

AUTOIMMUNE PNEUMONITIS AS A FATAL ADVERSE REACTION TO DURVALUMAB AND TREMELIMUMAB IN ADVANCED HEPATOCELLULAR CARCINOMA: A CASE REPORT

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Background and Importance

Durvalumab and tremelimumab are monoclonal antibodies used as first-line systemic immunotherapy for advanced hepatocellular carcinoma (HCC). These agents are known to cause immune-mediated adverse drug reactions (ADRs), including severe pneumonitis, which can be life-threatening. Published reports on fatal autoimmune pneumonitis following this combination in HCC patients remain scarce. This case report describes a case of immune-mediated pneumonitis with fatal outcome.

Material and methods

In 06/2025, the patient began treatment with tremelimumab and durvalumab. Three weeks after the first cycle he developed cough and desaturation. When evaluated in the clinic for the second cycle of therapy, the patient was heavily symptomatic and was sent to ER. He underwent bronchoscopy and TC-scan revealing a bilateral interstitial pneumonitis. High-dose methylprednisolone and broad-spectrum antibiotics were initiated. Despite therapy, progressive respiratory failure required invasive ventilation in the ICU (07/2025). A clinical pharmacological evaluation was performed through a detailed medication review to identify potential drug interactions.

Time line

Jun 2025



Jul 2025

Section 5: Patient Safety and Quality Assurance

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Aim and objectives

A 58-year-old male with obesity (history of sleeve gastrectomy), resolved diabetes and hypertension), NSAID allergy, and prior heavy smoking was diagnosed with a nodule of HCC in 11/2024 following investigations for abnormal liver function tests. After multidisciplinary evaluation, he underwent transarterial radioembolisation (TARE) as neoadjuvant treatment to surgery (01/2025). In the following month he experienced atrial fibrillation and a right-sided lacunar stroke, requiring apixaban. Further cardiac assessment in 05/2025 did not reveal significant coronary disease. HCC reevaluation after TARE showed disease progression.

RESULTS

- ✓ Despite therapies and respiratory support, the patient's condition deteriorated.
- ✓ Radiologic follow-up revealed increasing pulmonary consolidation, pericardial effusion, ascites, and further worsening of HCC (TC-scan on 15/07/2025).
- ✓ Further escalation of vital support was excluded after multidisciplinary evaluation and the patient died on 18/07/2025.
- ✓ The Naranjo algorithm scored 6, indicating a probable causality for an immune-mediated ADR. No alternative causal factors emerged.

Naranjo's algorithm			
Question	Yes	No	Don't Know
1. Are there previous <i>conclusive</i> reports on this reaction?	+1	0	0
2. Did the adverse event appear when the suspected drug was administered?	+2	-1	0
3. Did the adverse reaction improve when the drug was discontinued or a specific antagonist was administered?	+1	0	0
4. Did the adverse reaction reappear when the drug was readministered?	+2	-1	0
5. Are there alternative causes (other than the drug) that could on their own have caused the reaction?	-1	+2	0
6. Did the reaction reappear when a placebo was given?	-1	+1	0
7. Was the drug detected in the blood (or other fluids) in concentrations known to be toxic?	+1	0	0
8. Was the reaction more severe when the dose was increased, or less severe when the dose was decreased?	+1	0	0
9. Did the patient have a similar reaction to the same or similar drugs in any previous exposure?	+1	0	0
10. Was the adverse event confirmed by any objective evidence?	+1	0	0
Total Score	6		

The total score calculated from this table defines the category an adverse reaction belongs to. The categories are defined as follows:

Definite (Certain)	(total score >5)
Probable	(total score 5-6)
Possible	(total score 1-4)
Doubtful (Unlikely)	(total score <1)

Conclusion and relevance

This case details fatal immune-mediated pneumonitis as an adverse reaction to tremelimumab and durvalumab in HCC. The chronology, diagnostic exclusion, pharmacovigilance actions and medication review collectively reinforce the evidence for an immune-mediated mechanism. This case highlights the role of pharmacovigilance and systematic medication review in identifying and managing serious ADRs during cancer immunotherapy to enhance patient safety in these clinical settings.

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