VIA MEDICA

CASE REPORT

Anna Grenda[1], Ewelina Iwan[2], Paweł Krawczyk[1], Arkadiusz Bomba[2], Izabela Chmielewska[1], Katarzyna Bielińska[2], Aleksandra Grzywna[1], Michał Szczyrek[1], Tomasz Jankowski[1], Robert Kieszko[1], Natalia Galant[1], Janusz Milanowski[1]

[1]Department of Pneumonology, Oncology and Allergology, Medical University of Lublin, Poland
[2]Department of Omics Analysis, National Veterinary Research Institute, Pulawy, Poland

Association between gut microbiome components and immunotherapy efficacy in two small cell lung cancer cases with divergent outcomes

Address for correspondence:
Anna Grenda, PhD
Department of Pneumonology, Oncology and Allergology, Medical University of Lublin
ul. Jaczewskiego 8, 20–950 Lublin, Poland
e-mail: anna.grenda@umlub.pl

Oncology in Clinical Practice
DOI: 10.5603/ocp.105103

ISSN 2450–1654
e-ISSN 2450–6478

ABSTRACT

Introduction. Immunotherapy can be effective in some patients with small-cell lung cancer (SCLC) with good performance status. However, the factors contributing to sustained treatment responses remain unclear. The intestinal microbiome profile has emerged as a potential biomarker for the effectiveness of chemoimmunotherapy in SCLC. Evidence suggests that microbiome diversity, both in richness and abundance, may influence immunotherapy outcomes. The presence or absence of specific bacterial populations may also be linked to treatment success or failure. This pilot study compared the gut microbiome profile in two SCLC patients with partial responses to chemoimmunotherapy but had distinctly different outcomes.

Material and methods. Metagenomic analysis of the gut microbiome was performed using stool samples from two patients collected prior to treatment initiation. Gut microbiome composition was determined based on next-generation sequencing of the hypervariable regions of the 16S rRNA gene. Both patients received a treatment regimen consisting of atezolizumab, carboplatin and etoposide.

Results. The progression-free survival (PFS) and overall survival (OS) were 5.7 and 10.2 months for the first patient and 19.9 and 34.9 months for the second patient, respectively. The patient with early progression exhibited reduced species-level diversity compared to the long-term responder. Additionally, bacteria from the families *Lachnospiraceae*, *Akkermansiaceae* were found to be more prevalent in the patient with greater immunotherapy benefit. Conversely, the families *Enterobacteriaceae*, *Succinivibrionaceae*, *Streptococcaceae,* and *Desulfovibrionaceae* were more abundant in the patient with short survival than in patients with prolonged response.

Conclusions. Bacteria residing in the gut may affect the efficacy of chemoimmunotherapy in SCLC patients and represents a promising candidate for predictive biomarkers of treatment response and efficacy.

Keywords: microbiome, 16S rRNA, small cell lung cancer, SCLC, immunotherapy

Oncol Clin Pract

Introduction

Lung cancer is classified into two main subtypes: non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC). Small cell lung cancer accounts for approximately 15% of all lung cancer cases and is an aggressive malignancy with rapid progression and poor prognosis. Current chemotherapy regimens show limited effectiveness against SCLC, and disease progression is typically very rapid. The five-year survival rate

Received: 26.02.2025 Accepted: 16.06.2025 Early publication: 04.09.2025

remains low (at around 7%) for both limited (LD) and extensive disease (ED) stages [1–3], and approximately 75% of patients present with advanced or metastatic disease at diagnosis [1, 4, 5]. Given this poor prognosis, the 1year survival rate serves as a more clinically relevant metric, showing modest improvement from 34.4% in 2000 to 38.4% in 2020 [6].

Until recently, the sole therapeutic option available for SCLC patients with extensive disease was debilitating and often ineffective chemotherapy. Currently however, according to IMpower133 and CASPIAN trial results, first-line treatments now include anti-programmed death ligand 1 (PD-L1) immune checkpoint inhibitors (ICIs), such as atezolizumab or durvalumab, in combination with chemotherapy (CTH). These studies have demonstrated that chemoimmunotherapy significantly reduces the risk of disease progression and death compared to chemotherapy alone [7–10].

Despite advancements, SCLC patients are less likely to benefit from chemoimmunotherapy compared to NSCLC cases, likely due to the distinct biological characteristics. Factors influencing the efficacy of immunotherapy in SCLC include tumor mutations burden (TMB), major histocompatibility complex (MHC) class I and PD-L1 expression, tumor infiltration by effector T cells, as well as the presence of myeloid-derived suppressor cells and regulatory T cells, which inhibit immune system activation by ICIs. In addition, SCLC tumors often develop nonvascular areas that exert an immunosuppressive effect and limit lymphocyte and antibody access [11].

Recently, the composition of the gut microbiome has been identified as a factor influencing the success of immunotherapy, though there is limited information available on this topic in SCLC patients [12–14].

Nevertheless, bacteria of the genera *Barnesiella, Butyricimonas* or the family *Lachnospiraceae* have been suggested to protect against SCLC, whereas the genera *Intestinibacter*, *Bilophila, Eubacterium oxidoreducens* group, and the order *Bacillales* have been associated with the development of SCLC [12].

In NSCLC, responders to ICI therapy typically show elevated *Faecalibacterium* counts in their gut microbiota and increased blood levels of short-chain fatty acids (SCFA). Additionally, fecal microbiota transplant (FMT) has been shown to potentially exert anticancer effects, as confirmed in mice [15]. Microbiome is increasingly being considered as a potential biomarker for predicting the efficacy of immunotherapy and a possible target for enhancing treatment outcomes. Strategies of microbiome enrichment via probiotic or prebiotic supplementations, and dietary interventions, are regarded as supportive treatments for immunotherapy [14].

The role of the microbiome in modulating immunotherapy response in SCLC patients is poorly understood. However, emerging evidence suggests its potential utility both as a predictive biomarker for ICI effectiveness and as an adjuvant therapy (such as FMT).

Here, under analysis, are the gut microbial profiles of two SCLC patients who presented partial responses to chemoimmunotherapy but with markedly different progression-free survival (PFS) and overall survival (OS). The present findings highlight distinct microbial signatures that may underlie these differential treatment responses, with particular focus on bacterial taxa whose presence or absence correlates with clinical outcomes.

Material and methods

Patient characteristics

Two patients diagnosed with extensivestage small cell lung cancer (ED-SCLC) received first-line chemoimmunotherapy consisting of carboplatin, etoposide and atezolizumab. Fecal samples were collected before the start of the treatment.

The first patient was a 55-year-old male who was a current cigarette smoker was diagnosed in August 2021 with a tumor in the right lung, accompanied by metastatic lesions in the mediastinal lymph nodes, liver, and spinal canal. The patient remained in good performance status [grade 1, according to the Eastern Cooperative Oncology Group (ECOG)]. He completed four cycles of chemoimmunotherapy, followed by four cycles of atezolizumab monotherapy, both well-tolerated, achieving partial response that transitioned to stable disease. However, central nervous system (CNS) metastases led to disease progression six months after treatment initiation. The patient underwent palliative brain radiotherapy but was deemed ineligible for further systemic treatment. The patient passed away 10 months after starting the treatment, 4.5 months following immunotherapy discontinuation.

The second patient was a 73-year-old male smoker with good performance status diagnosed with ED-SCLC in July 2021. The disease included infiltration of the left lung hilum, lymph node metastases, and left pleural effusion. He underwent four cycles of chemoimmunotherapy, followed by atezolizumab therapy for 24 cycles, which he tolerated well. Partial remission of infiltrative lesions and complete remission of pleural effusion were observed. During immunotherapy, the patient received palliative radiotherapy to the left hilar region. A stable renal mass without histopathological

confirmation was concurrently observed. Local disease progression occurred after 20 months of treatment. The patient was started on second-line chemotherapy with carboplatin and etoposide in March 2023 but received only two cycles due to severe hematologic toxicity, after which treatment was discontinued. The disease remained stable until November 2023 when progression of thoracic lesions and CNS metastases developed. The patient was qualified for CAV (cyclophosphamide, doxorubicin, and vincristine) chemotherapy and whole brain radiotherapy, achieving a partial response.

The patient also received treatment with acyclovir for shingles during the course of therapy. The patient completed four cycles of CAV therapy before discontinuation due to significant clinical deterioration, including deterioration of performance status, grade II anemia and grade I neutropenia. The patient died 35 months after the initiation of chemoimmunotherapy. The interval between immunotherapy progression and death was 15 months, with 4 months elapsing between termination of anticancer treatment and death.

Comparative PFS and OS outcomes for both patients are presented in Figure 1.

16S rRNA sequencing

Stool samples were collected prior to the treatment and stored at –80°C. Sample aliquots (20 mg) were homogenized (FastPrep 24, MP Biomedicals) and pre-treated with a mix of lysozyme (10 μg/ml, A&A Biotechnology) and lysostaphin (2000 U, Sigma-Aldrich) for 30 min at 37°C. Total DNA was isolated using a Maxwell RCS 48 instrument (Promega) with the RSC Tissue DNA Kit (Promega). DNA concentration was measured with a Qubit 3.0 fluorometer (Thermo Fisher Scientific) using the High Sensitivity DNA Assay (Thermo Fisher Scientific).

Sequencing libraries were prepared from 15 ng of total DNA following the 16S metagenomics protocol (Illumina). Library quality was assessed by gel electrophoresis (Fragment Analyzer, Agilent Technologies) using dsDNA 935 Reagent Kits. Quantitative normalization of the libraries was performed using the Qubit 3.0 with the High Sensitivity Assay (Thermo Fisher Scientific).

Pair-end sequencing (2 × 300 bp) was performed using a V3 kit on the MiSeq platform (Illumina). The resulting fastQ files were quality-checked using FastQC. The V3 and V4 regions of the 16S rRNA gene were analyzed with Qiime 2.0, utilizing the Silva database.

Sequencing data were deposited in the ENA repositories (BioProject ID: PRJNA1096150). The study received approval from the Bioethics Committee at the Medical University of Lublin (approval number KE-0254/58/2019).

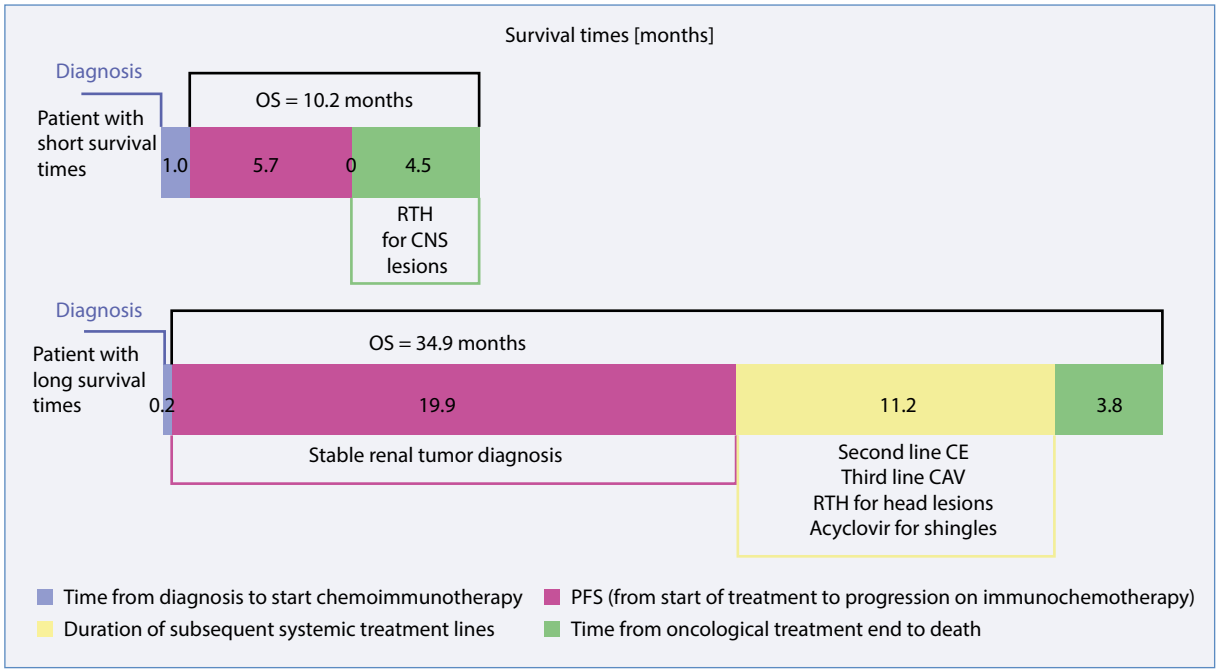

Figure 1. Survival times of the studied patients with corresponding treatment regimens; CAV — cyclophosphamide, doxorubicin, vincristine; CE — carboplatin and etoposide; CNS — central nervous system; OS — overall survival; PFS — progression-free survival; RTH — radiotherapy

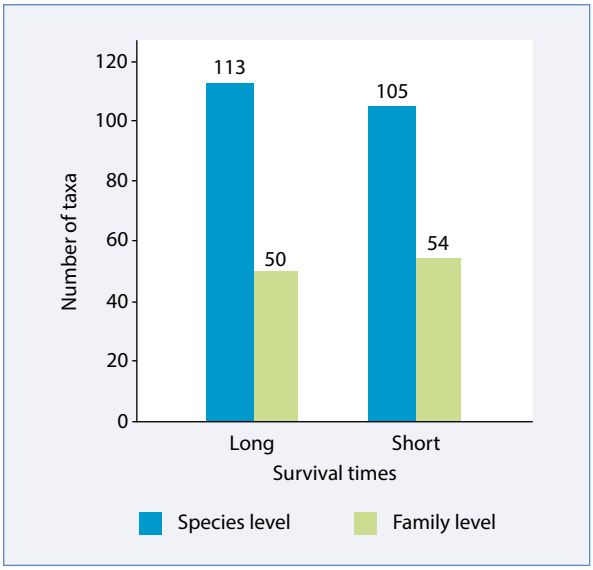

Figure 2. Comparison of the number of taxa between the studied patients

Results

The patient with a higher number of taxa at the species level and fewer bacterial families (by four) had longer PFS, OS and time from progression to death compared to the patient with a lower number of taxa (Fig. 2).

Notable differences were observed in the abundance of bacterial groups at the family level (Fig. 3). The long-surviving patient exhibited greater microbial diversity with significantly elevated proportions of bacteria from the families *Lachnospiraceae* (23.91% *vs.* 1.39%) and *Akkermansiaceae* (19.27% *vs.* 0.01%). Conversely, the short-surviving patient showed marked enrichment of the families *Enterobacteriaceae* (20.61% *vs.* 0.69%), *Succinivibrionaceae* (12.56% *vs.* 0.00%), *Streptococcaceae* (11.77% *vs.* 0,95%), and *Desulfovibrionaceae* (6.64% *vs.* 0.04%).

Discussion

Next-generation sequencing (NGS) has revolutionized microbiome research, providing unprecedented insights into microbial diversity and systematics, including non-culturable organisms [16]. While knowledge about intestinal bacteria has expanded substantially, numerous aspects remain to be explored. Although microbiome analysis is complex, it holds significant potential for advancing clinical approaches to cancer treatment.

The composition of the gut microbiome has recently emerged as a potential predictor of immunotherapy efficacy in various cancer types. Depending on the histopathological diagnosis, distinct bacterial taxa may exert either beneficial or detrimental effects on tumor progression. This dynamic is further complicated by numerous factors influencing microbiome composition, including tumor location, treatment type and regimen, as well as immune system activity. Additionally, lifestyle, environmental pollutants and clinical factors such as diet, comorbidities or medication use (particularly antibiotics), may significantly affect the microbiome composition.

Numerous studies have demonstrated the microbiome's influence on the efficacy of ICI therapies across various malignancies, including NSCLC. However, data remain limited for SCLC, as chemoimmunotherapy (platinum-etoposide with anti-PD-L1 agents) was only recently approved based on the CASPIAN and IMpower133 trials [7–10].

Specific bacterial taxa have been identified as potential predictive factors for immunotherapy efficacy in various cancer types. Next-generation sequencing provides a powerful platform for comprehensive microbiome profiling and identification of treatment-associated microbial signatures. One notable example is *Akkermansia muciniphila*, whose presence in the intestine has been associated with improved immunotherapy response, along with prolonged PFS and OS in NSCLC and renal cell carcinoma [17, 18].

The present analysis revealed a significantly higher abundance of the family *Akkermansiaceae* in the gut microbiome of the patient with an extended treatment response compared to the short-responding case (19.3% *vs.* 0.007%, respectively). This observation aligns with established evidence for *Akkermansia muciniphila*, the best-studied species in this family [17]. Multivariate analyses have established that the association of *A. muciniphila* with improved immunotherapy response remains significant after controlling for key clinical variables including age, sex, performance status, antibiotic use, and PD-L1 status [17].

The family *Lachnospiraceae*, consistently associated with improved ICI efficacy across multiple studies [14], was abundant in the current long-responding SCLC patient. Particularly noticeable in our study was the elevated abundance of specific beneficial species, including *Lachnoclostridium phocaeense*, (*Clostridium*) *scindens* or *Shuttleworthia* in patient with long PFS and OS compared to the patient with short survival times.

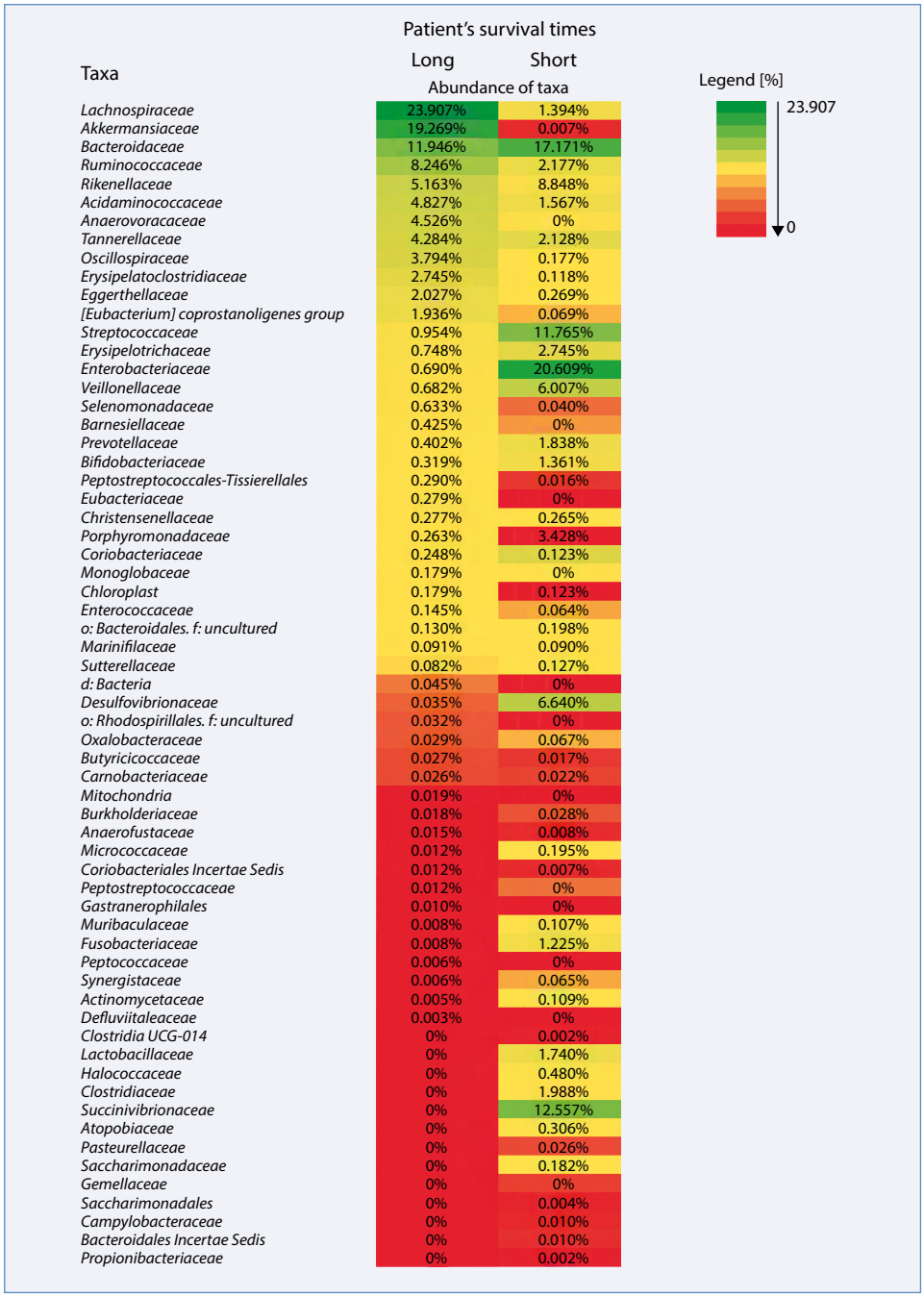

Figure 3. Comparison of gut microbiome diversity at the family level in small cell lung cancer patients with short and long progression-free survival (PFS) and overall survival (OS) following first-line chemoimmunotherapy

As a phylogenetically diverse family, *Lachnospiraceae* encompasses the probiotic-rich order *Lachnoclostridium* and the *Clostridium XIVa* cluster, involved in homeostasis maintenance in the human gut [19]. Their health-promoting effects are mediated through production of short-chain fatty acids (SCFAs), which function as immunomodulatory metabolites and prebiotics [19].

Lachnoclostridium phocaeense is a relatively recently described bacterium, with no existing reports linking it to the efficacy of immunotherapy in cancer patients [20]. However, reduced abundance of butyrate-producing bacteria (*Anaerostipes hadrus, Lachnoclostridium phocaeense*, and *Romboutsia ilealis*) has been observed in pancreatic cancer patients compared to controls [21]. It should be mentioned that these findings require

validation in larger cohorts, as the study involved only eight participants per group.

The present study observed that the patient with shorter survival time had an increased abundance of the family *Enterobacteriaceae*, including the genera *Shigella-Escherichia*. This family has been shown to be enriched in cancer patients compared to healthy individuals [22], and correlates with poorer anti-PD-1 response in lung cancer [23]. On the other hand, another study using 16S rRNA analyses, showed significantly higher numbers of *Escherichia-Shigella*, *Akkermansia* and *Olsenella* in patients with stable disease (SD) compared to those with progression [24]. This discrepancy may reflect the dynamic nature of immunotherapy responses, where initial disease stabilization often precedes rapid progression — a process potentially mediated by microbiome alterations.

Clinical studies demonstrate that probiotic interventions (e.g., JK5G — a blend of 21 inactivated *Lactobacillus* strains and metabolites) can modulate gut microbiota in NSCLC patients receiving immunotherapy. These treatments increase beneficial taxa (*Faecalibacterium*, *Ruminococcaceae*) and butyrate levels while reducing *Escherichia-Shigella* populations [25].

It should be noted that *Shigella* and *E. coli* cannot be reliably differentiated via 16S rRNA gene sequencing or whole-genome analysis due to their genetic similarity. While most *E. coli* strains are harmless gut commensals, specific pathotypes can cause severe infections, including diarrhea, dysentery, or even meningitis.

The current study identified *Succinivibrionaceae* as another bacterial family enriched in the patient with short survival times. While existing literature associates this bacterial family with increased cancer risk — including ovarian cancer (Mendelian randomization evidence) [26] and cervical cancer (case-control data) [27] — no direct evidence currently links *Succinivibrionaceae* to ICI treatment outcomes.

However, research shows that the genus *Streptococcus* is significantly more abundant in patients without response to ICIs [13]. In the present study, *Streptococcaceae* (and its representative *Streptococcus salivarius*) was more abundant in the patient with a short survival time. Furthermore, prior work indicates that *Streptococcus salivarius* and *Streptococcus vestibularis* are associated with short PFS in NSCLC patients treated with ICIs [13]. In the other hand the genus *Streptococcus* has also been found to be more abundant in bronchoalveolar lavage (BAL) samples from NSCLC patients responding to immunotherapy [28]. Bacteria of the family *Streptococcaceae* may infiltrate tissues through the bloodstream, potentially contributing to immunosuppression by inducing inflammation.

It is important to note that the genus *Streptococcus* represents a broad group of bacteria, with individual strains differing in their potential to support immunotherapy. For example, *S. salivarius* demonstrated significant abundance differences between pembrolizumab responders and non-responders in metastatic castration-resistant prostate cancer progressing after enzalutamide administration [29]. Furthermore, quantitative PCR analysis of DNA extracts from fecal samples confirmed increased *S. salivarius* levels in responders, confirming that specific bacterial strains can either enhance or hinder the effectiveness of ICIs.

Also observed were elevated counts of bacteria from the family *Desulfovibrioceae* in the short-surviving patient compared to the patient with prolonged survival. On the other hand, previous research indicated that these bacteria were more abundant in NSCLC patients responding to ICI therapy [30], or that *Bifidobacterium* and *Desulfovibrio* were enriched in patients without immune-related adverse events (irAEs) [31]. Although IrAEs can be life-threatening, they often indicate immune system activation and increased ICI efficacy. Strong evidence suggests that NSCLC patients with a history of irAEs achieve a significantly higher objective response rate and longer PFS and OS than those without irAEs [32]. Neither of the two patients developed irAEs, precluding any direct evaluation of the relationship between microbiome composition and irAE emergence. Future studies in SCLC patients should examine both gut microbiome composition and irAE occurrence.

There are several limitations in the present study. First, the analysis included only two patients. Second, the patients presented at different disease stages — the short-surviving patient had multiple distant metastases at diagnosis, while the long-responding patient was classified with ED based on pleural effusion. It is possible that the microbiome's composition was influenced by the disease stage or, conversely, that it may have contributed to the occurrence of multiple metastases at the time of diagnosis.

Despite these limitations, both patients showed initial treatment response, suggesting that the gut microbiome could influence response duration to ICI therapy. Present findings should be considered preliminary, highlighting the importance of conducting further investigations involving a larger cohort of patients. Future studies may focus on selected bacterial species, identified through methods other than NGS 16S rRNA screening. Such research could translate into clinical practice, potentially enabling implementation of FMT — an established gastroenterological therapy that may now prove valuable for oncology applications.

Conclusions

The gut microbiome shows significant potential as both a prognostic biomarker and predictor of immunotherapy response in SCLC patients. However, these preliminary observations require validation through larger, statistically powered clinical studies to establish definitive correlations between microbial profiles and treatment outcomes.

Article Information and Declarations

Ethics statement

The patients provided consent for participation in the study. The study received approval from the Bioethics Committee at the Medical University of Lublin (KE-0254/58/2019).

Author contributions

A.Grenda: conception and design of the study, drafting the article, revising and final approval; E.I.: conception and design of the study, acquisition of data, drafting the article, revising and final approval; P.K.: conception and design of the study, drafting the article, revising and final approval; A.B.: acquisition of data, analysis and interpretation of data, revising and final approval; I.C.: acquisition of data, revising and final approval; K.B.: analysis and interpretation of data; A.Grzywna: acquisition of data, revising and final approval; M.S.: acquisition of data, revising and final approval; T.J.: acquisition of data, revising and final approval; R.K.: acquisition of data, revising and final approval; N.G.: drafting the article; J.M.: revising and final approval.

Acknowledgments

None.

Funding

None.

Conflict of interest

The authors declare that there is no conflict of interest.

Supplementary material

None.

References

1. Jeon D, Kim H, Kim S, et al. Five-Year Overall Survival and Prognostic Factors in Patients with Lung Cancer: Results from the Korean Association of Lung Cancer Registry (KALC-R) 2015. Cancer Res Treat. 2023; 55(1): 103–111, doi: 10.4143/crt.2022.264, indexed in Pubmed: 35790197.
2. Lassen U, Osterlind K, Hansen M, et al. Long-term survival in small-cell lung cancer: posttreatment characteristics in patients surviving 5 to 18+ years--an analysis of 1,714 consecutive patients. J Clin Oncol. 1995; 13(5): 1215–1220, doi: 10.1200/JCO.1995.13.5.1215, indexed in Pubmed: 7738624.
3. Basumallik N, Agarwal M. Small Cell Lung Cancer. In: StatPearls. StatPearls Publishing, Treasure Island (FL) 2024.
4. Farago AF, Keane FK. Current standards for clinical management of small cell lung cancer. Transl Lung Cancer Res. 2018; 7(1): 69–79, doi: 10.21037/tlcr.2018.01.16, indexed in Pubmed: 29535913.
5. Saida Yu, Watanabe S, Kikuchi T. Extensive-Stage Small-Cell Lung Cancer: Current Landscape and Future Prospects. Onco Targets Ther. 2023; 16: 657–671, doi: 10.2147/OTT.S272552, indexed in Pubmed: 37551311.
6. Falchero L, Meyer N, Molinier O, et al. Real-life nationwide characteristics and outcomes of small cell lung cancer over the last 20 years: Impact of immunotherapy on overall survival in a real-life setting. Eur J Cancer. 2024; 210: 114277, doi: 10.1016/j.ejca.2024.114277, indexed in Pubmed: 39168000.
7. Jassem J, de Marinis F, Giaccone G, et al. Updated Overall Survival Analysis From IMpower110: Atezolizumab Versus Platinum-Based Chemotherapy in Treatment-Naive Programmed Death-Ligand 1-Selected NSCLC. J Thorac Oncol. 2021; 16(11): 1872–1882, doi: 10.1016/j.jtho.2021.06.019, indexed in Pubmed: 34265434.
8. Liu SV, Reck M, Mansfield AS, et al. Updated Overall Survival and PD-L1 Subgroup Analysis of Patients With Extensive-Stage Small-Cell Lung Cancer Treated With Atezolizumab, Carboplatin, and Etoposide (IMpower133). J Clin Oncol. 2021; 39(6): 619–630, doi: 10.1200/JCO.20.01055, indexed in Pubmed: 33439693.
9. Reck M, Liu SV, Mansfield AS, et al. IMpower133: Updated overall survival (OS) analysis of first-line (1L) atezolizumab (atezo) + carboplatin + etoposide in extensive-stage SCLC (ES-SCLC). Ann Oncol. 2019; 30: v710–v711, doi: 10.1093/annonc/mdz264.
10. Goldman JW, Dvorkin M, Chen Y, et al. CASPIAN investigators, CASPIAN investigators. Durvalumab plus platinum-etoposide versus platinum-etoposide in first-line treatment of extensive-stage small-cell lung cancer (CASPIAN): a randomised, controlled, open-label, phase 3 trial. Lancet. 2019; 394(10212): 1929–1939, doi: 10.1016/S0140-6736(19)32222-6, indexed in Pubmed: 31590988.
11. Hamilton G, Rath B. Immunotherapy for small cell lung cancer: mechanisms of resistance. Expert Opin Biol Ther. 2019; 19(5): 423–432, doi: 10.1080/14712598.2019.1592155, indexed in Pubmed: 30855195.
12. Yang W, Fan X, Li W, et al. Causal influence of gut microbiota on small cell lung cancer: a Mendelian randomization study. Clin Respir J. 2024; 18(5): e13764, doi: 10.1111/crj.13764, indexed in Pubmed: 38685730.
13. Dora D, Ligeti B, Kovacs T, et al. Non-small cell lung cancer patients treated with Anti-PD1 immunotherapy show distinct microbial signatures and metabolic pathways according to progression-free survival and PD-L1 status. Oncoimmunology. 2023; 12(1): 2204746, doi: 10.1080/2162402X.2023.2204746, indexed in Pubmed: 37197440.
14. Zhang M, Liu J, Xia Q. Role of gut microbiome in cancer immunotherapy: from predictive biomarker to therapeutic target. Exp Hematol Oncol. 2023; 12(1): 84, doi: 10.1186/s40164-023-00442-x, indexed in Pubmed: 37770953.
15. Ren S, Feng L, Liu H, et al. Gut microbiome affects the response to immunotherapy in non-small cell lung cancer. Thorac Cancer. 2024; 15(14): 1149–1163, doi: 10.1111/1759-7714.15303, indexed in Pubmed: 38572783.
16. Thomas AM, Segata N. Multiple levels of the unknown in microbiome research. BMC Biol. 2019; 17(1): 48, doi: 10.1186/s12915-019-0667-z, indexed in Pubmed: 31189463.
17. Derosa L, Routy B, Thomas AM, et al. Intestinal Akkermansia muciniphila predicts clinical response to PD-1 blockade in patients with advanced non-small-cell lung cancer. Nat Med. 2022; 28(2): 315–324, doi: 10.1038/s41591-021-01655-5, indexed in Pubmed: 35115705.
18. Fan S, Jiang Z, Zhang Z, et al. Akkermansia muciniphila: a potential booster to improve the effectiveness of cancer immunotherapy. J Cancer Res Clin Oncol. 2023; 149(14): 13477–13494, doi: 10.1007/s00432-023-05199-8, indexed in Pubmed: 37491636.
19. Guo P, Zhang Ke, Ma Xi, et al. species as probiotics: potentials and challenges. J Anim Sci Biotechnol. 2020; 11: 24, doi: 10.1186/s40104-019-0402-1, indexed in Pubmed: 32099648.
20. Brahimi S, Cadoret F, Fournier PE, et al. sp. nov. and sp. nov., two new bacterial species isolated from human urine after kidney transplantation. New Microbes New Infect. 2017; 16: 73–75, doi: 10.1016/j.nmni.2017.01.008, indexed in Pubmed: 28228968.
21. Wang XY, Sun ZX, Makale E, et al. Gut Microbial Profile in Patients with Pancreatic Cancer. Jundishapur Journal of Microbiology. 2022; 15(4), doi: 10.5812/jjm-122386.

22. Botticelli A, Vernocchi P, Marini F, et al. Gut metabolomics profiling of non-small cell lung cancer (NSCLC) patients under immunotherapy treatment. J Transl Med. 2020; 18(1): 49, doi: 10.1186/s12967-020-02231-0, indexed in Pubmed: 32014010.
23. Yin H, Yang Lu, Peng G, et al. The commensal consortium of the gut microbiome is associated with favorable responses to anti-programmed death protein 1 (PD-1) therapy in thoracic neoplasms. Cancer Biol Med. 2021 [Epub ahead of print]; 18(4): 1040–1052, doi: 10.20892/j.issn.2095-3941.2020.0450, indexed in Pubmed: 33960176.
24. He D, Li X, An R, et al. Response to PD-1-Based Immunotherapy for Non-Small Cell Lung Cancer Altered by Gut Microbiota. Oncol Ther. 2021; 9(2): 647–657, doi: 10.1007/s40487-021-00171-3, indexed in Pubmed: 34664203.
25. Chen M, Ma L, Yu H, et al. JK5G postbiotics attenuate immune-related adverse events in NSCLC patients by regulating gut microbiota: a randomized controlled trial in China. Front Oncol. 2023; 13: 1155592, doi: 10.3389/fonc.2023.1155592, indexed in Pubmed: 37601658.
26. Zhang L, Cao T, Liu K, et al. Genetically predicted blood metabolites mediate relationships between gut microbiota and ovarian cancer: a Mendelian randomization study. Front Cell Infect Microbiol. 2024; 14: 1451880, doi: 10.3389/fcimb.2024.1451880, indexed in Pubmed: 39364145.
27. Wang Z, Wang Q, Zhao J, et al. Altered diversity and composition of the gut microbiome in patients with cervical cancer. AMB Express. 2019; 9(1): 40, doi: 10.1186/s13568-019-0763-z, indexed in Pubmed: 30904962.
28. Jang HJ, Choi JiY, Kim K, et al. Relationship of the lung microbiome with PD-L1 expression and immunotherapy response in lung cancer. Respir Res. 2021; 22(1): 322, doi: 10.1186/s12931-021-01919-1, indexed in Pubmed: 34963470.
29. Peiffer LB, White JR, Jones CB, et al. Composition of gastrointestinal microbiota in association with treatment response in individuals with metastatic castrate resistant prostate cancer progressing on enzalutamide and initiating treatment with anti-PD-1 (pembrolizumab). Neoplasia. 2022; 32: 100822, doi: 10.1016/j.neo.2022.100822, indexed in Pubmed: 35908379.
30. Zhang C, Wang J, Sun Z, et al. Commensal microbiota contributes to predicting the response to immune checkpoint inhibitors in non-small-cell lung cancer patients. Cancer Sci. 2021; 112(8): 3005–3017, doi: 10.1111/cas.14979, indexed in Pubmed: 34028936.
31. Chau J, Yadav M, Liu B, et al. Prospective correlation between the patient microbiome with response to and development of immune-mediated adverse effects to immunotherapy in lung cancer. BMC Cancer. 2021; 21(1): 808, doi: 10.1186/s12885-021-08530-z, indexed in Pubmed: 34256732.
32. Lin Li, Liu Yu, Chen C, et al. Association between immune-related adverse events and immunotherapy efficacy in non-small-cell lung cancer: a meta-analysis. Front Pharmacol. 2023; 14: 1190001, doi: 10.3389/fphar.2023.1190001, indexed in Pubmed: 37284302.