

ECD treatment side effects

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#SociallyResponsible

What are we going to see today?

Introduction

- Side effect definition

Review

- ECD treatments

Side effects

- Side effects and their management

Future

- New treatments and strategies

THM

- Highlights & summary



Introduction

Review

Side effects

Future

THM



Side effect

an **unpleasant effect** of a drug, medical treatment, or vaccine that happens **in addition to the main intended effect**

- Types:

Dose-related

- Exposure is key

Allergic

- Person-dependent

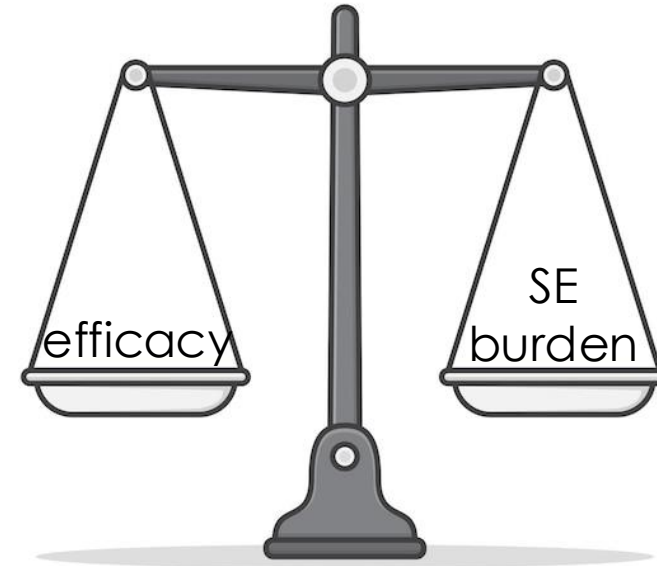
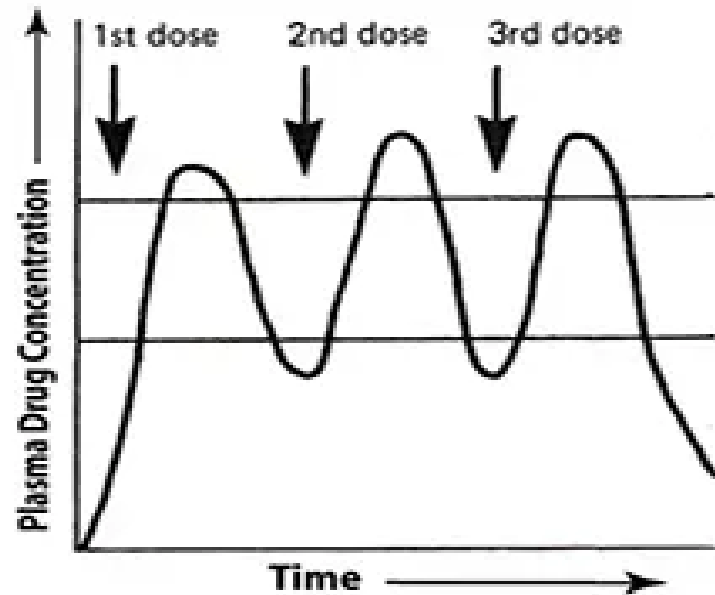
Idiosyncratic

- Not fully understood

Common misconception: 

Some medications are completely safe to take

A bit on medication exposure



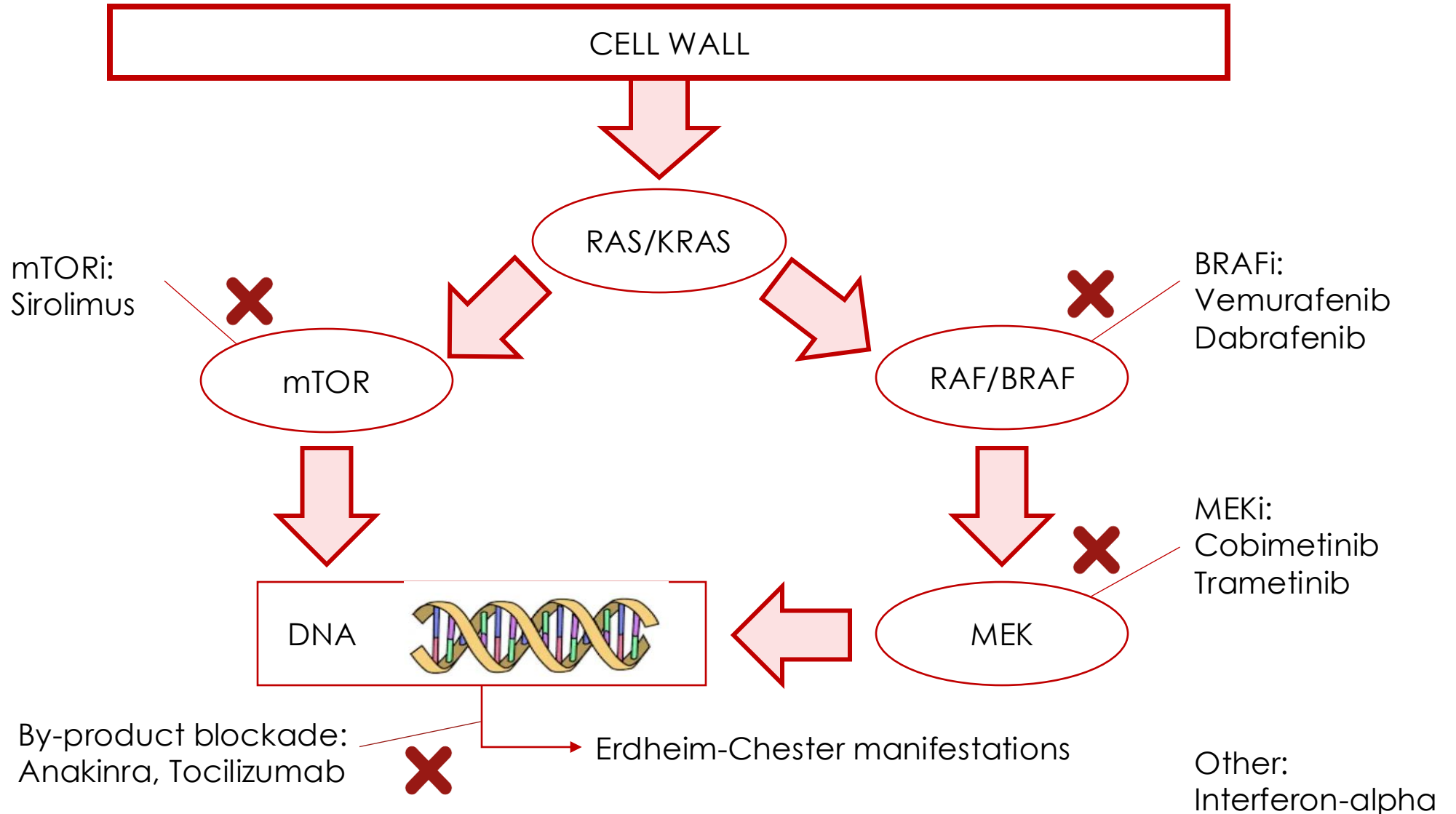
Therapeutic strategies:

Dose adjustment



Treatment "holidays"





BRAF_i

How to take?

- Vemurafenib 240-960mg
- Dabrafenib 50-150mg

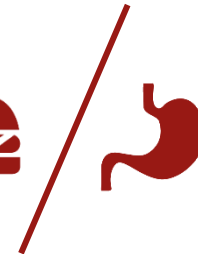
AM



PM



Vemurafenib:



Dabrafenib:






BRAFi Vemurafenib

Side effects

- Skin: rash, hair loss, skin tags, **hypersensitivity to sunlight**
- Digestive tract: nausea, vomiting, diarrhoea/constipation 
- Heart: **changes in electrical activity** (ECG) 
- General: **bone pain**, fatigue, arthralgia (joint pain)
- Eye: uveitis (inflammation)




BRAFi Dabrafenib

Side effects

- General: **Fever**, fatigue, arthralgia (joint pain) 
- Skin: **hand-foot syndrome**, rash, hair loss, skin thickening 
- Digestive tract: nausea/vomiting, diarrhoea, abdominal pain
- Metabolic: **high blood sugar**, low electrolytes in blood
- Eye: uveitis (inflammation), **visual alterations** 

BRAFi

Monitoring

- Complete bloodwork (haemogram, glucose, liver panel,...) periodically 
- **Skin exam** before treatment, then once monthly and up to 6 months after stopping. 
- **Eye exams** during treatment if changes in vision
- Vemurafenib: **ECG** before treatment, one month after and every dose change (more frequent if heart disease history) 

MEKi

How to take?

- Cobimetinib: 20-60 mg
- Trametinib: 1-2 mg (Store in fridge until use)



Once a day*

*Cobimetinib is taken in 28-day cycles: taken daily during **21 days** and not-taken the following **7 days**



Cobimetinib:






Trametinib:






MEKi (cobimetinib, dabrafenib)

Side effects

- General: bleeding, **muscle toxicity**, elevated blood pressure 
- Skin: rash, skin infection, nail changes, skin thickening, **hypersensitivity to sunlight** 
- Digestive tract: nausea, vomiting, diarrhoea, elevated liver enzymes
- Heart: **decreased cardiac output** 
- Eye: retinal toxicity including retinal detachment

MEKi (cobimetinib, dabrafenib)

Monitoring

- Complete bloodwork (haemogram, liver panel, muscle enzyme (CPK)...) monthly 
- **Left ventricle function** (FEVI) before treatment, one month after initiating and then every 3 months 
- Seek urgent **eye examination** if visual abnormalities
- **Skin exam** before treatment, then periodically and up to 6 months after stopping. Avoid sun exposure. 

So how do we deal with side effects?

Monitoring

- Mild
- Cause little disturbance
- Come and go

Treatment

- Moderate
- Affect comfort

Dose-adjustment

- Moderate-Severe
- Persistent
- QoL affected

Withhold treatment

- Severe
- Persistent
- QoL affected



Skin



- **Avoid hot water**, and **skin irritants** (solvents, disinfectants, OTC anti-acne medications)
- Alcohol and scent-free **skin moisturisers** at least twice daily
- **Avoid perfumes** or cologne
- Choose **loose-fit clothing**, preferably with breathable fibres
- Hand-foot syndrome – do not use tight shoes that may increase friction

Sunlight protection (UV-block):

- Wear at least 15 SPF all year round
- Avoid sunlight exposure between 10 and 16h
- Choose long-sleeved clothing



Fatigue

- **Physical activity** 3-5h weekly:
 - 150 min/week of aerobic exercise
 - 2 days/week of strength or flexibility exercises when aerobic is not carried out
- **Brisk walking** (5 km/h – 3 mph)
- **Stationary bike** with light effort
- Home-based exercises
- Within own physical capabilities and only if authorised by medical team
- According to International guidelines some patients may experience better outcomes and have fewer side-effects

Diarrhoea (more than 3 unformed stools a day)



When to **seek** urgent **care**:

- You have a temperature of **38°C** (100.5F) or higher
- Cramping and/or very painful **abdominal pain**
- **Oral rehydration**: only if you haven't been told to restrict your liquid intake.
 - Fruit juices or soft drinks with saltine crackers
 - Broths
 - Oral rehydration solutions
- Avoid high-fibre foods (whole grain cereals, beans, leafy vegetables, etc).
- Avoid fatty and spicy food, and other gastrointestinal irritants like coffee, alcohol or chocolate



Constipation (less than 3 bowel movements a week)



- **Increase fluid intake**, unless you've specifically been instructed not to do so
- **Increase dietary intake of fibres** (greens)
- **Physical activity** and mobility is encouraged, use a small footstool
- Refer to your GP to assess the need for laxatives



Nausea and vomiting



Tell your health care team if you have nausea for **more than 3 days** or if your nausea keeps you from doing things that are important to you.

- **Eat small quantities** of food spread out during the day
- Eat and drink what “works for you”
- Avoid fatty, fried, very spicy, or very sweet foods
- **Oral hygiene** – bacteria build up may worsen nausea
- Complementary therapies – beware of natural remedies taken by mouth, consult your pharmacist for an **interaction check**.
- You may need medication to control your symptoms, talk to your medical team if you feel the previous steps aren't “enough”



Heart

Let your doctor know immediately if you feel an **irregular heartbeat**.

Light-headedness. Loss of consciousness.

You've gained weight (more than 2kg – 5lbs) in a matter of days.

Swelling in your legs and feet.

Bloodwork

Some side effects are only detected this way. **Do not miss your appointment.**

- Blood cells
- Liver function
- Heart function



Interactions



What does this mean?

- **Exposure** to one (or many) medications can be **increased** or **decreased**
- More probability of **toxicity**
- Less **efficacy** of the treatment

Common “innocent-looking” troublemakers:

- Grapefruit
- St. John's wort



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Therapeutic Drug Monitoring – TDM?

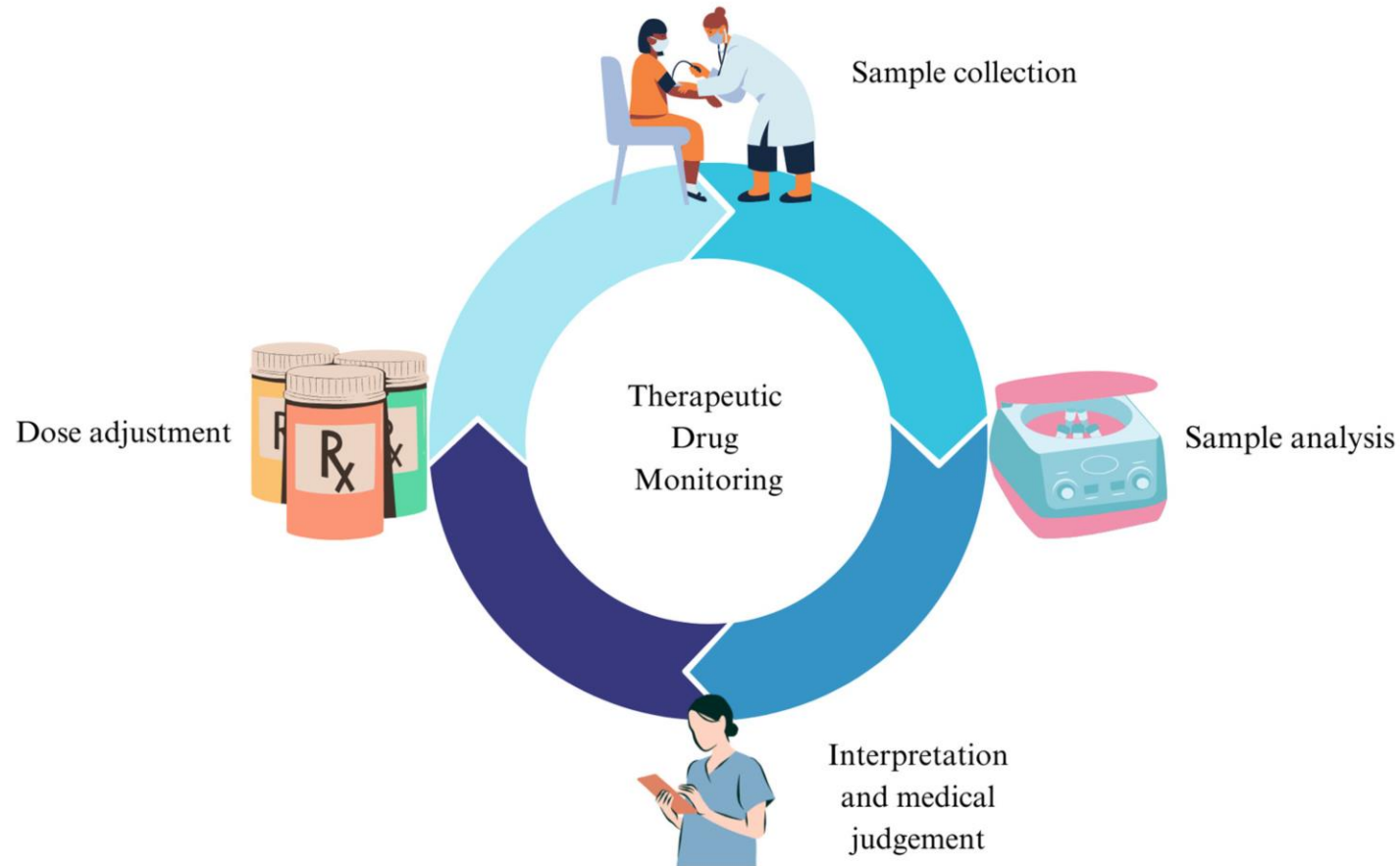


Diagram from Biso L, et al. Therapeutic Drug Monitoring in Psychiatry: Enhancing Treatment Precision and Patient Outcomes. *Pharmaceuticals*. 2024; 17(5):642.

Li G, et al. Development and validation of an UPLC-MS/MS method for simultaneous determination of fifteen targeted anti-cancer drugs in human plasma and its application in therapeutic drug monitoring. *J Pharm Biomed Anal*. 2022 Apr 1;212:114517.



- **Be vigilant in any changes in your body after starting a treatment**
- **Report anything out of your usual**
- **Talk to your doctor or pharmacist if you're concerned about a particular side effect and ask for advice/guidance**
- **Do not take any new medication or supplement without letting your healthcare providers know**
- **Do not hesitate to ask any doubts, they may arise at any time during the treatment**



THANK YOU!



Bellvitge University Hospital



Socialment
Responsables