Controvèrsies en IC

Com ha de ser la introducció dels diferents tractaments?

Esglaonadament, fins assolir la titulació objectiu?

I a la pràctica clínica… quin, quan i com?

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- Conflictes d'interés: Honoraris per presentacions i cursos d'Abbott i Novartis

ESC European Society of Cardiology

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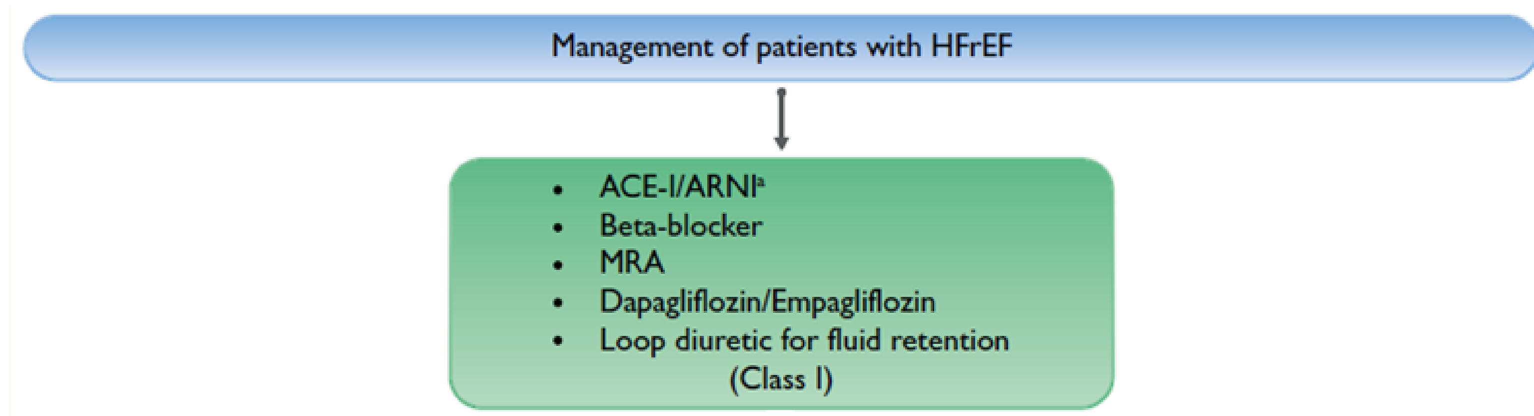
EDITORIAL

Heart failure drug treatment: the fantastic four

Controvèrsies en IC: Com ha de ser la introducció dels diferents tractaments?

- **Objectius del tractament:**
  - Reduir mortalitat
  - Reduir hospitalitzacions per IC
  - Millora clínica, funcional i en qualitat de vida
- **Abans que els dispositius**
- **Sempre amb les mesures no farmacològiques**



Pharmacological treatments indicated in patients with (NYHA class II–IV) heart failure with reduced ejection fraction (LVEF ≤40%)

Recommendations	Class[a]	Level[b]
An ACE-I is recommended for patients with HFrEF to reduce the risk of HF hospitalization and death.[110–113]	I	A
A beta-blocker is recommended for patients with stable HFrEF to reduce the risk of HF hospitalization and death.[114–120]	I	A
An MRA is recommended for patients with HFrEF to reduce the risk of HF hospitalization and death.[121,122]	I	A
Dapagliflozin or empagliflozin are recommended for patients with HFrEF to reduce the risk of HF hospitalization and death.[108,109]	I	A
Sacubitril/valsartan is recommended as a replacement for an ACE-I in patients with HFrEF to reduce the risk of HF hospitalization and death.[105]	I	B

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Pacients naïve per IECA/ARA-II, IC de novo, hospitalitzats: ARNI (IIbB)

McDonagh TA, Metra M, Adamo M, et al. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. Eur Heart J. 2021;42(36):3599-3726.

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Inici — **Transició** (2-3 m) → **Tractament Guía**

	Starting dose
ACE-I	
Captopril[a]	6.25 mg t.i.d.
Enalapril	2.5 mg b.i.d.
Lisinopril[b]	2.5 – 5 mg o.d.
Ramipril	2.5 mg b.i.d.
Trandolapril[a]	0.5 mg o.d.
ARNI	
Sacubitril/valsartan	49/51 mg b.i.d.[c]
Beta-blockers	
Bisoprolol	1.25 mg o.d.
Carvedilol	3.125 mg b.i.d.
Metoprolol succinate (CR/XL)	12.5 – 25 mg o.d.
Nebivolol[d]	1.25 mg o.d.
MRA	
Eplerenone	25 mg o.d.
Spironolactone	25 mg o.d.[f]
SGLT2 inhibitor	
Dapagliflozin	10 mg o.d.
Empagliflozin	10 mg o.d.
Other agents	
Candesartan	4 mg o.d.
Losartan	50 mg o.d.
Valsartan	40 mg b.i.d.

	Starting dose	Target dose
ACE-I		
Captopril[a]	6.25 mg t.i.d.	50 mg t.i.d.
Enalapril	2.5 mg b.i.d.	10 – 20 mg b.i.d.
Lisinopril[b]	2.5 – 5 mg o.d.	20 – 35 mg o.d.
Ramipril	2.5 mg b.i.d.	5 mg b.i.d.
Trandolapril[a]	0.5 mg o.d.	4 mg o.d.
ARNI		
Sacubitril/valsartan	49/51 mg b.i.d.[c]	97/103 mg b.i.d.
Beta-blockers		
Bisoprolol	1.25 mg o.d.	10 mg o.d.
Carvedilol	3.125 mg b.i.d.	25 mg b.i.d.[e]
Metoprolol succinate (CR/XL)	12.5 – 25 mg o.d.	200 mg o.d.
Nebivolol[d]	1.25 mg o.d.	10 mg o.d.
MRA		
Eplerenone	25 mg o.d.	50 mg o.d.
Spironolactone	25 mg o.d.[f]	50 mg o.d.
SGLT2 inhibitor		
Dapagliflozin	10 mg o.d.	10 mg o.d.
Empagliflozin	10 mg o.d.	10 mg o.d.
Other agents		
Candesartan	4 mg o.d.	32 mg o.d.
Losartan	50 mg o.d.	150 mg o.d.
Valsartan	40 mg b.i.d.	160 mg b.i.d.

Table 2 **Common comorbidities seen in heart failure and impact on use of guideline-directed medical therapy**

Comorbidity	GDMT	Precaution	Comment
Coronary artery disease and angina	✓		Beta-blockers and ivabradine may help control symptoms
Diabetes	✓		GDMT have shown similar benefits in diabetic patients
Lung disease		Asthma is a relative contraindication to beta-blocker; starting with low doses of cardio-selective beta-blocker may allow its use	Beta-blockers can be given in COPD
Depression	✓		Depression is associated with low adherence to medication
Erectile dysfunction	✓		Thiazides, spironolactone and beta-blockers (nebivolol preferred) may aggravate erectile dysfunction
Iron deficiency/anaemia	✓		
Kidney dysfunction		ACEi, ARB, ARNI, MRA may have some limitations (see text)	Diuretics may need higher doses to be effective
Cachexia		ACEi, ARB, ARNI should be up-titrated carefully because of orthostatic hypotension	

ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ARNI, angiotensin receptor–neprilysin inhibitor; COPD, chronic obstructive pulmonary disease; GDMT, guideline-directed medical therapy; MRA, mineralocorticoid receptor antagonist.

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	Baseline	3 months	6 months	12 months	24 months
Diuretics	78.2%	76.3%	73.5%	70.6%	70.1%
Beta-blockers	40.6%	57.9%	61.8%	67.8%	68.7%
ARB	18.7%	24.9%	26 1%	34.3%	34.4%
ACEI	27.0%	30.7%	31.9%	31.4%	31.0%
Aldosterone antagonists	11.2%	20,4%	25.1%	25.6%	27.4%
Sacubitril–valsartan	14.8%	14.1%	1.4%	11.9%	11.6%
Ivabradine	1.1%	1.1%	1.4%	2.2%	2.1%

Modificat d'A. Sicras-Mainar et al. Revista Española de Cardiología. 2020; S1885-5857(20)30521-1.

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Patient with symptomatic[a] HFrEF[b]

Class I

Class IIa

Therapy with ACE-I[c] and beta-blocker

(Up-titrate to maximum tolerated evidence-based dose)

Still symptomatic and LVEF ≤35%

Yes

Add MR ant

to maximum tol dose)

No

Able to tolerate ACEI (or ARB

Sinus rhythm,[h] HR ≥70 bpm

ARN

valuate CRT

Ivabradine

above treatments may be con

Resistant symptoms

Yes

Consider digoxin or H-ISDN or LVAD, or heart transplantation

No further action requir Consider reducing diuretic dose

Diuretics to relieve symptoms and signs of congestion

If LVEF ≤35% despite OMT or a history of symptomatic VT/VF, implant ICD

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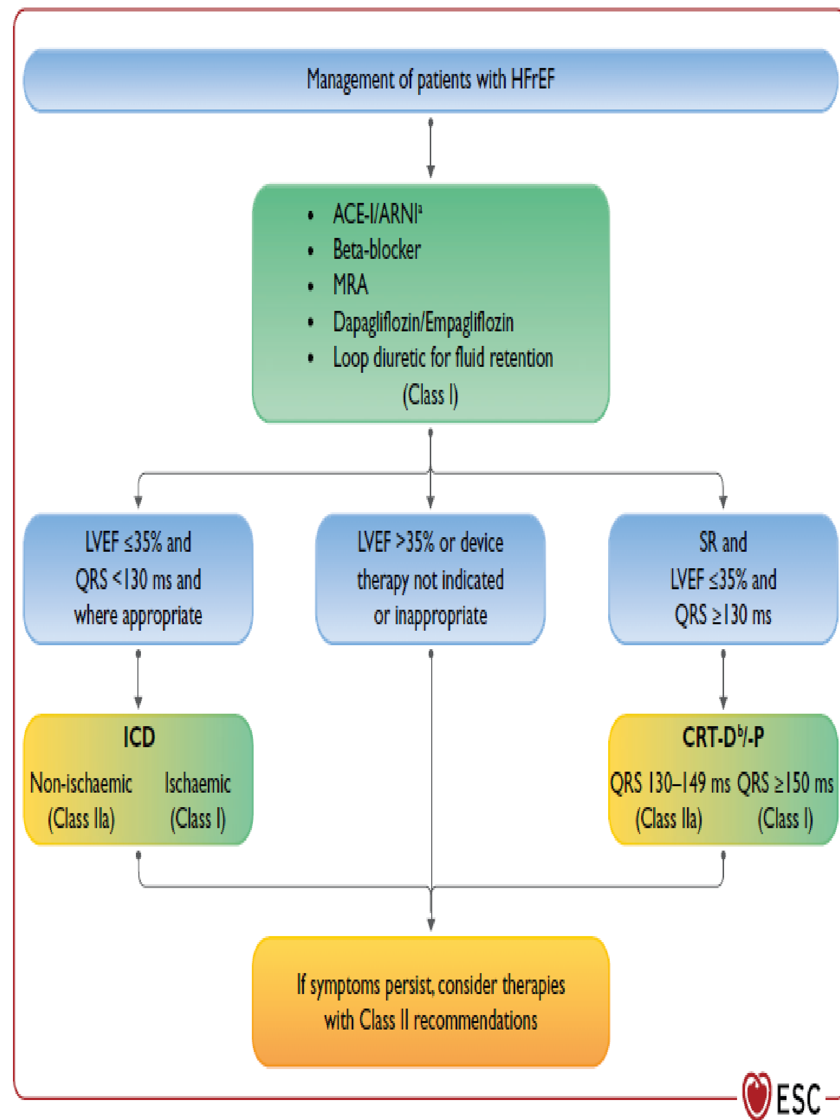

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Canadá 2021

TREAT COMORBIDITIES PER CCS HF RECOMMENDATIONS (INCL. AF, FUNCTIONAL MR, IRON DEF, CKD, DM)

DIURETICS TO RELIEVE CONGESTION (TITRATED TO MINIMUM EFFECTIVE DOSE TO MAINTAIN EUVOLEMIA)

HFrEF: LVEF ≤ 40% AND SYMPTOMS

Initiate Standard Therapies

Assess Clinical Factors for Additional Interventions

- HR >70 bpm and sinus rhythm
  - Consider ivabradine*
- Recent HF hospitalization
  - Consider vericiguat **
- Black patients on optimal GDMT, or patients unable to tolerate ARNI/ACEi/ARB
  - Consider combination hydralazine-nitrates
- Suboptimal rate control for AF, or persistent symptoms despite optimized GDMT
  - Consider digoxin

Initiate standard therapies as soon as possible and titrate every 2-4 weeks to target or maximally tolerated dose over 3-6 months

Reassess LVEF, Symptoms, Clinical Risk

NYHA III/IV, Advanced HF or High-Risk Markers

CONSIDER
- Referral for advanced HF therapy (mechanical circulatory support/transplant)
- Referral for supportive/palliative care

LVEF ≤ 35% and NYHA I-IV (ambulatory)

Refer to CCS CRT/ICD recommendations

LVEF > 35%, NYHA I, and Low Risk

Continue present management, reassess as needed

NON-PHARMACOLOGIC THERAPIES (EDUCATION, SELF-CARE, EXERCISE)

ADVANCE CARE PLANNING AND DOCUMENTATION OF GOALS OF CARE

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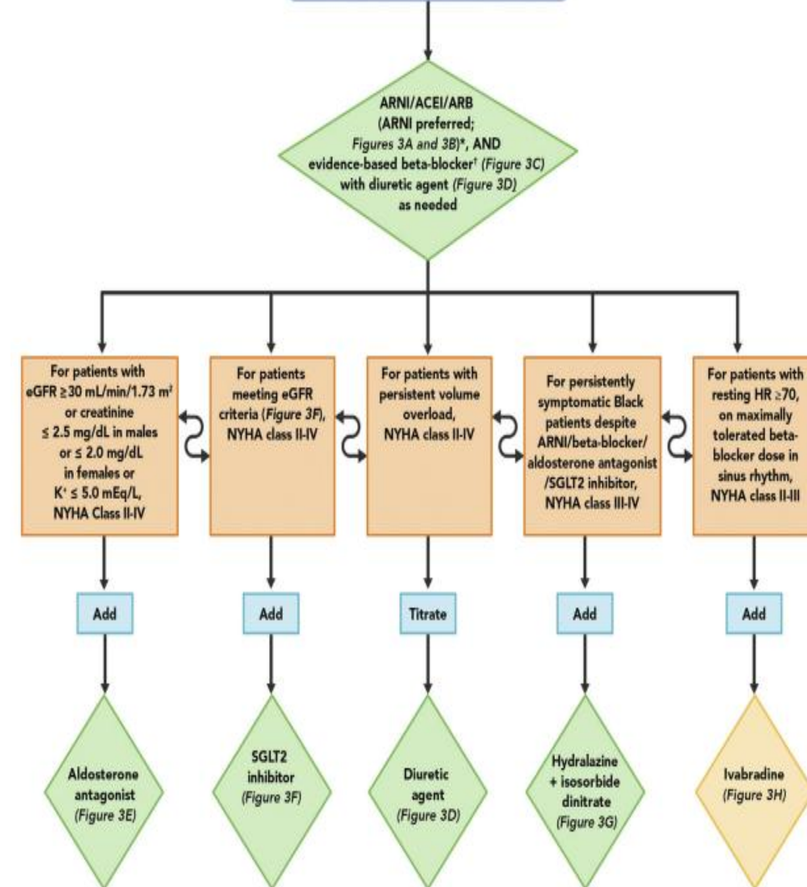
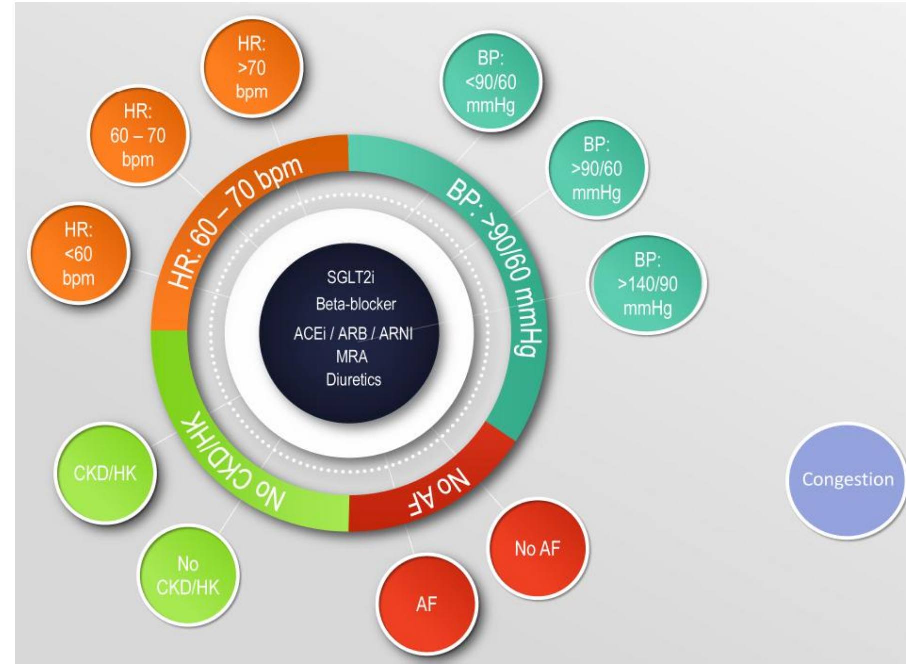
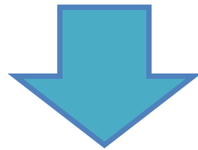


Millor combinació pel meu pacient?

PRIORITZAR
SECUENCIAR
INDIVIDUALITZAR

PA, FC
I. Renal, hiperK^+
FA





MEDICINA PERSONALITZADA

Rosano GMC, Moura B, Metra M, et al. Patient profiling in heart failure for tailoring medical therapy. A consensus document of the Heart Failure Association of the European Society of Cardiology. Eur J Heart Fail. 2021;23(6):872-881.

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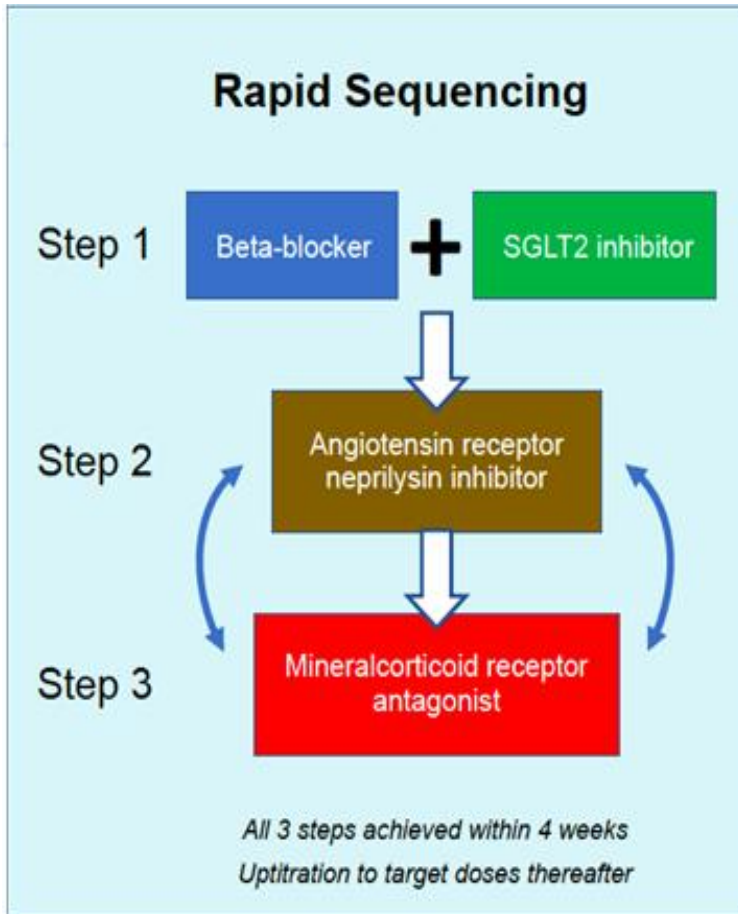

Recommended Total Time for Titration ≤ 12 weeks (3 months)

Cluster Scheme

Initiation and Titration of Foundational Therapy for Heart Failure with LVEF < 40%

Red- Face to face visit with prescriber preferred | Blue- Either face to face or virtual visit with prescriber | Orange- Virtual visit with prescriber preferred

Cluster A: Diuretic & SGLTi +	Cluster B: ARNi & MRA +	Cluster C: Beta Blocker & SNI*
Encounter 1 (Usually face-to-face, up to 3 medication initiations)		
Start Preferred Cluster A Medication	Start Preferred Cluster B Medication	Start Preferred Cluster Medication*
	1- 2 Weeks	
Encounter 2 (whenever feasible, up to 3 medication initiations)		
Titrate Cluster A Medication	Start Second Cluster B Medication	Adjust Cluster C Medication*
	1- 2 Weeks	
Encounter 3 & ongoing (whenever feasible, up to 3 medication titrations)		
Diuretic titration as needed	Cluster B Medication titration	Cluster C Medication Titration*
	1- 2 Weeks	

Goal Foundational Therapy- Continue to actively manage as necessary

Addition of Personalized Therapies as dictated by clinical presentation and setting (see Table 2)

Robert JH Miller, et al. A Novel Approach to Medical Management of Heart Failure with Reduced Ejection Fraction. Canadian Journal of Cardiology. 2021; 37: 632-643.
Milton Packer, et al. Rapid evidence-based sequencing of foundational drugs for heart failure and a reduced ejection fraction. European Heart Journal. 2021; 23: 882-894.

Consideracions en el MEU Pacient

Perfil	PA (>90/60)	FC (60-70 / AF)	MRC	Consideracions
1	PAS < 90	> 70	-	• Causes, revisar fàrmacs • Modificar tractament hipotensor si símptomes • Pujar BB (obj FC 60)
2	PAS < 90	< 60	-	• Causes, revisar fàrmacs • Modificar hipotensor si símptomes • Reducció de BB si FC < 50 o símptomes
3	Normal	< 60	-	• Revisar fàrmacs • Reducció-STOP Ivabradina 1r si FC < 50 o símptomes, 2n reduir BB
4	Normal	> 70	-	• Dosi objectiu BB (RS > 70 afegir Ivabradina) • Optimització IECA/ARNI/ARAII i ARM

Rosano GMC, Moura B, Metra M, et al. Patient profiling in heart failure for tailoring medical therapy. A consensus document of the Heart Failure Association of the European Society of Cardiology. Eur J Heart Fail. 2021;23(6):872-881.

Consideracions en el MEU Pacient

Perfil	PA	FC	MRC	Consideracions
5	Normal	FA	-	• FC objectiu 60-80 (vigilar amb BB)
6	PAS < 90	FA	-	• Reducció-STOP BB (digoxina) – objectiu FC 70 • Optimitzar resta tractament (ARM, iSGLT2)
7	-	-	Si	• Seguiment función renal, ionograma
8	Pre-alta	-	-	• Congestió (no BB)
9	Tractament HTA	-	-	• Adherència, dosis, altres fàrmacs, valorar HDLZ-Nitrats

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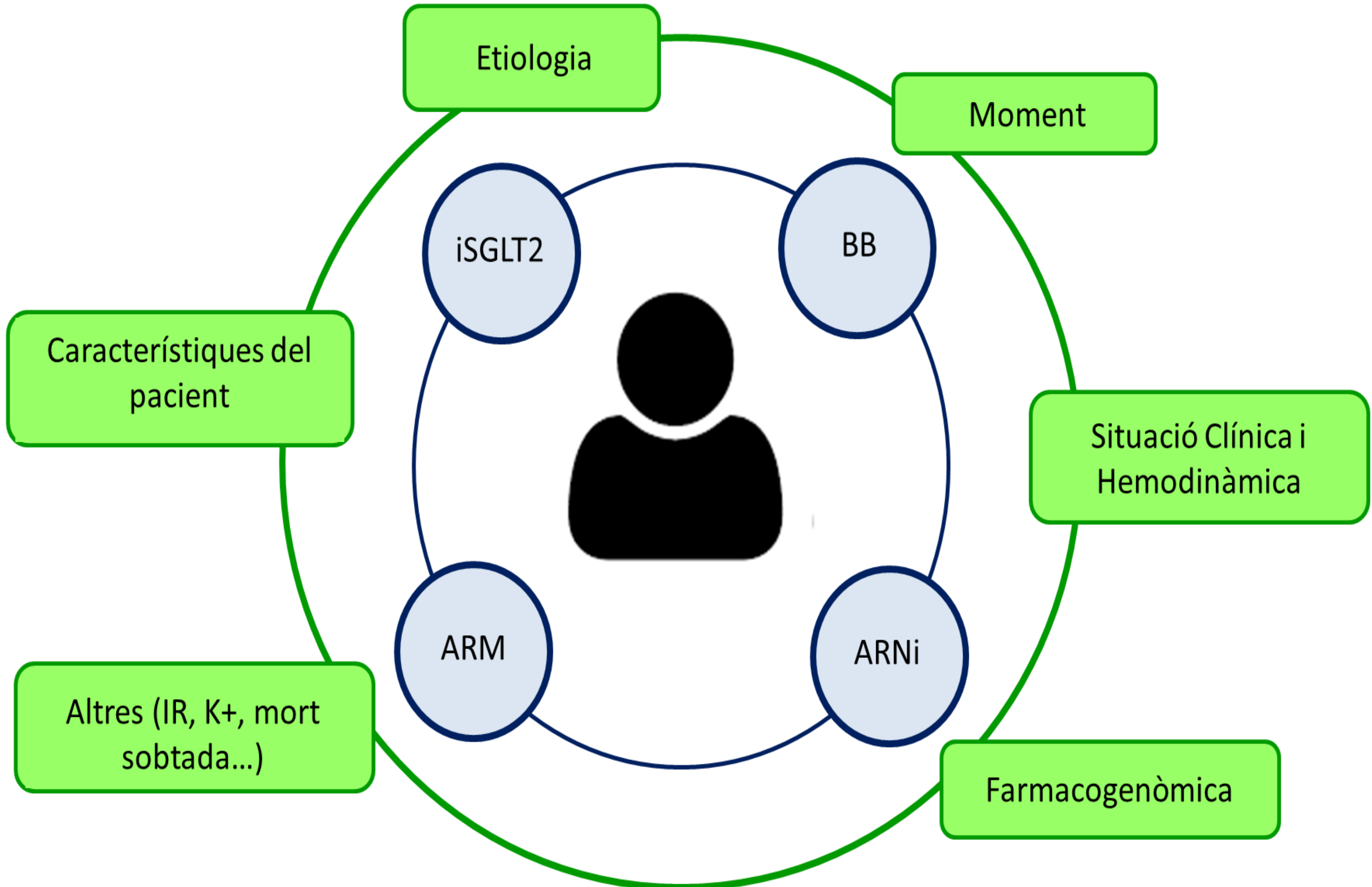
CONCLUSIONS



Moltes gràcies per la seva atenció