Summary on Immunotherapy for Palliative Care Teams

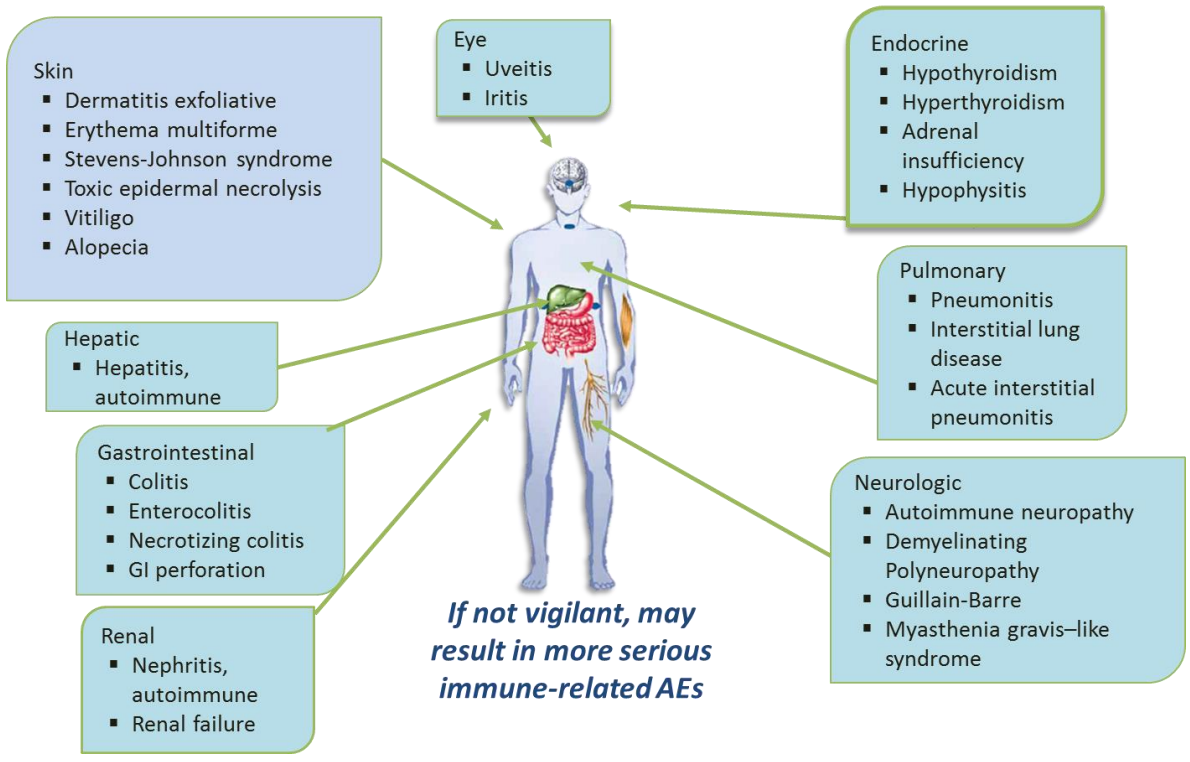
Dr Melanie Brooks (Bridgewater Community Healthcare NHS Trust/St. Rocco's Hospice)
Dr Anna Olsson-Brown (Clatterbridge Cancer Centre)

Treatment

1) Current treatments include ipilimumab, pembrolizumab, nivolumab, atezolizumab.
2) IV therapy usually given every 3 weeks (nivolumab is the only therapy given two weekly).
3) Works by making the patient's immune system target the tumour. The drug does not directly affect tumour.
4) Once the immune system is stimulated to produce the T calls to attack tumour the effect is self-propagating and effects can continue beyond a year after treatment has stopped.
5) These treatments do offer the potential for long term control in the metastatic setting. This is true in a number of malignant sites including those historically associated with limited prognoses including metastatic melanoma and NSCLC
6) Improves survival, especially in melanoma where survival has gone from 5% 1 year survival to up to 60% 2 year survival, 5y year survival not yet known.
7) It is also licenced by NICE for use in NSCLC, head and neck malignancies and RCC, but won't be long before other tumours are added as many are undergoing trials. There is also CDF approval of atezolizumab in urothelial cancers
8) Its uses are expanding and may include many tumour types in future
9) Doesn't appear to work in prostate, brain and some bowel cancers
10) These treatments are generally well tolerated with little day to day side effects which means patients who would not be able to tolerate chemotherapy may still be able to receive immunotherapy. The end point of treatment for individual patients is unknown and may continue into the terminal end point of treatment for individual patients unknown and may continue into terminal phase.
11) It has fewer side effects during administration and appears to be better tolerated than traditional chemotherapy, which means it can be given in patient's homes.

Side effects

As it stimulates the immune system it can lead to auto immune conditions including colitis, Addison's, hypothyroidism, hyperthyroidism, autoimmune hepatitis and pneumonitis as well as skin conditions. These can present up to a year after treatment has been discontinued.



Consequences

1) Patients living longer with metastatic disease, prolonged life with potential symptom burden, increasing need for palliative care support
2) Changing disease trajectory, disease where prognosis was short may live much longer, affecting prognostication.
3) Side effect profile may lead to confusion over disease progression versus autoimmune disease secondary to treatment as effects can appear to be non-specific.
    a. Any patient (having previously received immunotherapy) developing fatigue, weight loss (or gain), needs to have their serum cortisol/ACTH testing and thyroid function tests as well as a full profile, before a diagnosis of conditional deterioration can be made.
    b. Any patient developing abnormal LFTs needs to be considered as potentially having autoimmune hepatitis and treatment of this requires high dose steroids.
    c. Use the following guidance to help manage these patients https://www.clatterbridgecc.nhs.uk/professionals/guidance
    d. If any of these side effects occur, inform the patient's oncologist immediately.
4) Steroid management
    a. As immune therapy needs the patient to have an effective (not supressed) immune system at the time of treatment it is important that steroids are not given around the time of administration of immunotherapy if at all possible.
    b. The longer term tumour effects of immune therapy do not appear to be affected by short course steroids and they do not abort an established response to treatment. So if a patient has discontinued immunotherapy but the response is still ongoing steroids will not affect this in the long term.
    c. Doses of 7.5mg prednisolone/1mg dexamethasone can be given during immunotherapy, doses larger than this may make the treatment less effective and immunotherapy treatment cannot be given above this level thus the use of steroids in these patients must be avoided if possible.
    d. If a course of higher dose steroids is considered appropriate (e.g. liver capsular pain (exclude hepatitis)), then timing is important. A short course i.e. 5 days could be administered midway between the 2 IV immunotherapy infusions, however it is important that the oncologist is aware that steroids are being trialled and that response to steroids is noted and the course is not extended.
    e. Any case where steroids must be continued for longer this needs to be discussed with the oncologist as immunotherapy may need delaying.
5) Stopping treatment may become a future challenge as patients may become psychologically attached to the treatment and (as yet) there is no clear guidance as to when it should be discontinued and will vary across tumour sites. This will be the oncologists/patients decision in most cases but we may start to see patients wishing to receive treatment even as they enter the terminal phase of their illness. The evidence that the effects of treatment often extend beyond treatment cessation should allow HCPs to support patient and families going through this transition.