Inpatient Adverse Event (AE) Management Costs Associated with Immune Checkpoint Inhibitors (ICI) Approved for Various Advanced or Metastatic Cancers in the UK

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Introduction & Objective

- Immune checkpoint inhibitors (ICIs) enhance the immune system's ability to target tumors by modulating key regulatory pathways, significantly improving survival in patients with advanced and metastatic cancers. Currently, both the Medicines and Healthcare products Regulatory Agency (MHRA) and European Medicines Agency (EMA) has approved twelve ICIs for treating various malignancies.(1-3)
- ICIs are however associated with adverse events (AEs) of varying severity, which can impact patient quality of life and impose substantial financial burdens on healthcare systems.(4,5) Managing these AEs presents clinical challenges, often necessitating additional medical interventions and increasing healthcare costs.
- Existing studies indicate that AE-related costs vary due to factors such as event type and severity, the specific ICI used, and the cancer type being treated. However, comprehensive comparisons of these costs across different cancers remain limited. A systematic evaluation is essential to inform evidence-based clinical decision-making and healthcare policies.(6)
- This study assessed the economic burden associated with managing AEs in patients receiving ICIs for advanced or metastatic cancers in the United Kingdom (UK).

Methods

- The AE management costs for each ICI regimen were calculated by multiplying the frequency of each AE by its respective unit management cost and summing across all reported AEs. The analysis focused exclusively on grade 3–4 AEs, as lower-grade (grade 1–2) AEs do not typically result in substantial healthcare costs.
- The analysis included all MHRA-approved ICIs, with frequency of grade 3–4 AEs extracted from published data of registrational clinical trials cited in the product labels. These trials, conducted for each ICI regimen within its approved cancer indication, provide key insights into the safety profile and incidence rates of severe AEs.
- To standardize cost estimations and reflect the clinical burden associated with severe AEs requiring intensive medical management, it was assumed that all grade 3–4 AEs require hospitalization
- Unit hospitalization costs for each AE were obtained from NHS England's National Cost Collection dataset.(7) Inpatient stays associated with each AE were identified using NHS healthcare resource groups (HRGs) and relevant coding classifications, leveraging codes from previous NICE submissions. Unit costs were calculated using weighted averages of short- and long-duration non-elective inpatient stays to ensure accurate cost estimation.

Results

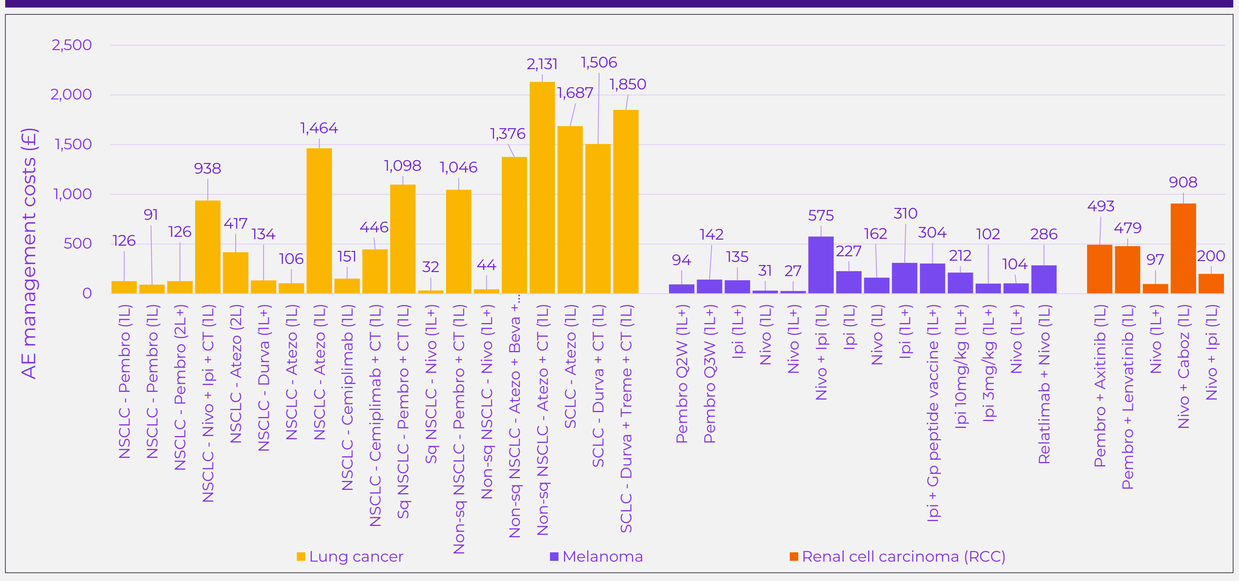
- The analysis revealed a broad spectrum of inpatient AE management costs across MHRA-approved ICI regimens, with substantial variability seen by cancer type, treatment regimen, and the frequency of grade 3–4 toxicities observed in registrational trials (Table 1).
- Overall, combination regimens, particularly those incorporating dual ICIs or ICIs with chemotherapy or targeted agents, were consistently associated with elevated inpatient AE costs (Figure 1 and Figure 2).

Table 1: Key AEs of ICI treatments

Indication	Most frequent grade 3-4 AEs
NSCLC (8-17)	Neutropenia, pneumonia, dyspnea, anemia
NSCLC squamous (18, 19)	Anemia, neutropenia, fatigue/asthenia
NSCLC non-squamous (20-23)	Neutropenia, anemia, thrombocytopenia
SCLC (24, 25)	Neutropenia, anemia
Melanoma (26, 32)	diarrhea, colitis, fatigue/asthenia
Renal cell carcinoma (33-37)	Hypertension, diarrhea, ALT increase
HCC(38-39)	Hypertension, AST/ALT increase, lipase increased
CRC (40)	Hypertension, abdominal pain, fatigue/asthenia
Esophageal carcinoma (41)	Neutropenia, anemia, leukopenia/lymphocytopenia/white blood cell decreased
ESCC (42, 43)	Anemia, decreased neutrophil count, decreased appetite
BTC (44, 45)	Decreased neutrophil count, anemia, neutropenia
Endometrial cancer (46, 47)	Hypertension, neutropenia, anemia
GEJ (48-50)	Anemia, thrombocytopenia/platelet count decreased, decreased neutrophil count
Urothelial cancer (51-55)	Anemia, fatigue/asthenia
R/M CC (56, 57)	Anemia, neutropenia, hypertension
TNBC (58, 59)	Neutropenia, decreased neutrophil count, anemia
HNSCC (60-62)	Anemia, neutropenia, fatigue/asthenia
cHL (63)	Pneumonitis, pneumonia, neutropenia
MPM(64)	Lipase increased, diarrhea, colitis

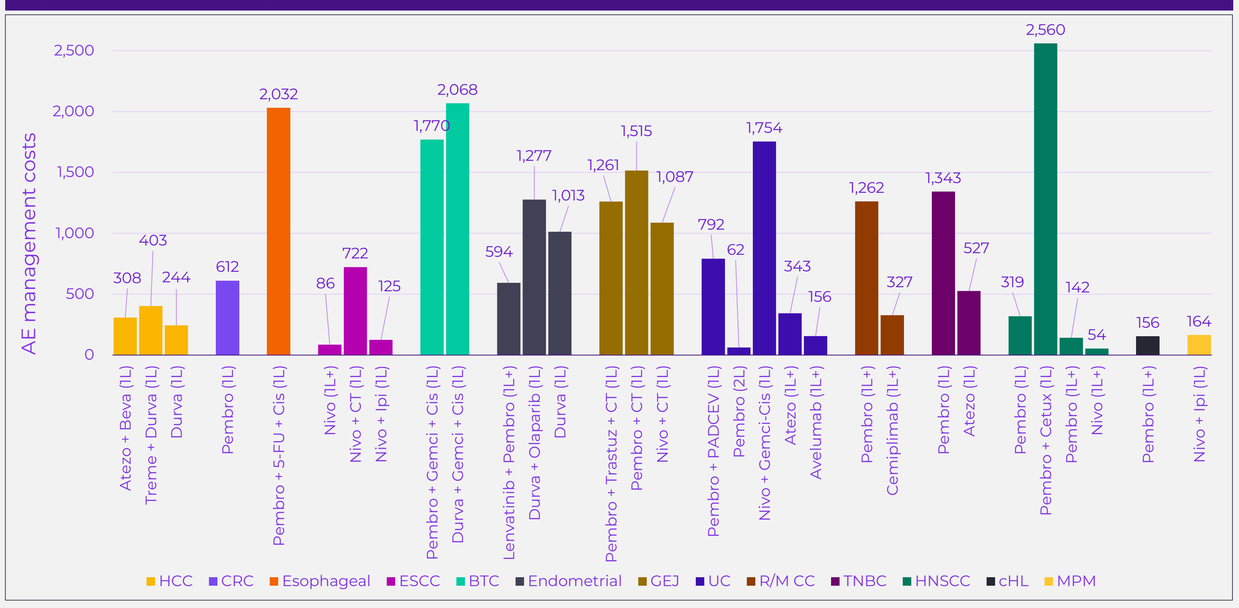
Abbreviations: BTC: Biliary tract carcinoma; cHL: classic Hodgkin Lymphoma; CRC: Colorectal cancer; ESCC: Esophageal squamous cell carcinoma; GEJ: Gastroesophageal junction; HCC: Hepatocellular carcinoma; HNSCC: Head and neck squamous cell carcinoma; MPM: Malignant Pleural Mesothelioma; NSCLC: Non-small cell lung cancer; R/M CC: Recurrent and metastatic cervical cancer; SCLC: Small cell lung cancer; TNBC: Triple negative breast cancer; UC: Urothelial cancer

Figure 1: AE management costs of ICI treatments approved in lung cancer, melanoma and RCC



Abbreviations: Atezo: Atezolizumab; Beva: Bevacizumab; Caboz: Cabozantinib; CT: Chemotherapy; Durva: Durvalumab; Ipi: Ipilimumab; Nivo: Nivolumab; NSCLC: Non-small cell lung cancer; Pacli: Paclitaxel; Pembro: Pembrolizumab; Q2W/Q3W: Once every 2/3 weeks; SCLC: Small cell lung cancer; Sq: Squamous; Treme: Tremelimumab; 1L: First line; 2L: Second line

Figure 2: AE management costs of ICI treatments approved in other cancers



Abbreviations: Atezo: Atezolizumab; Beva: Bevacizumab; BTC: Biliary tract carcinoma; Cetux: Cetuximab; cHL: classic Hodgkin Lymphoma; Cis: Cisplatin; CRC: Colorectal cancer; CT: Chemotherapy; Durva: Durvalumab; ESCC: Esophageal squamous cell carcinoma; GEJ: Gastroesophageal junction; Gemci: Gemcitabine; HCC: Hepatocellular carcinoma; HNSCC: Head and neck squamous cell carcinoma; Ipi: Ipilimumab; MPM: Malignant Pleural Mesothelioma; Nivo: Nivolumab; Pembro: Pembrolizumab; R/M CC: Recurrent and metastatic cervical cancer; TNBC: Triple negative breast cancer; Trastuz: Trastuzumab; Treme: Tremelimumab; UC: Urothelial cancer; 1L: First line; 2L: Second line

Conclusion

- AE management costs for ICI therapies vary by regimen and cancer type, with hematologic and cardiovascular toxicities frequently observed across indications.
- Combination regimens, particularly those involving dual immunotherapy or immunotherapy plus chemotherapy or targeted agents, are consistently associated with higher AE costs, underscoring the trade-off between clinical benefit and toxicity burden.
- These findings highlight the importance of considering AE management costs when selecting ICI regimens for cancer treatment

References

1. He X et al. Cell Res. 2020;30(8):660-9; 2. Shiravand Y et al. Curr Oncol. 2022;29(5):3044-60; 3. Marin-Acevedo JA et al. J Hematol Oncol. 2021;14:1-29; 4. Martins F et al. Nat Rev Clin Oncol. 2019;16(9):563-80; 5. George S et al. Oncologist. 2021;26(7):e1205-15; 6. Brahmer JR et al. N Engl J Med. 2012;366(26):2455-65; 7. National cost collection data publication: national schedule 2023/24 [Internet]. London: NHS England; [cited 2025 Feb 19]. Available from: https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/; 8. Reck M et al. N Engl J Med. 2016;375(19):1823-33; 9. Mok TS et al. Lancet. 2019;393(10183):1819-30; 10. Herbst RS et al. J Thorac Oncol. 2021;16(10):1718-1732; 11. Paz-Ares L et al. Lancet Oncol. 2021;22(2):198-211; 12. Rittmeyer A et al. Lancet. 2017;389(10066):255-65; 13. Antonia SJ et al. N Engl J Med. 2017;377(20):1919-29; 14. Herbst RS et al. N Engl J Med. 2020;383(14):1328-39; 15. Lee SM et al. Lancet. 2023;402(10400):451-63; 16. Sezer A et al. Lancet. 2021;397(10274):592-604; 17. Gogishvili M et al. Nat Med. 2022;28(11):2374-80; 18. Paz-Ares L et al. N Engl J Med. 2018;379(21):2040-51; 19. Brahmer J et al. N Engl J Med. 2015;373(2):123-35; 20. Gandhi L et al. N Engl J Med. 2018;378(22):2078-92; 21. Borghaei H et al. N Engl J Med. 2015;373(17):1627-39; 22. Socinski MA et al. N Engl J Med. 2018;378(24):2288-301; 23. West H et al. Lancet Oncol. 2019;20(7):924-37; 24. Horn L et al. N Engl J Med. 2018;379(23):2220-9; 25. Goldman JW et al. Lancet Oncol. 2021;22(1):51-65; 26. Robert C et al. N Engl J Med. 2015;372(26):2521-32; 27. Robert C et al. N Engl J Med. 2015;372(4):320-30; 28. Weber JS et al. Lancet Oncol. 2015;16(4):375-84; 29. Larkin J et al. N Engl J Med. 2019;381(16):1535-46; 30. Hodi FS et al. N Engl J Med. 2010;363(8):711-23; 31. Ascierto PA et al. J Immunother Cancer. 2020;8(1); 32. Tawbi HA et al. N Engl J Med. 2022;386(1):24-34; 33. Rini BI et al. N Engl J Med. 2019;380(12):1116-27; 34. Motzer RJ et al. N Engl J Med. 2021;384(14):1289-300; 35. Motzer RJ et al. N Engl J Med. 2015;373(19):1803-13; 36. Choueiri TK et al. N Engl J Med. 2021;384(9):829-41; 37. Motzer RJ et al. N Engl J Med. 2019;380(12):1103-15; 38. Finn RS et al. N Engl J Med. 2020;382(20):1894-905; 39. Abou-Alfa GK et al. NEJM Evidence. 2022;1(8); 40. André T et al. N Engl J Med. 2020;383(23):2207-18; 41. Janjigian YY et al. Nature. 600(7890):727-30; 42. Rha SY et al. Lancet Oncology. 24(11):1181-1195; 43. Janjigian YY et al. Lancet. 2021;398(10294):27-40; 44. Sun J et al. Lancet. 2021;398(10302):759-71; 45. Kato K et al. Lancet Oncol. 2019;20(11):1506-17; 46. Doki Y et al. N Engl J Med. 2022;386(5):449-62; 47. Kelley RK et al. Lancet. 2023;401(10391):1853-65; 48. Oh DY et al. NEJM Evidence. 2022;1(8); 49. Makker V et al. N Engl J Med. 2022;386(5):437-48; 50. Westin SN et al. J Clin Oncol. 2024;42(3):283-99; 51. Powles T et al. N Engl J Med. 2024;390(10):875-88; 52. Bellmunt J et al. N Engl J Med. 2017;376(11):1015-26; 53. Van Der Heijden M et al. N Engl J Med. 2023;389(19):1778-89; 54. Van Der Heijden M et al. European Urology. 2021;80(1):7-11; 55. Powles T et al. N Engl J Med. 2020;383(13):1218-30; 56. Colombo N et al. N Engl J Med. 2021;385(20):1856-67; 57. Tewari K et al. N Engl J Med. 2022;386(6):544-55; 58. Cortes J et al. N Engl J Med. 2022;387(3):217-26; 59. Schmid P et al. N Engl J Med. 2018;379(22):2108-21; 60. Burtness B et al. Lancet. 2019;394(10212):1915-28; 61. Cohen EE et al. Lancet. 2019;393(10167):156-67; 62. Ferris RL et al. N Engl J Med. 2016;375(19):1856-67; 63. Kuruvilla J et al. Lancet Oncol. 2021;22(4):512-24; 64. Baas P et al. Lancet. 2021;397(10272):375-86.

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