were PD-L1-positive. Of these, 60 patients with PD-L1-positive squamous cell carcinoma of the head and neck were enrolled and treated: 24 (35%) were HPV-positive and 37 (62%) were HPV-negative. Pembrolizumab was well tolerated, with 10 (17%) of 60 patients having grade 3-4 drug-related adverse events, the most common of which were increases in alanine aminotransferase and aspartate aminotransferase, and hyponatraemia, each occurring in two of 60 patients; one patient developed a grade 3 drug-related rash. The proportion of patients with an overall response by central imaging review was 18% (eight of 45 patients; 95% CI 8-32) in all patients and was 25% (four of 16 patients; 7-52) in HPV-positive patients and 14% (four of 29 patients; 4-32) in HPV-negative patients.

INTERPRETATION:
Pembrolizumab was well tolerated and demonstrated clinically meaningful antitumour activity in recurrent or metastatic squamous cell carcinoma of the head and neck, supporting further study of pembrolizumab as anticancer therapy for advanced head and neck cancers.

KEYNOTE-012: Pembrolizumab in Advanced TNBC: Study Design

- Pembrolizumab anti-PD-1 antibody with high affinity for receptor
  - Provides dual independent biologic of PD-L1 and PD-L2
  - No mutagenic activity, KAA0052
  - Clinical activity in metastatic tumours, resistant approach in melanoma

KEYNOTE-012: Pembrolizumab Efficacy

- Median time to response: 9 wks
- Response duration: 16.5, 13.1, 7.1 yrs
- 3 yrs remain on therapy
- Median OS 12.7 mos
- OS 6 mos: 63.8%; OS 12 mos: 52.0%
- Median PFS: 2 mos

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Presenté par le Dr Xavier Zasadny
Polyclinique Limoges – Chénieux
The expansion cohort of KEYNOTE 012

- included 132 patients who were unselected for PD-L1 expression and received a fixed dose of pembrolizumab (infusion of 200 mg every 3 weeks)
- Approximately 59% of the patients had received ≥2 previous therapies
- The overall objective response rate was 24.8%, and was 26.3% in HPV-negative patients and 20.6% in HPV-positive patients. Approximately 25% of patients had stable disease, for a disease control rate of approximately 50%
- 60% of patients having any adverse event, and 15% reporting fatigue. Other side effects included hypothyroidism (9.1%), decreased appetite (7.6%), and rash (7.6%)
- Serious side effects occurred in <10% of patients. A total of 4 patients experienced serious immune-related adverse events that included 2 patients with pneumonitis and 2 with swelling of the face

Phases en cours = M+

Phase 3
Pembrolizumab for First Line Treatment of Recurrent or Metastatic Squamous Cell Cancer of the Head and Neck (KEYNOTE-048)
Participants with recurrent or metastatic squamous cell cancer of the head and neck will be randomly assigned to receive pembrolizumab alone, or pembrolizumab + a platinum-based drug (cisplatin or carboplatin) + 5-Fluorouracil (5-FU), or cetuximab + a platinum-based drug (cisplatin or carboplatin) + 5-FU

Phase 3
Pembrolizumab Versus Standard Treatment for Recurrent or Metastatic Head and Neck Cancer After Treatment With Platinum-based and Therapy (KEYNOTE-040)
This is a study of pembrolizumab versus standard treatment (methotrexate, docetaxel or cetuximab) for the treatment of recurrent or metastatic head and neck squamous cell cancer. Participants will be randomly assigned to receive either pembrolizumab or investigator's choice of standard treatment

Phase 2
Study of Pembrolizumab in Recurrent or Metastatic Head and Neck Squamous Cell Carcinoma After Treatment With Platinum-based and Cetuximab Therapy (KEYNOTE-055)
This is a study of single-agent pembrolizumab in patients with recurrent and/or metastatic head and neck squamous cell carcinoma who have progressed on platinum-based and cetuximab therapy

Phases 2 en cours = Ass RXTH

Radiation Therapy and Pembrolizumab in Treating Patients with Head and Neck Squamous Cell Carcinoma That Is Recurrent or Cannot Be Removed by Surgery

Pembrolizumab and Radiation Therapy in Treating patients with Squamous Cell Cancer of the Head and Neck

Pembrolizumab, Cisplatin, and Intensity Modulated Radiation Therapy in Treating Patients with Previously Untreated Stage III/IV Head and Neck Cancer

Adjuvant Cisplatin and Radiation With Pembrolizumab in Resected Head and Neck Squamous Cell Carcinoma

The purpose of this research study is to test the safety and the benefit of adding pembrolizumab to standard of care treatment for head and neck cancer. The standard of care treatment will include surgery followed by radiation for 6 weeks. Some patients may also receive cisplatin as standard of care once a week for 6 weeks if the cancer is found to be "high risk"

AstraZeneca

Durvalumab (PD-L1 Antibody)

et

Tremelimumab (CTLA-4 Antibody)

Nivolumab (PD-1 Antibody)

indicé en monothérapie dans le traitement des patients adultes atteints d’un mélanome avancé (non résectable ou métastatique)

indicé dans le traitement des patients adultes atteints d’un cancer bronchique non à petites cellules (CBNPC) de type épidermoïde localement avancé ou métastatique après une chimiothérapie antérieure
Présentation du Dr Xavier ZASADNY
Polyclinique Limoges – Chénieux