Common Side Effects of Novel Therapies and Immunotherapies and Their Management in the Community

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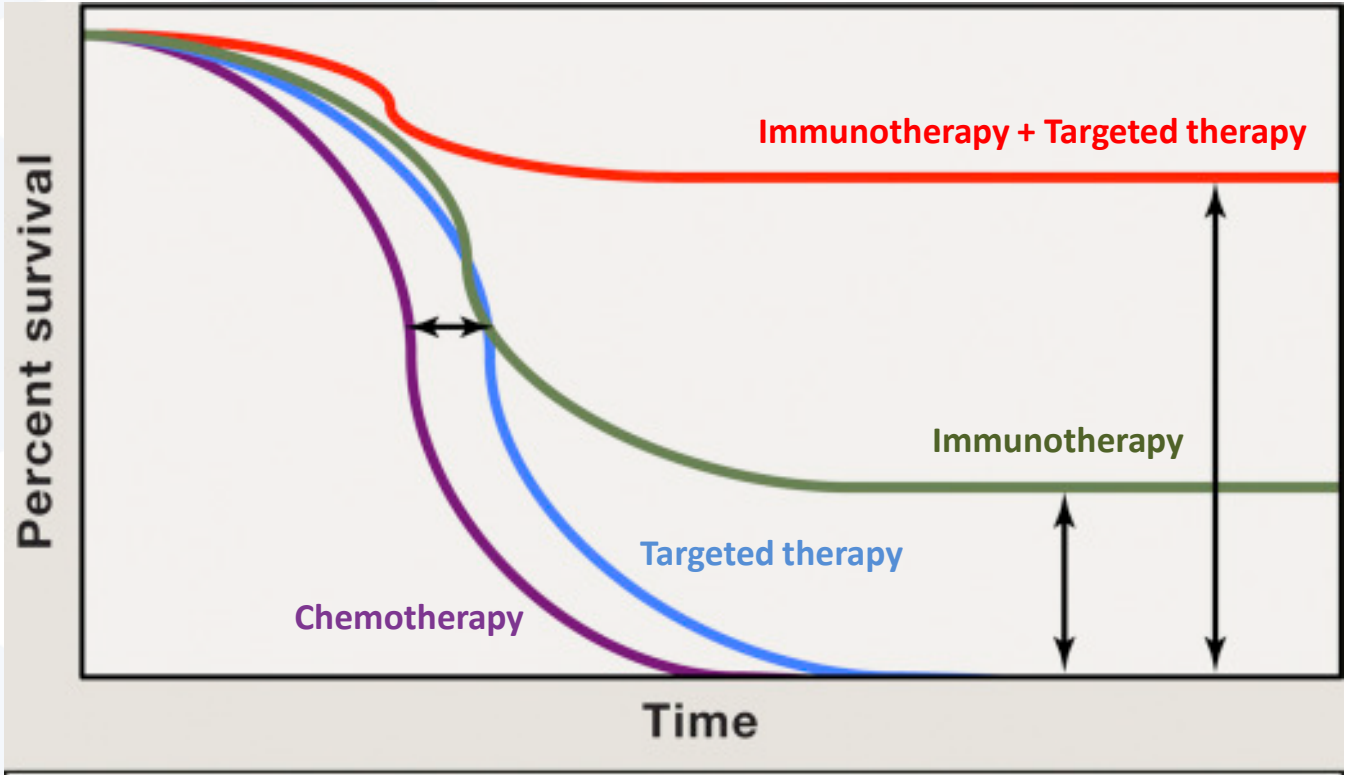
THIS IS MODERN MEDICINE



The survival outcomes

Objective: Answer 3 Important Questions

1. How does novel anti-cancer therapy and immunotherapy differ from chemotherapy?

2. What are the differences in toxicity profile between the different cancer therapies ?

3. How to manage the toxicities ?

Introduction: Cancer Therapy Has Evolved

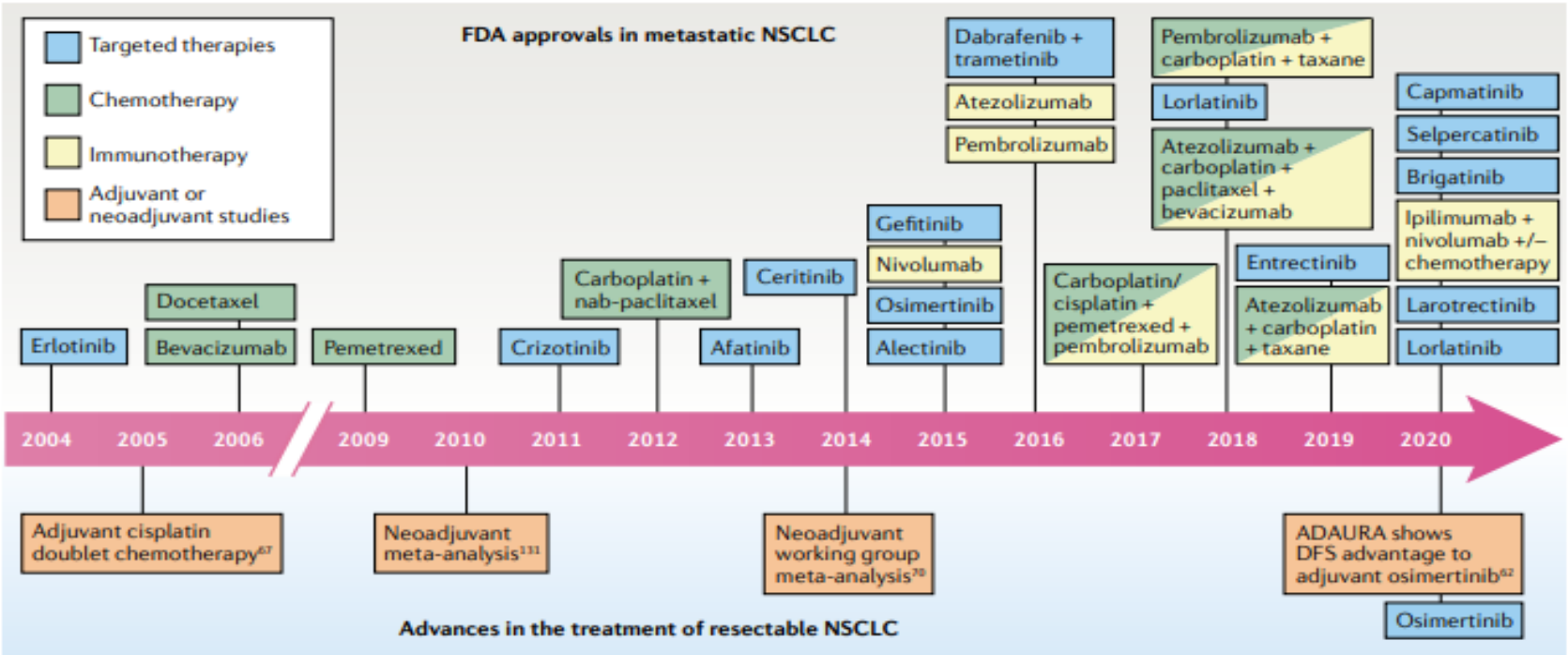


Fig. 1 | **Treatment of metastatic and non-metastatic NSCLC.** Timeline showing drugs approved or indicated for the treatment of metastatic and non-metastatic non-small-cell lung cancer (NSCLC) as of December 2020. When several approvals were made in a year, they are arranged chronologically from top to bottom. DFS, disease-free survival.

Chaft et al, Nature reviews clinical oncology April 2021

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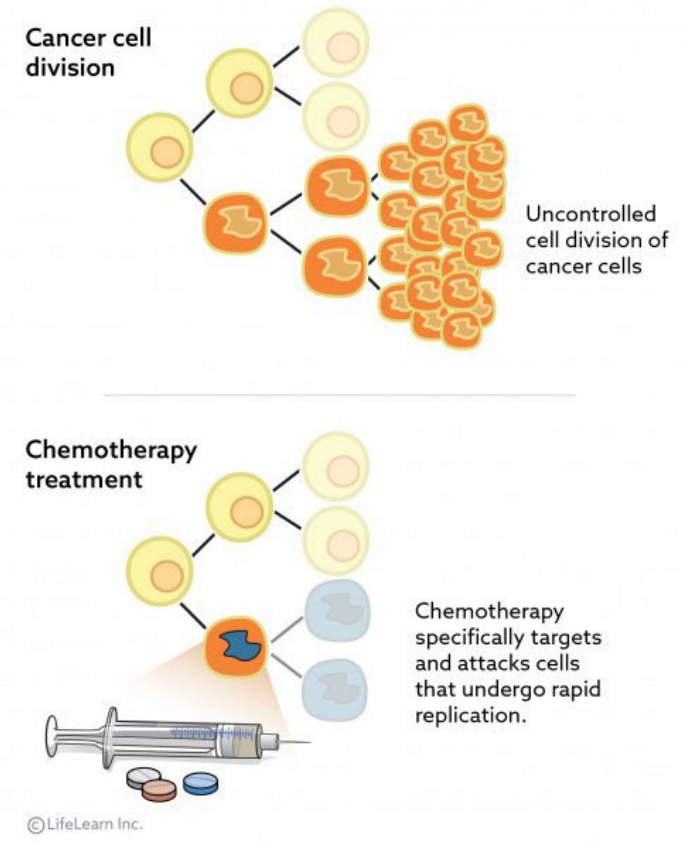
Chemotherapy

Examples: Capecitabine (po), cisplatin, paclitaxel, docetaxel etc

- Non-selectively interfere with the proliferation of all rapidly dividing cells
- Can affect normal cells
- Limited by narrow therapeutic index, significant toxicities and frequently acquired resistance
- Remain the backbone of many treatments



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Molecular Targeted Therapies

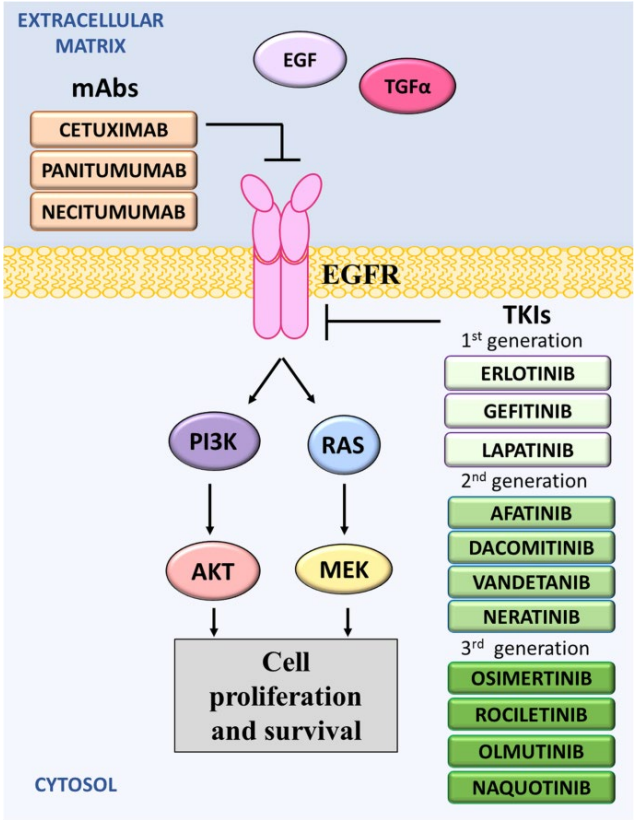
Examples:

Herceptin: anti-her2 (monoclonal antibody)

Erlotinib: anti-EGFR (TKI)

Palbociclib: inhibitor of the cyclin-dependent kinases CDK4 and CDK 6

- Target cancer cells - targeting molecules required for cell growth and tumorigenesis
- Easier to tolerate compared to chemo
- Different toxicity profile



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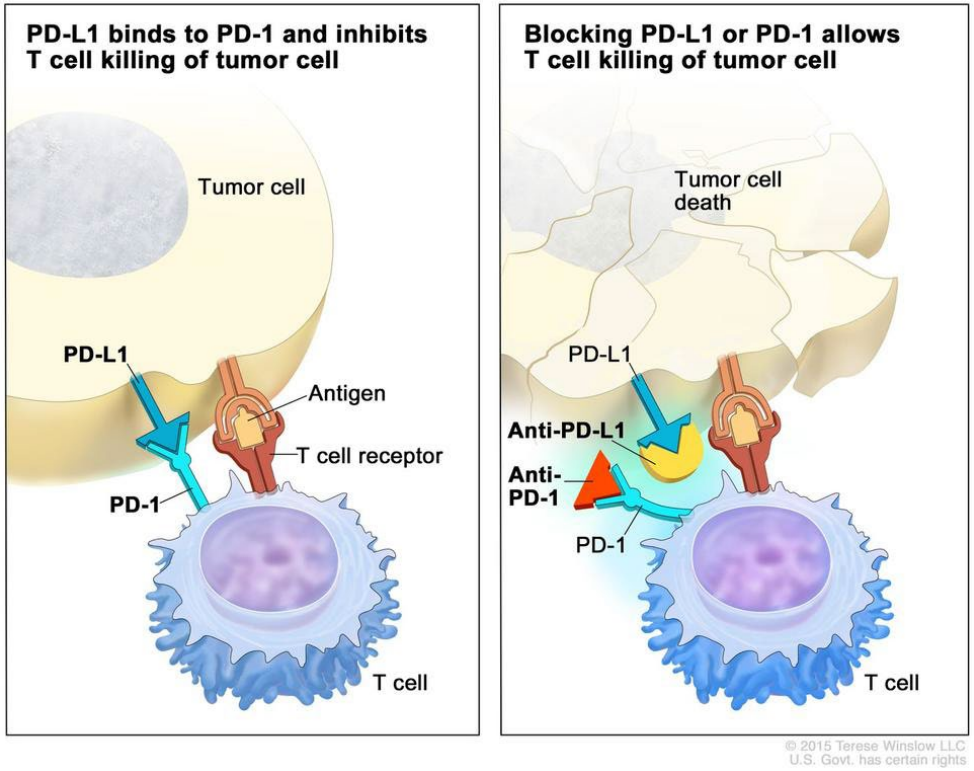
Immunotherapy

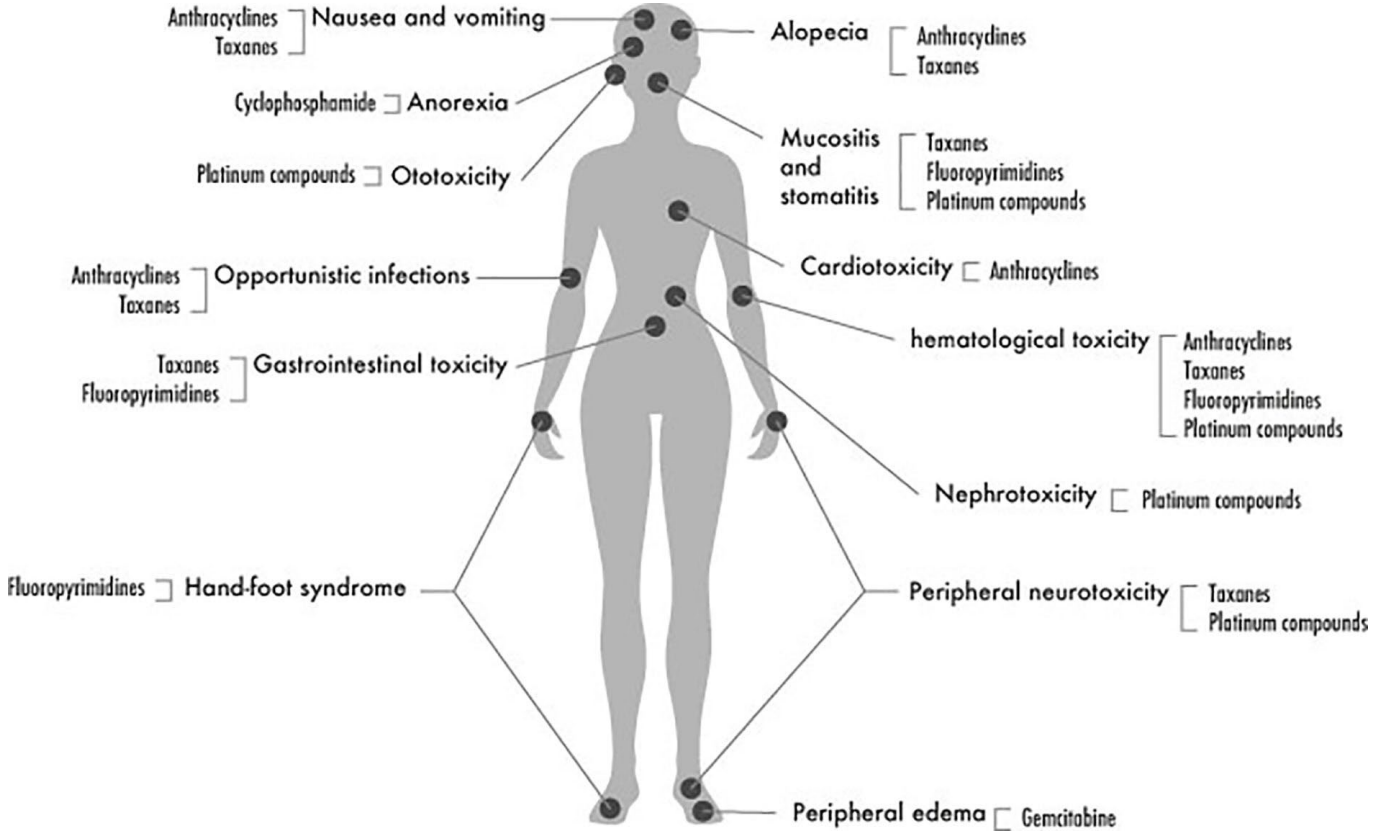


Example: Nivolumab, Pembrolizumab, Ipilimumab

- Enhances anti-tumour immune response - helps the immune system recognize cancer cells for subsequent destruction
- Cancer selectivity and long-lasting effects
- Immune related toxicities

2. What are the differences in toxicity profiles between the different cancer therapies?

Chemotherapy Toxicity



Al-Mahayri, Front. Pharmacol 2020.

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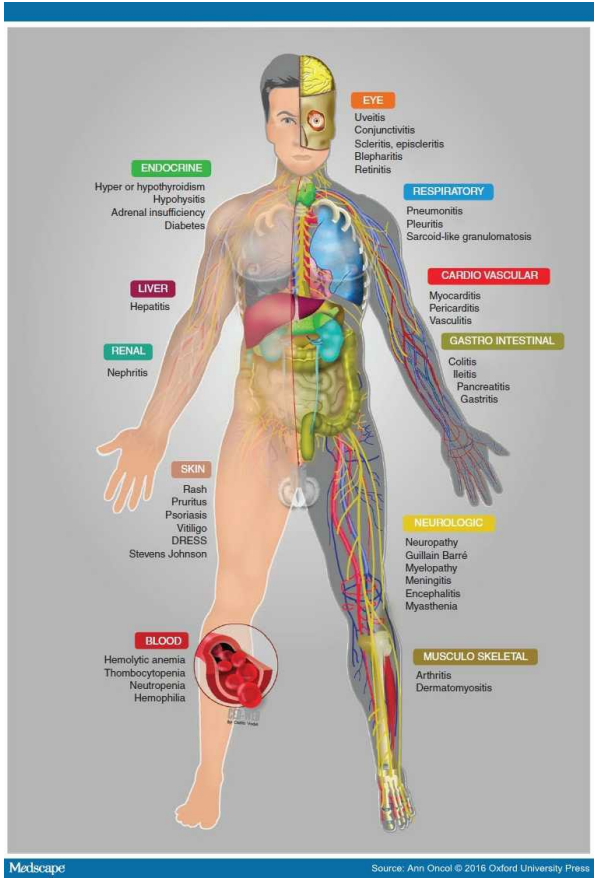
Immunotherapy Toxicity



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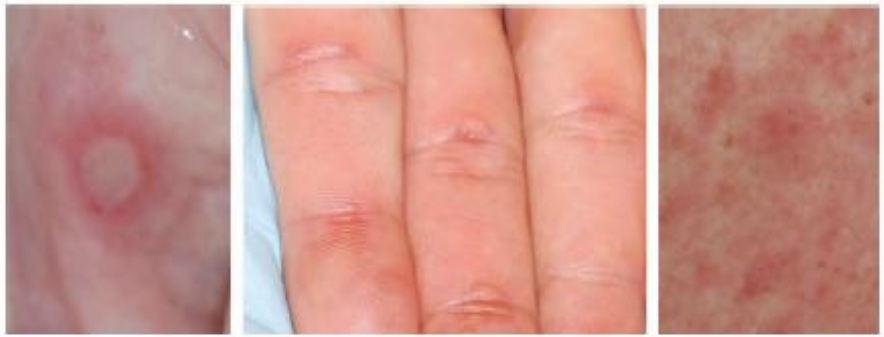
Targeted Therapy Toxicity

RELATED SIDE-EFFECTS



Stomatitis in a patient on an mTOR inhibitor (left), and hand-foot skin reaction (centre) and rash (right) in patients on sorafenib. These side-effects often occur simultaneously, and if any one of these is found, the patient should be checked for the others.

Courtesy of ME Lacouture, Memorial Sloan Kettering Cancer Center

Dermatology	Rash, Dry skin, Palmar-plantar syndrome, Paronychia
Systemic	Fatigue
Endocrine	Thyroid dysfunction, elevated sugar level
GI	Diarrhoea, Nausea, Hepatitis
Cardiovascular	Hypertension, QTc prolongation, cardiomyopathy
	Drug Interaction (Cytochrome p450)

3. How do we manage the toxicity?

Toxicity Management – Grading of Toxicities

Common terminology criteria for adverse events (CTCAE v5)

- ***Grade 1: continue treatment***
- ***Grade 2: may continue or hold***
- ***Grade 3: hold treatment/discontinue***
- ***Grade 4: Permanently discontinue***

Toxicity Management – Guidelines and Resources

Guidelines / Sources

- Summary of Product Characteristic (SPC)
- The HSE National Cancer Control Programme (NCCP) Guideline
- European Society of Medical Oncology (ESMO)Guideline
  - https://www.esmo.org/guidelines/supportive-and-palliative-care/toxicities-from-immunotherapy

NCCP Chemotherapy Regimen

Palbociclib Therapy - 28 day

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	Reimbursement Status
Treatment of hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative locally advanced or metastatic breast cancer in combination with an aromatase inhibitor	C50	00414a	CDS 01/06/2018
Treatment of hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative locally advanced or metastatic breast cancer in combination with fulvestrant in women who have received prior endocrine therapy	C50	00414b	CDS 01/06/2018

TREATMENT:

The starting dose of the drugs detailed below may be adjusted downward by the prescribing clinician, using their independent medical judgement, to consider each patients individual clinical circumstances.

Palbociclib is taken once daily for 21 consecutive days followed by 7 days off treatment to comprise a complete cycle of 28 days until disease progression or unacceptable toxicity develops.

Day	Drug	Dose	Route and Method of administration	Cycle
1-21	*Palbociclib	125mg daily	PO taken with food, preferably a meal to ensure consistent palbociclib exposure	Every 28 days
*Please note palbociclib should be administered in combination with either an aromatase inhibitor or fulvestrant. In pre-or perimenopausal women, the endocrine therapy should be combined with a luteinizing hormone-releasing hormone (LHRH) agonist.				
Palbociclib should not be taken with grapefruit or grapefruit juice. Pabloclib capsules should be swallowed whole (should not be chewed, crushed, or opened prior to swallowing). No capsule should be ingested if it is broken, cracked, or otherwise not intact.				

CLINICAL PRACTICE GUIDELINES

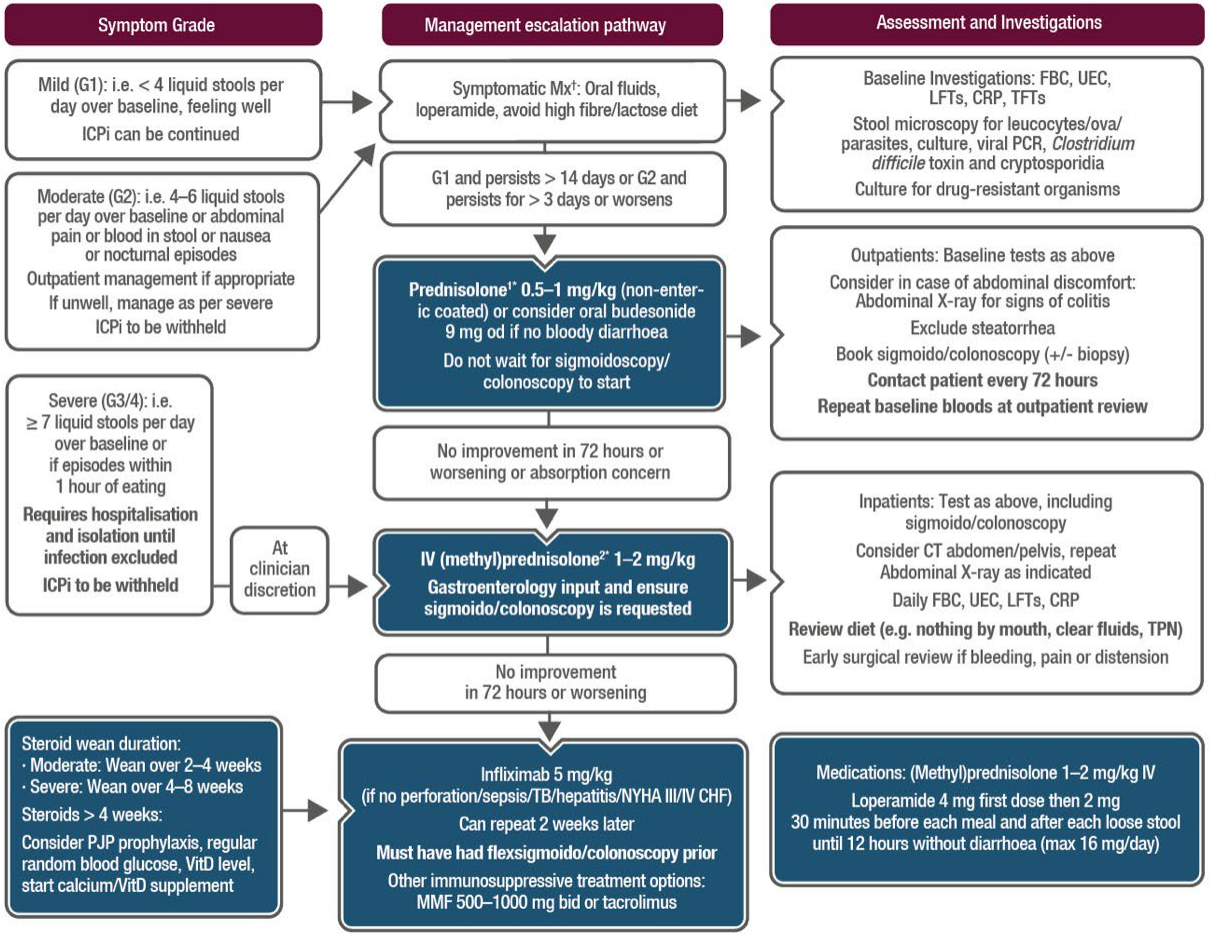
Immune related gastrointestinal toxicities

ICPi-related toxicity: Management of diarrhoea and colitis

†Loperamide 4 mg first dose then 2 mg 30 minutes before each meal and after each loose stool until 12 hours without diarrhoea (max 16 mg/day)

Steroid wean duration:
[1]Moderate: wean over 2–4 weeks
[2]Severe: wean over 4–8 weeks

*Steroids > 4 weeks: Consider PJP prophylaxis, regular random blood glucose, VitD level, start calcium/VitD supplement



Toxicity Management – Molecularly Targeted Therapies

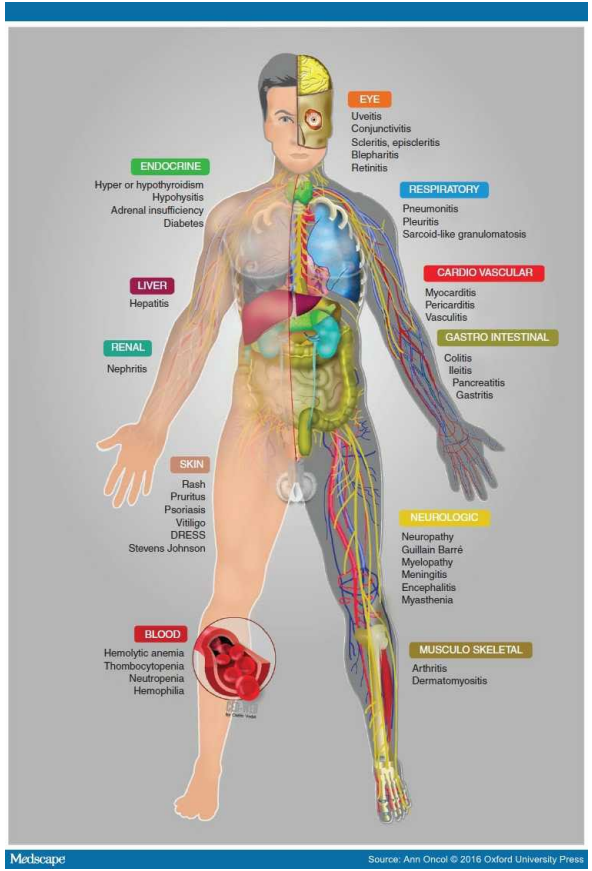
Common toxicities

- Thyroid – hypothyroidism
- Diarrhoea
- Rash
- Hypertension

- Interactions with other medications – induction/inhibition of cytochrome p450 enzymes

- Prolongation of QTc

Toxicity Management - Immunotherapy



Common toxicities

- Hypothyroidism
- Colitis
- Skin rash
- Hepatitis

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Conclusion: Cancer Therapies are Constantly Evolving

Immunotherapy and targeted therapy are different to chemotherapy in MOA and toxicity profile.

Finding the right information supports your management of cancer therapy toxicities:

- Grade toxicity – CTCAE
- SPC (Summary of product characteristics)
- NCCP (National Cancer Control Program)
- Guidelines - ESMO

Contact us – level 6 ward (01-2937530) & liaison nurses
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Thank you

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