

# Cancer treatment and diabetes

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# Diabetes and cancer

- Cancer and its treatment also poses challenges to managing diabetes
  - Surgery
  - Altered appetite
  - Cachexia
  - Artificial Nutrition
  - Weight Loss / Gain
  - Nausea and Vomiting
  - Palliative Care



# Cancer treatments and diabetes

- Steroids
- mTOR inhibitors
- PI3 Kinase Inhibitors
- Others



# Steroids

- Widely used in oncology
  - As part of chemotherapy regimes
    - Lymphoma
    - Myeloma
  - To improve tolerability of chemotherapy
  - To manage symptoms of cancer
    - Reduce inflammation (brain, spine metastases)
  - To manage side effects eg immunotherapies



# Steroid induced hyperglycaemia

- Multiple mechanisms
  - Increased hepatic gluconeogenesis
  - Insulin resistance – reduced insulin stimulated glucose uptake
  - Increased lipolysis, leading to intracellular lipids
  - Reduced insulin secretion



# Risk factors

- Pre-existing diabetes
- Those at increased risk of diabetes (obesity, family history, previous gestational diabetes, PCOS)
- Impaired fasting glycaemia or glucose tolerance
- At risk on Diabetes UK Risk Calculator



## Your risk explained

These are the risk factors that you can't change, so focus on the things that you can change or maintain.

	Points
<b>Age: 41</b>	
49 or younger	0
50 - 59	5
60 - 69	9
70 or older	13
<b>Gender</b>	
Male	1
Female	0
<b>Ethnicity</b>	
Only white European	0
Oth	
<b>Relatives with diabetes</b>	
Yes	5
No	0

These are the risk factors that you can change. Even small changes can help reduce your risk.

	Points
<b>Waist measurement: 78.7cm</b>	
Less than 90cm (35.3in)	0
90 - 99.9cm (35.4 - 39.3in)	4
100 - 109.9cm (39.4 - 42.9in)	6
110cm (43in) or above	9
<b>BMI: 19.0</b>	
Less than 25	0
25 - 29.9	3
30 - 34.9	5
35 or above	8
	5
No	0

**Low** : 0 - 6

**Increased** : 7 - 15

**Moderate** : 16 - 24

**High** : 25 - 47

# Definitions

- **Steroid induced diabetes**
  - New onset diabetes identified after starting steroids
  - May or may not resolve when steroids stop
- **Steroid induced hyperglycaemia**
  - Deteriorating glycaemic control in those with established diabetes after starting steroids





# Patterns

- Depend on administration regime
- May be relatively mild impact on fasting glycaemia
- More dramatic effects of post-prandial levels, especially during day
- Onset can be within 4 hours
- Usually return to normal within 24 hours of stopping



# Practical implications

- Need to monitor glucose both in those with diabetes and those at risk
- Fasting glucose may miss much of the effect
- Testing post-lunch or pre-evening meal more useful
- HbA1c no value in detecting effects of short steroid courses



# Cancer drugs and diabetes

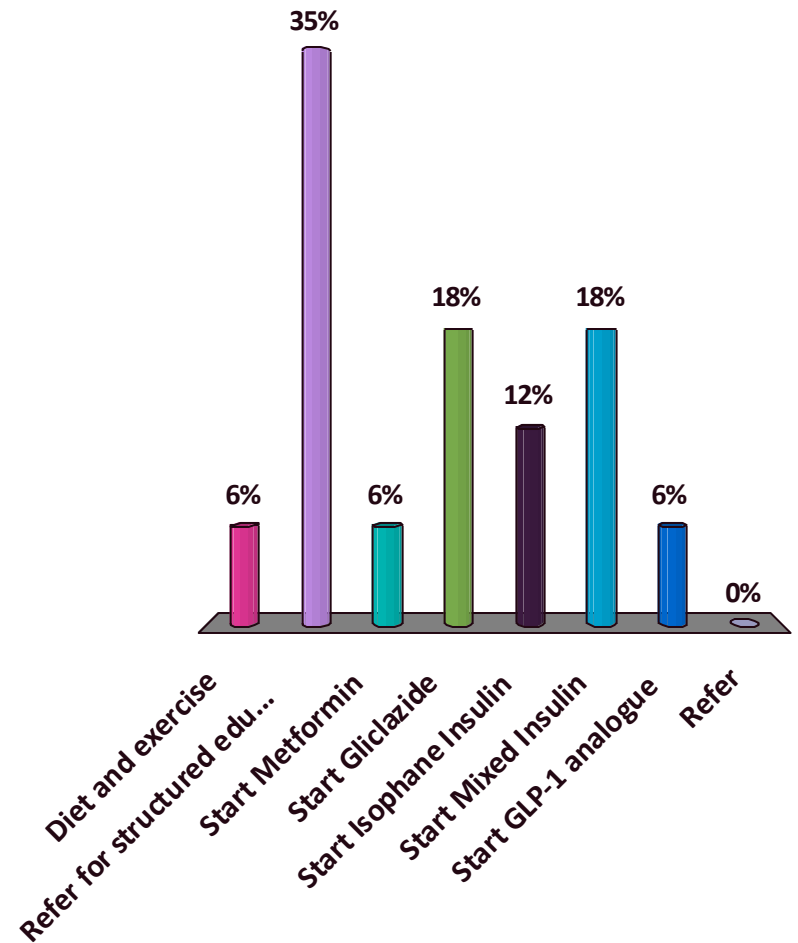
- Male, 60s
- Previous diabetes controlled on Metformin
- Colorectal cancer
- Commenced chemotherapy on d2 with Dexamethasone 4mg tds for 3 days

Mornin g	Evenin g	Day
8.6	8.3	1
6.8	14.4	2
10.1	26.1	3
11.2	15.4	4
9.3	19.3	5
6.9	5.8	6



# How would you treat?

1. Diet and exercise
2. Refer for structured education
3. Start Metformin
4. Start Gliclazide
5. Start Isophane Insulin
6. Start Mixed Insulin
7. Start GLP-1 analogue
8. Refer



# How to treat:

- Difficult!!
- Oral Agents
  - Metformin useful if tolerated
  - Sulphonylureas - may only be needed whilst taking steroids
- Insulin
  - Once daily AM human
  - isophane insulin
  - BD Mixed Insulin
  - Basal Bolus



## How common?

- Surprisingly little data
- .....perhaps because rarely do blood tests at time of peak risk
- Bounrmouth Study
  - 39 Patients, after 5 cycles 8 had glucose in diabetes range and 6 with impaired glucose tolerance
- RMH Data (same regime)
  - 14 % developed steroid induced diabetes



## Other effects

- Putative effects of hyperglycaemia on effectiveness of chemotherapy
- Small studies have suggested increased toxicities eg neuropathy, but not consistent



# Hyperglycaemia in newer cancer agents

- How are adverse events reported?
- Common terminology Criteria for Adverse Events – CTCAE Grade 1-5 (5=Death)
- Define either:
  - Hyperglycaemia – cut offs of glucose level that do not correlate with diagnostic criteria for diabetes OR
  - Impaired Glucose Tolerance – define by need for treatment
- Questionable how relevant these are to long term treatments





# mTOR Inhibitors

- mTOR inhibitors (Everolimus) used to treat
  - Renal Cell Cancer
  - Breast Cancer
  - Neuroendocrine tumours
- >10 % develop Grade III Hyperglycaemia (Glucose >13.8 mmol/l)
- Meta-analysis
  - RR 3.06 for any hyperglycaemia and 7.80 for high grade hyperglycaemia



# mTOR Inhibitors

- Greatest risk in those with pre-existing diabetes
- Try to establish normoglycaemia before treatment
- Standard algorithms suggested – but consider role of TZDs and SGLT-2 inhibitors



# PI3K Inhibitors

- In advanced stages of trials for multiple cancers
- Unsurprisingly hyperglycaemia commonly reported – around 30% in Phase 1 studies reported to date
- Increased Insulin levels



# Other cancer drugs and diabetes

- Streptozocin used in some pancreatic NETS
- Small molecule inhibitors of IGF-1 receptor in Phase 1 trials
- AKT Inhibitors
- Immunotherapies – rare cases of Type 1 Diabetes



# Evaluation: Cancer Treatment and Diabetes

Please rate this session for **relevance to you as a GP:**

1. Poor
2. Fair
3. Good
4. Very good
5. Excellent

