SCOMPENSO CARDIACO

IL TRATTAMENTO NELLE LINEE GUIDA

LE NUOVE STRATEGIE TERAPEUTICHE

M.MILANO
M.CRISTINA ROSA BRUSIN

ANNA

- 68 anni
- Ipertesa, diabetica in ipo-orali
- Atenololo 50mg/die e Metformina 500mg
- Da circa 2 mesi sintomatica per dispnea NYHA II-III
- ECOTT: Vsx marcatamente ipertrofico, FE 55%,

disfunzione diastolica, non valvulopatie di rilievo

Quale terapia inizierà il cardiologo?

1) ACE-I o Sartano
2) Digitale
3) Doxazosina
4) ASA

Televoto

ANNA

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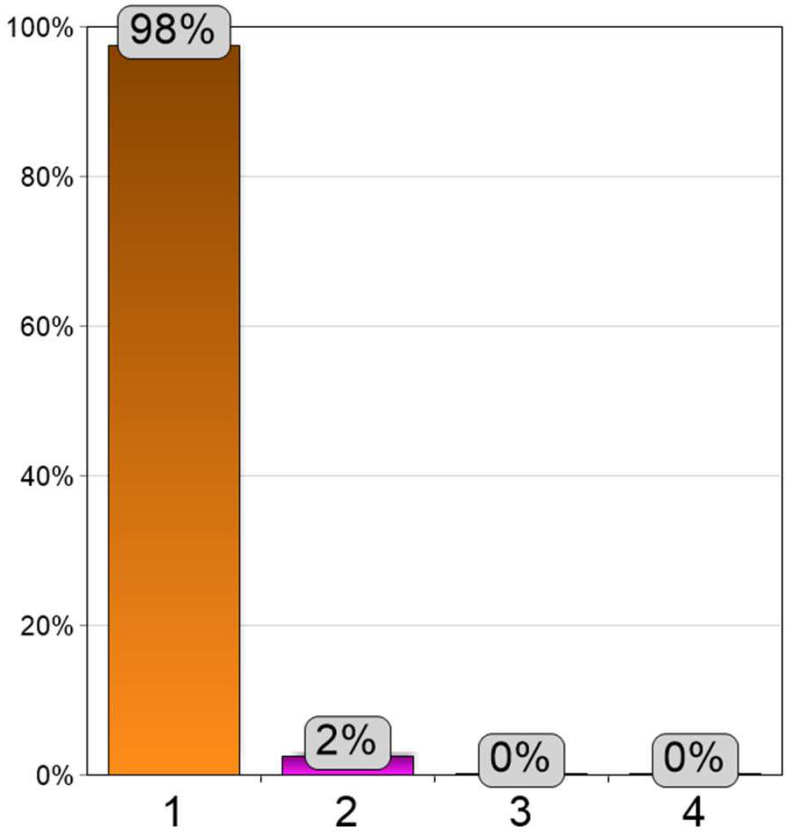

QUALE E' LA TERAPIA CORRETTA SECONDO LE LINEE GUIDA?

ANNA

Table 3.1 Definition of heart failure with preserved (HFpEF), mid-range (HFmrEF) and reduced ejection fraction (HFrEF)

Type of HF		HFrEF	HFmrEF	HFpEF
CRITERIA	1	Symptoms ± Signs[a]	Symptoms ± Signs[a]	Symptoms ± Signs[a]
	2	LVEF <40%	LVEF 40–49%	LVEF ≥50%
	3	–	1. Elevated levels of natriuretic peptides[b]; 2. At least one additional criterion: a. relevant structural heart disease (LVH and/or LAE), b. diastolic dysfunction (for details see Section 4.3.2).	1. Elevated levels of natriuretic peptides[b]; 2. At least one additional criterion: a. relevant structural heart disease (LVH and/or LAE), b. diastolic dysfunction (for details see Section 4.3.2).

European Heart Journal (2016) 37, 2129–2200
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ESC GUIDELINES

2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)

Treatment of heart failure with preserved ejection fraction

Recommendations for treatment of patients with heart failure with preserved ejection fraction and heart failure with mid-range ejection fraction

Recommendations	Class [a]	Level [b]	Ref [c]
it is recommended to screen patients with HFpEF or HFmrEF for both cardiovascular and non-cardiovascular comorbidities, which, if present, should be treated provided safe and effective interventions exist to improve symptoms, well-being and/or prognosis.	I	C	
Diuretics are recommended in congested patients with HFpEF or HFmrEF in order to alleviate symptoms and signs.	I	B	178, 179

HFmrEF = heart failure with mid-range ejection fraction; HFpEF = heart failure with preserved ejection fraction.
[a]Class of recommendation.
[b]Level of evidence.
[c]Reference(s) supporting recommendations.

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9.2 Effect of treatment on hospitalization for heart failure in heart failure with preserved ejection fraction

For patients in sinus rhythm, there is some evidence that nebivolol,[173,312,313] digoxin,[314] spironolactone[301] and candesartan[310] might reduce HF hospitalizations. For patients in AF, beta-blockers do not appear to be effective and digoxin has not been studied. The evidence in support of either ARBs[315] or ACEIs[311] is inconclusive.

9.3 Effect of treatment on mortality in heart failure with preserved ejection fraction

Trials of ACEIs, ARBs, beta-blockers and MRAs have all failed to reduce mortality in patients with HFpEF or HFmrEF. However, in older patients with HFrEF, HFpEF or HFmrEF, nebivolol reduced the combined endpoint of death or cardiovascular hospitalization,[173,312] with no significant interaction between treatment effect and baseline LVEF.[313]

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ANTONIO

- 65 anni, iperteso, diabetico
- Marzo 2016: STEMI anteriore ad arrivo tardivo, PTCA primaria su IVA occlusa, FE 30%.
- Dimesso in Doppia Anti Aggregazione (DAT), statina, ACE-I e beta bloccante
- Giugno 16: FE 30% nonostante terapia medica massimale, impianto ICD monocamerale (QRS stretto)
- Settembre 2017: HF, peggioramento funzionalità epatica e renale, FE 30% ed IM grave. Ottimizzazione del compenso con diuretici e vasodilatatori. Coronarografia: buon esito pregresso stenting

Dimesso in ASA, metoprololo, statina, diuretici (furosemide e riasparmiatore di potassio), ACE-I. Dopo normalizzazione della funzionalità epato-renale, quale farmaco aggiungereste?

1) Digitale
2) Sartano
3) Clonidina
4) Sostutuirei ACE-I con Sacubitril/Valsartan

Televoto

ANTONIO

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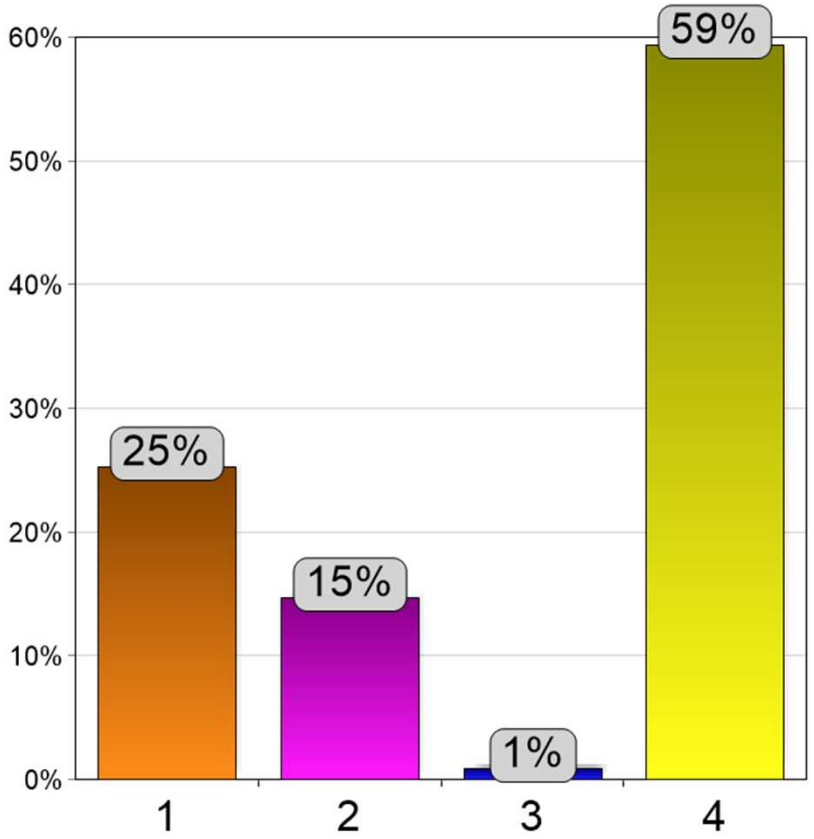

HFrFE: QUALE E' LA TERAPIA OTTIMALE?

ANTONIO

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Type of HF		HFrEF	HFmrEF	HFpEF
CRITERIA	1	Symptoms ± Signs[a]	Symptoms ± Signs[a]	Symptoms ± Signs[a]
	2	LVEF <40%	LVEF 40–49%	LVEF ≥50%
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TERAPIA OTTIMALE HFrFE

- Correzione co morbilità e cause scatenanti
- Terapia medica ottimale con ACE-I o sartano, B bloccante ed eventualmente diuretici (se segni/sintomi di HF)
- CONSIDERARE NUOVA CLASSE DI FARMACI: ARNI

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ESC GUIDELINES

2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

Angiotensin receptor neprilysin inhibitor			
Sacubitril/valsartan is recommended as a replacement for an ACE-I to further reduce the risk of HF hospitalization and death in ambulatory patients with HFrEF who remain symptomatic despite optimal treatment with an ACE-I, a beta-blocker and an MRA[4]	I	B	62

The landmark PARADIGM-HF trial was the largest clinical trial ever conducted in HF[1]

The trial stopped early due to compelling efficacy: risk of CV death was significantly reduced and the primary end point was met[2]

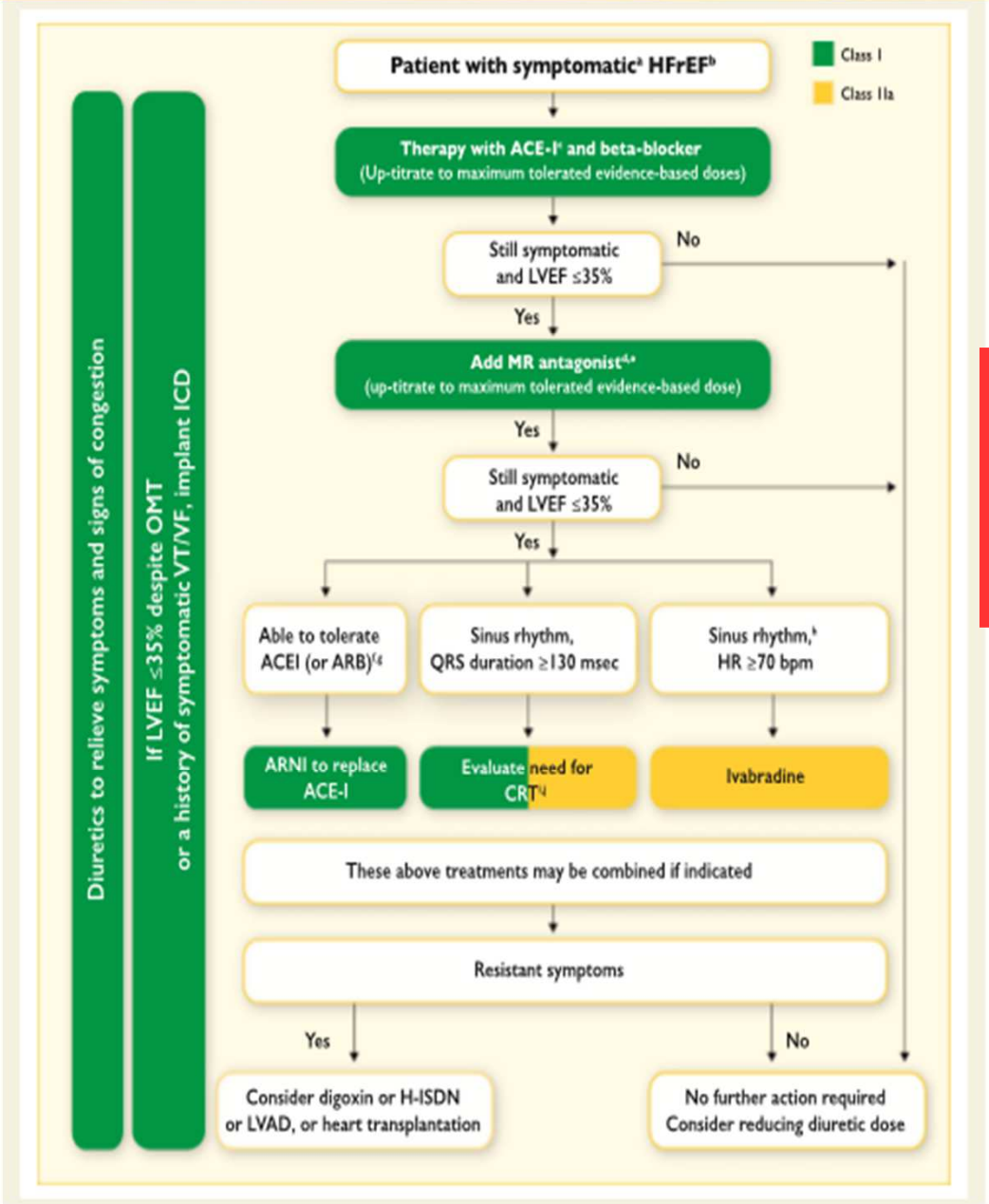
8442 ADULT HF PATIENTS WITH REDUCED EJECTION FRACTION[3]

HFrFE: SCELTE OTTIMALI

Recommendations to prevent or delay the development of overt heart failure or prevent death before the onset of symptoms

Recommendations	Class[a]	Level[b]	Ref[c]
Treatment of hypertension is recommended to prevent or delay the onset of HF and prolong life.	I	A	126, 129, 150, 151
Treatment with statins is recommended in patients with or at high-risk of CAD whether or not they have LV systolic dysfunction, in order to prevent or delay the onset of HF and prolong life.	I	A	137–140, 152
Counselling and treatment for smoking cessation and alcohol intake reduction is recommended for people who smoke or who consume excess alcohol in order to prevent or delay the onset of HF.	I	C	131–134
Treating other risk factors of HF (e.g. obesity, dysglycaemia) should be considered in order to prevent or delay the onset of HF.	IIa	C	130, 141, 153–155
Empagliflozin should be considered in patients with type 2 diabetes in order to prevent or delay the onset of HF and prolong life.	IIa	B	130
ACE-I is recommended in patients with asymptomatic LV systolic dysfunction and a history of myocardial infarction in order to prevent or delay the onset of HF and prolong life.	I	A	5, 144, 145
ACE-I is recommended in patients with asymptomatic LV systolic dysfunction without a history of myocardial infarction, in order to prevent or delay the onset of HF.	I	B	5
ACE-I should be considered in patients with stable CAD even if they do not have LV systolic dysfunction, in order to prevent or delay the onset of HF.	IIa	A	142
Beta-blocker is recommended in patients with asymptomatic LV systolic dysfunction and a history of myocardial infarction, in order to prevent or delay the onset of HF or prolong life.	I	B	146
ICD is recommended in patients: a) with asymptomatic LV systolic dysfunction (LVEF ≤30%) of ischaemic origin, who are at least 40 days after acute myocardial infarction, b) with asymptomatic non-ischaemic dilated cardiomyopathy (LVEF ≤30%), who receive OMT therapy, in order to prevent sudden death and prolong life.	I	B	149, 156–158

ESC HFrEF Treatment Algorithm



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ESC GUIDELINES

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The NEW ENGLAND JOURNAL of MEDICINE

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Angiotensin–Neprilysin Inhibition versus Enalapril in Heart Failure

John J.V. McMurray, M.D., Milton Packer, M.D., Akshay S. Desai, M.D., M.P.H., Jianjian Gong, Ph.D., Martin P. Lefkowitz, M.D., Adel R. Rizkala, Pharm.D., Jean L. Rouleau, M.D., Victor C. Shi, M.D., Scott D. Solomon, M.D., Karl Swedberg, M.D., Ph.D., and Michael R. Zile, M.D., for the PARADIGM-HF Investigators and Committees*

2016 ACC/AHA/HFSA Focused Update on New Pharmacological Therapy for Heart Failure: An Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure

A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America

RAAS inhibition- 2016

7.3.2. Pharmacological Treatment for Stage C HF With Reduced Ejection Fraction: Recommendations

7.3.2.10. Renin-Angiotensin System Inhibition With Angiotensin-Converting Enzyme Inhibitor or Angiotensin Receptor Blocker or ARNI: Recommendations

See the *Online Data Supplement* (http://jaccjacc.acc.org/Clinical_Document/2016_Heart_Failure_Focused_Update_Data_Supplement_New_Therapy_Only_S5.pdf) for evidence supporting these recommendations.

Recommendations for Renin-Angiotensin System Inhibition With ACE Inhibitor or ARB or ARNI		
COR	**LOE**	**Recommendations**
I	ACE: A	The clinical strategy of inhibition of the renin-angiotensin system with ACE inhibitors *(Level of Evidence: A)* (9-14), OR ARBs *(Level of Evidence: A)* (15-18), OR ARNI *(Level of Evidence: B-R)* (19) in conjunction with evidence-based beta blockers (20-22), and aldosterone antagonists in selected patients (23, 24), is recommended for patients with chronic HF*r*EF to reduce morbidity and mortality.
	ARB: A	
	ARNI: B-R	

CARATTERISTICHE DEL PAZIENTE IDEALE PER SACUBITRIL/VALSARTAN

Classe NYHA: **II-III**
FE: **≤35%***

PAS: **≥100** mmHg

eGFR: **≥30** ml/min/1,73m²

Potassio sierico: **≤5,4** mmol/l

In trattamento con dosi stabili di **ACE-I** o **sartani**

Quale è il paziente ENTRESTO?

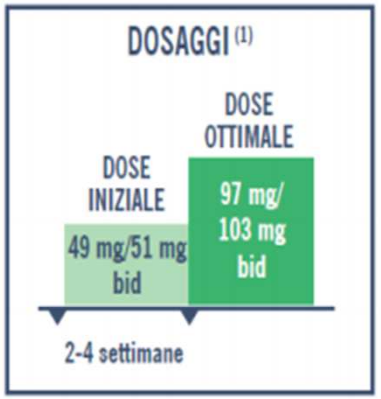
Entresto®
sacubitril/valsartan

Indicato in pazienti adulti per il trattamento di insufficienza cardiaca sintomatica cronica con ridotta frazione di eiezione (1)

PAZIENTE ENTRESTO (1)

- Classe NYHA II-III
- FE: ≤35%
- PAS: ≥100 mmHg
- eGFR: ≥30 ml/min/1,73 m²*
- Potassio sierico ≤5,4 mmol/l
- In trattamento con dosi stabili di ACE-I o sartani

DOSAGGI (1)



SACUBITRIL/VALSARTAN
Controindicazioni-Cautela

- **Insufficienza epatica**
- **Insufficienza renale**
- **Iperpotassiemia**
- **Ipotensione (PA < 100mmHg)**
- **Gravidanza; età < 18 anni**
- **Storia di Angioedema da ACE-I/ARB o angioedema ereditario o idiopatico**

SACUBITRIL/VALSARTAN

3 DIFFERENTI DOSAGGI

. 24mg sacubitril/26mg valsartan

. 49mg sacubitril/51mg valsartan

. 97mg sacubitril/103mg valsartan

Le compresse possono essere assunte con o senza cibo, devono essere deglutite con un bicchiere d'acqua

La dose va raddoppiata ogni 2-4 settimane fino alla dose ottimale (TITOLAZIONE!!!!)

DOSAGGI ENTRESTO

49 mg/51 mg[1]

DOSE INIZIALE

Confezioni:
- **28 compresse**
- **56 compresse**

2 cpr al giorno

97 mg/103 mg[1]

DOSE OTTIMALE

- **Confezione: 56 compresse**

Casi speciali

- Basse dosi di ACEi o Sartani
- Compromissione renale (**eGFR**<60ml/min/1,73m2)
- Compromissione epatica (Child-Pugh B o AST-ALT>2ULN)
- 100 mmHg ≤ **PAS** ≥ 110 mmHg

- **Confezione: 28 compresse**

SACUBITRIL/VALSARTAN

Basso dosaggio 24/36mg

- **PA compresa fra 100-110mmHg**
- **GFR compresa fra 30-60ml/min/m2**
- **Insufficienza epatica moderata (Child Pugh B o AST/ALT > x 2 vn)**
- **Pazienti naive**
- **Pazienti che assumono basso dosaggio di ACE-I o di sartano**

Nei pazienti in cui è indicato il basso dosaggio, più cautela nella titolazione

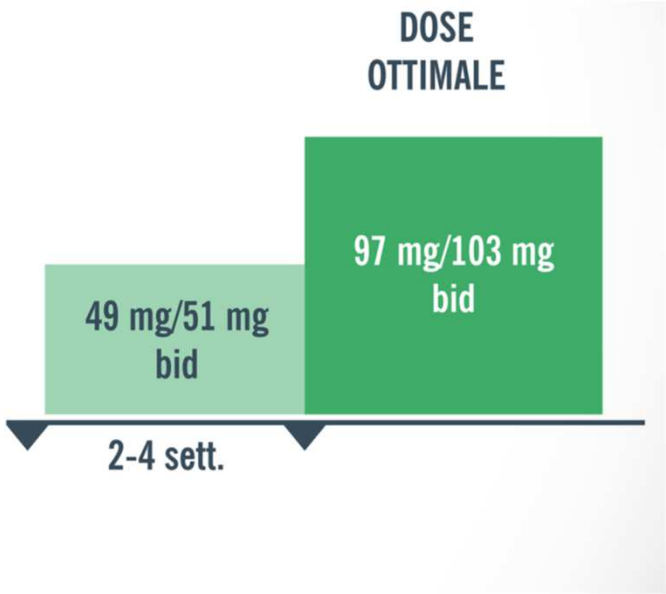
COME INIZIAMO SACUBITRIL/VALSARTAN????

- Il paziente sta assumendo un ACE-I
- Il paziente sta assumendo un sartano
- Paziente naïve

PAZIENTE IN ACE-I

SACUBITRIL/VALSARTAN NELLA PRATICA CLINICA
TITOLAZIONE

Come iniziare la terapia con sacubitril/valsartan
Già in terapia con ACE-I



PAZIENTE IN SARTANO

SACUBITRIL/VALSARTAN NELLA PRATICA CLINICA: TITOLAZIONE

Come iniziare la terapia con Sacubitril/valsartan
Già in terapia con sartano

RACCOMANDAZIONI

- Il trattamento non va iniziato se PA< 100
- Cautela nelle popolazioni “speciali” (IR, ipoteso...)
- Monitorare la pressione e titolare il farmaco

EFFETTI COLLATERALI

- Ipotensione
- Peggioramento fx renale
- IperK+
- Angioedema
- Tosse

Tabella 1 Elenco delle reazioni avverse

Classificazione per sistemi e organi	Termine preferito	Categoria di frequenza
Patologie del sistema emolinfopoietico	Anemia	Comune
Disturbi del sistema immunitario	Ipersensibilità	Non comune
Disturbi del metabolismo e della nutrizione	Iperkaliemia*	Molto comune
	Ipokaliemia	Comune
	Ipoglicemia	Comune
Patologie del sistema nervoso	Capogiro	Comune
	Cefalea	Comune
	Sincope	Comune
	Capogiro posturale	Non comune
Patologie dell'orecchio e del labirinto	Vertigini	Comune
Patologie vascolari	Ipotensione*	Molto comune
	Ipotensione ortostatica	Comune
Patologie respiratorie, toraciche e mediastiniche	Tosse	Comune
Patologie gastrointestinali	Diarrea	Comune
	Nausea	Comune
	Gastrite	Comune
Patologie della cute e del tessuto sottocutaneo	Prurito	Non comune
	Eruzione cutanea	Non comune
	Angioedema*	Non comune
Patologie renali e urinarie	Compromissione renale*	Molto comune
	Insufficienza renale (insufficienza renale, insufficienza renale acuta)	Comune
Patologie sistemiche e condizioni relative alla sede di somministrazione	Affaticamento	Comune
	Astenia	Comune

*Vedere la descrizione di reazioni avverse selezionate

PIANO TERAPEUTICO

- CARTACEO (NO piano AIFA come i DOAC)
- VALIDITA’ 6 MESI
- VIENE INDICATO IL DOSAGGIO CON CUI SI INIZIA MA IL FARMACO ANDRA’ TITOLATO DAL MMG (indipendentemente dal dosaggio segnalato sul PT)
- CONTROLLO FX RENALE ED ELETTROLITI
- CONTROLLO PA

GRAZIE PER L'ATTENZIONE