

# A Revolution in the Management of Lung Cancer

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October 2017

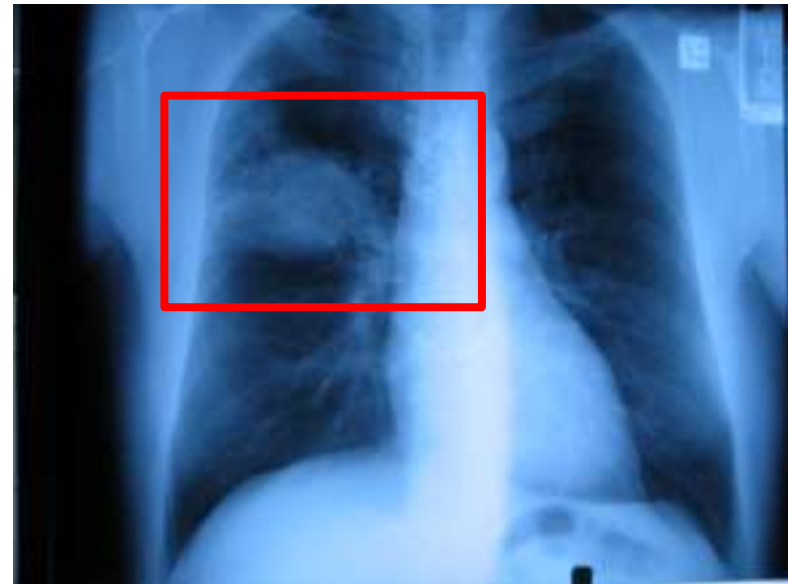
# A Revolution in Lung Cancer

Dr Michael Bayne

October 2017

# 20 years ago 1997

- \* Metastatic Lung Cancer.
  - \* Chemotherapy controversial
  - \* Palliative thoracic radiotherapy
  - \* Whole Brain radiotherapy
- \* Median survival 6 months
- \* 1 year survival 25%
- \* 5 year survival <1%



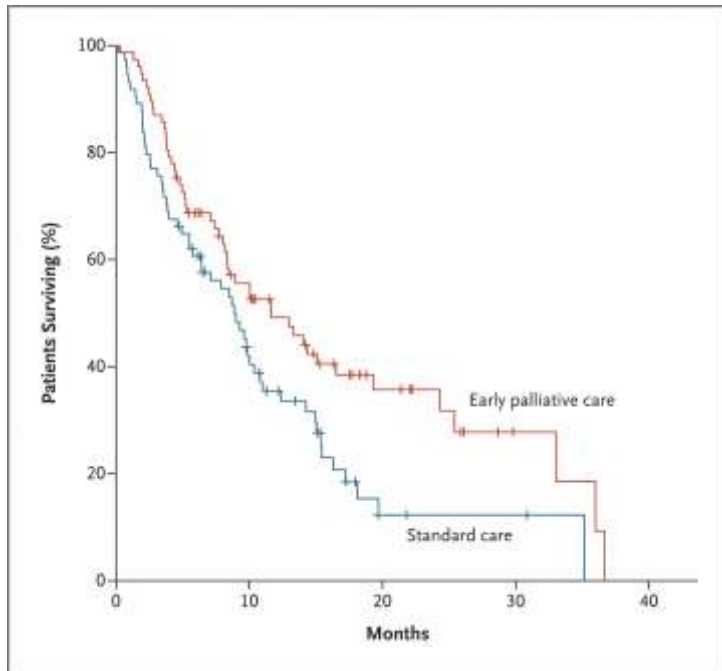
# Whats Changed?

- \* Imaging
  - \* PET
- \* Chemotherapy
  - \* Selection based on histology
  - \* Maintenance chemotherapy
  - \* Improved antiemetics
- \* Radiotherapy
  - \* Stereotactic radiotherapy
    - \* Brain = SRS Body = SABR
  - \* Intensity Modulated Radiotherapy (IMRT)
  - \* Image guided radiotherapy (IGRT)
- \* Tyrosine kinase inhibitors (ibs)
  - \* EGFR inhibitors
  - \* ALK inhibitors
- \* Liquid Biopsies
- \* Immunotherapy (abs)

# What is the same?

- 50% present late with poor PS often following emergency admission
- Early Palliative Care for Patients with Metastatic Non–Small-Cell

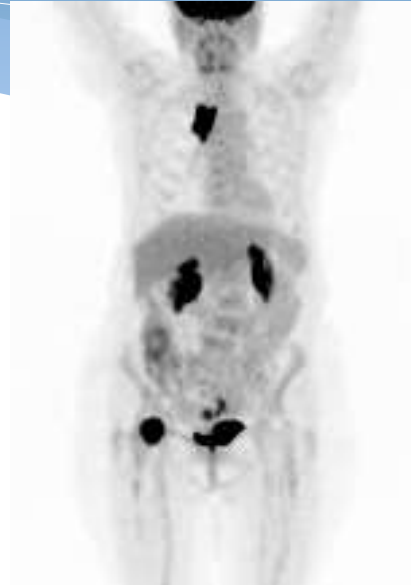
Jennifer S. Temel et al NEJM 2010.



- \* Supportive care and symptom management remain as important as drugs and radiotherapy.
- \* But for some treatment can transform metastatic Lung cancer into a chronic disease

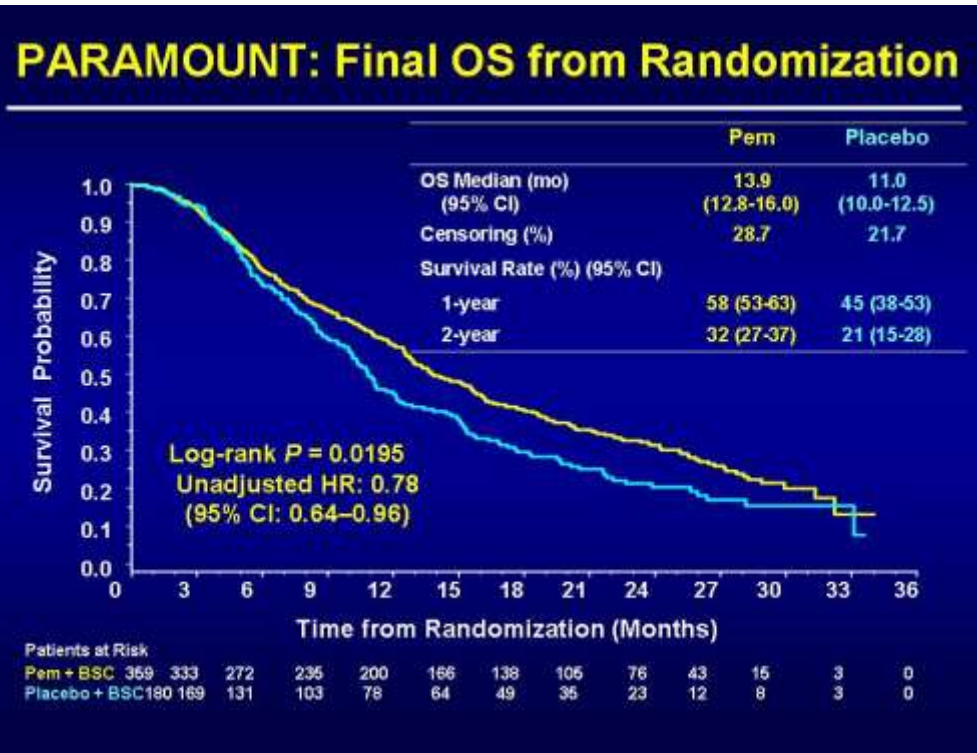
# Positron Emission Tomography PET

- \* Improves patient selection for radical treatment
- \* Better than a bone scan for identifying bone metastases and directing palliative radiotherapy



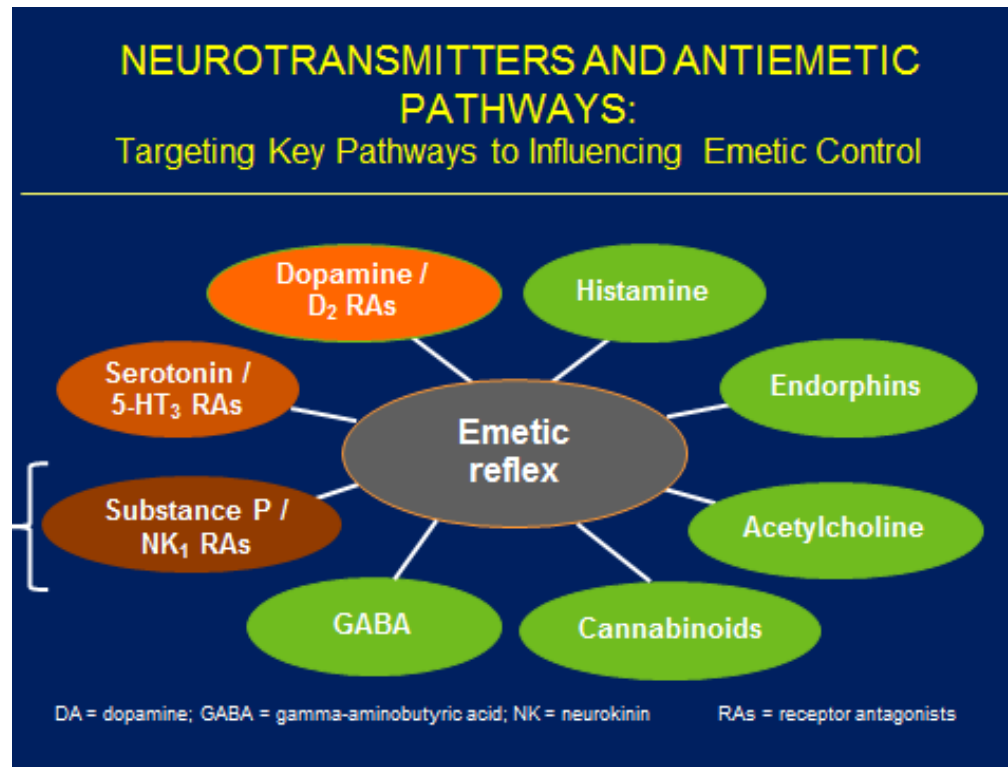
# Chemotherapy

- \* The optimum regimen is based on histology
  - \* Small cell v non small cell
  - \* Adenocarcinoma v squamous carcinoma
  - \* For those with adenocarcinoma best outcomes are seen with maintenance pemetrexed continued till progression.



# Chemotherapy

- \* Antiemetics have improved beyond recognition
  - \* 5HT<sub>3</sub> inhibitors - ondansetron
  - \* Neurokinin 1 antagonists – aprepitant
  - \* NEPA = netupitant + palonosetron in a single tablet





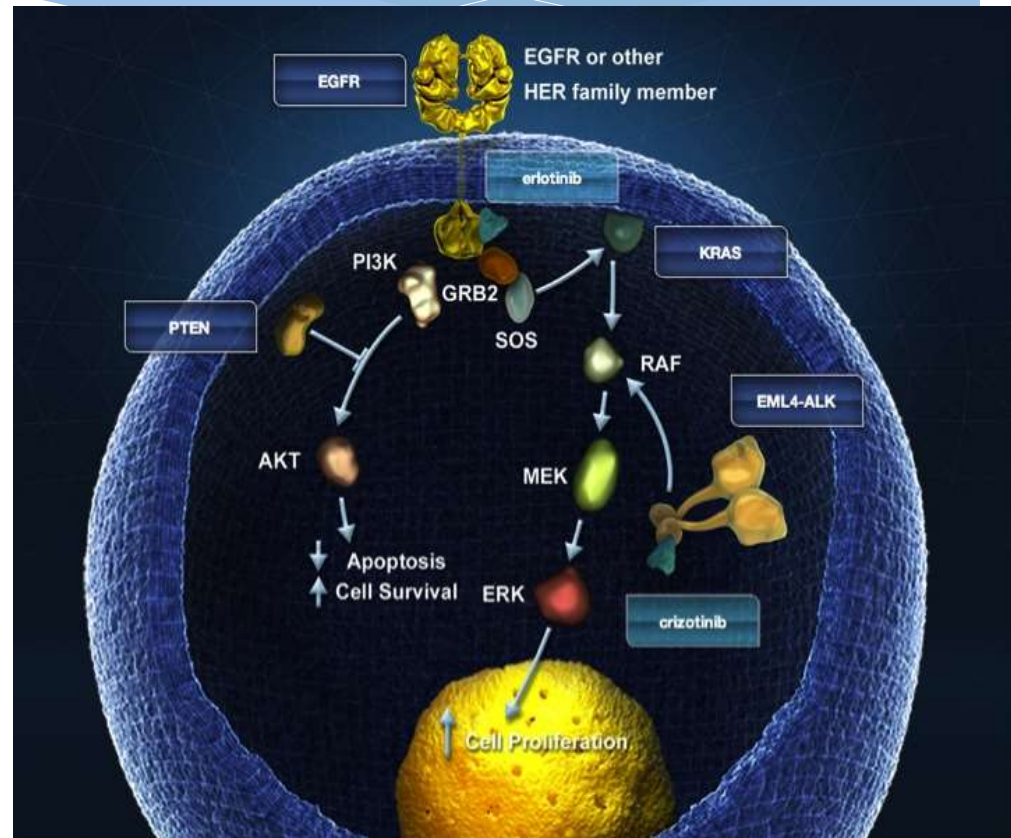
# Not chemotherapy

- \* Chemotherapy

- \* Damages cellular machinery for DNA replication
- \* Cancer cells vulnerable
- \* Narrow therapeutic window

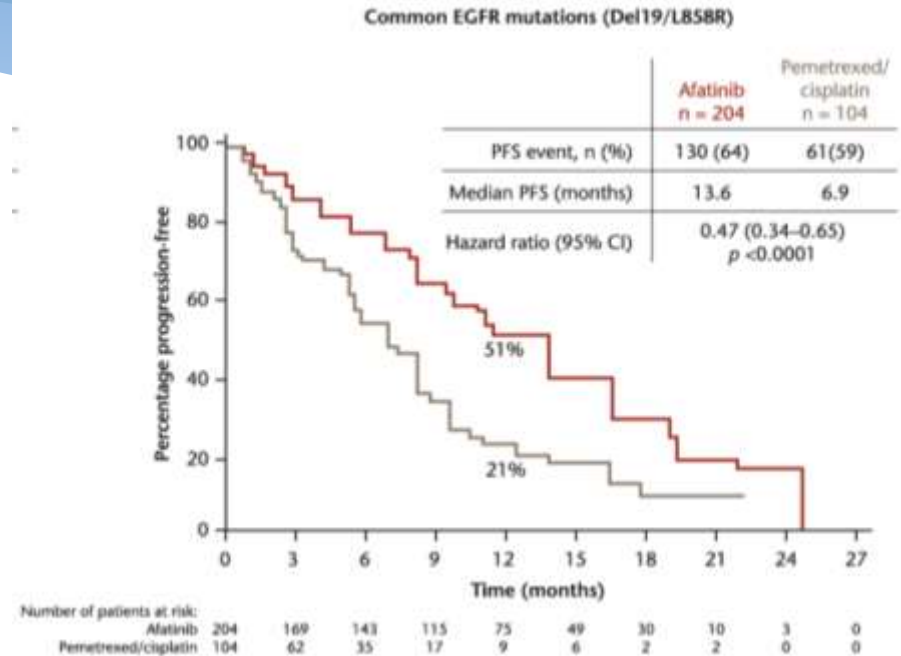
- \* Tyrosine kinase inhibitors

- \* Switch off over active signalling pathway
- \* Wide therapeutic window



# Tyrosine kinase inhibitors

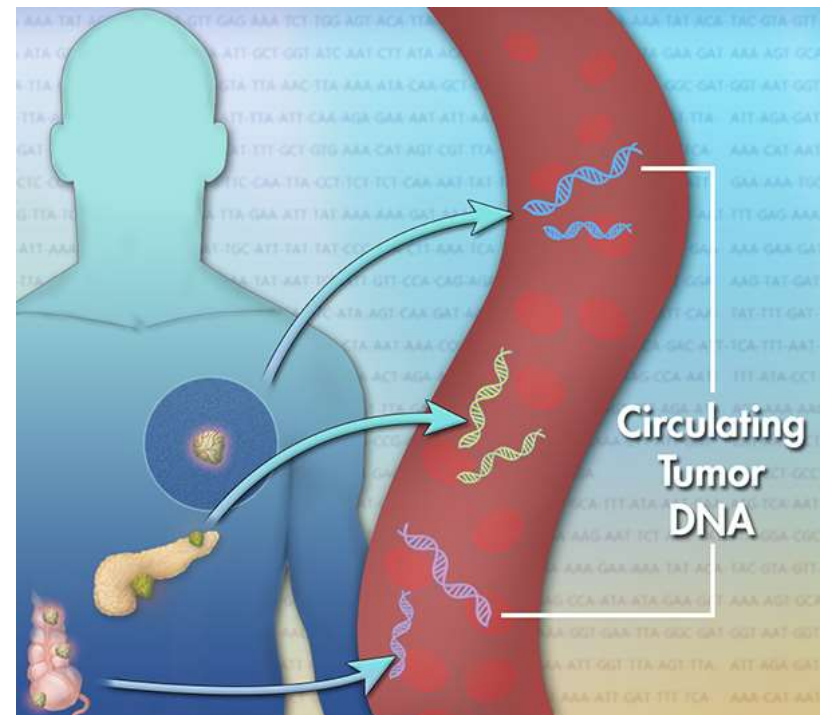
- \* EGFR inhibitors
  - \* erlotinib, gefitinib, afatinib
  - \* osimertinib
- \* ALK inhibitors
  - \* crizotinib, ceritinib, alectinib
- \* Others on the way



For the lucky ones (up to 10%) these drugs bring about a rapid often durable benefit with manageable side effects.

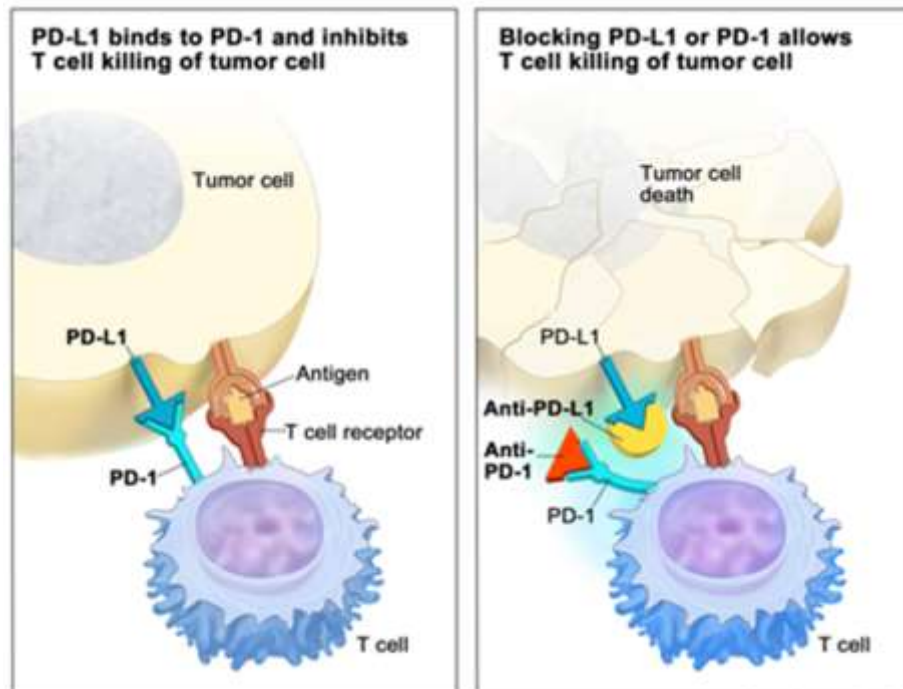
# Liquid Biopsy

- \* Circulating tumour
  - \* Identify sensitising EGFR mutation
  - \* Identify resistance mutation



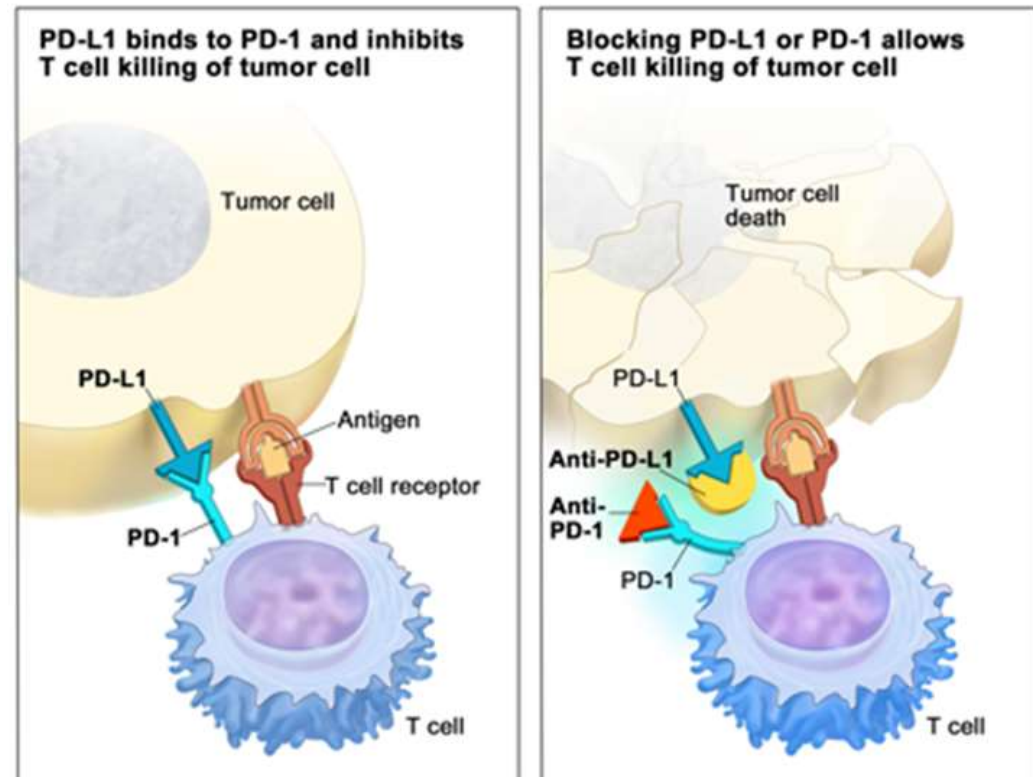
# Immunotherapy

- \* Chemotherapy damages machinery for DNA replication
- \* Tyrosine kinase inhibitors block signalling pathways
- \* Immunotherapy enhances the immune response against cancer cells.



# Immunotherapy

- \* Checkpoint inhibitors
  - \* PD1 inhibitors
    - \* Pembrolizumab
    - \* Nivolumab
  - \* PDL1 inhibitors
    - \* Atelolizumab
    - \* Darvalumab



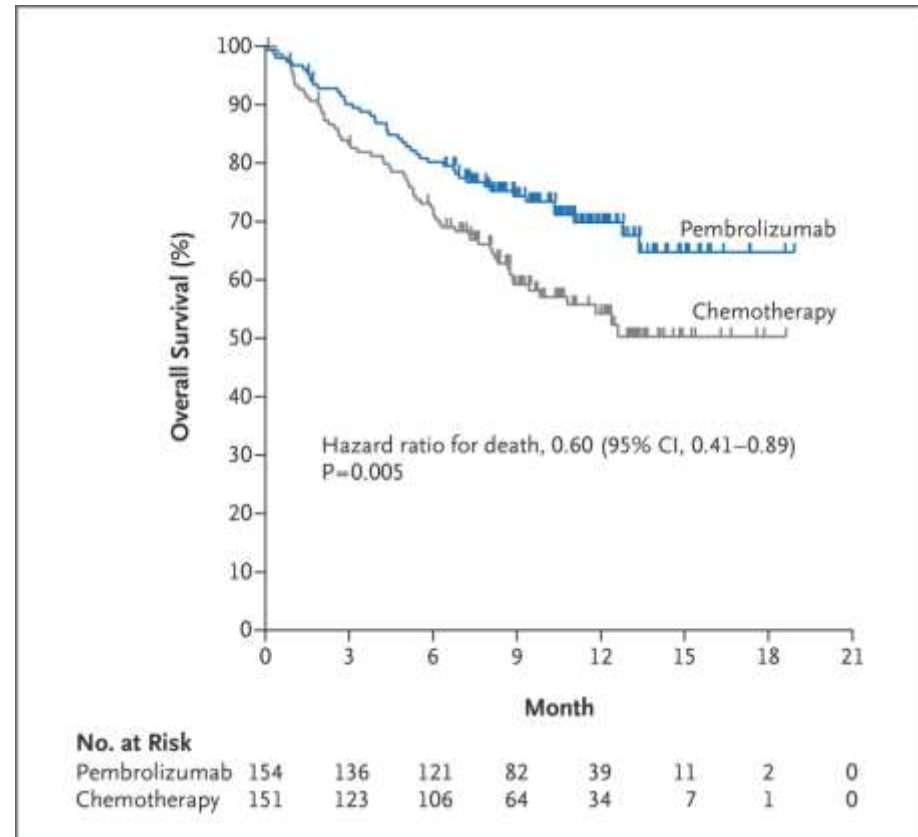
# Immunotherapy

- \* Tumours with high expression of PDL1 most likely to benefit
- \* Seem to work best in the smoking related tumours with a high mutation burden.
- \* There may be a synergy with radiotherapy.
  - \* abscopal effect
- \* Currently approved in NHS for
  - \* 1<sup>st</sup> line
    - \* >50% PDL1 expression
  - \* 2<sup>nd</sup> line
    - \* all squamous lung cancer
    - \* Adenocarcinoma with PDL1 expression >1%

> 75% of patients with lung cancer may be eligible for immunotherapy provided they are PS0-1 with controlled brain metastases.

# How good is immunotherapy?

- \* For selected patients clearly better than chemotherapy
- \* Clearly less toxic than chemotherapy



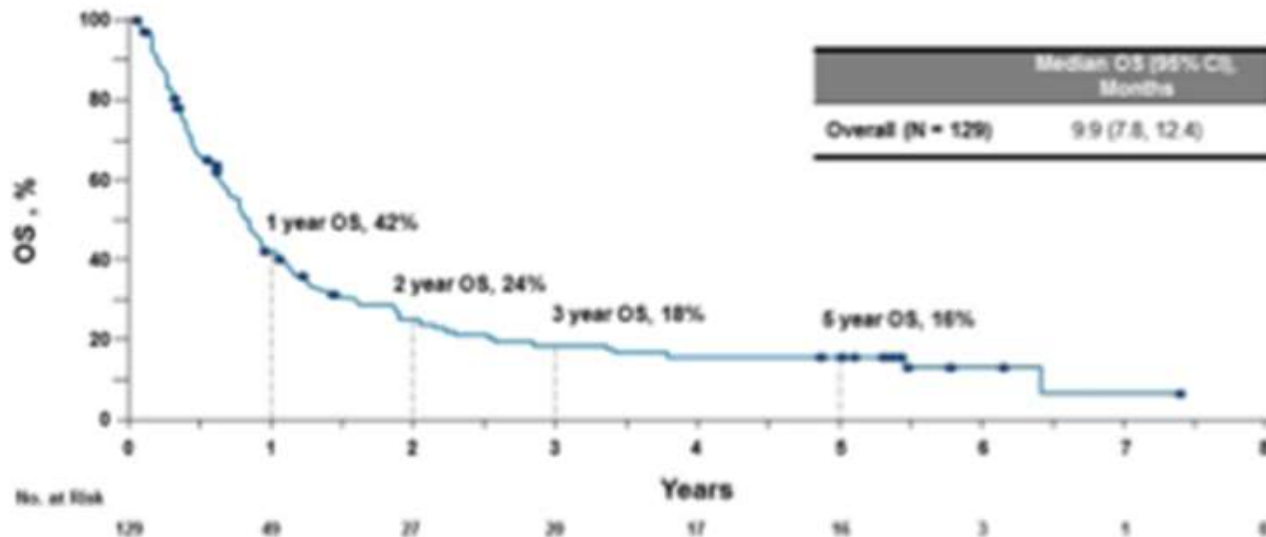
# Immunotherapy Toxicity



# How good is immunotherapy?

- \* For some it may turn metastatic lung cancer into a chronic disease

## CA209-003 Five-Year OS Update: Phase I Nivolumab in Advanced NSCLC



# 2017

- \* Metastatic Lung Cancer.

- \* Immunotherapy
- \* Targeted TKIs
- \* Refined radiotherapy
- \* Improved imaging

- \* Median survival >18months

- \* 1 year survival 70% ( for patients with PDL1>50%)

- \* 5 year survival 16%!

# 1997

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# Lung Cancer as a chronic disease

\* Cases