



PLATFORM OF LABORATORIES FOR ADVANCES IN CARDIAC EXPERIENCE

ROMA

Centro Congressi
di Confindustria

**Auditorium
della Tecnica**

9^a Edizione

**30 Settembre
1 Ottobre
2022**

CARDIONCOLOGIA: UPDATE 2022 Parte II

**IPERTENSIONE E DISLIPIDEMIA NEL PAZIENTE ONCOLOGICO:
DOBBIAMO SEGUIRE LE LINEE GUIDA O FARE QUALCOSA DI PIÙ
(O DI MENO)?**

Tarantini Luigi IAS «Cardioncologia»

AUSL-IRCCS (Tecnologie avanzate e modelli assistenziali in Oncologia) – Reggio Emilia



**SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA**
Azienda Unità Sanitaria Locale di Reggio Emilia
IRCCS Istituto in tecnologie avanzate e modelli assistenziali in oncologia



I Fattori di rischio CV nei pazienti oncologici in Italia

Prevalence of Cardiovascular Risk factors in Patients With Cancer: the PASSI Registry (2012-2016)



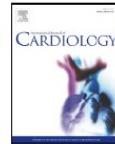
Fattori di rischio cardiovascolari (n=6867)



Chronic Comorbid Conditions Among Adult Cancer Survivors in the United States: Results From the National Health Interview Survey, 2002-2018

TABLE 2. Trends in Each Chronic Condition From 2002 to 2018 in US Adult Cancer Survivors

	Population Size (2012), 1000s	Population Size (2018), 1000s	Prevalence (2002-2003) ^a	Prevalence (2016-2018) ^a	Average Annual Prevalence Change ^b	P for Trend ^b
Hypertension *	4062	7730	36.90%	40.60%	0.296	<.001
Diabetes *	1358	2570	18.40%	15.80%	0.149	.003
Insulin-dependent diabetes	413	695	4.30%	4.00%	0.027	.36
Stroke	555	1263	4.90%	6.30%	0.052	.14
Heart disease *	2481	3767	20.60%	18.40%	-0.166	.007
Ischemic heart disease *	1441	2089	12.30%	10.60%	-0.169	.001
Other heart disease	1588	2543	12.80%	11.90%	-0.056	.29
Lung disease	1589	2624	14.30%	14.20%	-0.051	.33
COPD *	1078	1431	9.40%	6.90%	-0.181	<.001
Active asthma	851	1617	8.30%	10.10%	0.063	.14
Kidney disease *	319	940	4.20%	5.00%	0.066	.03
Liver disease *	248	625	3.10%	4.40%	0.087	.001
Hepatitis	474	622	5.90%	4.50%	-0.062	.04
Arthritis	4323	6865	31.80%	35.10%	0.026	.72
Morbid obesity *	716	1429	5.90%	9.50%	0.209	<.001



Arterial hypertension in cancer: The elephant in the room☆•☆☆

Giacomo Tini ^a, Matteo Sarocchi ^a, Giuliano Tocci ^{b,c}, Eleonora Arboscello ^d, Giorgio Ghigliotti ^a, Giuseppina Novo ^e, Claudio Brunelli ^a, Daniel Lenihan ^f, Massimo Volpe ^{b,c}, Paolo Spallarossa ^{a,*}



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- ❖ Arterial hypertension is a risk factor for cancer therapy-related heart failure.
- ❖ Arterial hypertension is a common adverse effect of many anticancer drugs.

Highlights

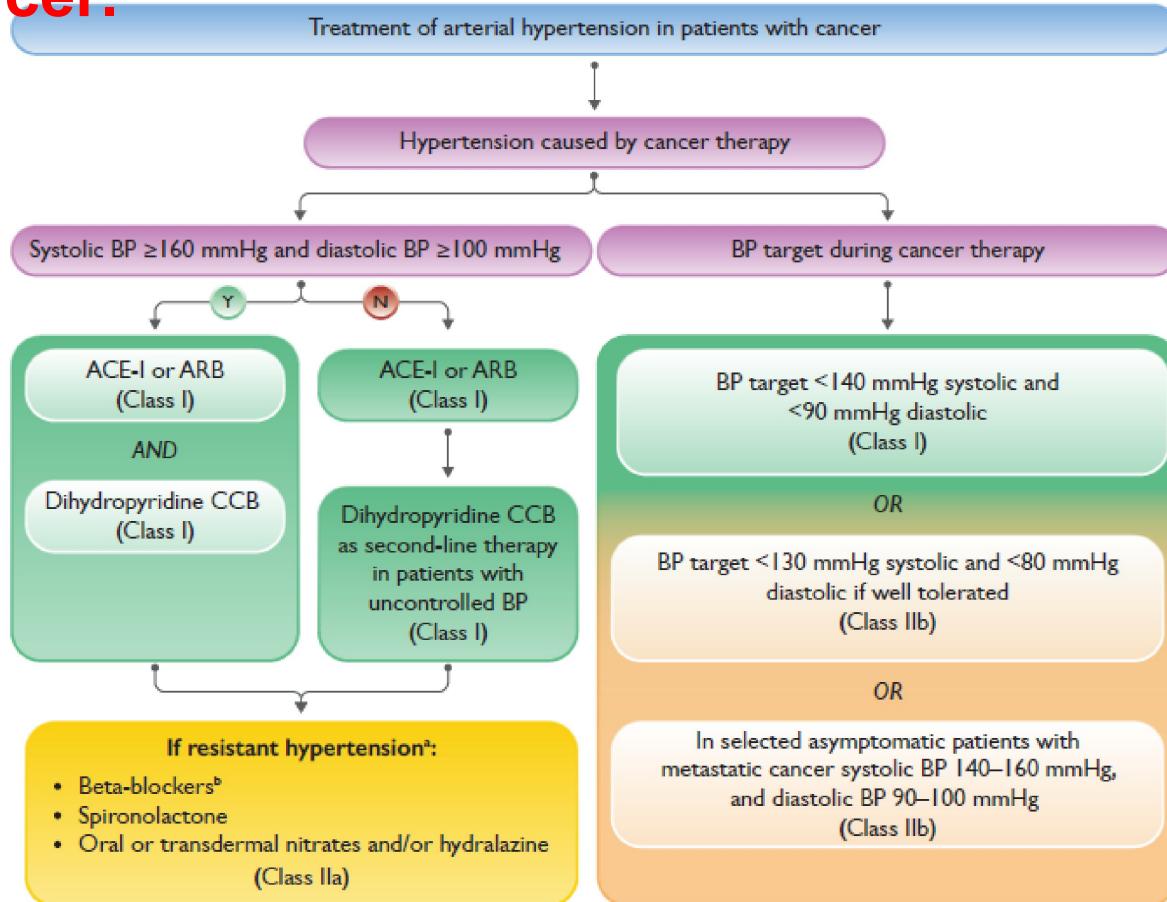
- ❖ Arterial hypertension is the most common comorbidity of cancer patients.
- ❖ It is significantly associated with both cancer incidence and mortality.
- ❖ Anti-hypertensive therapy prevents from premature discontinuation of cancer therapy.

Recommended threshold for asymptomatic hypertension treatment

in different clinical scenarios

Home BP mmHg	CS	Curable cancer during treatment	Metastatic cancer Prognosis >3 years	Metastatic cancer Prognosis 1–3 years	Metastatic cancer Prognosis <1 year	
160+	Treat	Treat	Treat	Treat	Treat	Class IIb
140–159	Treat	Treat	Treat	Consider treatment	May treat	Class IIa
135–139	Treat	May treat	Consider treatment	May treat	None	Class I
130–134	May treat	None	None	None	None	
<130	None	None	None	None	None	

Treatment of arterial hypertension in patients with cancer.

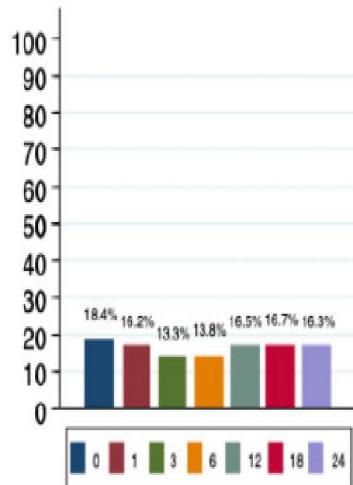


Cardiovascular risk factors during cancer treatment. Prevalence and prognostic relevance

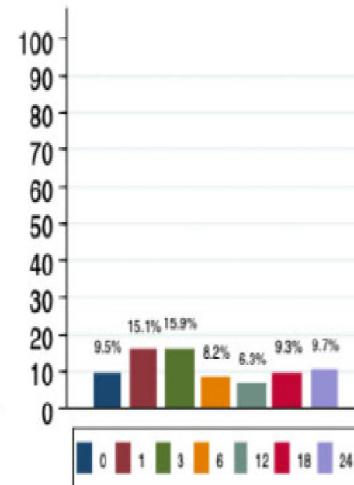
1324 patients underwent follow-up in a dedicated cardio-oncology clinic from April 2012 to October 2017 at CV risk factor in 67% of pts

Patients with poor control of CV Risk Factors

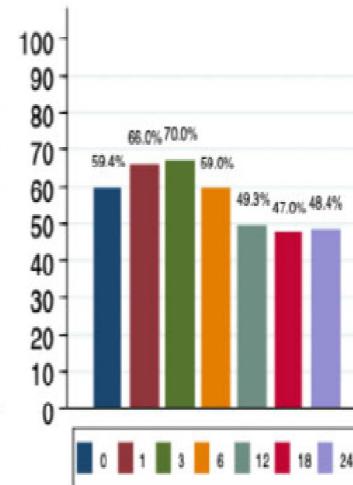
Hypertension



Diabetes



Hypercholesterolemia



Reassessing Human Adipose Tissue

Aaron M. Cypess, M.D., Ph.D.

Components of WAT

- T cell
- B cell
- M2 macrophage
- Preadipocyte
- M1 macrophage
- Adipocyte
- Endothelial cell
- Precursor
- ECM
- Cytosol
- Dendritic cell
- Eosinophil

Factors released by WAT

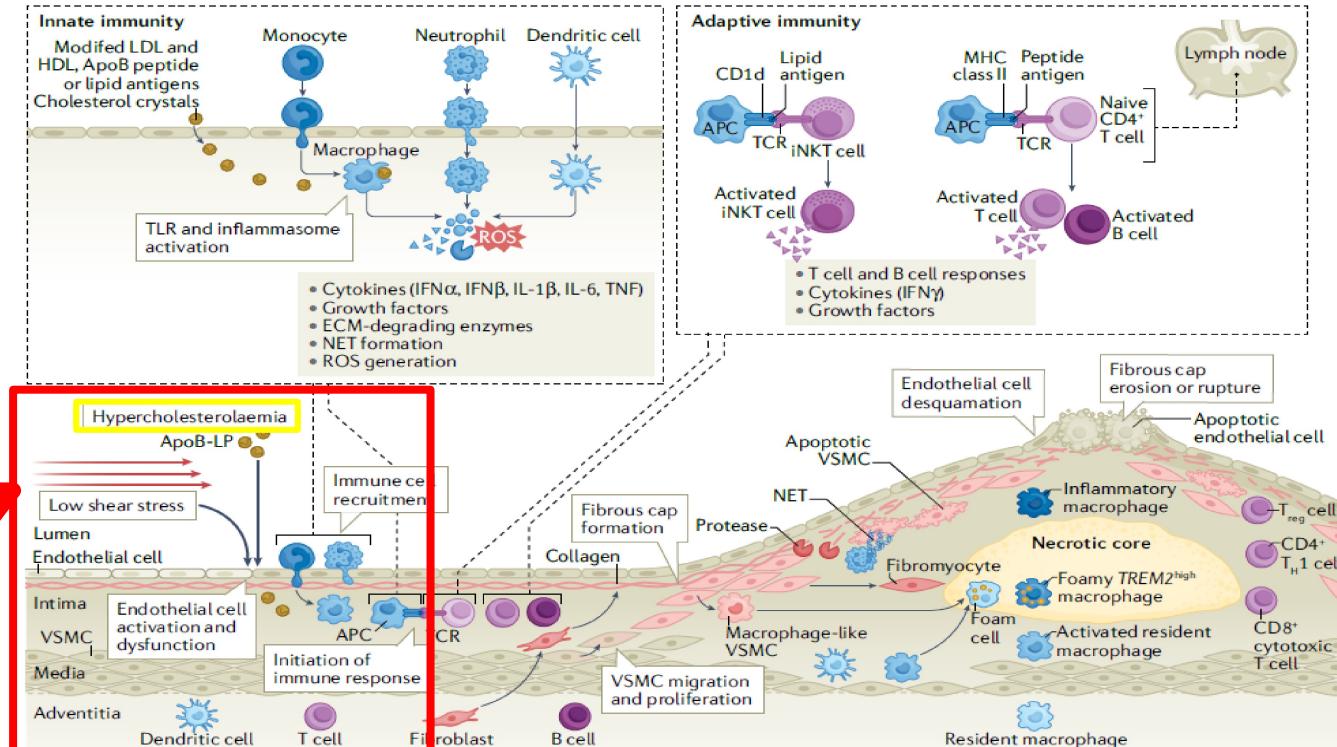
- Adipokines or hormones**
 - Leptin
 - Adiponectin
 - Resistin
 - Hepcidin
 - RPB4
 - Estrogen
- Cytokines**
 - TNF- α
 - MCP-1
 - CCL2, CXCL8
 - Interleukin-1, interleukin-6
- Enzymes or inhibitors**
 - LPL
 - DPP-4
 - PAI-1
- Lipid transport**
 - ApoE
 - CETP
 - Cholesterol
 - Bile acids
- Others**
 - HIF1 α
 - Anandamide
 - Lipid-derived species

Organ systems affected by WAT adipokines

- Appetite, satiety, EE, temperature, activity, glucose metabolism
- Immune cell attraction, differentiation, systemic inflammation, wound healing
- Blood pressure, heart muscle contractility, smooth muscle tone
- Insulin sensitivity, lipid accumulation, hepatokine release, lipid metabolism, growth factors
- Insulin secretion, glucagon secretion
- Absorption, incretin secretion
- Insulin sensitivity, myokine secretion, lipid storage

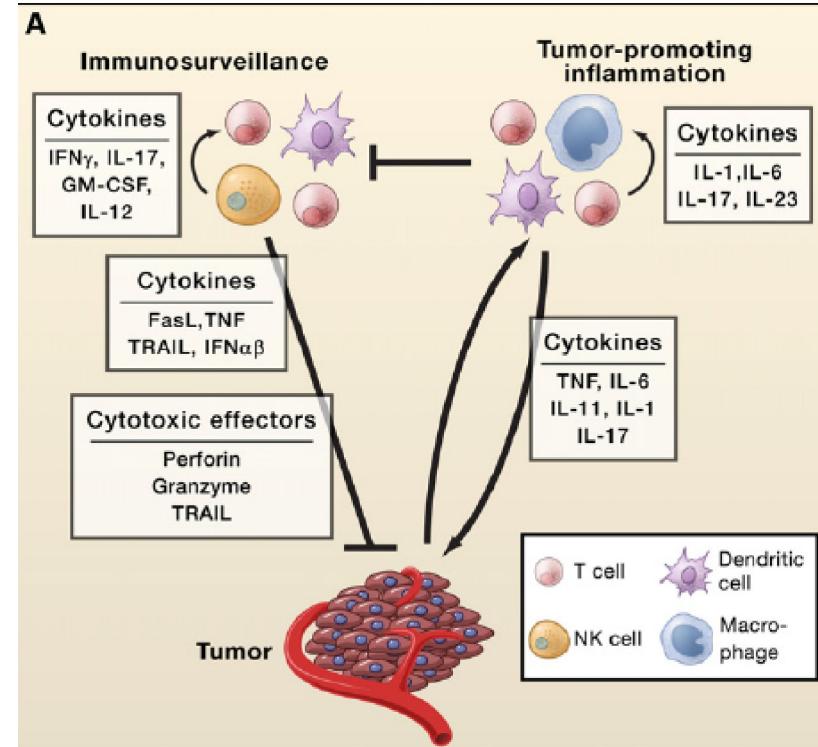
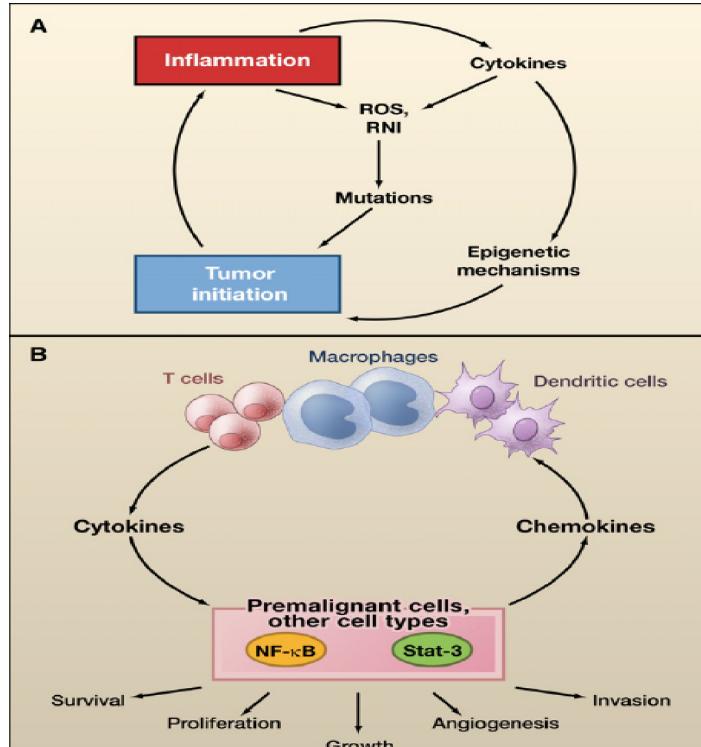
Cancro e Malattie CV: la teoria del «Common Soil» 1

Inflammation and Immunity in Atherosclerosis



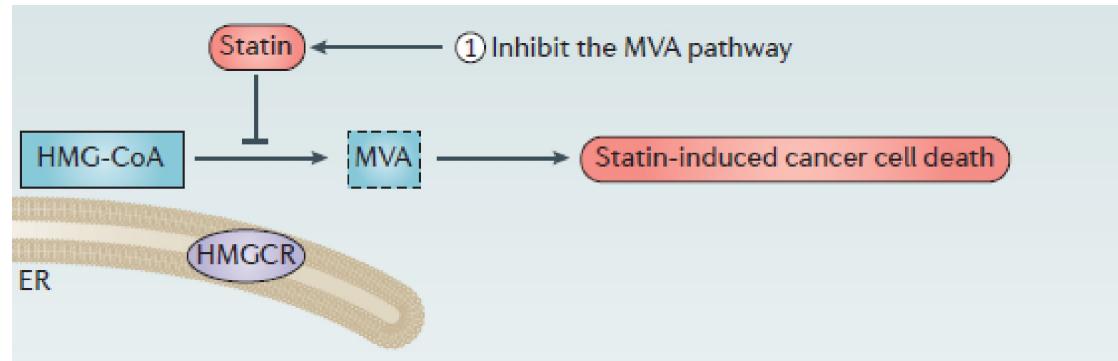
Cancro e Malattie CV: la teoria del «Common Soil» 2

Inflammation and Immunity in Tumorigenesis



The interplay between cell signalling and the mevalonate pathway in cancer

Cancer cells, with their aberrant growth and metabolism, are primed to upregulate the MVA pathway to provide essential building blocks for continued proliferation.



Statins have potential anticancer properties. They inhibit 3-hydroxy-3-methylglutaryl-CoA reductase (HMGCR), thereby reducing mevalonate production

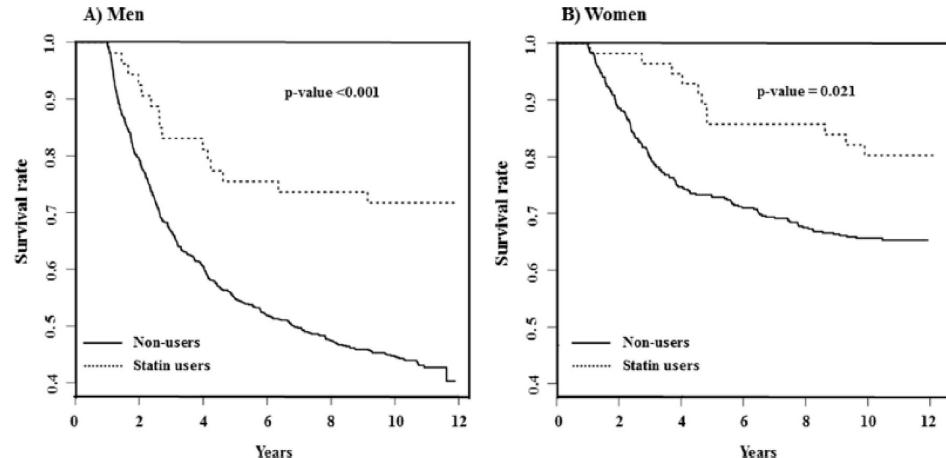
Association between statin use and all-cause mortality in cancer survivors, based on the Korean health insurance service between 2002 and 2015

Joungyoun Kim ^{a,1}, Eun-A. Choi ^{a,1}, Ye-Eun Han ^a, Jae-woo Lee ^b, Ye-seul Kim ^b,
Yonghwan Kim ^b, Hyo-Sun You ^b, Hyeong-Jin Hyun ^c, Hee-Taik Kang ^{b,d,*}

Table 1 Baseline characteristics according to statin use by sex.

	Men		p-values	Women		p-values
	Non-users	statin users		Non-users	statin users	
Number	755	53	n.a.	438	56	n.a.
Age, years	56.0 ± 7.5	57.9 ± 6.3	0.069	53.0 ± 7.7	56.4 ± 7.6	0.002
BMI, kg/m ²	23.7 ± 3.0	24.7 ± 2.4	0.016	23.9 ± 3.0	25.5 ± 3.2	<0.001
SBP, mmHg	128.9 ± 17.4	134.7 ± 14.2	0.018	123.3 ± 17.9	132.9 ± 17.3	<0.001
Glucose, mg/dL	102.9 ± 40.0	112.8 ± 39.2	0.084	92.5 ± 16.7	112.4 ± 48.5	<0.001
Total cholesterol, mg/dL	188.5 ± 36.0	206.9 ± 38.3	<0.001	192.6 ± 37.0	233.6 ± 44.6	<0.001
ALT, U/L	32.9 ± 40.7	36.6 ± 52.0	0.533	21.9 ± 17.5	24.1 ± 21.2	0.385
DM, %	43 (5.7)	9 (17.0)	0.005	8 (1.8)	6 (10.7)	0.002
Hypertension, %	57 (7.6)	11 (20.8)	0.003	37 (8.4)	15 (26.8)	<0.001
Ever smokers, %	454 (60.1)	33 (62.3)	0.885	19 (4.3)	1 (1.8)	0.715
Drinking status, %			0.064			0.033
Rare	261 (34.6)	26 (49.1)		365 (83.3)	53 (94.6)	
Sometimes	292 (38.7)	13 (24.5)		66 (15.1)	2 (3.6)	
Often	202 (26.8)	14 (26.4)		7 (1.6)	1 (1.8)	
Physical activity, %			0.065			0.166
Rare	381 (50.5)	22 (41.5)		294 (67.1)	32 (57.1)	
Sometimes	282 (37.4)	28 (52.8)		100 (22.8)	14 (25.0)	
Regular	92 (12.2)	3 (5.7)		44 (10.0)	10 (17.9)	
Economic status, %			0.225			0.613
Low	161 (21.3)	16 (30.2)		93 (21.2)	14 (25.0)	
Middle	236 (31.3)	12 (22.6)		161 (36.8)	17 (30.4)	
High	358 (47.4)	25 (47.2)		184 (42.0)	25 (44.6)	

Abbreviation: BMI, body mass index; SBP, systolic blood pressure; ALT, alanine aminotransferase; DM, diabetes mellitus.



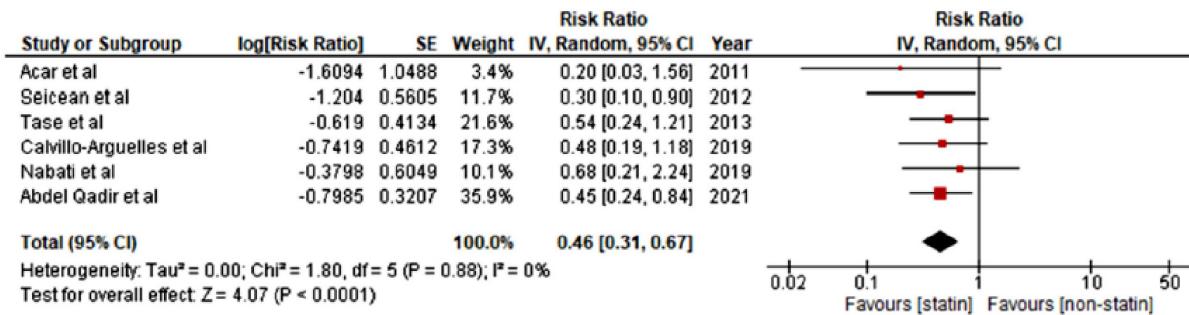
Statin adherence and risk of all-cause, cancer, and cardiovascular mortality among dyslipidemia patients: A time-dependent analysis

Young Ran Lee ^{a,b,1}, Sarah Soyeon Oh ^{a,c,1}, Sung-In Jang ^{a,d}, Eun-Cheol Park ^{a,d,*}

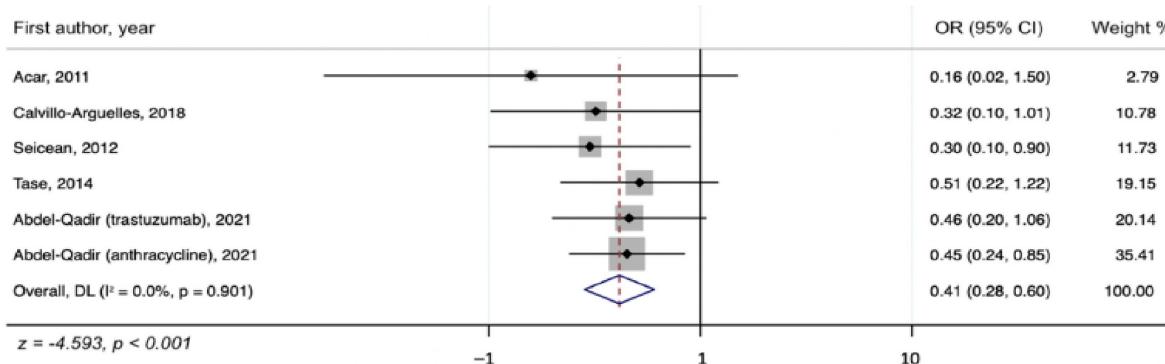
	Proportion of days covered (PDC) for statin							
	Good (>80%)	Moderate (50–80%)			Poor (<50%)			
		Adjusted HR	95% CI	p-Value	Adjusted HR	95% CI	p-Value	
Lower–Upper								
Mortality (cancer)								
Sex								
Men	1.00	1.29	1.02–1.64	0.0357	1.58	1.40–3.42	0.0021	
Women	1.00	1.04	0.85–1.29	0.7007	1.32	1.11–1.56	0.0018	
BMI								
Underweight (BMI < 18.5)	1.00	0.78	0.33–1.84	0.5715	0.53	0.23–1.19	0.1213	
Normal (18.5 ≤ BMI < 25.0)	1.00	1.21	0.99–1.47	0.0640	1.31	1.10–1.56	0.0024	
Overweight (25.0 ≤ BMI < 30)	1.00	0.93	0.70–1.25	0.6331	1.40	1.10–1.77	0.0060	
Obese (30 ≤ BMI)	1.00	0.83	0.35–1.94	0.6626	1.25	0.61–2.55	0.5494	
Smoking status								
Non-smoker	1.00	1.13	0.84–1.53	0.4207	1.27	0.98–1.64	0.0699	
Current smoker	1.00	1.10	0.91–1.33	0.3486	1.37	1.16–1.62	0.0002	
Past smoker	1.00	0.97	0.50–1.87	0.9311	1.08	0.62–1.89	0.7785	
Physical activity								
Active	1.00	1.04	0.83–1.32	0.7169	1.31	1.09–1.58	0.0049	
Inactive	1.00	1.15	0.93–1.42	0.2090	1.35	1.12–1.64	0.0022	

Statins attenuate Cardiotoxicity in Cancer Patients receiving Anthracyclines and Trastuzumab-based Chemotherapy

Incidence of cardiotoxicity



Shadid I. et AL. Am. J. Cardiol 2021



Kim J. Et AL. J. Clin. Med. 2021,

Caveat!! Gli RCT sottostimano gli eventi avversi CV da ICI !!

Association Between Immune Checkpoint Inhibitors With Cardiovascular Events and Atherosclerotic Plaque

CONCLUSIONS: Cardiovascular events were higher after initiation of ICIs, potentially mediated by accelerated progression of atherosclerosis. Optimization of cardiovascular risk factors and increased awareness of cardiovascular risk before, during, and after treatment should be considered among patients on an ICI.

Drobni S et AL. Circulation 2020

Incidence of Cardiovascular Events in Patients Treated With Immune Checkpoint Inhibitors

CONCLUSION Cardiovascular events during and after ICI treatment are more common than currently appreciated. Patients at risk are those with a history of cardiovascular disease. Compared with matched cancer and population controls, MACE incidence rates are significantly higher, suggesting a potential harmful effect of ICI treatment besides the underlying risk.

Laenens D. et AL. JCO 2022

ORIGINAL RESEARCH ARTICLE

Association Between Immune Checkpoint Inhibitors With Cardiovascular Events and Atherosclerotic Plaque

Table 5. Subgroup Analysis of the Change in Plaque Volume After Starting an ICI by Statin

Plaque measure, median (IQR)	Drug, yes	Drug, no	P value
Statin			
Total aortic plaque volume			
Before ICI, mm ³	1903 (1038 to 2661)	1281 (358 to 2691)	0.38
After ICI, mm ³	2214 (1730 to 4090)	1644 (588 to 4211)	0.32
Absolute change in total plaque, mm ³ /y	79.2 (0 to 524)	115 (0 to 509)	0.001
Relative change in total plaque volume, %/y	5.2 (0.6 to 23.7)	8.3 (4.7 to 42.5)	0.04
Noncalcified aortic plaque volume			
Before ICI, mm ³	1233 (956 to 1835)	998 (353 to 2663)	0.68
After ICI, mm ³	1781 (1180 to 3517)	1631 (576 to 3652)	0.62
Absolute change in noncalcified plaque, mm ³ /y	45.3 (-38 to 387)	69.5 (0 to 377)	0.002
Relative change in noncalcified plaque volume, %/y	3.1% (-2.3 to 30.4)	7.0% (2.6 to 43.6)	0.04

Integrated analysis of concomitant medications and oncological outcomes from PD-1/PD-L1 checkpoint inhibitors in clinical practice

real-world, multicenter, retrospective observational data collection aimed at evaluating the impact of concomitant medications at immunotherapy
Initiation in **1012 pts**

Table 2 Univariate and multivariate analyzes of ORR

Variable (Comparator)	ORR		Multivariate analysis aOR (95% CI); p value
	Univariate analysis Response/ratio—ORR (%) (95% CI)	OR (95% CI); p value	
Statins			
(No)	275/774—35.5 (31.4 to 39.9)	1.56 (1.13 to 2.15); p=0.0070	1.60 (1.14 to 2.25); p=0.0064
Yes	86/186—46.2 (36.9 to 57.1)		
Other lipid lowerings			
(No)	345/915—37.7 (33.9 to 41.9)	1.22 (0.66–2.24); p=0.5130	1.11 (0.59 to 2.09); 0.7271
Yes	19/45—42.2 (25.4 to 65.9)		
Aspirin			
(No)	281/780—36.0 (31.9 to 40.5)	1.42 (1.02 to 1.97); p=0.0361	1.47 (1.04 to 2.08); 0.0267
Yes	80/180—44.4 (35.2 to 55.3)		

Objective response rate (ORR)

Cortellini A, et AL. *Journal for ImmunoTherapy of Cancer* 2020

Take Home Messages

Malattie CV e Cancro non sono più da considerare come entità cliniche separate ma interconnesse dalla condivisione di fattori di rischio e da comuni meccanismi fisiopatologici

Con il progressivo invecchiamento della popolazione ed il miglioramento della sopravvivenza dei pazienti con malattie croniche degenerative i pazienti oncologici attuali del mondo reale sono sempre più clinicamente «complessi»

Le evidenze disponibili indicano che l'ipertensione e la dislipidemia devono essere trattate adeguatamente tenendo soprattutto in considerazione l'Assetto Cardio-metabolico

Le evidenze disponibili per l'ipertensione sono da ritenersi sufficienti, non così per la gestione della dislipidemia il cui trattamento è spesso inadeguato.

Alla luce delle recentissime evidenze cliniche e della prorompente evoluzione della immuno-terapia, è necessario colmare al più presto tale lacuna con studi mirati.



Grazie per l'attenzione!!!!