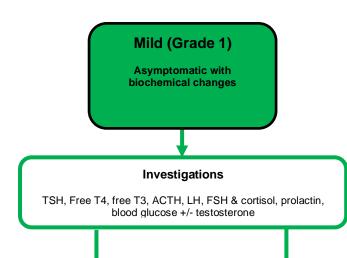


Immune-Related Adverse Event: Endocrinopathies-Thyroid Dysfunction

Immunotherapy has been causatively associated with a number of endocrinopathies, including hypo/hyperthyroidism. Observational studies have shown that there is a typical pattern of thyroid specific biochemical disturbance presenting with asymptomatic hyperthyroidism before return to normal levels for a brief period. This is nearly always followed by the development of, in some cases profound, hypothyroidism, which is frequently persistent and requires long-term thyroid replacement. Smaller subsets of patients develop isolated hypothyroidism over a period of weeks. Both groups appear to require long-term replacement in a majority of cases. These guidelines are in the basis of a clinically well patient and not experiencing thyroid disturbance due to being clinically unwell, if this is a concern, Endocrinology advice should be sought.



Hyperthroidism

TSH <0.40 mU/L and Free T4 > 22pmol/L

(If TSH low and T4 normal or low, need to exclude pituitary dysfunction)

Treatment:

 Steroids are not needed in this setting unless expressly advised by endocrinology.

Actions:

- Recheck TFT's and cortisol within 3 weeks and then 3 weekly thereafter. N.B. the majority of cases become hypothyroid within a matter of weeks.
- Refer to IO Toxicity Service.

Once hypothyroidmanage as per hypothyroidism algorithm

Continue Immunotherapy

Hypothyroidism

TSH of >10mU/L and Free T4 < 12 pmol/L

Treatment:

Levothyroxine 50mcg/day

Actions:

- Recheck TFT's and cortisol with next cycle of treatment
- Increase Levothyroxine in 25mcg increments
- Discuss with endocrinologist to identify best pathway for long-term management and monitoring (primary/secondary care)
- Consider referral to endocrinologist if unable to stabilise thyroid function
- Refer to IO Toxicity Service.

Continue Immunotherapy

Moderate (Grade 2)

Symptomatic or severe biochemical disturbance

Investigations

TSH, Free T4, free T3, ACTH, LH, FSH & cortisol, prolactin, blood glucose +/- testosterone

Hyperthroidism

TSH <0.40 mU/L and Free T4 > 22pmol/L

(if TSH low and T4 normal or low, need to exclude pituitary dysfunction)

Treatment:

- B-blocker- Propranolol 40-80mg daily
- Carbimazole-rarely indicated due to the transient nature of hyperthyroidism. If persistent or associated with anti-TSH antibodies consider in collaboration with an endocrinologist

Actions:

- Recheck TFT's and cortisol within 2 weeks and fortnightly thereafter. N.B. the majority of cases become hypothyroid within a matter of weeks.
- Refer to IO Toxicity Service.

Continue Immunotherapy

Once hypothyroidmanage as per hypothyroidism algorithm

Hypothyroidism

TSH of >10mU/L and Free T4 < 12 pmol/L

Treatment:

Levothyroxine 50mcg/day

Actions:

- Recheck TFT's and cortisol with next cycle of treatment
- Increase Levothyroxine in 25mcg increments
- Consider referral to endocrinologist if unable to stabilise thyroid function.
- Refer to IO Toxicity Service.

Continue Immunotherapy

Interrupt SACT immunotherapy until discussed with Acute Oncology Team. Please contact <u>on-call oncology/haematology</u> <u>team</u> for advice. Ensure that the patient has monitoring/follow up planned with their oncology/immuno-oncology team.

Issue Date: 11th July 2023	Page 1 of 1	Filename: GAMATHYRO	Version No: 1.3
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