Radioactive iodine and other thyroid cancer treatments, and their side effects: frequently asked questions

How are patients prepared for radioactive iodine (RAI)?

Table 1 summarises the preparation of patients who will be treated with RAI (\(^{131}I\)).

<table>
<thead>
<tr>
<th>Increase thyroid stimulating hormone (TSH) levels to &gt;30 mIU/L</th>
<th>Increasing TSH levels ensures that RAI is maximally taken up by thyroid cells. This can be achieved by:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Injecting recombinant human TSH 24 and 48 hours before RAI, while the patient receives levothyroxine(^{1})</td>
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<tr>
<td></td>
<td>• Withdrawing thyroid hormone(^{2})</td>
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<table>
<thead>
<tr>
<th>Reduce iodine stores in the body</th>
<th>This can be achieved by:</th>
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<tr>
<td></td>
<td>• Following a low iodine diet for 1–2 weeks before RAI(^{2}); (this advice can differ between centres)</td>
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<td></td>
<td>• Not performing imaging using RAI contrast medium during 8 weeks before RAI(^{2})</td>
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<td>• Discontinuing medications that are high in iodine(^{2})</td>
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<table>
<thead>
<tr>
<th>Provide patients with support and advice</th>
<th>Education, support and advice could include:</th>
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<tbody>
<tr>
<td></td>
<td>• Explaining the rationale for the above steps and the potential side effects of RAI(^{1,3})</td>
</tr>
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<td></td>
<td>• Advising what to bring into the isolation room</td>
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<td></td>
<td>• Advising about pregnancy and breast feeding (see below)(^{2})</td>
</tr>
<tr>
<td></td>
<td>• Highlighting the importance of avoiding close contact with others for a time after receiving RAI(^{2}) and other practicalities after discharge</td>
</tr>
</tbody>
</table>

### Table 1: Preparation of patients for RAI

**Which patients are unsuitable for RAI?**

RAI scans are contraindicated during pregnancy and breastfeeding. Healthcare professionals (HCPs) must exclude pregnancy before radioiodine remnant ablation (RRA) or RAI in women of reproductive potential. All patients (regardless of gender) should not attempt conception for at least 6 months after RRA or 4 months after RAI. Women should stop breastfeeding at least 8 weeks before RRA or RAI and not resume until after a future pregnancy.\(^{2}\)
Funding statement: This independent educational activity is supported by an educational grant provided by Eisai and Sanofi. PCM Scientific is the medical education company acting as scientific secretariat and organiser for this programme. The activity is run independently of the financial supporter and all content is created by the faculty. No funder has had input into the content of the activity.

What are common post-operative complications?

Post-operative complications are generally rare. A study of 27,912 people who underwent thyroidectomy for differentiated or medullary thyroid cancer reported that 6.5% developed general surgical complications within 30 days of the procedure. During the year after the procedure, 12.3% of patients experienced complications specific to thyroidectomy.

A review of surgery for thyroid cancer noted that:

- The most serious complications of thyroidectomy are injury to the recurrent laryngeal nerve (RLN) and hypocalcaemia.
- Up to 5% of people show temporary nerve palsy following thyroidectomy, while less than 2–3% experience permanent RLN injury and vocal cord paralysis.
- Bilateral RLN damage occurs after about 1 in 1000 thyroidectomies but requires permanent tracheotomy.

Less common important complications include:

- Neck haematoma (<1% of cases).
- Seroma.
- Injury to the external branch of the superior laryngeal nerve (SLN). About a third of patients experience vocal symptoms following thyroidectomy, even without obvious nerve damage. Half of these still have symptoms 3 months after thyroidectomy, which may suggest SLN injury, especially among patients with, for example, reduced tone, vocal fatigue and problems projecting their voice.
- Wound infections (e.g. cellulitis), while rare (0.1%-2%), are most common in immunocompromised patients and those with diabetes.

What is the post-operative advice to patients?

Complications following thyroidectomy performed by experienced surgeons are generally uncommon and can be corrected. Most scars are barely visible six months to a year after thyroidectomy. Some patients, particularly those with red hair and those from Africa or the West Indies, can develop a hypertrophic (keloid) scar. Steroid tape and injections, and laser treatment may improve the appearance of keloid scar.

Patients who undergo thyroidectomy should inform their HCP immediately if they experience muscle cramping or tingling in their hands, fingers or face, especially the lips. Adequate calcium concentrations are essential for normal nerve and muscle functioning. These symptoms may indicate low calcium levels and patients may need supplements.

HCPs should also stress the importance of:

- Attending the follow up appointments and visits for thyroid function monitoring.
- Reporting any symptoms that may suggest hypothyroidism.
- Seeking urgent medical attention if the neck swelling seems excessive or they experience problems breathing.

How should persistently increases in thyroglobulin (Tg) or Tg antibody (TgAb) levels in differentiated thyroid cancer be managed?

Rising Tg or TgAb levels may indicate the cancer’s progression and, therefore, indicate that further investigations, such as imaging, are needed. These investigations will indicate if further therapy, such as local excision or localised external beam radiation therapy, is required. RAI will typically continue until the disease becomes RAI-refractory, but the dose may need to be increased. Expert opinion suggests continuing TSH suppression while closely monitoring Tg levels if the thyroid cancer becomes RAI-refractory and the patient is asymptomatic.
What are the main side-effects of tyrosine kinase inhibitors (TKI) and how can they be managed?

Table 2 summarises main side-effects associated with TKIs and their management. If the specific measures in Table 2 do not alleviate or control the side effects, the HCP can consider adjusting the dose and duration of the TKI.\textsuperscript{11,12} The next question considers skin problems that may be associated with TKIs.

<table>
<thead>
<tr>
<th>Side-effect</th>
<th>Prophylactic measures and side effect Management for patients taking TKIs\textsuperscript{11,12}</th>
</tr>
</thead>
</table>
| **Hypertension** | Ensure blood pressure is normal before starting TKI treatment  
Aim to maintain a blood pressure of 140/90 mmHg or less, using anti-hypertensives if blood pressure exceeds this threshold |
| **Fatigue** | Encourage a nutritious diet and optimal hydration, with regular mild-moderate exercise  
Recommend energy management strategies, such as rest periods during the day  
Support the patient to manage other TKI side effects  
Investigate other potential factors that may contribute to fatigue  
Consider TKI administration in the evening, which may reduce daytime fatigue |
| **Diarrhoea** | Regularly assess diarrhoea frequency and monitor electrolytes  
Encourage adequate fluid intake  
Avoid foods and drinks that could contribute to diarrhoea  
Prescribe anti-diarrhoea medication |
| **Decreased appetite and weight loss** | Encourage a nutritious diet  
Monitor appetite and weight loss at each assessment  
Treat any underlying nausea |
What is the management of skin problems associated with TKIs?

TKIs can cause several dermatological adverse events including:

- Palmar-plantar erythrodysesthesia (hand-foot) syndrome (PPES).  
- Rash (e.g. acneiform).  
- Erythema.  
- Pruritus.  
- Paronychia.  
- Telangiectasia.  
- Alopecia and changes in hair growth or pigmentation.  
- Skin discolouration and dryness (xerosis).

Many dermatological adverse events can be treated or prevented (tables 3 and 4). HCPs should advise patients that acneiform rash and PPES generally develop within the first 8 weeks of treatment. Sun protection includes using a non-alcohol-based sunblock (SPF≥30) applied at least every two hours or every hour if sweating or swimming, protective clothing, including a hat, and avoiding direct sunlight.

Limit time in baths and showers; use cool or warm (not hot) water

Keep fingernails short

Use mild soaps and low pH cleansers and moisturisers; avoid cleansers containing alcohol

Wear gloves and socks when exercising

Apply moisturisers twice daily; apply after bathing while skin is damp

Wear hat and gloves in cold weather

Reduce skin friction; pat rather than rub with a towel

Use fragrance-free and vitamin-free lip balm

Maintain humidity (reduce temperature in the home; use a humidifier)

Use moisturisers containing salicylic acid or ammonium lactate for very dry, scaly skin or xerosis of the palms or soles

Table 3: Managing xerosis in patients taking TKIs
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<table>
<thead>
<tr>
<th>Reaction</th>
<th>Grade 0</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3*</th>
<th>Grade 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>No adverse events</td>
<td>Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only</td>
<td>Moderate; minimal, local or noninvasive intervention needed; limits age-appropriate instrumental activities of daily living (ADL)§</td>
<td>Severe or medically significant but not immediately life-threatening; hospitalisation or prolongation of hospitalisation; disabling; limiting self-care ADL¶</td>
<td>Life-threatening consequences; urgent intervention needed</td>
<td></td>
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<tr>
<td>Photosensitivity</td>
<td>Topical steroids</td>
<td>Topical steroids</td>
<td>Topical steroids</td>
<td>Oral antihistamines</td>
<td>Oral steroids</td>
</tr>
<tr>
<td></td>
<td>Sun protection</td>
<td>OTC moisturisers†</td>
<td>Oral antihistamines</td>
<td>Oral antihistamines</td>
<td>Oral steroids</td>
</tr>
<tr>
<td>PPES</td>
<td>Urea cream</td>
<td>Urea cream</td>
<td>Urea cream</td>
<td>Clobetasol cream</td>
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<tr>
<td></td>
<td>Ammonia lactate cream</td>
<td>Clobetasol cream</td>
<td>Clobetasol cream</td>
<td>Lidocaine (topical or patch)</td>
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<tr>
<td></td>
<td>Heavy moisturiser</td>
<td>Lidocaine (topical or patch)</td>
<td>Analgesia (NSAIDs; GABA agonists; narcotics)</td>
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<tr>
<td></td>
<td>Oral doxycycline or oral minocycline†</td>
<td>Hydrocortisone cream</td>
<td>Hydrocortisone cream</td>
<td>Hydrocortisone cream</td>
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<tr>
<td></td>
<td>Low-potency topical steroid‡</td>
<td>Clindamycin gel</td>
<td>Oral doxycycline or oral minocycline</td>
<td>Oral doxycycline or oral minocycline</td>
<td></td>
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<tr>
<td></td>
<td>Sunscreen (SPF ≥30)‡</td>
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<tr>
<td>Acneiform rash</td>
<td>Moisturiser cream†</td>
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</tbody>
</table>

* Or intolerable grade 2; † containing aloe vera or pramoxine; ‡ Prophylactic; § preparing meals, shopping for groceries or clothes, using the telephone, managing money, etc; ¶ bathing, dressing and undressing, feeding self, using the toilet, taking medications, and not bedridden. Please see reference for specific recommendations (e.g. dose), monitoring, discontinuation and referral.13 Paper uses National Cancer Institute Common Terminology Criteria for Adverse Events v 4.0.14 NSAID: Non-steroidal anti-inflammatory drug; OTC: Over-the-counter; PPES: palmar-plantar erythrodysaesthesia (hand-foot) syndrome

**Table 4: Management of dermatological adverse events in patients taking TKI13,14**
References


6. Reeve T and Thompson NW. Complications of thyroid surgery: how to avoid them, how to manage them, and observations on their possible effect on the whole patient. World Journal of Surgery 2000;24:971-5


10. Cooper MS and Gittoes NJ. Diagnosis and management of hypocalcaemia. Bmj 2008;336:1298-302


