FACULTEIT GENEESKUNDE EN GEZONDHEIDSWETENSCHAPPEN

PHYSICAL MEDICINE AND REHABILITATION
GHENT UNIVERSITY HOSPITAL

# ASYMMETRICAL POLYRADICULOPATHY FOLLOWING TREATMENT WITH IMMUNE CHECKPOINT INHIBITORS

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# 1. INTRODUCTION

- Yearly 18.1 million new oncological diagnoses
- Chemotherapy, radiotherapy and surgery
- Immune checkpoint inhibitors

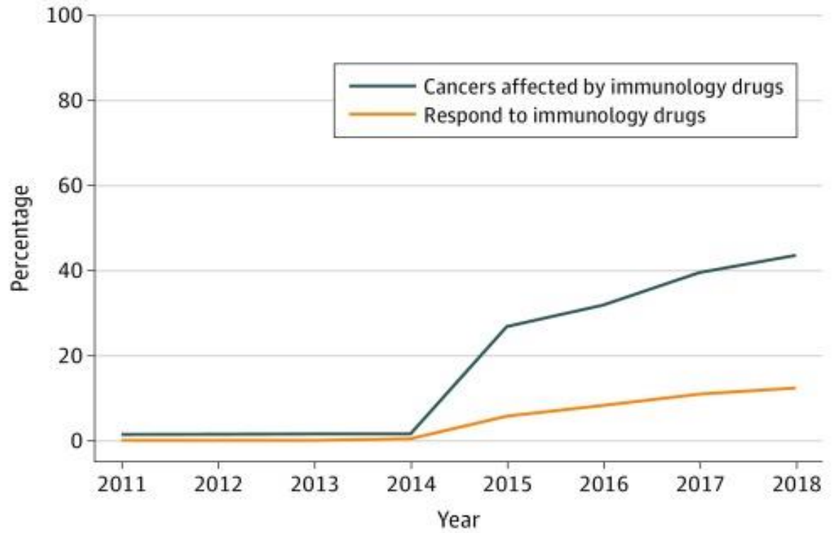


**Figure: Percentage of US Patients With Cancer Who May Benefit From and Respond to Checkpoint Inhibitor Immunology Drugs (2011-2018)**

Haslam A, Prasad V. Estimation of the Percentage of US Patients With Cancer Who Are Eligible for and Respond to Checkpoint Inhibitor Immunotherapy Drugs. JAMA Netw Open. 2019 May 3;2(5):e192535. doi: 10.1001/jamanetworkopen.2019.2535. PMID: 31050774; PMCID: PMC6503493.

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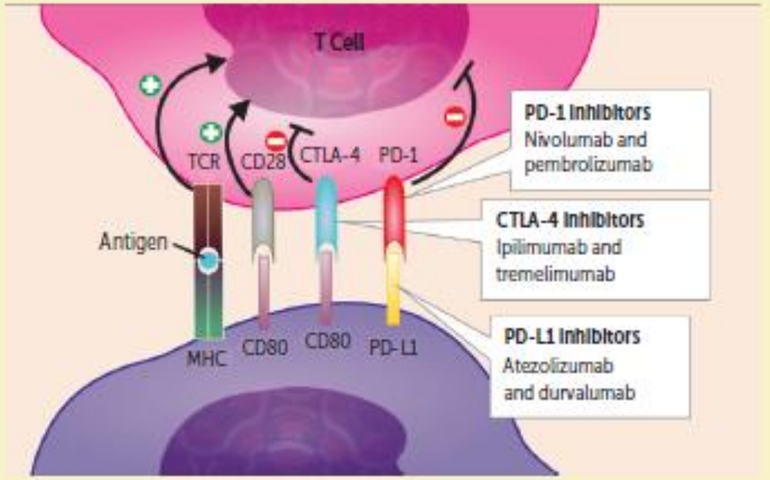
# 1. INTRODUCTION

- Monoclonal antibodies
- Inhibit regulatory effects on t-cell activation
  - Leading to enhanced anti-tumor immune respons
- Targets
  - CTLA-4
  - PD-1
  - PDL-1

**FIGURE 1.**
MECHANISMS OF ACTION OF IMMUNE CHECKPOINT INHIBITORS




CD—cluster of differentiation; CTLA-4—cytotoxic T-lymphocyte antigen 4; FDA—U.S. Food and Drug Administration; MHC—major histocompatibility complex; PD-1—programmed cell death protein 1; PD-L1—programmed cell death ligand 1; TCR—T-cell receptor
**Note.** Since original publication of this figure, the PD-L1 inhibitor avelumab has been approved by the FDA. Tremelimumab is not approved by the FDA at the time of this writing.
**Note.** Republished with permission of *OncoTargets and Therapy*, from Potential role of immunotherapy in advanced non-small-cell lung cancer; de Mello, R.A., Veloso, A.F., Catarina P.E., Nadine, S., and Antoniou, G.; volume 10, 2016: 21–30.

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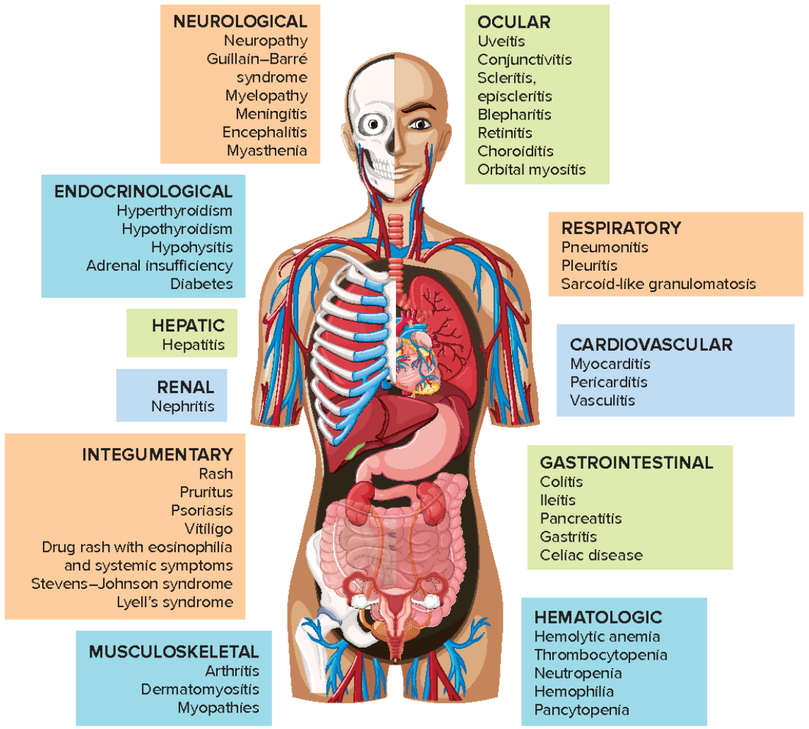
# 1. INTRODUCTION

- Disruption of the normal immunoserveillance and self-tolerance can result in adverse events
- 70-90% have related adverse events
  - Gastro-intestinal: most frequent
  - Respiratory
  - Endocrine
  - Neurological



# 2.CASE

- 62-year old ♂
- Renal cell carcinoma with metastasis
- Treatment
  - Radical nephrectomy
  - PD-1 and CTLA-4 inhibitors
- Acute pain right leg

# 2. CASE

- First clinical presentation
  - Hypo-esthesia L4 dermatome
  - Paresis knee extension and ankle dorsiflexion
    - MRC scale 4
- Second clinical presentation 6 weeks later
  - Paresis in L2-S1 myotomes
    - MRC scale 3

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# 2. CASE

- Technical investigations
  - MRI lumbar spine and pelvis negative
  - ENMG
    - Acute denervation characteristics in L2-S1 muscles of the right leg
    - Decreased recruitment in L2-S1 muscles of the right leg
- Treatment
  - Discontinuation of the immunotherapy
- Outcome
  - No strength deficits 5 months after onset
  - Normal daily functioning

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# 3. DISCUSSION

- Chemotherapy-induced peripheral neuropathy
  - Predominantly axonal sensory
  - Dorsal root ganglion less protected by blood-brain barrier
  - Nerve conduction studies

- Immunotherapy-induced peripheral neuropathy
  - Acute demyelinisation
  - Sensory and/or motor axonal neuropathy (AMAN/AMSAN)

# 3. DISCUSSION

- Better clinical outcome (⇔ chemotherapy)
  - Following discontinuation or administration of corticosteroids
- Greater understanding of predisposing mechanisms will be important in future management
  - Loss of immunologic tolerance to myeline or axonal antigens

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