Peertechz

CLINICAL GROUP

INTERNATIONAL JOURNAL OF Oral and Craniofacial Science OPEN ACCESS JOURNAL

ISSN: 2455-4634 DOI: https://dx.doi.org/10.17352/ijocs

Research Article

# Tolerance to First-Line Immunotherapy in Elderly Patients with Advanced Solid Tumours

**Angelina Towadros, Sandra Boles, Salman Anwar and Dalia Kamel***

Medical Oncology, St Vincent University, Ireland

**Received:** 17 November, 2025
**Accepted:** 02 December, 2025
**Published:** 03 December, 2025

***Corresponding author:** Dalia Kamel, Medical Oncology, St Vincent University, Ireland,
E-mail: dsskamel@hotmail.com

**Keywords:** Immunotherapy; Geriatric oncology; Immune-related adverse events; Immune-senescence; Checkpoint inhibitors; Treatment tolerance; Treatment outcomes; Real-world data



https://www.organscigroup.us

Check for updates

## Abstract

**Aim of the study:** This review examines how ageing-related changes in the immune system impact the response to immunotherapy and assesses the potential challenges to treatment tolerance in elderly patients.

**Methodology:** This is a retrospective study of patients with advanced solid cancer treated at Blackrock and St Vincent Private Hospital with immunotherapy as first line in elderly patients. An electronic database search identified patients treated with monotherapy between March 2024 and February 2025. We collected demographics, treatment details, baseline laboratory investigations, adverse events and the outcome of disease for each patient. Data were analysed to determine associations between therapy, clinical characteristics, and baseline laboratory investigations related to disease outcome using the chi-square test and independent samples t-tests.

**Results:** We identified 17 elderly patients with advanced solid cancers who received immunotherapy as first-line systemic treatment. The mean age of the cohort was 77 ± 11 years, with 12 (70%) males. In terms of Eastern Cooperative Oncology Group (ECOG) performance status, 4 (24%) had an ECOG score of 0, 7 (41%) had an ECOG score of 1, and 6 (35%) had an ECOG score of 2. Additionally, 13 (76%) of the patients had pre-existing comorbidities. The cancer types included 6 (36%) head and neck cancer, 4 (24%) malignant melanoma, 4 (24%) renal cell carcinoma, 2 (11%) lung cancers, and 1 (5%) colon cancer. Radical surgery was offered to 6 (35%) patients, radical radiotherapy to 7 (41%), and concomitant chemotherapy to 4 (24%). The mean duration of immunotherapy was 65 weeks (ranging from 5 to 292 weeks). Among the patients, 11 (64%) experienced autoimmune side effects, with 3 (17%) reporting more than one side effect. The most common adverse effects included fatigue in 6 (35%), skin rash of grades 1-2 in 3 (17%), hypothyroidism in 3 (17%), diarrhoea in 3 (17%), and arthralgia in 1 (5%). The severity of side effects was classified as grade 1 in 6 (35%) patients, grade 2 in 9 (52%), and grade 3 in 1 (5%). Four patients (24%) discontinued immunotherapy, with 3 (17%) due to disease progression and 1 (5%) due to toxicity. Notably, there was no significant difference in demographics, treatment modalities or laboratory findings between patients who experienced adverse events and those who did not.

## Introduction

Cancer incidence increases drastically with age [1]. Of the many possible reasons for this, there is the accumulation of senescent cells in tissues and the loss of function and proliferation potential of immune cells, often referred to as immuno-senescence. With the global ageing population on the rise, the efficacy, tolerance, and response to immunotherapy in geriatric patients remain a critical area of investigation. Ageing is associated with immune-senescence, which may influence immune checkpoint inhibitors' (ICIs) effectiveness and safety profiles [2-4].

Clinical studies indicate that while older patients can benefit from immunotherapy, their response rates and adverse effects may differ from those observed in younger cohorts [5-7]. Additionally, comorbidities and polypharmacy are frequently seen in geriatric patients, complicating treatment regimens, increasing the risk of immune-related adverse events (irAEs) [8].

## Methodology

This retrospective study examined the outcomes of elderly patients with advanced solid cancer who received immunotherapy as first-line treatment at Blackrock and St



**Citation:** Towadros A, Boles S, Anwar S, Kamel D. Tolerance to First-Line Immunotherapy in Elderly Patients with Advanced Solid Tumours. Int J Oral Craniofac Sci. 2025;11(1):004-007. DOI: https://dx.doi.org/10.17352/2455-4634.000066

Vincent Private Hospital. We conducted an electronic database search to identify patients treated with immunotherapy as a monotherapy between March 2024 and February 2025.

For each patient, data were collected on demographics, treatment details, baseline laboratory results, adverse events, and disease outcomes. We analysed the data to explore potential associations between immunotherapy, clinical characteristics, and baseline laboratory investigations in relation to disease outcome. Statistical analysis included chi-square tests and independent samples t-tests to identify significant relationships between these factors.

## Results

We identified 17 elderly patients with advanced solid cancers who received immunotherapy as first-line systemic treatment. The mean age of the cohort was 77 ± 11 years, with 12 (70%) males. In terms of Eastern Cooperative Oncology Group (ECOG) performance status, 4 (24%) had an ECOG score of 0, 7 (41%) had an ECOG score of 1, and 6 (35%) had an ECOG score of 2. Additionally, 13 (76%) of the patients had pre-existing comorbidities. The cancer types included 6 (36%) head and neck cancer, 4 (24%) malignant melanoma, 4 (24%) renal cell carcinoma, 2 (11%) lung cancers, and 1 (5%) colon cancer. Radical surgery was offered to 6 (35%) patients, radical radiotherapy to 7 (41%), and concomitant chemotherapy to 4 (24%). The mean duration of immunotherapy was 65 weeks (ranging from 5 to 292 weeks) (Table 1).

Among the patients, 11 (64%) experienced autoimmune side effects, with 3 (17%) reporting more than one side effect. The most common adverse effects included fatigue in 6 (35%), skin rash of grades 1-2 in 3 (17%), hypothyroidism in 3 (17%), diarrhoea in 3 (17%), and arthralgia in 1 (5%). The severity of side effects was classified as grade 1 in 6 (35%) patients, grade 2 in 9 (52%), and grade 3 in 1 (5%). Four patients (24%) discontinued immunotherapy, with 3 (17%) due to disease progression and 1 (5%) due to toxicity. Notably, there was no significant difference in demographics, treatment modalities or laboratory findings between patients who experienced adverse events and those who did not (Table 2).

**Table 1:** Patients' demographics and types of solid cancer.

| Parameters | Value |
|---|---|
| Total number | 17 |
| Mean age | 77±11 years |
| Males | 12 (70%) |
| Females | |
| ECOG 0 | 4 (24%) |
| ECOG 1 | 7 (41%) |
| ECOG 2 | 6 (35%) |
| Pre-existing co-morbidities | 13 (76%) |
| Head and neck cancer | 6 (36%) |
| Malignant melanoma | 4 (24%) |
| Renal cell cancer | 4 (24%) |
| Lung cancer | 2 (11%) |
| Colon cancer | 1 (5%) |

**Table 2:** Immunotherapy duration and immune-related adverse events.

| Mean duration | 65 weeks (5-292 weeks) |
|---|---|
| Discontinuation due to adverse events | 1 (5%) |
| Discontinuation Due to Progression | 3 (17%) |
| All autoimmune events | 11 (64%) |
| Grade 1 | 6 (35%) |
| Grade 2 | 9 (52%) |
| Grade 3 | 1 (5%) |
| Fatigue | 6 (35%) |
| Skin rash | 3 (17%) |
| Hypothyroidism | 3 (17%) |
| Diarrhoea | 3 (17%) |
| Arthralgia | 1 (5%) |

## Discussion

This study investigated the tolerance and side effects of first-line immunotherapy in elderly patients with advanced solid tumours. While elderly patients could tolerate immunotherapy for extended periods, 64% experienced autoimmune side effects. Notably, these side effects were generally mild to moderate, though some patients (5%) discontinued treatment due to severe toxicity. This real-world data highlights the potential for immunotherapy in geriatric oncology, with a need for close monitoring.

This study highlights the impact of immune-senescence — the age-related decline in immune system function — that may influence both the therapeutic response to immune checkpoint inhibitors (ICIs) and the profile of irAEs. As patients age, immune functions diminish, leading to the accumulation of senescent immune cells, reduced naïve T-cell reserves, and altered immune regulation. These age-related changes may not necessarily increase the severity of toxicity but could influence the type and timing of immune-related adverse events. Emerging evidence also suggests that older adults may experience different patterns of irAEs (e.g., more endocrine and cutaneous events), whereas younger patients may have more gastrointestinal or hepatic irAEs, highlighting age-related variability in toxicity presentation [9].

In our cohort, 11 (64%) patients developed irAEs, which underscores that, while older adults can benefit from immunotherapy, vigilance in monitoring remains key. While some real-world data in older adult ICI recipients show no significant increase in high-grade toxicity or treatment discontinuation across age groups [1], other reviews highlight that immuno-senescence may contribute to distinct patterns of irAEs in elderly patients [10]. More recent real-world studies further support this, showing that frailty, comorbidities, and immune function—rather than chronological age—play a greater role in predicting toxicity and treatment outcomes [11,12].

Together, these findings suggest that chronological age alone is insufficient to predict safety; rather, comprehensive assessment of immune reserve, functional status, and comorbidity should inform the use of ICIs in older adults.



**Citation:** Towadros A, Boles S, Anwar S, Kamel D. Tolerance to First-Line Immunotherapy in Elderly Patients with Advanced Solid Tumours. Int J Oral Craniofac Sci. 2025;11(1):004-007. DOI: https://dx.doi.org/10.17352/2455-4634.000066

A major challenge identified in this study is the frequent presence of comorbidities in elderly patients, with 13/17 76% of the cohort having pre-existing conditions. This high rate is clinically important because multiple chronic illnesses complicate treatment regimens and may increase susceptibility to immune-related adverse events (irAEs) [8,13]. The presence of comorbidities, combined with polypharmacy, can exacerbate treatment complications, making the management of adverse effects more difficult.

Our findings align with previous research emphasising the importance of individualised treatment in older adults. Yildiz et al reported that most geriatric cancer patients receiving immunotherapy have significant comorbidities and that treatment decisions should account for overall health status rather than chronological age alone [3]. Similarly, Granier et al discussed how age-related immune changes, frailty, and comorbid conditions necessitate a tailored approach to immunotherapy, as older patients often differ from those represented in clinical trials [14]. Collectively, these observations support the need for personalised, comorbidity-aware, and polypharmacy-conscious treatment strategies to balance efficacy with safety in elderly cancer patients.

In our cohort, 11/17 (64%) patients experienced immune-related adverse events (irAEs)—most commonly fatigue (6/17, 35%), skin rash (3/17, 17%; grades 1–2), hypothyroidism (3/17, 17%), diarrhoea (3/17, 17%), and arthralgia (1/17, 5%). Most irAEs were grade 1–2, and only 1/17 (5%) patients had a grade ≥ 3 adverse event. These findings are consistent with prior studies in older adults receiving ICIs, which generally report similar overall and high-grade toxicity compared with younger patients [6,15].

In our study, adverse-event incidence did not differ by demographics, treatment modality, or baseline laboratory parameters. Importantly, emerging evidence indicates that chronological age alone does not dictate irAE risk; functional vulnerability and certain patient-level factors may be more informative [11,12]. These data support close monitoring and individualised toxicity management in older adults to sustain treatment adherence and outcomes.

A notable finding from this study is that 24% of patients discontinued treatment, primarily due to disease progression (17%) and toxicity (5%). This discontinuation rate is comparable to other studies examining immunotherapy in older populations, such as Elkrief, et al. who observed that elderly patients are more likely to discontinue treatment due to toxicity [5].

While the rate of discontinuation in our cohort was not markedly high, even a small percentage of toxicity-related discontinuations underscores the importance of close monitoring and early detection of immune-related adverse events (irAEs) to improve treatment adherence and overall patient outcomes [16]. An additional aspect that may influence treatment outcomes in elderly patients is the type of ICI used, treatment cycles, and the lack of standardised biomarker use in this population. Emerging studies suggest that these variables may predict both toxicity patterns and response rates, yet such data remain limited in older cohorts [7].

### Study limitations and areas for future research

This study has some notable limitations that should be considered when interpreting the findings. The retrospective design is a key limitation, as it is prone to biases associated with the use of existing patient data, such as incomplete records or inconsistencies in how information was recorded. Additionally, the small sample size of only 17 patients reduces the statistical power of the study and limits its ability to generalise the results to a broader elderly cancer population. To confirm the findings and improve their applicability, larger, prospective studies with more diverse patient cohorts are necessary.

Further research should aim to identify predictive biomarkers that could help identify elderly patients at higher risk of severe immune-related adverse events (irAEs). Biomarkers that predict adverse outcomes would allow clinicians to tailor immunotherapy regimens more effectively, reducing the incidence of toxicity while maintaining efficacy. Moreover, exploring ways to optimise treatment schedules for elderly patients, adjusting dosages or treatment frequency to account for age-related changes in drug metabolism and immune function, could improve tolerance and minimise side effects.

Another critical area for future research is polypharmacy, which is common in elderly patients. Polypharmacy increases the risk of drug interactions and complicates the management of cancer treatment. Research into simplifying medication regimens or finding safer alternatives for comorbidities could significantly improve the overall safety and effectiveness of immunotherapy. Additionally, closer monitoring of comorbid conditions is crucial, as they can affect how elderly patients respond to immunotherapy and exacerbate adverse effects.

## Conclusion

In conclusion, this study offers valuable insights into the use of first-line immunotherapy in elderly patients with advanced solid tumours. While many elderly patients tolerate immunotherapy well, autoimmune-related side effects remain a significant challenge. As the ageing population grows and immunotherapy becomes more common in oncology, further research is crucial to refine treatment strategies for older patients. This will help maximise the therapeutic benefits of immunotherapy while minimising associated risks.

This study suggests that elderly patients receiving immunotherapy for advanced solid cancers can tolerate the treatment for an extended period (mean 65 weeks), although a majority (64%) develop autoimmune side effects. While these effects were mostly mild to moderate, a small percentage (5%) developed severe toxicity, leading to treatment discontinuation in some cases (24%).

This highlights the need for close monitoring but supports immunotherapy feasibility in elderly cancer patients.



**Citation:** Towadros A, Boles S, Anwar S, Kamel D. Tolerance to First-Line Immunotherapy in Elderly Patients with Advanced Solid Tumours. Int J Oral Craniofac Sci. 2025;11(1):004-007. DOI: https://dx.doi.org/10.17352/2455-4634.000066

This 'real-world' data can provide a foundation for further research into predicting tolerance to immunotherapy in elderly cancer patients.

## References


1. Samani A, Zhang S, Spiers L, Suwaidan AA, Merrick S, Tippu Z, et al. Impact of age on the toxicity of immune checkpoint inhibition. J Immunother Cancer. 2020;8(2):e000871. Available from: https://jitc.bmj.com/content/8/2/e000871

2. Abraham G, Jobanputra K, Noronha V, Patil VM, Menon NS, Gattani SC, et al. Immune checkpoint inhibitors in older patients with solid tumours: real-world experience from India. Cancer Res Stat Treat. 2021;4(2):270–276. Available from: https://journals.lww.com/crst/fulltext/2021/04000/immune_checkpoint_inhibitors_in_older_patients.15.aspx

3. Yildiz B, Acar R. Immunotherapy in geriatric patients with advanced cancer. EJMO. 2020;4(3):209-214. Available from: https://www.ejmo.org/10.14744/ejmo.2020.44446

4. Guégan M, Bichon M, Chaput N, Houot R, Lemoine J. Cancer immunotherapy in elderly patients: The concept of immune senescence challenged by clinical experience. Eur J Cancer. 2024;214:115145. Available from: https://www.sciencedirect.com/science/article/pii/S0959804924000202

5. Elkrief A, Richard C, Malo J, Cvetkovic L, Florescu M, Blais N, et al. Efficacy of immune checkpoint inhibitors in older patients with non-small cell lung cancer: real-world data from multicentric cohorts in Canada and France. J Geriatr Oncol. 2020;11(5):802-806. Available from: https://www.sciencedirect.com/science/article/pii/S1879406820300146

6. Betof AS, Nipp RD, Giobbie-Hurder A, Johnpulle RAN, Rubin K, Rubinstein SM, et al. Impact of age on outcomes with immunotherapy for patients with melanoma. Oncologist. 2017;22(8):963–971. Available from: https://theoncologist.onlinelibrary.wiley.com/doi/10.1634/theoncologist.2016-0450

7. Elias R, Giobbie-Hurder A, McCleary NJ, Ott P, Hodi FS, Rahma O. Efficacy of PD-1 & PD-L1 inhibitors in older adults: a meta-analysis. J Immunother Cancer. 2018;6(1):26. Available from: https://jitc.bmj.com/content/6/1/26

8. Tran Van Hoi N, Fabbri E, Basso U, Cortiula F, Esposito G, Calvetti L, et al. Toxicity in older patients with cancer receiving immunotherapy: an observational study. Drugs Ageing. 2024;41(3):215-225. Available from: https://link.springer.com/article/10.1007/s40266-024-01114-z

9. Hakozaki T, Hosomi Y, Fujimoto D. Differential immune-related adverse events between younger and older patients treated with PD-1/PD-L1 inhibitors: a real-world cohort study. Front Oncol. 2021;11:619385. Available from: https://www.frontiersin.org/articles/10.3389/fonc.2021.619385

10. Gao J, Yuan Y, Wang X, He L, Li L. Impact of immunosenescence on immune-related adverse events in elderly patients with cancer. Aging Med. 2025;8(1):e70000. Available from: https://onlinelibrary.wiley.com/doi/10.1002/agm2.70000

11. Johns AC, Yang M, Wei L, Grogan M, Spakowicz D, Patel SH, et al. Risk factors for immune checkpoint inhibitor immunotherapy toxicity among older adults with cancer. Oncologist. 2023;28(8):e625-e632. Available from: https://academic.oup.com/oncolo/article/28/8/e625/7239216

12. Matsukane R, Oyama T, Tatsuta R, Kimura S, Hata K, Urata S, et al. Real-world prevalence and tolerability of immune-related adverse events in older adults with non-small cell lung cancer: a multi-institutional retrospective study. Cancers (Basel). 2024;16(11):2159. Available from: https://www.mdpi.com/2072-6694/16/11/2159

13. Rong Y, Bentley JP, Bhattacharya K, Yang Y, Chang Y, Earl S, et al. Incidence and risk factors of immune-related adverse events in older cancer patients: a multicenter retrospective study. Cancer Med. 2024;13(14):16147-16158. Available from: https://onlinelibrary.wiley.com/doi/10.1002/cam4.6879

14. Granier C, Gey A, Roncelin S, Weiss L, Paillaud E, Tartour E. Immunotherapy in older patients with cancer. Biomed J. 2020;43(4):435-442. Available from: https://www.sciencedirect.com/science/article/pii/S2319417020301086

15. Elias R, Morales J, Rehman Y, Khurshid H. Immune-related adverse events and their management in older adults receiving immune checkpoint inhibitors. J Geriatr Oncol. 2018;9(5):421-427. Available from: https://www.sciencedirect.com/science/article/pii/S1879406818300877

16. Noronha V, Abraham G, Patil V, Joshi A, Menon N, Mahajan A, et al. Real-world data of immune checkpoint inhibitors in solid tumours from India. Cancer Med. 2021;10(5):1525-1534. Available from: https://onlinelibrary.wiley.com/doi/10.1002/cam4.3617






**Citation:** Towadros A, Boles S, Anwar S, Kamel D. Tolerance to First-Line Immunotherapy in Elderly Patients with Advanced Solid Tumours. Int J Oral Craniofac Sci. 2025;11(1):004-007. DOI: https://dx.doi.org/10.17352/2455-4634.000066