Trattamento Precoce con PCSK9 Inibitori nel Paziente a Rischio CV Molto Alto: Il Problema

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Caserta

Anamnesi

- Paziente di 46 anni, sesso maschile, BMI 19
- FDR: Familiarità per CAD in età giovanile, dislipidemia non in trattamento
- In apparente buona salute fino al 04.04.2021 quando per insorgenza di dolore toracico a riposo, irradiato al giugulo, si reca in PS dove veniva posta diagnosi di STEMI inferiore
- Stenosi occlusiva di CDx al tratto medio s/p PTCA-DES (culprit)
- Stenosi significativa su IVA s/p PTCA-DES (staged)

Esami ematochimici al ricovero

- Colesterolo totale 324 mg/dl
- Colesterolo LDL 237 mg/dl
- Colesterolo HDL 57 mg/dl
- Trigliceridi 150 mg/dl
- Lp(a) 0.522 g/dl (v.r. 0.000-0.300)

Linee guida: Cosa ci dicono?

Very-high-risk	People with any of the following: Documented ASCVD, either clinical or unequivocal on imaging. Documented ASCVD includes previous ACS (MI or unstable angina), stable angina, coronary revascularization (PCI, CABG, and other arterial revascularization procedures), stroke and TIA, and peripheral arterial disease. Unequivocally documented ASCVD on imaging includes those findings that are known to be predictive of clinical events, such as significant plaque on coronary angiography or CT scan (multivessel coronary disease with two major epicardial arteries having >50% stenosis), or on carotid ultrasound. DM with target organ damage,[a] or at least three major risk factors, or early onset of T1DM of long duration (>20 years). Severe CKD (eGFR <30 mL/min/1.73 m^2). A calculated SCORE ≥10% for 10-year risk of fatal CVD. FH with ASCVD or with another major risk factor.

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Linee guida: Cosa ci dicono?

Recommendations for treatment goals for low-density lipoprotein cholesterol

Recommendations	Class[a]	Level[b]
In secondary prevention for patients at very-high risk,[c] an LDL-C reduction of ≥50% from baseline[d] and an LDL-C goal of <1.4 mmol/L (<55 mg/dL) are recommended.[33–35,119,120]	I	A
In primary prevention for individuals at very-high risk but without FH,[c] an LDL-C reduction of ≥50% from baseline[d] and an LDL-C goal of <1.4 mmol/L (<55 mg/dL) are recommended.[34–36]	I	C
In primary prevention for individuals with FH at very-high risk, an LDL-C reduction of ≥50% from baseline and an LDL-C goal of <1.4 mmol/L (<55 mg/dL) should be considered.	IIa	C
For patients with ASCVD who experience a second vascular event within 2 years (not necessarily of the same type as the first event) while taking maximally tolerated statin-based therapy, an LDL-C goal of <1.0 mmol/L (<40 mg/dL) may be considered.[119,120]	IIb	B
In patients at high risk,[c] an LDL-C reduction of ≥50% from baseline[d] and an LDL-C goal of <1.8 mmol/L (<70 mg/dL) are recommended.[34,35]	I	A
In individuals at moderate risk,[c] an LDL-C goal of <2.6 mmol/L (<100 mg/dL) should be considered.[34]	IIa	A
In individuals at low risk,[c] an LDL-C goal <3.0 mmol/L (<116 mg/dL) may be considered.[36]	IIb	A

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Linee guida: Cosa ci dicono?

Recommendations for pharmacological low-density lipoprotein cholesterol lowering

Recommendations	Class[a]	Level[b]
It is recommended that a high-intensity statin is prescribed up to the highest tolerated dose to reach the goals set for the specific level of risk.[32,34,38]	I	A
If the goals[c] are not achieved with the maximum tolerated dose of a statin, combination with ezetimibe is recommended.[33]	I	B
For primary prevention patients at very-high risk, but without FH, if the LDL-C goal is not achieved on a maximum tolerated dose of a statin and ezetimibe, a combination with a PCSK9 inhibitor may be considered.	IIb	C
For secondary prevention, patients at very-high risk not achieving their goal[c] on a maximum tolerated dose of a statin and ezetimibe, a combination with a PCSK9 inhibitor is recommended.[119,120]	I	A
For very-high-risk FH patients (that is, with ASCVD or with another major risk factor) who do not achieve their goal[c] on a maximum tolerated dose of a statin and ezetimibe, a combination with a PCSK9 inhibitor is recommended.	I	C
If a statin-based regimen is not tolerated at any dosage (even after rechallenge), ezetimibe should be considered.[197,265,353]	IIa	C
If a statin-based regimen is not tolerated at any dosage (even after rechallenge), a PCSK9 inhibitor added to ezetimibe may also be considered.[197,265,353]	IIb	C
If the goal[c] is not achieved, statin combination with a bile acid sequestrant may be considered.	IIb	C

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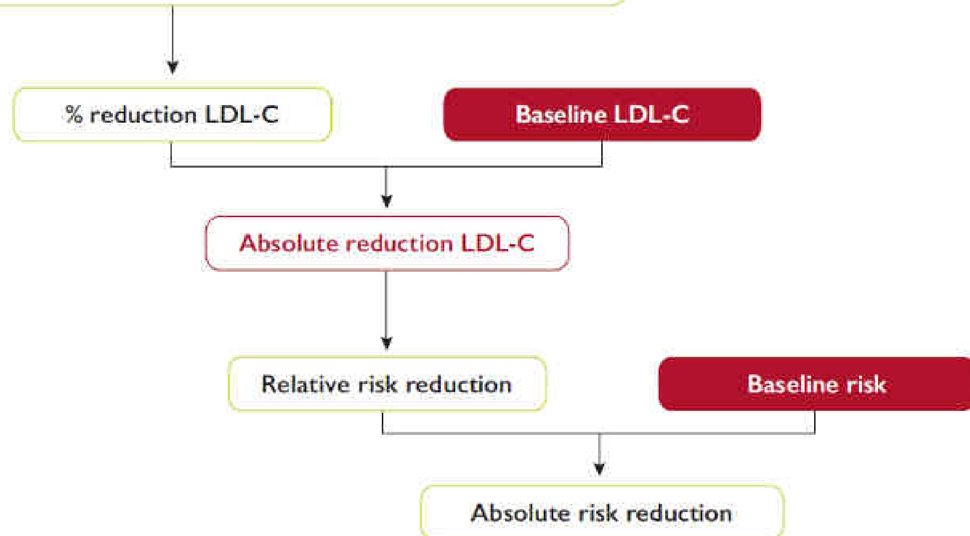
Linee guida: Cosa ci dicono?

Intensity of lipid lowering treatment

Treatment	Average LDL-C reduction
Moderate intensity statin	≈ 30%
High intensity statin	≈ 50%
High intensity statin plus ezetimibe	≈ 65%
PCSK9 inhibitor	≈ 60%
PCSK9 inhibitor plus high intensity statin	≈ 75%
PCSK9 inhibitor plus high intensity statin plus ezetimibe	≈ 85%



LDL: 237 mg/dl

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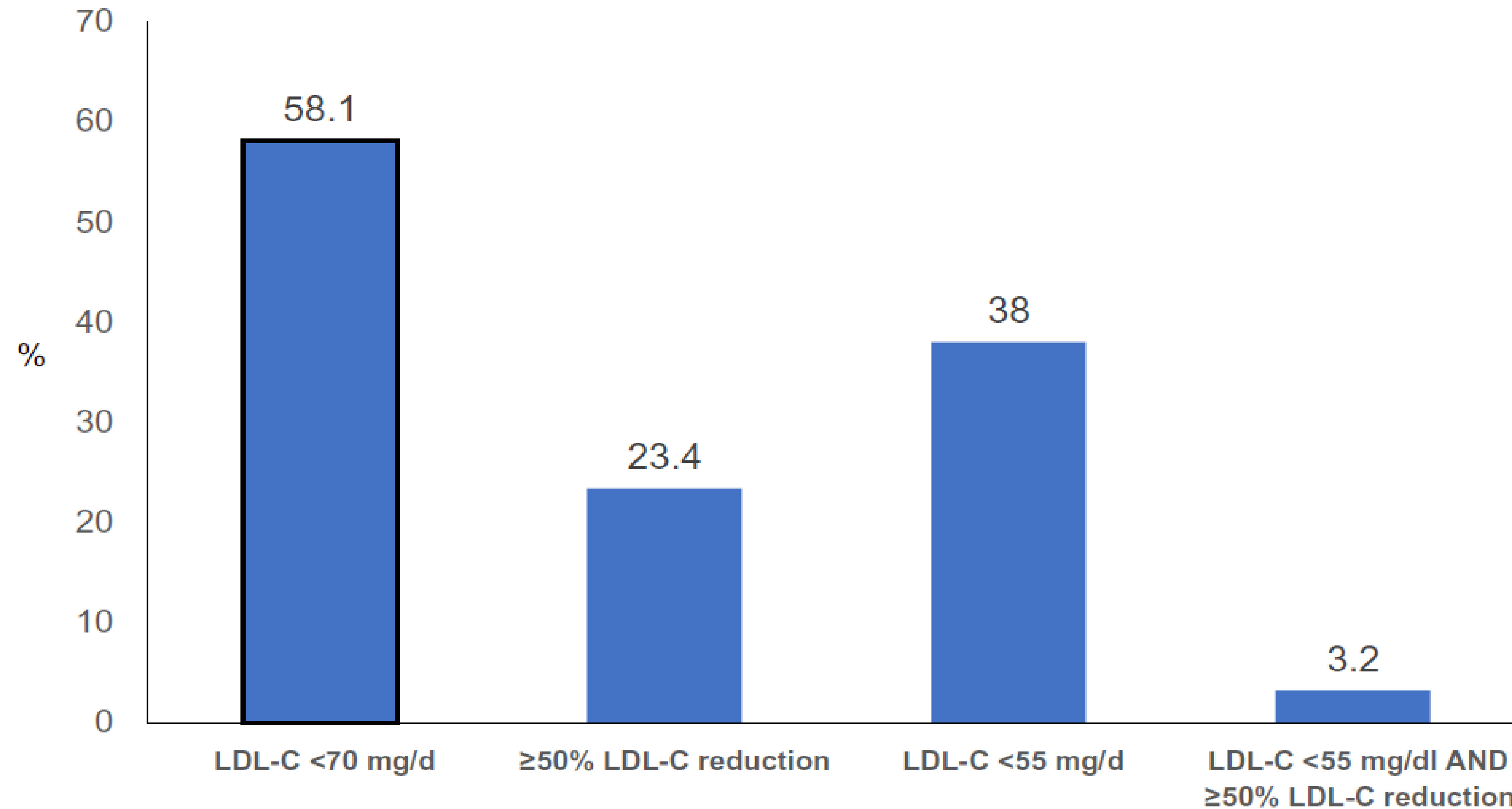
Problema

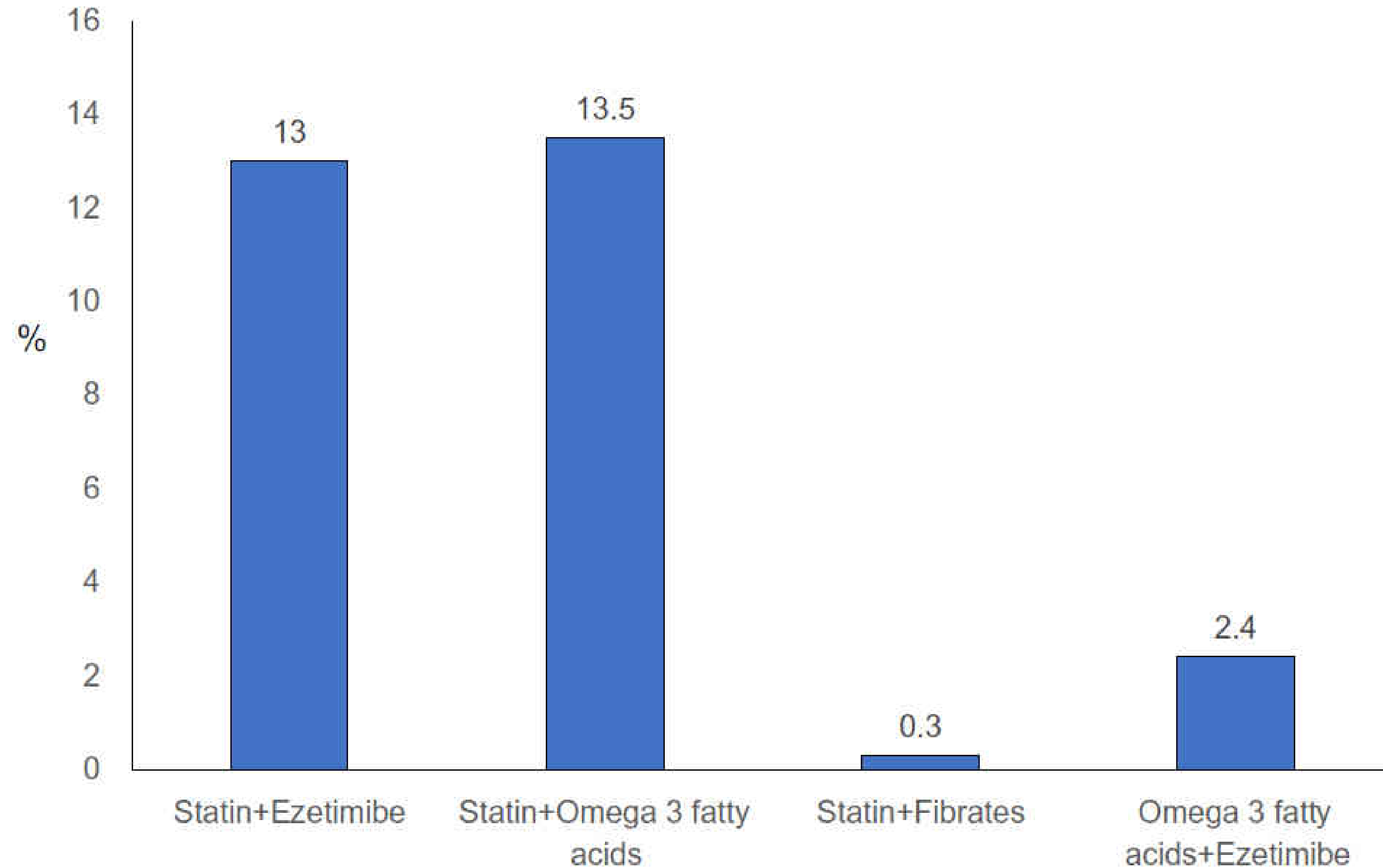
Quanti pazienti con rischio cardiovascolare molto alto raggiungono il target suggerito dalle linee guida?

Frequency of Very High Risk* Patients Reaching LDL-C Goals Recommended by 2016 and 2019 ESC/EAS Guidelines



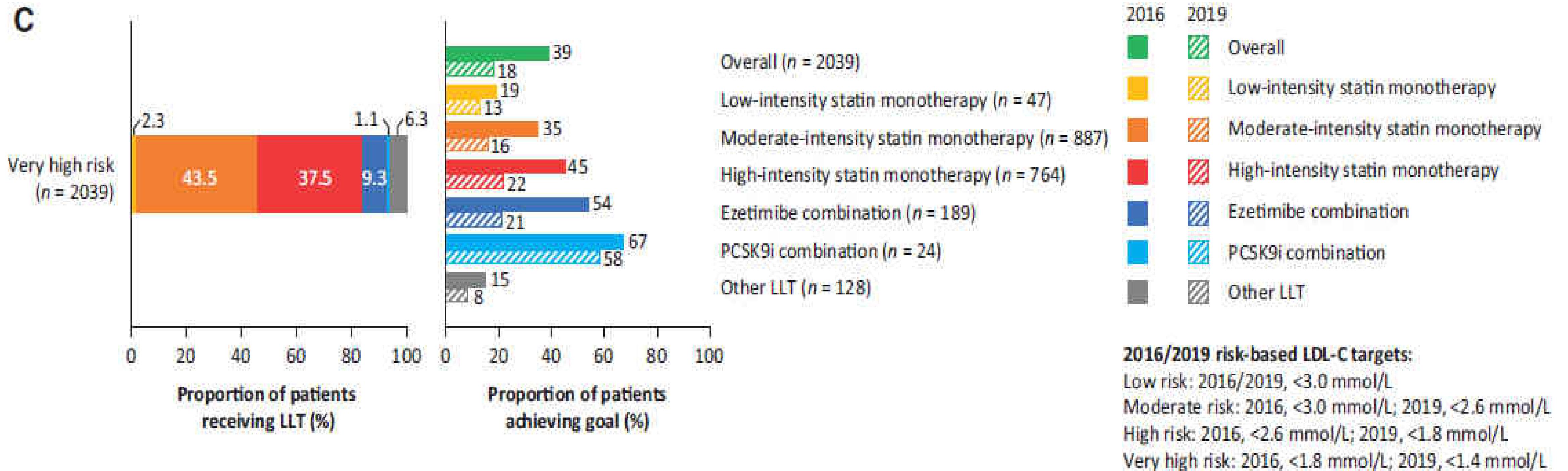
De Luca L et al. Int J Cardiol. 2020

Associations of Lipid Lowering Strategies in Patients at Very High Risk



De Luca L et al. Int J Cardiol. 2020

EU-Wide Cross-Sectional Observational Study of Lipid-Modifying Therapy Use in Secondary and Primary Care: the DA VINCI Study



Kausik K. R. et al. EJPC, 2020

Trattamento

- Rosuvastatina/Ezetimibe 20/10 mg 1 cp ore 22

Follow up (I)

- Controllo clinico del 04/05/2021
- Paziente asintomatico, non eventi cardiovascolari dalla dimissione
- Colesterolo totale 256 mg/dl (↓)
- Colesterolo LDL 170 mg/dl (↓)
- Colesterolo HDL 56 mg/dl
- Trigliceridi 150 mg/dl
- Lp(a) 0,495 g/dl

Attivazione web e pubblicazione schede di monitoraggio - Registro Praluent (CVD)

Si informano gli utenti dei Registri Farmaci sottoposti a Monitoraggio che, a seguito della pubblicazione della Determina AIFA nella GU n. 95 del 09/04/2020, a partire dal 10/04/2020 è possibile utilizzare, in regime di rimborsabilità SSN, il medicinale PRALUENT per le seguenti indicazioni terapeutiche:

- in prevenzione primaria in pazienti di età ≤80 aa con ipercolesterolemia familiare eterozigote e livelli di LDL-C ≥130 mg/dL nonostante terapia da almeno 6 mesi con statina ad alta potenza alla massima dose tollerata + ezetimibe oppure con dimostrata intolleranza alle statine (vedere successivamente la definizione di intolleranza) **e/o all'ezetimibe**;
- in prevenzione secondaria in pazienti di età ≤80 aa con ipercolesterolemia familiare eterozigote o ipercolesterolemia non familiare o dislipidemia mista e livelli di LDL-C ≥100 mg/dL nonostante terapia da almeno 6 mesi con statina ad alta potenza alla massima dose tollerata + ezetimibe **oppure dopo una sola rilevazione di C-LDL in caso di IMA recente (ultimi 12 mesi) o eventi CV multipli** oppure con dimostrata intolleranza alle statine (vedere successivamente la definizione di intolleranza) **e/o all'ezetimibe**.

N.B: In grassetto sono evidenziate le modifiche apportate rispetto alle precedenti indicazioni già rimborsate SSN.

Si specifica che, a partire dal 10/04/2020, il registro in oggetto è disponibile sulla piattaforma web; pertanto si invitano i referenti regionali a procedere all'abilitazione dei Centri sanitari autorizzati, accedendo al sistema.

Infine si ricorda che è possibile consultare la scheda clinica, scaricabile in formato .zip, dalla lista dei "Registri e PT Attivi", raggiungibile dal box "*Link correlati*".

Ufficio Registri di Monitoraggio

Follow up (I)

- Statina alta intensità + Ezetimibe
- Aggiunge PCSK9 i

Follow up (II)

- Controllo clinico del 07/06/2021
- Asintomatico, non eventi cardiovascolari dall'ultimo controllo
- Colesterolo totale 170 mg/dl (↓)
- Colesterolo LDL 68 mg/dl (↓)
- Colesterolo HDL 58 mg/dl
- Trigliceridi 125 mg/dl
- Lp(a) 0,366 g/dl (↓)

Problema

Quanto l'utilizzo precoce di PCSK9 inibitori influenzi gli outcome nei pazienti a rischio cardiovascolare molto alto?

Quali sono gli effetti dei PCSK9 inibitori sulla placca ateromasica?

Grazie per l’attenzione