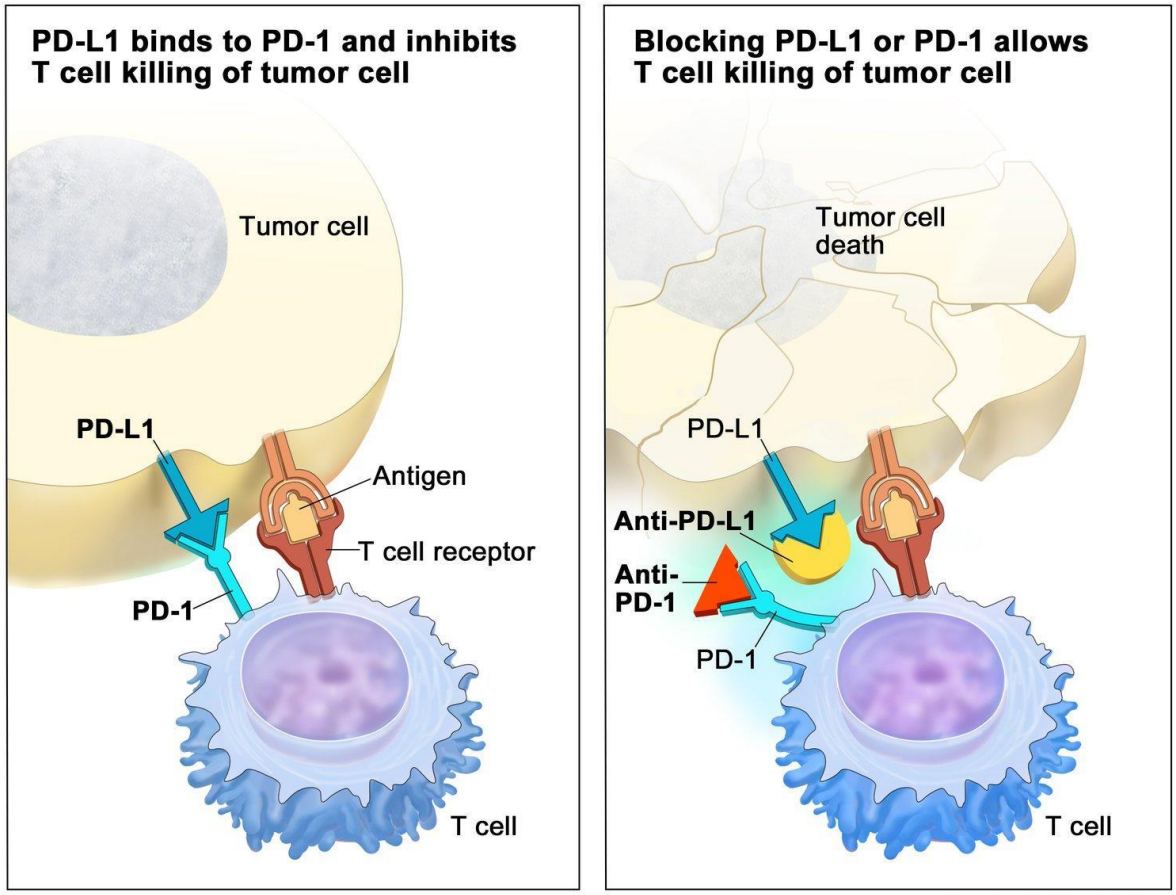
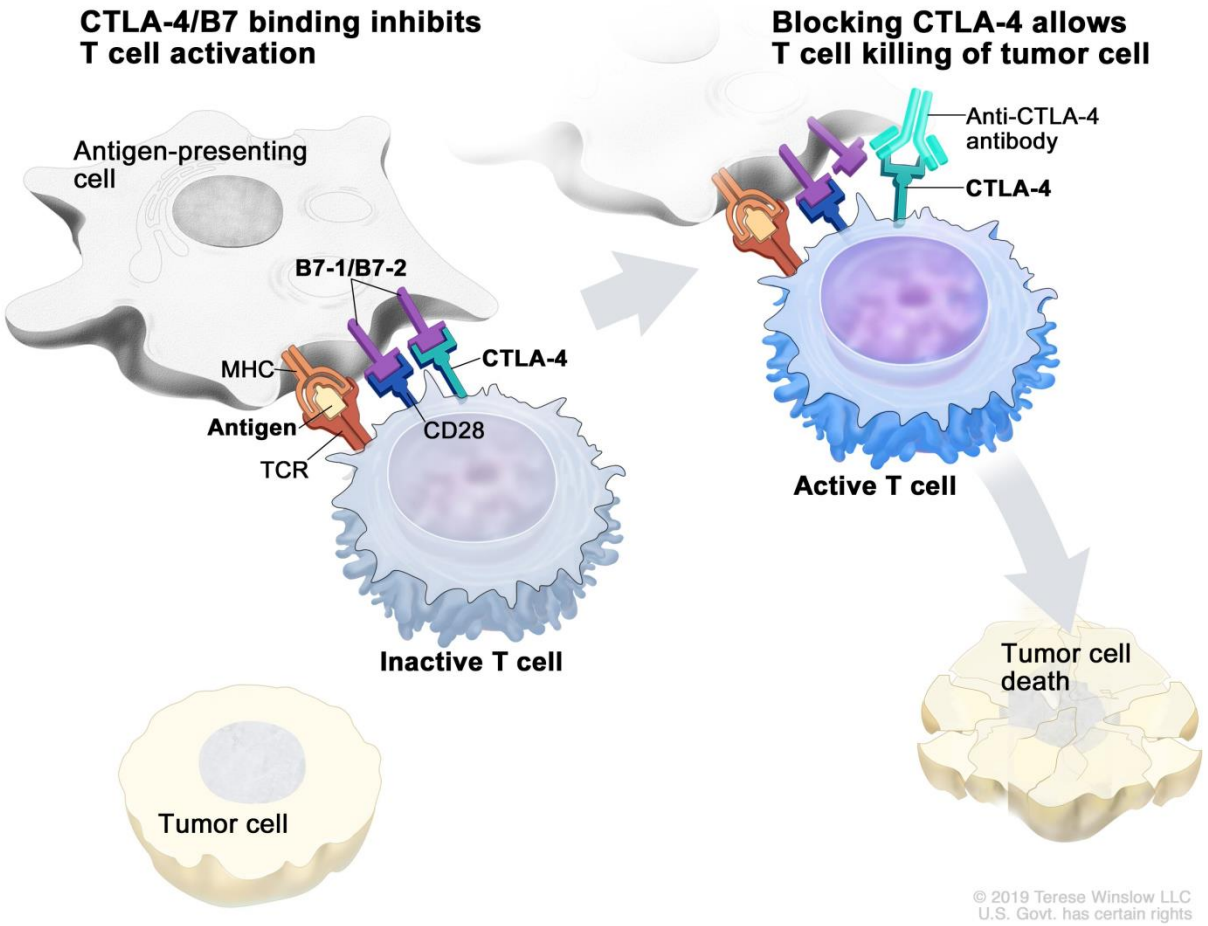
Immunotherapy: When and how

Prof. Jonathan Strosberg, MD
Moffitt Cancer Center
Tampa, FL

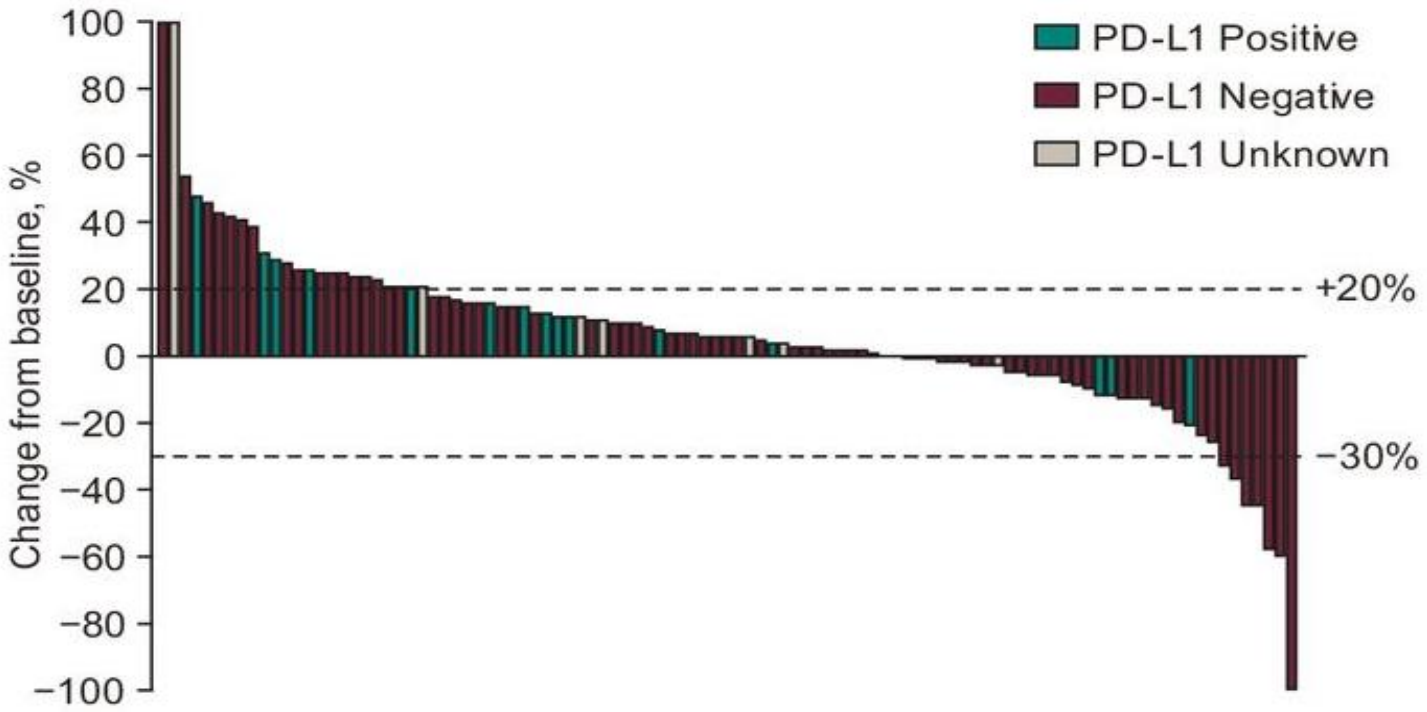
Checkpoint inhibitors: PD-1/PD-L1



Checkpoint inhibitors: CTLA-4



PD-1 inhibition in well-diff. NETs.



Strosberg et al. Clin Cancer Res. 2020 May 1;26(9):2124-2130

PD-1 inhibition in high grade neuroendocrine tumors/carcinomas

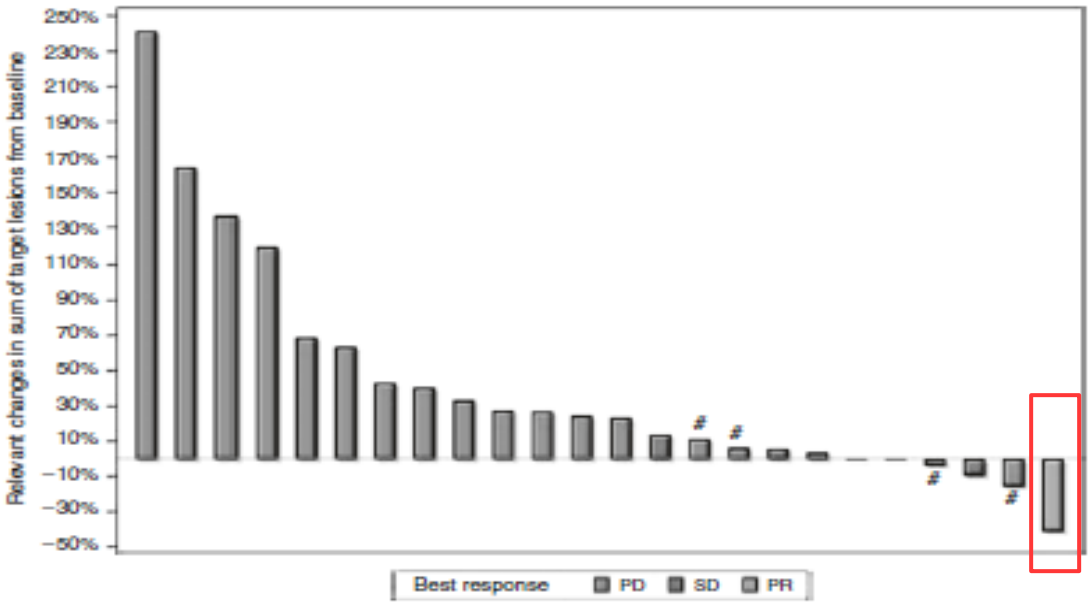
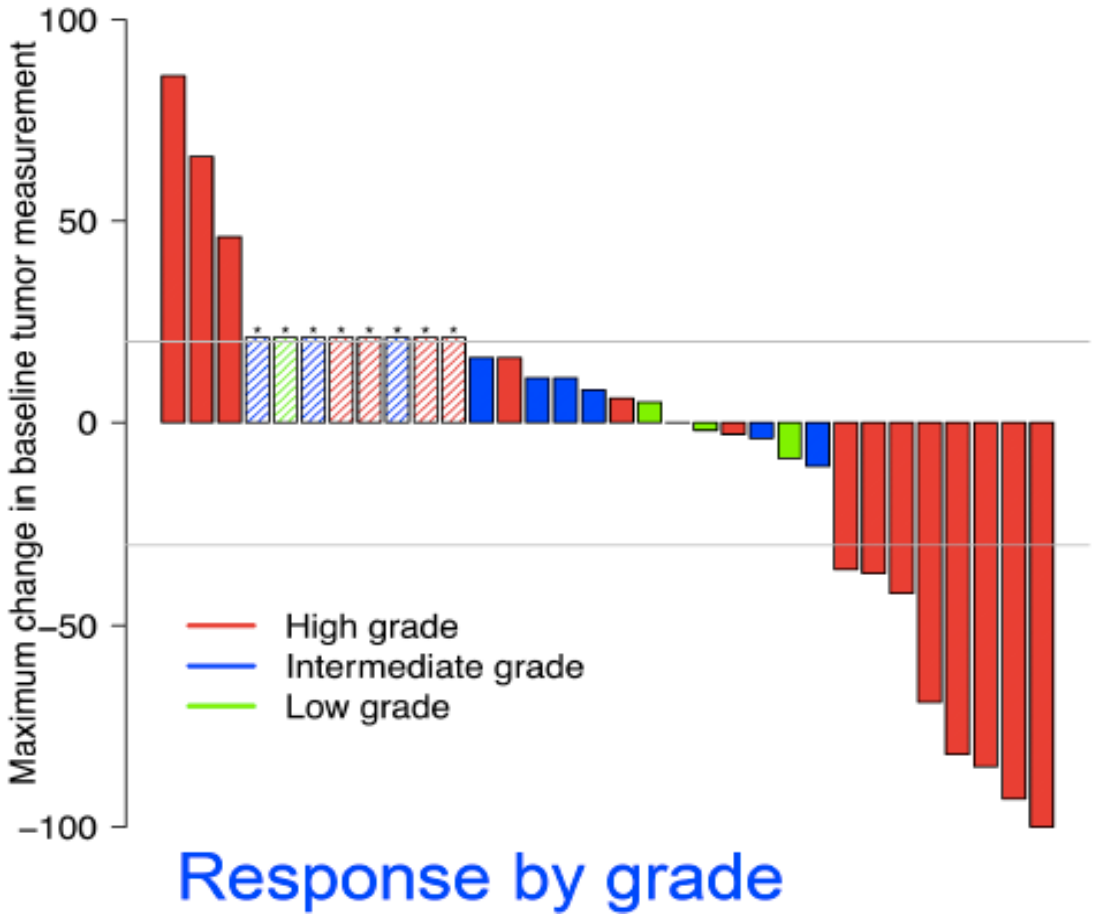


Fig. 1 Waterfall plot depicting best overall response to therapy by patient. Five patients were not evaluable for response. # represents patients who progressed due to appearance of new lesions despite reduction or less than 20% increase in tumor size. PD progressive disease, SD stable disease, PR partial response.

Vijayvergia et al. Br J Caner 2020 Apr;122(9):1309-1314

Ipilimumab/Nivolumab in high-grade NENs



Patel et al. Clin Cancer Res 2020 May 15;26(10):2290-2296

A multi-cohort phase II study of durvalumab plus tremelimumab for the treatment of patients (pts) with advanced neuroendocrine neoplasms (NENs) of gastroenteropancreatic or lung origin: The DUNE trial (GETNE 1601)

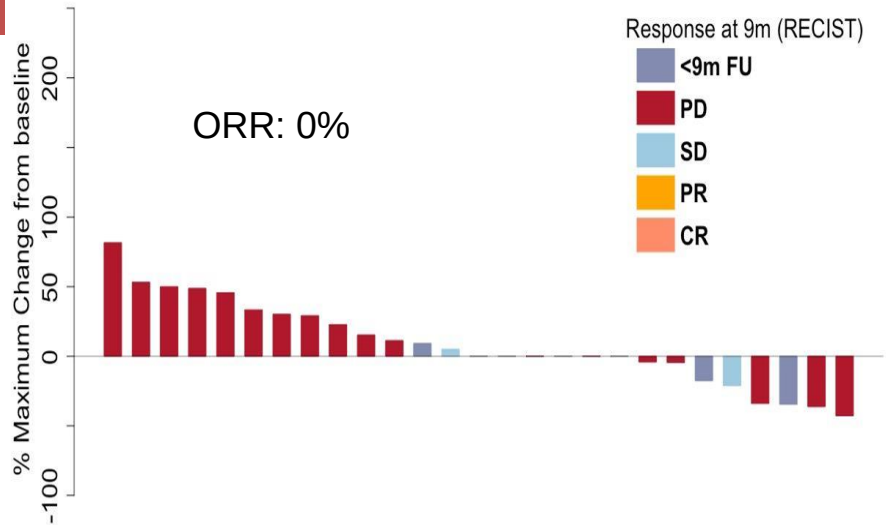
Jaume Capdevila, Alexandre Teulé, Carlos López, Rocío García-Carbonero, Marta Benavent, Ana Belén Custodio, Antonio Cubillo, Vicente Alonso, Teresa Alonso Gordoa, Alberto Carmona, Guillermo Crespo, Montserrat Blanco-Codesido, Paula Jimenez-Fonseca, Antonio Viúdez, Adelaida La Casta Muñoa, Isabel Sevilla, Marta Llanos, Ángel Segura, Jorge Hernando-Cubero, Jose Luis Manzano

Jaume Capdevila, MD, PhD
Medical Oncology Department
Gastrointestinal and Endocrine Tumor Unit
Vall d'Hebron University Hospital
Vall d'Hebron Institute of Oncology (VHIO) - Barcelona

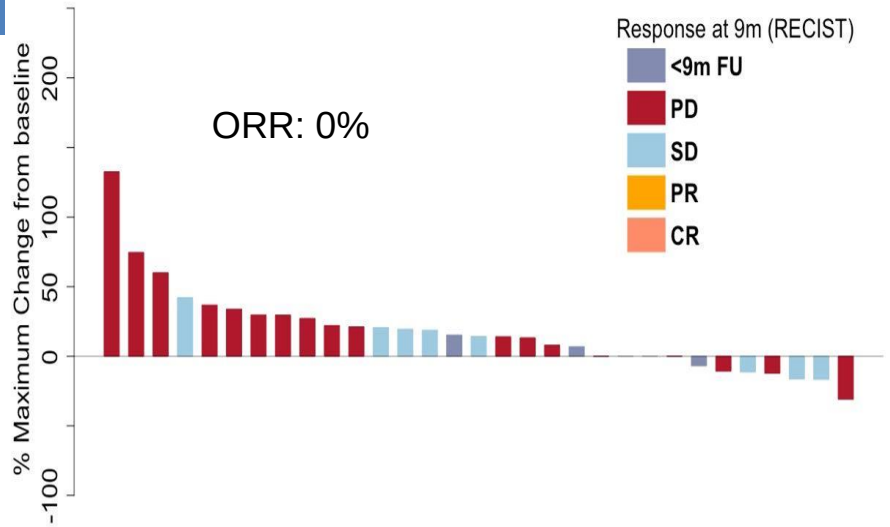
ESMO VIRTUAL CONGRESS 2020
Proffered Paper Presentation

Best % change from baseline in target lesions per cohort

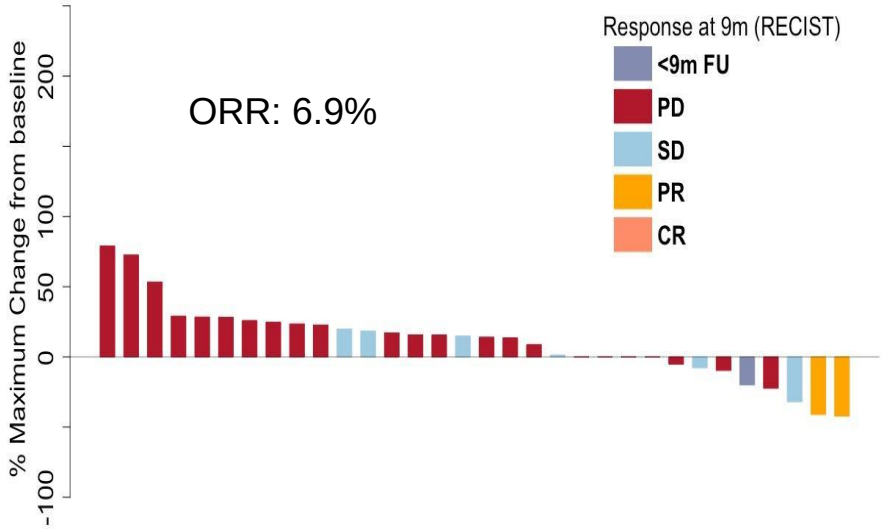
Cohort 1: Typical/atypical lung carcinoids



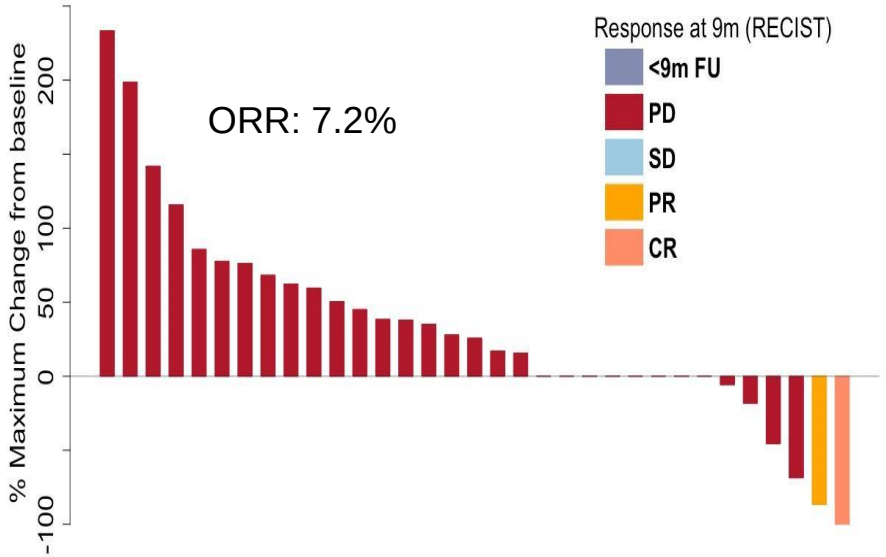
Cohort 2: G1/2 gastrointestinal



Cohort 3: G1/2 pancreatic



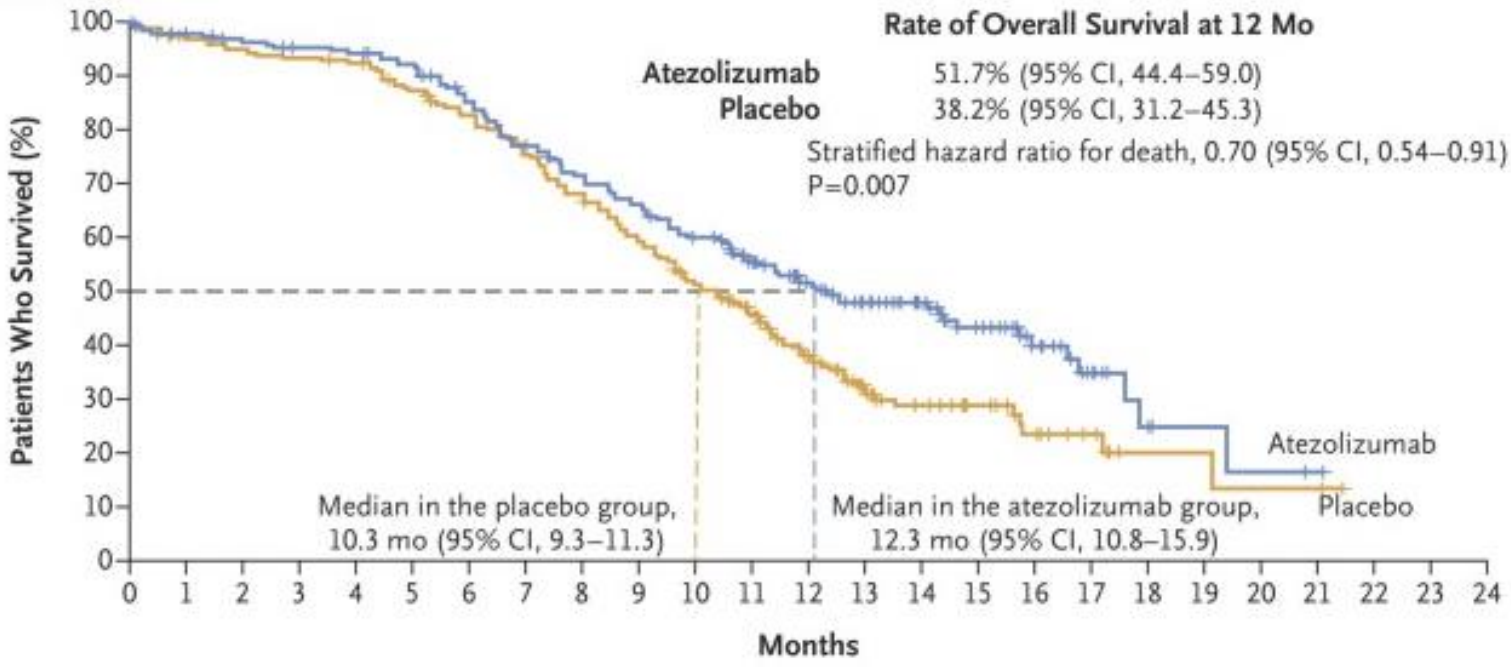
Cohort 4: G3 gastroenteropancreatic



Side effects

- Autoimmune (inflammation):
  - GI tract: diarrhea
  - Skin: rash
  - Lung: cough, shortness of breath
  - Endocrine: loss of pituitary/adrenal/thyroid function
- Usually treatable with steroids

First-line chemo-immunotherapy: Data only in small cell lung cancer.



Horn et al. N Engl J Med 2018; 379:2220-2229

Predictive markers?

- PD-L1 expression: 
- Microsatellite instability
- High tumor mutation burden (>10 per megabase)

FDA Approval Summary: Pembrolizumab for the Treatment of Microsatellite Instability-High Solid Tumors

- The FDA approved pembrolizumab on May 23, 2017, for the treatment of adult and pediatric patients with unresectable or metastatic, microsatellite instability-high (MSI-H), or mismatch repair deficient (dMMR) solid tumors
- The ORR was 40% among 149 patients with 15 different tumor types with a 7% complete response rate. The duration of response ranged from 1.6+ months to 22.7+ months, with 78% of responses lasting ≥6 months.

FDA approves pembrolizumab for adults and children with TMB-H solid tumors

- On June 16, 2020, the Food and Drug Administration granted accelerated approval to pembrolizumab for the treatment of patients with tumor mutational burden-high (TMB-H) [≥10 mutations/megabase (mut/Mb)] solid tumors
- A total of 102 patients (13%) had tumors identified as TMB-H, defined as TMB ≥10 mut/Mb. The ORR for these patients was 29% with a 4% complete response rate and 25% partial response rate. 57% of patients had response durations ≥12 months and 50% of patients having response durations ≥24 months.

Summary

- Responses to PD-1/PD-L1 inhibitors very rare both in well and poorly differentiated NENs
  - Exception are MSI-high and high TMB cancers: *very* rare and probably only seen in poorly differentiated NEC
- Combination PD-1/CTLA-4 inhibition has *some* activity in high-grade disease. Probably in the 10-20% range
- No data on combination chemo-immunotherapy