

Immunotherapy & Radiation Therapy

Understanding Your Combined Treatment, Side Effects &
Self-Monitoring

Anthony Ricco, MD
Radiation Oncology
Main Line Health — Lankenau Medical Center & Riddle Hospital

Version 1.1 | March 2026

Evidence-based guidance from NCCN (v1.2026 ICI toxicity), ASCO (2021 irAE update), PACIFIC, ADRIATIC,
KEYNOTE trials, and MSK

Section 1: How Immunotherapy Works

Immunotherapy is one of the most important advances in cancer treatment in the past decade. Unlike chemotherapy, which directly kills cancer cells, immunotherapy works by helping YOUR OWN immune system recognize and attack cancer.

Checkpoint Proteins & Cancer's Invisibility Cloak

Your immune system has natural 'off switches' called checkpoint proteins. These prevent your immune system from attacking healthy cells. But cancer cells are clever — they exploit these switches to hide, essentially putting on an invisibility cloak. **Checkpoint inhibitors block these switches, releasing the brakes on your immune system.**

Two Main Types of Checkpoint Inhibitors

- **PD-1/PD-L1 inhibitors:** Pembrolizumab (Keytruda), nivolumab (Opdivo), durvalumab (Imfinzi), atezolizumab (Tecentriq), cemiplimab (Libtayo)
- **CTLA-4 inhibitors:** Ipilimumab (Yervoy) — works earlier in immune activation, tends to have more side effects

Checkpoint inhibitors don't kill cancer directly. They remove the 'invisibility cloak' cancer uses to hide from your immune system. Your body's trained immune cells do the actual fighting.

Section 2: Why Radiation & Immunotherapy Work Together

The abscopal effect: Radiation kills cancer in a specific area, but also releases cancer 'fingerprints' (antigens) that prime your immune system to recognize cancer cells EVERYWHERE in your body.

How the Combination Works (Step by Step)

1. Radiation destroys tumor cells in the radiation field
2. This releases cancer antigens (like fingerprints of the tumor)
3. Your immune system's 'scout cells' (dendritic cells) pick up these antigens
4. T cells are activated and learn to recognize cancer throughout your body
5. Checkpoint inhibitors prevent cancer from suppressing these newly activated T cells
6. The combination creates a body-wide anti-cancer immune response

Radiation can sometimes help the immune system recognize cancer better — almost like an in-situ vaccine — but true abscopal responses (tumors shrinking outside the radiation field) are uncommon and unpredictable. The combination works best when both treatments are given as your oncologist plans.

Combining radiation with immunotherapy is increasingly the standard of care across many cancers. The two treatments amplify each other, leading to better outcomes than either alone.

***Important note:** The PACIFIC-2 trial tested starting durvalumab concurrently with chemoradiation (rather than after) and did not establish benefit. Consolidation after chemoradiation remains the standard approach for stage III NSCLC.*

Section 3: Common Combinations by Cancer Type

Different cancers use different checkpoint inhibitors at different times. Here are the most common combinations:

Cancer Type	Immunotherapy Drug	How Combined	Key Trial Data
Stage III NSCLC	Durvalumab (Imfinzi)	Consolidation after chemoradiotherapy	PACIFIC: 5-yr OS 42.9% vs 33.4%
Limited SCLC	Durvalumab (Imfinzi)	Consolidation after cCRT (no progression)	ADRIATIC: median OS 55.9 vs 33.4 mo
H&N; SCC (PD-L1 CPS\geq1)	Pembrolizumab (Keytruda)	Before, during, after surgery/RT	KEYNOTE-689 (1st interim): 36-mo EFS 57.6% vs 46.4% (HR 0.73)
Cervical (III-IVA)	Pembrolizumab (Keytruda)	During & after chemoRT	KEYNOTE-A18: 3-yr OS 82.6% vs 74.8%
Melanoma brain mets	Ipi + Nivo	With stereotactic radiosurgery	Retrospective data: 1-yr LC ~92% vs 64% (no phase III yet)
Muscle-invasive bladder	Durvalumab + tremelimumab	With radiotherapy	IMMUNOPRESERVE (phase II): 2-yr bladder-intact DFS 65%
High-risk skin SCC	Cemiplimab (Libtayo)	Adjuvant after surgery + RT (high recurrence risk)	C-POST: 2-yr DFS 87% vs 64% (FDA approved Oct 2025)

Ask your radiation oncologist which combination is being used for YOUR specific cancer and why this specific timing was chosen. Every cancer and every patient is different.

Section 4: Side Effects — What to Expect

Because immunotherapy activates your immune system broadly, it can cause inflammation in virtually any organ. These are called **immune-related adverse events (irAEs)**. The good news: most are manageable when caught early.

The Numbers

- Immune side effects of some kind are common; severity depends on the specific drugs used
- Severe events (Grade 3-4) are less common with single-agent PD-1/PD-L1 inhibitors
- Higher rates with combination IO (ipilimumab + nivolumab) or CTLA-4-containing regimens
- Most irAEs appear within 3-6 months, but can occur at ANY time — even months after stopping treatment

By Organ System

Organ System	Common Side Effect	Prevalence	Typical Onset
Thyroid	Hypo/hyperthyroidism	32-40%	4-10 weeks
Skin	Rash, itching, vitiligo	20-30%	2-6 weeks
Gastrointestinal	Diarrhea, colitis	10-30%	6-12 weeks
Lung	Pneumonitis (see Section 5)	10-20%	2-6 months
Liver	Hepatitis	5-10%	6-14 weeks
Kidney	Nephritis	10-15%	Variable
Endocrine	Adrenal insufficiency, pituitary	5-10%	Variable
Heart	Myocarditis	1-5%	2-8 weeks
Nervous system	Neuropathy, encephalitis	1-5%	Variable

Section 5: Pneumonitis — The Critical Side Effect

This is **THE** most important side effect to understand when combining radiation and immunotherapy, especially for lung and chest cancers. Both radiation AND immunotherapy can cause lung inflammation. When combined, the risk is additive.

How to Tell Them Apart

Feature	Radiation Pneumonitis	Immunotherapy Pneumonitis
Onset	1-3 months post-RT	Unpredictable, any time
Location on imaging	Confined to radiation field, sharp borders	Bilateral, multiple lobes, blurry borders
Severity range	Usually mild-moderate	Can be severe
Primary treatment	Steroids, observation	Hold IO + high-dose steroids

PACIFIC Trial Data (Durvalumab + Chemoradiation)

- Any-grade pneumonitis/radiation pneumonitis: 33.9% (durvalumab) vs 24.8% (placebo)
- Grade ≥ 2 symptomatic pneumonitis: 19.8% vs 14.1% — the more clinically relevant number
- Grade 3-4 severe: only 3.4% vs 2.6% — rare
- **Critical finding:** Grade 2+ pneumonitis did NOT compromise survival benefit

Symptoms to Watch

- New persistent cough (not related to cold/infection)
- Worsening shortness of breath
- Chest pain when breathing
- Fever with respiratory symptoms

Report ANY new respiratory symptoms to your care team immediately. Early detection of pneumonitis allows early treatment and better outcomes. Do not wait.

Radiation Recall Pneumonitis

A reaction called **radiation recall** can occur when immunotherapy 'reactivates' inflammation in areas previously treated with radiation — sometimes months or even years later. In a retrospective study of 80 previously irradiated lung cancer patients who received PD-1/PD-L1 inhibitors, radiation recall pneumonitis occurred in **18.8%** (15/80).

- **Key concern:** On imaging, radiation recall can look like cancer recurrence — in one study, 53% of cases were initially misdiagnosed
- If you develop new cough or shortness of breath after starting IO, tell your team about your prior radiation history
- Your radiation oncologist can help distinguish recall from true recurrence based on the imaging pattern

Section 6: Managing Side Effects at Home

Skin (Rash, Itching, Dermatitis)

- **Mild:** moisturizers (CeraVe, Cetaphil), avoid irritants, oatmeal baths, OTC hydrocortisone cream (1%)
- **Moderate:** prescription topical steroids, oral antihistamines (cetirizine, fexofenadine)
- **Call if:** rapidly spreading rash, blistering, signs of infection (warmth, pus, increasing redness)

Gastrointestinal (Diarrhea, Colitis)

- **Mild (<4 stools/day):** hydration, low-residue diet, loperamide (Imodium) if no blood
- **Moderate (4-6/day):** call your team — you may need prednisone, IO may be held temporarily
- **Call immediately:** blood in stool, severe abdominal pain, fever, dehydration

Thyroid Dysfunction

- Most common lasting irAE (32-40% of patients)
- Often starts as hyperthyroidism (fatigue, palpitations, weight loss) → transitions to hypothyroidism (fatigue, weight gain, cold intolerance)
- Symptoms: fatigue, weight changes, cold/heat intolerance, mood changes, constipation (hypo)
- Treatment: levothyroxine replacement — often **lifelong**
- Usually does NOT require stopping immunotherapy

Liver (Hepatitis)

- May have no symptoms — often detected on routine blood work
- Symptoms if present: jaundice (yellow skin/eyes), dark urine, right-sided abdominal pain, fatigue
- Treatment: hold IO + steroids if Grade 2+

Adrenal Insufficiency (Hypophysitis/Adrenalitis)

- Fatigue, low blood pressure, salt craving, dizziness, syncope
- Treatment: hydrocortisone replacement — often **lifelong**
- **CRITICAL:** NEVER skip doses — can cause life-threatening adrenal crisis
- Call if: severe dizziness, chest pain, confusion — go to ER

Section 7: The Steroid Question

You may worry that steroids used to treat side effects could reduce the effectiveness of your immunotherapy. Here's what the evidence says.

Steroids for Managing irAEs (After IO Has Started)

Prednisone and related steroids are the standard treatment for many immune side effects. Starting them promptly when your team recommends them is often safer than waiting. Developing an irAE may actually indicate your immune system is responding to treatment. **Controlling a severe side effect is more important than the theoretical concern about immunosuppression.** Steroids still require monitoring and are usually tapered slowly over 4–6 weeks or longer.

Baseline Steroids (Before Starting IO)

High-dose steroids (>10 mg prednisone) BEFORE starting immunotherapy may be associated with worse outcomes. Discuss with your oncologist if you need steroids before starting IO.

Prednisone Taper Protocol

If you're prescribed steroids for an irAE, follow your taper schedule exactly. NEVER stop abruptly — this can cause adrenal crisis. Your care team will provide a written schedule.

Don't be afraid of steroids for side effect management. Controlling an irAE is more important than the theoretical concern about immunosuppression. Trust your care team's judgment.

Section 8: Long-Term & Late-Onset Effects

Side effects can appear months or even a year after your LAST dose of immunotherapy. This is unique to IO and requires ongoing vigilance. Your immune system has been 'trained' by the treatment.

Late Immune-Related Adverse Events

- Late irAEs are more common than many patients expect: a 2025 cohort found hospitalized irAEs presenting 6–12 months after first ICI exposure in 14.7%, and >1 year in 10.8%
- Most common delayed: joint pain/arthralgia, colitis, rash, pneumonitis
- Chronic irAEs persisting >3 months after stopping treatment are also common and may require ongoing management

Permanent Endocrine Effects

- **Hypothyroidism:** ICI thyroiditis often progresses to long-term hypothyroidism requiring lifelong levothyroxine replacement
- **Adrenal insufficiency:** Hypophysitis-related ACTH deficiency is often persistent and may require long-term hydrocortisone replacement
- **Pituitary dysfunction:** Often persistent; may require multiple hormone replacements (thyroid, cortisol, growth hormone)

What If I Had a Side Effect — Can I Restart IO?

If immunotherapy was stopped due to a side effect, your oncologist may consider restarting it. Here's what the data shows:

- In the largest updated cohort, **31.8%** experienced recurrence of the same irAE after rechallenge
- Some patients develop a different irAE than the original one
- Rechallenge is generally considered safe after mild-moderate (Grade 1-2) irAEs
- **Usually NOT restarted** after cardiac (myocarditis), severe neurologic, or any Grade 4 irAE
- If restarted, side effects tend to appear sooner — your team will monitor you closely

Monitoring Schedule Post-IO

- First 3 months: monthly visits + labs
- Months 3-12: every 3 months (TSH, liver tests, creatinine, glucose)
- Year 1-2+: every 6 months, **lifelong thyroid monitoring**

Even after immunotherapy stops, continue reporting new symptoms to your care team indefinitely. Late irAEs are treatable when caught early.

Section 9: Red Flags — When to Call Immediately

These symptoms require urgent evaluation. If you're unsure, call. It's always better to check than to miss something serious.

Warning Sign	What It May Mean
New persistent cough or worsening SOB	Possible pneumonitis; needs imaging
Diarrhea >4 episodes/day or blood in stool	Possible colitis; may need steroids/IO hold
Jaundice (yellow skin/eyes) or dark urine	Possible hepatitis; needs urgent labs
Severe fatigue + dizziness + low BP	Possible adrenal crisis; seek emergency care
New chest pain, palpitations, fainting, or new profound muscle weakness	Possible myocarditis/myositis overlap (mortality 30–50%); needs URGENT ECG + troponin + CK
Severe headache + vision changes + fever	Possible hypophysitis; needs MRI + hormone panel
Rapidly spreading rash or blistering	Possible severe dermatologic reaction; needs evaluation
New weakness or numbness (limbs/face)	Possible neurologic irAE; needs assessment
Fever >100.4°F with chills	Infection or inflammatory irAE; needs evaluation
Confusion, seizures, or loss of consciousness	EMERGENCY — go to ER immediately

When in doubt, CALL. It's always better to report a symptom that turns out to be nothing than to miss an irAE that needs treatment.

IMPORTANT: Tell any ER or urgent-care clinician that you are receiving (or recently received) immunotherapy. This information is critical for your emergency care.

Section 10: Recommended Products & Resources

These products may help manage side effects. Most are over-the-counter; some may be covered by insurance.

Category	Product/Service	Est. Cost
Skin care	Fragrance-free moisturizer (CeraVe, Cetaphil)	~\$12-16
Skin care	OTC hydrocortisone cream (1%)	~\$8
Skin care	Oatmeal bath (Aveeno Oatmeal Bath)	~\$8
GI	Loperamide (Imodium)	~\$10
GI	Probiotics (if diarrhea)	~\$15-25
Thyroid	Levothyroxine (generic, if prescribed)	~\$10-20/month
Monitoring	Digital thermometer	~\$10
Monitoring	Home blood pressure monitor	~\$30-50
Organization	Medication tracking app	Free
Support	CancerCare counseling	Free
Support	Cancer Support Community	Free
Education	National Cancer Institute IO resources (cancer.gov)	Free

Contact Information

Anthony Ricco, MD

Radiation Oncology

Main Line Health

Lankenau Medical Center & Riddle Hospital

100 East Lancaster Ave · Rosengarten Bldg, Basement · Wynnewood, PA 19096

1078 West Baltimore Pike · Health Center 1, Ground Floor · Media, PA 19063

Phone: 1.866.CALL.MLH (1.866.225.5654)

Immunotherapy combined with radiation represents one of the most exciting advances in cancer treatment. Your care team is monitoring you closely. Stay vigilant, report symptoms early, and know that most side effects are manageable when caught quickly. You've got this.

My Treatment Journal

A place to notice patterns, remember questions, and track what helps.

You do not need to fill this out perfectly. Even a few notes can help you see patterns, remember what worked, and tell your care team what is actually happening at home.

This Week

Week of / goals / anything I especially want help with

Daily Check-In

Day / Date	Energy (0-10)	Pain (0-10)	Eating / Drinking	Sleep	Main note
Mon					
Tue					
Wed					
Thu					
Fri					
Sat					
Sun					

Symptoms I Want to Watch

<input type="checkbox"/> Cough / breathing	<input type="checkbox"/> Diarrhea	<input type="checkbox"/> Rash / skin
<input type="checkbox"/> Fatigue	<input type="checkbox"/> Fever	<input type="checkbox"/> New or unusual symptoms
<input type="checkbox"/> Other: _____		

What I Tried / What Helped

Use this page to test small changes and keep track of what helps, what does not, and what you want to ask about next.

Problem or symptom	What I tried	Did it help?	Next step / question

Examples: taking pain medicine before meals, changing skin care timing, drinking earlier in the day, using a humidifier, adjusting fiber, walking after treatment, or asking for a refill.

Questions for My Care Team

Bring this page to visits. Small questions are worth writing down, especially when treatment days start to run together.

Symptoms or side effects I want to mention

Medication, refill, or product questions

Eating, drinking, bowel, bladder, skin, sleep, or activity questions

Logistics: appointments, transportation, work, family, forms

One thing I keep forgetting to ask
