

CIRCULATING LIPID PROFILE AS A PROGNOSTIC FACTOR IN PATIENTS WITH ADVANCED SOLID TUMORS TREATED WITH IMMUNE CHECKPOINT INHIBITORS

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Background Components of lipid profile seem to impact differently on phenotype and activity of immune cells in cancer.^{1,2} Their prognostic role in solid cancer patients treated with immune checkpoint inhibitors (ICIs) is still matter of debate.

Methods We retrospectively collected baseline clinicopathological characteristics including circulating lipid profile [total cholesterol (TC), triglycerides (TGs), low-density lipoproteins (LDL), high-density lipoproteins (HDL)] of consecutive solid cancer patients treated with ICIs and we investigated their impact on clinical outcomes. Cut-off values showing alteration of plasma lipid profile were ≥ 200 mg/dl for TC, ≥ 170 mg/dl for TGs, ≥ 130 mg/dl for LDL, < 40 mg/dl for HDL in males, < 45 mg/dl for HDL in females.

Results Among 432 patients enrolled, 67% (N=289) were men, 61% (N=266) were diagnosed with advanced non-small cell lung cancer and 86.6% (N=374) of patients were treated with ICIs as monotherapy. Patients' circulating lipid assessments were described in tables (tables 1–3). At a median follow-up of 46 months, patients with $TC \geq 200$ mg/dl showed an improved, although not significant, progression free survival (PFS) (6.61 versus 4.67 months, $p=0.4$) and longer overall survival (OS) (19.4 versus 10.8 months, $p=0.02$) compared to those with $TC < 200$ mg/dl. Conversely, patients with $TGs \geq 170$ mg/dl showed a shorter PFS (2.8 versus 5.07 months, $p=0.006$) and OS (5.92 versus 12.99 months, $p < 0.001$) compared to those with $TGs < 170$ mg/dl. Then, we combined TC and TGs in a LIPID-score that identified three subgroups: good risk (GR) ($TC \geq 200$ mg/dl and $TGs < 170$ mg/dl), intermediate risk (IR) ($TC < 200$ mg/dl and $TGs < 170$ mg/dl or $TC \geq 200$ mg/dl and $TGs \geq 170$ mg/dl) and poor risk (PR) ($TC < 200$ mg/dl and $TGs \geq 170$ mg/dl). The median PFS of GR, IR and PR groups was 7.76, 4.18 and 2.40 months, respectively ($p < 0.001$). Moreover, median OS of GR, IR and PR was 20.36, 11.18 and 4.14 months, respectively ($p < 0.001$) (figure 1). At multivariate analyses, after adjusting for baseline performance status, histology, treatment line, sex, statin use, number of metastatic sites and body mass index, the impact of LIPID score remained significant for both PFS and OS (table 4). Looking at TC components, HDL and LDL, a significant association was detected only for HDL and OS, with patients characterized by higher HDL levels showing longer OS (15.3 vs 10.1 months, $p=0.02$).

Conclusions LIPID score seems to strongly define subgroups of patients treated with ICIs with different prognosis. Further mechanistic insights are needed to clarify the prognostic and predictive role of lipid profile components in patients treated with ICIs.

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Ethics Approval Ethical approval to conduct this study was obtained by the respective local ethical committees on human experimentation of each participating center, after previous approval by the coordinating center ('Comitato Etico Regionale delle Marche – C.E.R.M.', Reference Number 792). All study related procedures and data collection were conducted in accordance with the Declaration of Helsinki and in accordance with Good Clinical Practice.

Consent Not applicable

Abstract 91 Tables 1,2,3 Patients circulating lipid assessment

Tables 1-2-3

Table 1: Patients circulating lipid profile and body mass index according to total cholesterol levels

	Total cholesterol ≥ 200 mg/dl	Total cholesterol < 200 mg/dl	p
Age	62.1 (14.5)	61.7 (14.2)	0.52
Sex			
Male	168 (58.3)	167 (57.8)	0.98
Female	10 (3.4)	10 (3.4)	0.98
TC (mg/dl)	212.1 (52.1)	167.1 (41.2)	<0.001
TG (mg/dl)	162.1 (112.1)	102.1 (72.1)	<0.001
LDL (mg/dl)	112.1 (72.1)	72.1 (42.1)	<0.001
HDL (mg/dl)	42.1 (22.1)	52.1 (32.1)	0.02
BMI	22.1 (3.1)	22.1 (3.1)	0.98

Table 2: Patients circulating lipid profile and body mass index according to triglycerides levels

	Triglycerides ≥ 170 mg/dl	Triglycerides < 170 mg/dl	p
Age	62.1 (14.5)	61.7 (14.2)	0.52
Sex			
Male	168 (58.3)	167 (57.8)	0.98
Female	10 (3.4)	10 (3.4)	0.98
TC (mg/dl)	212.1 (52.1)	167.1 (41.2)	<0.001
TG (mg/dl)	162.1 (112.1)	102.1 (72.1)	<0.001
LDL (mg/dl)	112.1 (72.1)	72.1 (42.1)	<0.001
HDL (mg/dl)	42.1 (22.1)	52.1 (32.1)	0.02
BMI	22.1 (3.1)	22.1 (3.1)	0.98

Table 3: Patients circulating lipid profile and body mass index according to sex

	Male	Female	p
Age	62.1 (14.5)	61.7 (14.2)	0.52
Sex			
Male	168 (58.3)	167 (57.8)	0.98
Female	10 (3.4)	10 (3.4)	0.98
TC (mg/dl)	212.1 (52.1)	167.1 (41.2)	<0.001
TG (mg/dl)	162.1 (112.1)	102.1 (72.1)	<0.001
LDL (mg/dl)	112.1 (72.1)	72.1 (42.1)	<0.001
HDL (mg/dl)	42.1 (22.1)	52.1 (32.1)	0.02
BMI	22.1 (3.1)	22.1 (3.1)	0.98

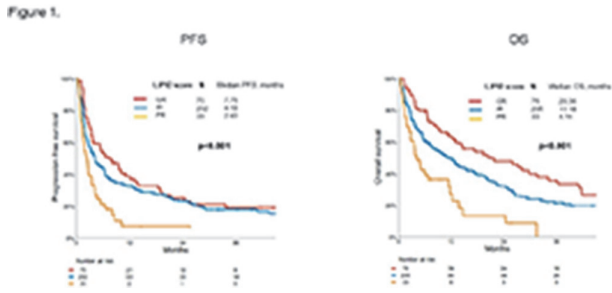
BMI, body mass index; TC, total cholesterol; TGs, triglycerides; LDL, low-density lipoproteins; HDL, high-density lipoproteins, NA, not available

Abstract 91 Table 4 Multivariate analysis for PFS and OS

Table 4.

Test variables	Multivariate analysis					
	PFS			OS		
	HR	95% CI	p	HR	95% CI	p
Histology						
NSCLC (ref.)/Others*	0.59	0.44-0.80	<0.001	0.58	0.42-0.79	<0.001
Sex						
Female (ref.)/Male	1.15	0.87-1.52	0.330	1.45	1.07-1.96	0.018
Treatment lines						
1st(ref.) \geq 2nd	1.37	1.05-1.80	0.022	1.36	1.02-1.81	0.035
ECOG PS						
0-1 (ref.) \geq 2	2.41	1.62-3.59	<0.001	2.48	1.67-3.69	<0.001
Metastatic sites						
0-1 (ref.) \geq 2	1.58	1.07-2.32	0.021	1.80	1.17-2.75	0.007
BMI						
<25 (ref.) \geq 25	0.92	0.70-1.21	0.566	0.78	0.58-1.04	0.086
Statin use						
no (ref.)/yes	1.02	0.76-1.38	0.888	0.89	0.65-1.21	0.445
LIPID-score						
GR (ref.)						
IR	1.21	0.86-1.68	0.270	1.51	1.05-2.17	0.024
PR	2.03	1.26-3.26	0.004	2.81	1.71-4.64	<0.001

PFS, progression free survival; OS, overall survival; HR, hazard ratio; CI, confidence interval; NSCLC, non-small cell lung cancer; ECOG PS; Eastern Cooperative Oncology Group Performance Status; BMI, body mass index; GR, good risk; IR, intermediate risk; PR, poor risk. All variables referred to baseline characteristics of patients.
*Others; melanoma, renal cell carcinoma, urothelial carcinoma, head and neck cancer
Statistically significant ($P < 0.05$).



Abstract 91 Figure 1 PFS and OS according to LIPID score
 GR, good risk; IR, intermediate risk; PR, poor risk

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