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Immunotherapy in oesophago-gastric
adenocarcinoma
DISCLOSURE OF INTEREST

- No conflicts of interest to declare
Clinical history

- **May 2015:** 63-years-old, T3N0M0 poorly differentiated adenocarcinoma of the distal oesophagus. Treated with 3 cycles neo-adjuvant ECX (cycle 3 discontinued early at 10 days due to severe PPE, constipation, fatigue, anorexia and decline in performance status).
  - PMHx: Hypertension, gastro-oesophageal reflux, diet-controlled diabetes mellitus

- **October 2015:** Ivor Lewis oesophagectomy. ypT3N0 (0/34 lymph nodes) poorly differentiated adenocarcinoma, R1 resection.
  - Slow post-operative recovery.
  - Did not receive post-operative radiotherapy or chemotherapy.
Clinical history (2)

- **January 2018**: CT scan identified recurrent disease at the site of anastomosis with large volume mediastinal lymphadenopathy.

- **February 2018**: Biopsy confirmed poorly differentiated adenocarcinoma at 25cm, HER2 negative.

- **February - April 2018**: Weekly Paclitaxel.

- **May 2018**: CT after 3 cycles of paclitaxel treatment demonstrated progressive disease with omental metastases.
Clinical history (3)

- **June 2018**: 5# palliative radiotherapy for tracheal compression secondary to mediastinal disease. Care transferred to RMH.
  - Fatigue, hoarse voice, dysphagia and regurgitation
  - 10kg weight loss in 6 months. PS2.

- **July 2018**: Commences nivolumab 3mg/kg 2-weekly on Expanded Access Programme
  - Symptomatic improvement after two doses
  - Partial response in mediastinal and peritoneal disease at 3-month CT
  - CA19-9: 2147 at baseline (20/06/2018) → 8 (25/09/2018)

- **August 2019**: 29 cycles of nivolumab completed
  - Asymptomatic aside from voice hoarseness. Well-tolerated.
  - Ongoing partial response radiologically.
Clinical history (4)

- **September 2019:**
  - Supplementary report: MMR proficient

- Cycle 34 on 22/10/2019
## Baseline CT:

2\textsuperscript{nd} July 2018

## Post 6 cycles:

19\textsuperscript{th} September 2018

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Discussion

- **ATTRACTION-2**
  - nivolumab vs. best supportive care
    - ≥2 regimens refractory to/intolerant of standard therapy
    - Asian patients
  - Responses seen irrespective of PD-L1 status

- **KEYNOTE-059**
  - ≥2 prior lines of chemotherapy, pembrolizumab monotherapy
    - ORR 15.4% vs. 6.4% in patients with PD-L1 positive tumours
    - Combined positivity score (CPS) >1%

- **Timing of anti-PD-1 therapy**
  - **KEYNOTE-061**: pembrolizumab vs. paclitaxel, 2L
    - No survival benefit with pembrolizumab, if biomarker unselected
    - MSI-H: median OS not reached vs. 8.1 (2-16.7) months (pembrolizumab vs. paclitaxel)
    - CPS≥10: mOS 10.4 (5.9–17.3) vs. 8.0 (5.1–9.9) months
  - **KEYNOTE-062**: pembrolizumab vs. pembrolizumab + chemotherapy (cisplatin+ 5-FU/capecitabine) vs. placebo + chemotherapy; PD-L1 positive (CPS ≥1), 1L
    - Pembrolizumab non-inferior to chemotherapy if CPS >1 (median OS 11.1 vs. 10.6 months; HR 0.91); clinically meaningful survival benefit if CPS ≥10 (17.4 vs 10.8 months; HR 0.69)
Discussion

- **Combination therapies**
  - anti-PD-1 + anti-CTLA 4
    - CHECKMATE-032
      - ORR 24% in nivolumab 1 mg/kg plus ipilimumab 3 mg/kg vs. 12% in nivolumab 3mg/kg

- **Biomarkers** – how do we better define patients who will benefit?
  - MSI-H
  - PD-L1
  - T cell inflamed signature
  - Tumour mutational burden