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Lung

Case history

- 61 year old male patient
- Worked up for coronary artery bypass operation but persistent cough and shortness of breath -> abnormal CXR and CT CAP shows right upper lobe mass and bilateral pulmonary metastases
- CT guided biopsy and histology confirms Squamous Cell carcinoma of the lung
- PDL1 expression 100%
- Past Medical History
  - Ischaemic heart disease, known angina, awaiting CABG
  - Diabetes type 2
  - Hypercholesterolaemia
  - HTN
- Performance status 1
- Drug history
  - ISMN, Ranolazine, Nicorandil
  - Bisoprolol, Ramipril, Atorvastatin
  - Insulin, Metformin
- Social History
  - Lives with wife and children
  - Ex smoker

Management

- CHECKMATE 227 trial
  - Phase III open labelled multicenter RCT
  - Chemotherapy treatment naive patients with advanced Stage IV or recurrent Non-Small Cell Lung Cancer
  - Nivolumab alone vs Nivolumab and Ipilimumab combination vs Nivolumab in combination with Platinum doublet chemotherapy vs Platinum doublet chemotherapy

- Patient enrolled in August 2016
  - Randomised to Nivolumab/Ipilumumab combination arm
  - Tolerated #1 well with CT post #1 showing stable disease in lungs
  - Noticed increased shortness of breath and reduced exercise tolerance
  - ECHO showed biatrial enlargement ? Immunotherapy related myocarditis
  - Reviewed by cardiology. Cardiac MRI – nil evidence myocardial inflammation
  - Continued with #2 Nivolumab and Ipilimumab. CT post #2 shows some bibasal groundglass shadowing, retrospectively also found to be present on previous CT after #1
  - Admitted as inpatient for high dose methylprednisolone for possible immune mediated pneumonitis.
  - Patient developed acute chest pain associated with dynamic ECG changes (CT depression in anterolateral leads) and Troponin rise ? MI

Management

- Patient reviewed by cardiology as inpatient
  - Non ST Elevation Anterolateral Myocardial infarction
  - Started ACS protocol and sliding scale due to poorly controlled BMs on high dose steroids
  - Coronary angiogram showed extensive atheromatous coronary disease – 7 stents inserted
  - Good post operative recovery
  - Steroids weaned down over 6 weeks
  - Breathing and exercise tolerance improved despite persistent ground glass changes in lungs on CT
  - Restarted Nivolumab only CHECKMATE 227 trial -> doing well

Learning points

- Important to consider all differentials in patients who develop new shortness of breath with pre-existing comorbidities whilst on immunotherapy
  - ? Coronary artery disease/ Arrhythmias
  - PE
  - Pneumonitis
  - Myocarditis/ heart failure
  - Disease progression

- Reduced exercise tolerance may have been in part related to ischaemic heart disease as well as pneumonitis

- Need to address both issues to help alleviate symptoms

- Awareness that patients on Nivolumab and Ipilimumab combination may be at higher risk of developing immune related toxicities
  - Pneumonitis symptoms vague, delays in diagnosis (overall incidence 5%, 10% for combined IO, 3% for Nivo alone)
  - Myocarditis (1 in 1000) symptoms often vague, deterioration can be rapid, risk factors include pre-exiting cardiovascular disease

European Society for Medical Oncology

Thank you