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The Effect of Malnutrition on Treatment Efficacy and Toxicity in Geriatric Patients Treated With Immune Checkpoint Inhibitors

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Abstract

Background/Aim: Immune checkpoint inhibitors (ICIs) have been shown to be effective in various cancer subtypes and their use in clinical practice has become widespread in recent years. However, discussions on their effectiveness in geriatric patients and in cases of malnutrition are still ongoing. The aim of the study was to evaluate the association of geriatric nutritional index (GNRI) detected malnutrition risk with progression-free survival (PFS) and immune related adverse events (irAEs) in geriatric solid tumor patients treated with ICIs.

Patients and Methods: The study was conducted retrospectively and included patients with metastatic solid tumors who received second- or third-line immunotherapy between 2018 and 2024 at the Dr. Abdurrahman Yurtaslan, Ankara Oncology Education and Research Hospital and Etlik City Hospital. The GNRI score of the patients at the start of immunotherapy was calculated, and the relationship between the GNRI score and PFS and irAEs was evaluated.

Results: No significant association was found between sex (p=0.28), comorbidity (p=0.34), polypharmacy (p=0.09), antibiotic (p=0.24) use and PFS. A significant association was found between ECOG PS (p<0.05) and GNRI (p=0.012) and PFS. In multivariate analysis, ECOG PS [hazard ratio (HR)=1.5, 95% confidence interval (CI)=1.0-2.2, p=0.036] and GNRI (HR=0.6, 95% CI=0.4-0.9, p=0.033) were statistically significant. The incidence of irAEs was statistically higher in patients with GNRI <98 (p=0.019).

continued

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Conclusion: Geriatric solid tumor patients are not fully represented in prospective clinical drug trials. Prospective studies are needed in which only geriatric patients are included, treatment efficacy and toxicity are assessed stepwise according to nutritional status, and malnutrition is treated to increase treatment efficacy and reduce toxicity.

Keywords: Geriatric-nutritional index, malnutrition, geriatric cancer patients, immune-related adverse events, immune checkpoint inhibitors, immunotherapy, lung cancer, RCC, malignant melanoma.

Introduction

The efficacy of immune checkpoint inhibitors (ICIs) in various cancer subtypes has been demonstrated and their use in clinical practice has become widespread in recent years (1). The use of ICIs in geriatric patients is a matter of debate due to hypotheses that both treatment efficacy may decrease, and toxicity may increase. It was expected that the treatment response with ICIs would be lower due to the weaker vaccine response in the elderly (2). However, the results obtained from clinical studies and their meta-analyses showed that, regardless of the tumor subtype, treatment efficacy in patients aged 65-75 is similar to that in patients under 65 (3). The debates are still ongoing regarding the age of 75 and above (4). The idea that geriatric patients included in clinical studies do not fully reflect the entire geriatric patient population continues the debate on this subject. It is thought that malnutrition also increases ICI response and toxicity in geriatric patients (5).

Malnutrition is a common problem especially in advanced cancer patients. In geriatric cancer patients, malnutrition is important both in terms of treatment efficacy and toxicity (6). Geriatric nutritional risk index (GNRI) is a simple and objective method recommended to evaluate the nutritional status of elderly patients. It was developed by combining body mass index (BMI) and albumin and can be used to determine the risk of malnutrition (7). The prognostic efficacy of GNRI in geriatric patients is also superior to albumin and BMI alone. There are studies in the literature showing that GNRI is prognostic in lung cancer (8), prostate cancer (8), head and neck cancer (9) patients. At the same time, although there are studies showing that the efficacy of ICIs decreases in patients with low GNRI in the entire population of lung cancer and head and neck cancer, it has not yet been evaluated specifically for geriatric cancer patients.

Although there are studies on the prognostic effect of GNRI in patients with solid cancer, we see that the relationship between immunotherapy efficacy and GNRI has not been addressed in depth. The aim of our study was to evaluate the effect of malnutrition determined by GNRI on treatment efficacy and toxicity in geriatric solid tumor patients treated with ICIs.

Patients and Methods

Study population. The study included 142 patients aged 65 years and older with solid tumors treated with metastatic second or third-line ICIs between 2018 and 2024. Patients under 65 years of age were excluded from the study. Patients receiving immunotherapy as monotherapy were selected because the study aimed to compare treatment efficacy and toxicity according to GNRI. Patients receiving chemoimmunotherapy as first-line therapy, tyrosine kinase inhibitors combined with immunotherapy, or dual ICIs were excluded because they were considered likely to bias both treatment efficacy and the incidence of immune related adverse events (irAEs). This patient group was selected because patients receiving ICIs as monotherapy were predominantly metastatic second- or third-line patients.

Variable measurement and definition. The patients' files were examined retrospectively. Age, sex, Eastern Cooperative Oncology Group (ECOG) performance status, diagnosis date, comorbidities, history of polypharmacy,

history of proton pump inhibitor (ppi) use, history of antibiotic use, line of treatment at ICIs was received, irAEs and grades and progression-free survival (PFS) time with ICIs were recorded. The use of five or more drugs in addition to immunotherapy was considered polypharmacy. In the case of antibiotic or ppi use, the use was based on the period starting 30 days before the start of treatment and ending at the end of treatment.

GNRI assessment of malnutrition. GNRI was calculated for each patient according to the data at the beginning of the period during which he/she received ICIs. GNRI was calculated using the formula: GNRI=14.89 × serum albumin (g/dl) + 41.7 × [present body weight (kg)/ideal body weight (kg)]. The Lorentz formula [for men: w=(height [cm]− 100) − ((height −150)/4); for women: w=(height − 100) − ((height − 150)/2)]; was used to calculate ideal weight. This formula was used because the researchers who developed GNRI used the Lorentz formula to calculate ideal weight (7). IrAEs were assessed and graded according to common terminology criteria for adverse events (CTCAE) 4.

The Clinical Research Ethics Committee of Dr. Abdurrahman Yurtaslan, Ankara Oncology Education and Research Hospital approved the study, prior to initiation of the research work. This is a retrospective study, and the ethics committee did not require consent from patients. Ethics Approved Number: 2025-02/20.

Statistical analysis. IBM-SPSS statistics, version 23.0 was used for data analysis. In the descriptive statistics of the study, continuous variables were used as mean (standard deviation), and median (range); categorical variables were presented as frequency (percentage). Comparisons of continuous variables between two independent groups were made using the Mann-Whitney *U*-test, and comparisons of categorical data were made using the chi-square test. PFS was calculated by the Kaplan-Meier method and log-rank test. The relationship between PFS and irAEs was examined using the cut-off value of <98 (malnutrition risk present), ≥98 (no malnutrition risk) determined during the development of GNRI (7). In addition, the relationship between GNRI and PFS was examined in each solid tumor subtype. In univariate analysis, $p<0.05$ was considered statistically significant. Variables found to be significantly associated with PFS in univariate analysis were evaluated using Cox regression analysis in multivariate analysis.

Results

One hundred and forty-two patients were included in the study. The basic characteristics of the patients are summarized in Table I. 47 (33.0%) had no comorbidities, and 105 (67.0%) had various comorbidities. The most common comorbidities were hypertension (22.5%) and coronary artery disease (20%). All patients received nivolumab monotherapy. GNRI was <82 in 4 (2.8%) patients, GNRI was 82-92 in 27 (19.0%) patients, GNRI was 92-98 in 28 (19.8%) patients, and GNRI was ≥98 in 83 (58.4%) patients. When evaluated in disease subgroups; GNRI was <98 in 34 (23.9%) lung cancer patients, 12 (8.4%) RCC patients, and 13 (9.2%) malignant melanoma patients. The distribution of patient characteristics according to GNRI groups is summarized in Table II. IRAEs were seen in 34 (23.9%) patients in the entire patient group. Grade 3 and 4 IRAEs were seen in 9 (6.3%) patients. There were no patients with grade 5 side effects. 6 of them had dermatitis, 1 had thrombocytopenia, 4 had hepatitis, 9 had pneumonitis, and 13 had thyroiditis. In the GNRI <98 group, 20 (33.9%) patients had ırAEs, while in the GNRI ≥98 group, 14 (16.9%) patients had irAEs. The incidence of irAEs was statistically higher in patients with GNRI <98 ($p=0.019$) (Table III). 8 of Grade 3-4 irAEs were seen in patients with GNRI <98, and 1 was seen in patients with GNRI ≥98.

The median PFS in lung cancer patients was 5.0 [95% confidence interval (CI)=2.4-7.6] months, in malignant melanoma patients was 4.6 (95% CI=2.2-6.9) months, and in RCC patients was 6.6 (95% CI=3.5-9.7) months. The median PFS in lung cancer patients with GNRI <98 was 3.2 (95% CI=2.4-3.9) months, in malignant melanoma patients was 3.0 (95% CI=2.0-4.0) months, and in RCC

Table I. *Demographic characteristics of patients.*

	Lung (N=85)	Malignant melanoma (N=32)	RCC (N=25)
Age (median) (min-max)	70 (65-86)	72 (65-92)	70 (65-82)
Age			
<75	65 (76.5)	17 (53.1)	21 (84.0)
≥75	20 (23.5)	15 (46.9)	4 (16.0)
ECOG PS			
0-1	58 (68.2)	23 (71.8)	20 (80.0)
≥2	27 (31.8)	9 (28.2)	5 (20.0)
Sex			
Female	14 (16.4)	13 (40.6)	3 (12.0)
Male	71 (83.6)	19 (59.4)	22 (88.0)
Comorbidity			
Yes	54 (63.5)	25 (78.1)	16 (64.0)
No	31 (36.5)	7 (22.9)	9 (36.0)
Cigarette			
Yes	74 (87.0)	9 (28.2)	14 (56.0)
No	11 (13.0)	23 (71.8)	11 (44.0)
Polypharmacy			
Yes	38 (44.7)	12 (37.5)	12 (48.0)
No	47 (55.3)	20 (62.5)	13 (52.0)
PPI using			
Yes	42 (49.5)	15 (46.8)	8 (32.0)
No	43 (50.5)	17 (53.2)	17 (68.0)
Antibiotic using			
Yes	20 (23.5)	6 (18.75)	5 (20.0)
No	65 (77.5)	26 (71.25)	20 (80.0)

ECOG PS: Eastern Cooperative Oncology Group performance status; RCC: renal cell carcinoma; Min: minimum; Max: maximum; ppi: proton pump inhibitor.

patients was 5.7 (95% CI=1.7-9.8) months. Median PFS in lung cancer patients with GNRI ≥98 was 6.7 (95% CI=4.1-9.2) months, in malignant melanoma patients it was 8.2 (95% CI=6.4-10.0) months, and in RCC patients it was 14.7 (95% CI=1.3-28.1) months. The relationship between GNRI and PFS was statistically significant in lung cancer (p=0.031), malignant melanoma(p=0.02) and RCC (p=0.045). Kaplan-Meier curves of lung cancer (A), malignant melanoma (B), and RCC (C) patients are shown in Figure 1. In patients aged 75 years and older, median PFS was 5.7 (95% CI=0-11.7) months. In the group with GNRI <98, median PFS was 3.0 (95% CI=2.0-4.0) months, and in the group with GNRI ≥98, median PFS was 9.1 (95% CI=4.2-14.0) months. The difference between the two groups was also statistically significant in patients aged 75 years and older (p=0.011). Kaplan-Meier curve is shown in Figure 2.

In univariate analysis, no significant association was found between sex (p=0.28), comorbidity (p=0.34), polypharmacy (p=0.09), antibiotic (p=0.24) use, ppi use (p=0.58) and PFS. A significant association was found between ECOG PS (p<0.05) and GNRI (p=0.012) and PFS. In multivariate analysis, ECOG PS [hazard ratio (HR)=1.5, 95% CI=1.0-2.2, p=0.036) and GNRI (HR=0.6, 95% CI=0.4-0.9, p=0.033) were statistically significant.

Discussion

In this study, we found that ICIs efficacy decreased and the incidence of irAEs increased in geriatric cancer patients with low GNRI. There are several studies in the literature investigating the relationship between GNRI and survival in cancer subgroups. However, this is the first study to demonstrate the relationship between GNRI and PFS and

Table II. *Patient characteristics according to GNRI groups.*

	GNRI <98	GNRI ≥98	*p*-Value (χ^2)
Age (Median)	71	70	
Sex			0.28
Female	15 (25.4)	15 (18.0)	
Male	44 (74.6)	68 (72.0)	
ECOG PS			0.37
0-1	38 (64.4)	63 (75.9)	
≥2	21 (35.6)	20 (24.1)	
Comorbidity			0.36
Yes	42 (71.2)	53 (63.9)	
No	17 (28.8)	30 (36.1)	
IO treatment line			0.36
Second	52 (88.1)	74 (89.2)	
Third	7 (11.9)	9 (10.8)	
Cigarette			0.91
Yes	40 (67.8)	57 (68.7)	
No	19 (32.2)	26 (31.3)	
Polypharmacy			0.44
Yes	28 (47.5)	34 (41.0)	
No	31 (52.5)	49 (59.0)	
PPI using			0.49
Yes	29 (49.2)	36 (43.4)	
No	30 (50.8)	47 (56.6)	
Antibiotic using			0.64
Yes	14 (23.7)	17 (20.5)	
No	45 (76.3)	66 (79.5)	

GNRI: Geriatric Nutritional Index; ECOG PS: Eastern Cooperative Oncology Group performance status; RCC: renal cell carcinoma; IO: immunotherapy; ppi: proton pump inhibitors.

Table III. *GNRI and irAEs rates in tumor subtypes.*

	Lung (N=85)	Malignant melanoma (N=32)	RCC (N=25)
GNRI			
<98	34 (40.0)	13 (40.6)	12 (48.0)
≥98	51 (60.0)	19 (59.4)	13 (52.0)
irAEs (n, %)			
Yes	20 (23.6)	6 (18.75)	8 (32.0)
No	65 (77.5)	26 (71.25)	17 (68.0)

RCC: Renal cell carcinoma; GNRI: Geriatric Nutritional Index, irAEs: immune related adverse events.

irAEs in geriatric cancer patients. Since the frequency of malnutrition is high in geriatric cancer patients, this study also indicates a very valuable result. A study of geriatric small cell lung cancer patients treated with platinum doublet found that patients with lower GNRI index had inferior PFS and OS (10). In another study conducted on patients with resectable colorectal cancer, it was determined that the GNRI score calculated before surgery was a determinant of prognosis (11). In a study conducted in patients with resectable gastric cancer, GNRI was shown to predict poor prognosis after curative surgery (12).

Both innate and acquired immune function decrease with aging (13). There is a decrease in the release of neoantigens, and the initiation of antitumor immune responses is impaired (14) This suggested that the efficacy of immunotherapy in geriatric patients may be low. Some of the clinical studies were re-examined to investigate the efficacy in geriatric subgroups. In the subgroup analysis of the study investigating the efficacy of nivolumab as monotherapy in previously treated RCC patients, the reduction in HR in the ≥65 age group was better than in the <65 age group. However, the efficacy decreased in the ≥75 age group [HR=1.23 (0.66-2.31)] (15). In melanoma patients, the efficacy of nivolumab in geriatric patients was also much better than expected. In the ≥65 age group, the reduction in HR was similar to that in the <65 age group. In the ≥75 age group, there was a better reduction than in the whole population [HR=0.25 (0.10-0.61)] (16). In a study evaluating the efficacy of nivolumab in non-squamous (17) and squamous (18) NSCLC patients who had previously received platinum-based chemotherapy, the reduction in HR in the ≥65 age group was similar to that in the <65 age group. In the ≥75 age group, the treatment efficacy was lower compared to the whole population. In the safety analysis of nivolumab in geriatric patients, no increase in grade 3-5 adverse events were found in the ≥65 age group compared to the 65-age group. However, the frequency of grade 3-5 adverse events was higher in the ≥70 age group compared to the <65 age group (71.7% *vs.* 58.4%) (19).

It is known that malnutrition is strongly associated with survival in cancer patients. In addition, it has been investigated in recent years that malnutrition may also be effective in ICIs response. A study by Johannet *et al*. showed that low BMI and prognostic nutritional index

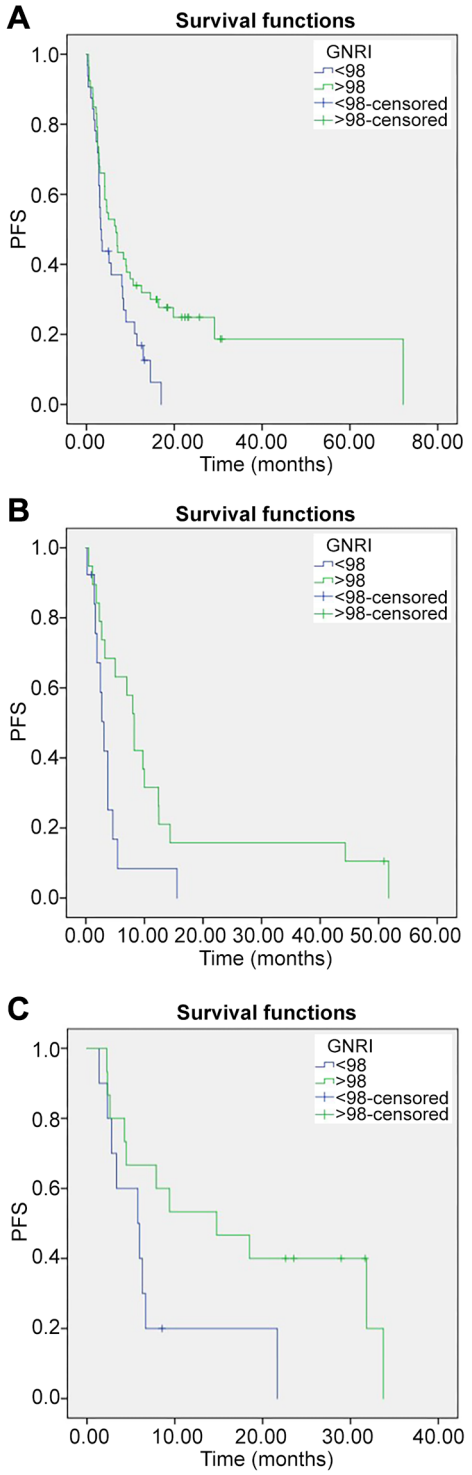

Figure 1. *Progression free survival (PFS) curve according to geriatric nutritional index (GNRI) in patients with lung (A), malignant melanoma (B) and renal cell carcinoma (RCC) (C).*

(PNI) are associated with poor response to ICIs treatment (20). In another study conducted on NCSLC patients, malnutrition assessed by BMI, weight loss and hypoalbuminemia were found to reduce objective response rates (ORR) and OS in ICIs treatment (21). Another method used to assess nutritional status, the NRS2002 score, was also found to be prognostic in patients treated with ICIs in a study conducted by Tang *et al.* (22). The results in our study were similar to these studies. In patients in whom the GNRI score indicated the risk of malnutrition, both PFS was shorter, and toxicities were increased with ICIs. It is known that in cases of malnutrition, blood plasma levels of drugs increase depending on fat and muscle distribution (23). It is also an expected result that this will increase the frequency of adverse events.

The effect of polypharmacy on the efficacy of ICIs has been investigated in various studies. In a study conducted on lung cancer patients receiving ICIs, OS was found to be shorter in patients with polypharmacy. However, it is not clear whether these patients had shorter OS because of their high comorbidities or because the treatment efficacy was reduced (24). Another study found that OS and irAEs were similar in patients with and without polypharmacy. In our study, we evaluated the relationship between polypharmacy and PFS; PFS was numerically shorter in the polypharmacy group, but it did not reach statistical significance. The relationship between antibiotic use and OS and PFS is also a subject of research in patients treated with ICIs. In a meta-analysis, it was found that antibiotic use caused a 1.2-month decrease in PFS and was associated with a 6.7-month decrease in OS (25). In our study, we did not find a significant relationship between antibiotic use and PFS. We may not have obtained a significant result because the number of patients using antibiotics was low. PPI use has also been shown to be associated with lower PFS and OS in patients treated with ICIs in a meta-analysis (26). In our study, we could not detect a significant relationship between PFS and PPI use. We thought that the small number of patients might have caused a significant relationship not to be detected.

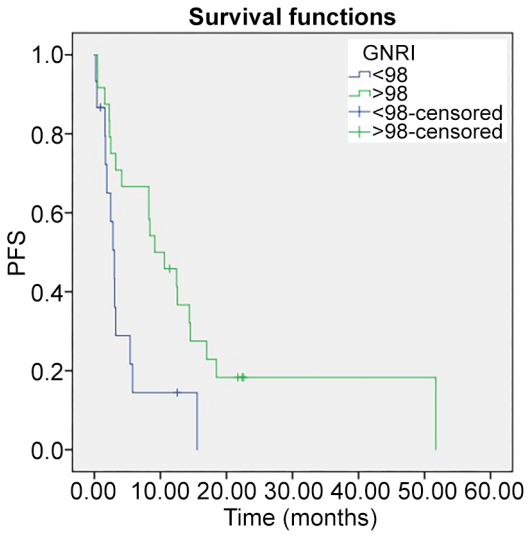

Figure 2. *Progression free survival (PFS) curve according to geriatric nutritional index (GNRI) in patients with ≥75 years old.*

ICIs have become quite widespread in oncology practice in recent years, and it is expected that standard chemotherapeutics will be replaced by ICIs and targeted therapies in the next century (27). As the use of ICIs becomes widespread in clinical practice, appropriate patient selection will also become more important. In individualized treatments, it is necessary to consider the age, nutritional status and comorbidities of the patients in the selection of treatment (28). Since malnutrition is an important problem in geriatric patients, the aim of our study was to emphasize that the nutritional status of geriatric patients who will be treated with ICIs should be evaluated before treatment. In addition, it was to emphasize that GNRI is a simple but effective index that can be used in nutritional assessment. The limitations of our study were that it was retrospective, and the number of patients was small. Since it was a retrospective study, we could not use dynamic tests to determine nutritional status. In addition, it was a valuable study because it included only geriatric patients treated with ICIs. Since geriatric patients are not fully represented in clinical studies, prospective studies evaluating the efficacy of ICIs in the geriatric population, stratified by nutritional status, are needed in the future.

Conclusion

This study concludes that the risk of malnutrition detected by GNRI is associated with poorer PFS and increased irAEs in geriatric solid tumor patients treated with ICIs. Geriatric solid tumor patients are not fully represented in prospective clinical drug trials. Prospective studies are needed in which only geriatric patients are included, treatment efficacy and toxicity are assessed stepwise according to nutritional status, and malnutrition is treated to increase treatment efficacy and reduce toxicity.

Conflicts of Interest

The Authors declare no conflicts of interest.

Authors' Contributions

IDO: Conception, design, supervision, resources, materials, data collection and processing, analysis and interpretation, literature search, writing manuscript, and critical review. EM, KB, Mİ, OS, BÇÖ: Resources, materials, data collection, and processing. FY: Conception, design, supervision, resources, materials, data collection and processing, literature search, writing manuscript, and critical review.

Artificial Intelligence (AI) Disclosure

No artificial intelligence (AI) tools, including large language models or machine learning software, were used in the preparation, analysis, or presentation of this manuscript.

References

1 Robert C: A decade of immune-checkpoint inhibitors in cancer therapy. Nat Commun 11(1): 3801, 2020. DOI: 10.1038/s41467-020-17670-y

2 Granier C, De Guillebon E, Blanc C, Roussel H, Badoual C, Colin E, Saldmann A, Gey A, Oudard S, Tartour E: Mechanisms of action and rationale for the use of checkpoint inhibitors in cancer. ESMO Open 2(2): e000213, 2017. DOI: 10.1136/esmoopen-2017-000213

3 Daste A, Domblides C, Gross-Goupil M, Chakiba C, Quivy A, Cochin V, De Mones E, Larmonier N, Soubeyran P, Ravaud A: Immune checkpoint inhibitors and elderly people: A review. Eur J Cancer 82: 155-166, 2017. DOI: 10.1016/j.ejca.2017.05.044
4 Landre T, Taleb C, Nicolas P, Des Guetz G: Is there a clinical benefit of anti-PD-1 in patients older than 75 years with previously treated solid tumour? J Clin Oncol 34(15_suppl): 3070-3070, 2016. DOI: 10.1200/JCO.2016.34.15_suppl.3070
5 Granier C, Gey A, Roncelin S, Weiss L, Paillaud E, Tartour E: Immunotherapy in older patients with cancer. Biomed J 44(3): 260-271, 2021. DOI: 10.1016/j.bj.2020.07.009
6 Dunne RF, Roussel B, Culakova E, Pandya C, Fleming FJ, Hensley B, Magnuson AM, Loh KP, Gilles M, Ramsdale E, Maggiore RJ, Jatoi A, Mustian KM, Dale W, Mohile SG: Characterizing cancer cachexia in the geriatric oncology population. J Geriatr Oncol 10(3): 415-419, 2019. DOI: 10.1016/j.jgo.2018.08.008
7 Bouillanne O, Morineau G, Dupuy C, Coudray-Lucas C, Berchery D, Rambaud C, Lahaye L, Lemoine-Morel S, Lemoine A, Lahaye J: Geriatric Nutritional Risk Index: a new index for evaluating at-risk elderly medical patients. Am J Clin Nutr 82(4): 777-783, 2005. DOI: 10.1093/ajcn/82.4.777
8 Lee GW, Go SI, Kim DW, Kim HG, Kim JH, An HJ, Jang JS, Kim BS, Hahn S, Heo DS: Geriatric Nutritional Risk Index as a prognostic marker in patients with extensive-stage disease small cell lung cancer: Results from a randomized controlled trial. Thorac Cancer 11(1): 62-71, 2020. DOI: 10.1111/1759-7714.13229
9 Nakayama M, Gosho M, Adachi M, Ii R, Matsumoto S, Miyamoto H, Hirose Y, Nishimura B, Tanaka S, Wada T, Tabuchi K: The Geriatric Nutritional Risk Index as a prognostic factor in patients with advanced head and neck cancer. Laryngoscope 131(1): E151-E156, 2021. DOI: 10.1002/lary.28587
10 Kinoshita R, Nakao M, Kiyotoshi H, Sugihara M, Kuriyama M, Takeda N, Muramatsu H: Geriatric Nutritional Risk Index as prognostic marker for elderly patients with small cell lung cancer. Cancer Diagn Progn 4(4): 482-488, 2024. DOI: 10.21873/cdp.10352
11 Kataoka M, Hirano Y, Ishii T, Ishikawa S, Kataoka A, Fujii T, Shimamura S: Prognostic utility of Geriatric Nutritional Risk Index after curative resection of colorectal cancer: a propensity score-matched study. Cancer Diagn Progn 1(5): 479-484, 2021. DOI: 10.21873/cdp.10064
12 Furuke H, Matsubara D, Kubota T, Kiuchi J, Kubo H, Ohashi T, Shimizu H, Arita T, Yamamoto Y, Konishi H, Morimura R, Shiozaki A, Kuriu Y, Ikoma H, Fujiwara H, Okamoto K, Otsuji E: Geriatric Nutritional Risk Index predicts poor prognosis of patients after curative surgery for gastric cancer. Cancer Diagn Progn 1(2): 43-52, 2021. DOI: 10.21873/cdp.10007
13 Pera A, Campos C, López N, Hassouneh F, Alonso C, Tarazona R, Solana R: Immunosenescence: Implications for response to infection and vaccination in older people. Maturitas 82(1): 50-55, 2015. DOI: 10.1016/j.maturitas.2015.05.004
14 Fang M, Roscoe F, Sigal LJ: Age-dependent susceptibility to a viral disease due to decreased natural killer cell numbers and trafficking. J Exp Med 207(11): 2369-2381, 2010. DOI: 10.1084/jem.20100282
15 Motzer RJ, Escudier B, McDermott DF, George S, Hammers HJ, Srinivas S, Tykodi SS, Sosman JA, Procopio G, Plimack ER, Castellano D, Choueiri TK, Gurney H, Donskov F, Bono P, Wagstaff J, Gauler TC, Ueda T, Tomita Y, Schutz FA, Kollmannsberger C, Larkin J, Ravaud A, Simon JS, Xu LA, Waxman IM, Sharma P, CheckMate 025 Investigators: Nivolumab versus everolimus in advanced renal-cell carcinoma. N Engl J Med 373(19): 1803-1813, 2015. DOI: 10.1056/NEJMoa1510665
16 Robert C, Long GV, Brady B, Dutriaux C, Maio M, Mortier L, Hassel JC, Rutkowski P, McNeil C, Kalinka-Warzocha E, Savage KJ, Hernberg MM, Lebbé C, Charles J, Mihalcioiu C, Chiarion-Sileni V, Mauch C, Cognetti F, Arance A, Schmidt H, Schadendorf D, Gogas H, Lundgren-Eriksson L, Horak C, Sharkey B, Waxman IM, Atkinson V, Ascierto PA: Nivolumab in previously untreated melanoma without *BRAF* mutation. N Engl J Med 372(4): 320-330, 2015. DOI: 10.1056/NEJMoa1412082
17 Borghaei H, Paz-Ares L, Horn L, Spigel DR, Steins M, Ready NE, Chow LQ, Vokes EE, Felip E, Holgado E, Barlesi F, Kohlhäufl M, Arrieta O, Burgio MA, Fayette J, Lena H, Poddubskaya E, Gerber DE, Gettinger SN, Rudin CM, Rizvi N, Crinò L, Blumenschein GR Jr, Antonia SJ, Dorange C, Harbison CT, Graf Finckenstein F, Brahmer JR: Nivolumab *versus* docetaxel in advanced nonsquamous non-small-cell lung cancer. N Engl J Med 373(17): 1627-1639, 2015. DOI: 10.1056/NEJMoa1507643
18 Brahmer J, Reckamp KL, Baas P, Crinò L, Eberhardt WE, Poddubskaya E, Antonia S, Pluzanski A, Vokes EE, Holgado E, Waterhouse D, Ready N, Gainor J, Arén Frontera O, Havel L, Steins M, Garassino MC, Aerts JG, Domine M, Paz-Ares L, Reck M, Baudelet C, Harbison CT, Lestini B, Spigel DR: Nivolumab versus docetaxel in advanced squamous-cell non-small-cell lung cancer. N Engl J Med 373(2): 123-135, 2015. DOI: 10.1056/NEJMoa1504627
19 Singh H, Kim G, Maher VE, Beaver JA, Pai-Scherf LH, Balasubramaniam S, Theoret MR, Blumenthal GM, Pazdur R: FDA subset analysis of the safety of nivolumab in elderly patients with advanced cancers. J Clin Oncol 34(15_suppl), 2016. DOI: 10.1200/JCO.2016.34.15_suppl.10010
20 Johannet P, Sawyers A, Qian Y, Kozloff S, Gulati N, Donnelly D, Zhong J, Osman I: Baseline prognostic nutritional index and changes in pretreatment body mass index associate with immunotherapy response in patients with advanced cancer. J Immunother Cancer 8(2): e001674, 2020. DOI: 10.1136/jitc-2020-001674
21 Mahé M, Seegers V, Vansteene D: Correlation between changes in nutritional status and tumor response in patients receiving immunotherapy for lung cancer (NUTIMMUNO

study). Support Care Cancer 32(5): 312, 2024. DOI: 10.1007/s00520-024-08519-x
22 Tang W, Li C, Huang D, Zhou S, Zheng H, Wang Q, Zhang X, Fu J: NRS2002 score as a prognostic factor in solid tumors treated with immune checkpoint inhibitor therapy: a real-world evidence analysis. Cancer Biol Ther 25(1): 2358551, 2024. DOI: 10.1080/15384047.2024.2358551
23 Hopkins JJ, Sawyer MB: A review of body composition and pharmacokinetics in oncology. Expert Rev Clin Pharmacol 10(9): 947-956, 2017. DOI: 10.1080/17512433.2017.1347503
24 Morikawa N, Naito T, Morita M, Sekikawa M, Doshita K, Yabe M, Kodama H, Miura K, Iida Y, Mamesaya N, Kobayashi H, Ko R, Wakuda K, Ono A, Kenmotsu H, Murakami H, Takahashi T: Effect of polypharmacy on the outcomes of older patients with advanced non-small-cell lung cancer treated with PD-1/PD-L1 inhibitors: A retrospective cohort study. J Geriatr Oncol 15(7): 101832, 2024. DOI: 10.1016/j.jgo.2024.101832
25 Lurienne L, Cervesi J, Duhalde L, De Gunzburg J, Andremont A, Zalcman G, Buffet R, Bandinelli PA: NSCLC immunotherapy efficacy and antibiotic use: a systematic review and meta-analysis. J Thorac Oncol 15(7): 1147-1159, 2020. DOI: 10.1016/j.jtho.2020.03.002
26 Rizzo A, Santoni M, Mollica V, Ricci AD, Calabrò C, Cusmai A, Gadaleta-Caldarola G, Palmiotti G, Massari F: The impact of concomitant proton pump inhibitors on immunotherapy efficacy among patients with urothelial carcinoma: a meta-analysis. J Pers Med 12(5): 842, 2022. DOI: 10.3390/jpm12050842
27 Ventola CL: Cancer immunotherapy, part 3: challenges and future trends. P T 42(8): 514, 2017.
28 Sathyanarayanan V, Neelapu SS: Cancer immunotherapy: Strategies for personalization and combinatorial approaches. Mol Oncol 9(10): 2043-2053, 2015. DOI: 10.1016/j.molonc.2015.10.009