Case based discussion

Cardiologist/Endo/Nephrologist

Moderator Prof Upendra Kaul

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HF Essentials
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*Not a real patient. Image for illustration only.

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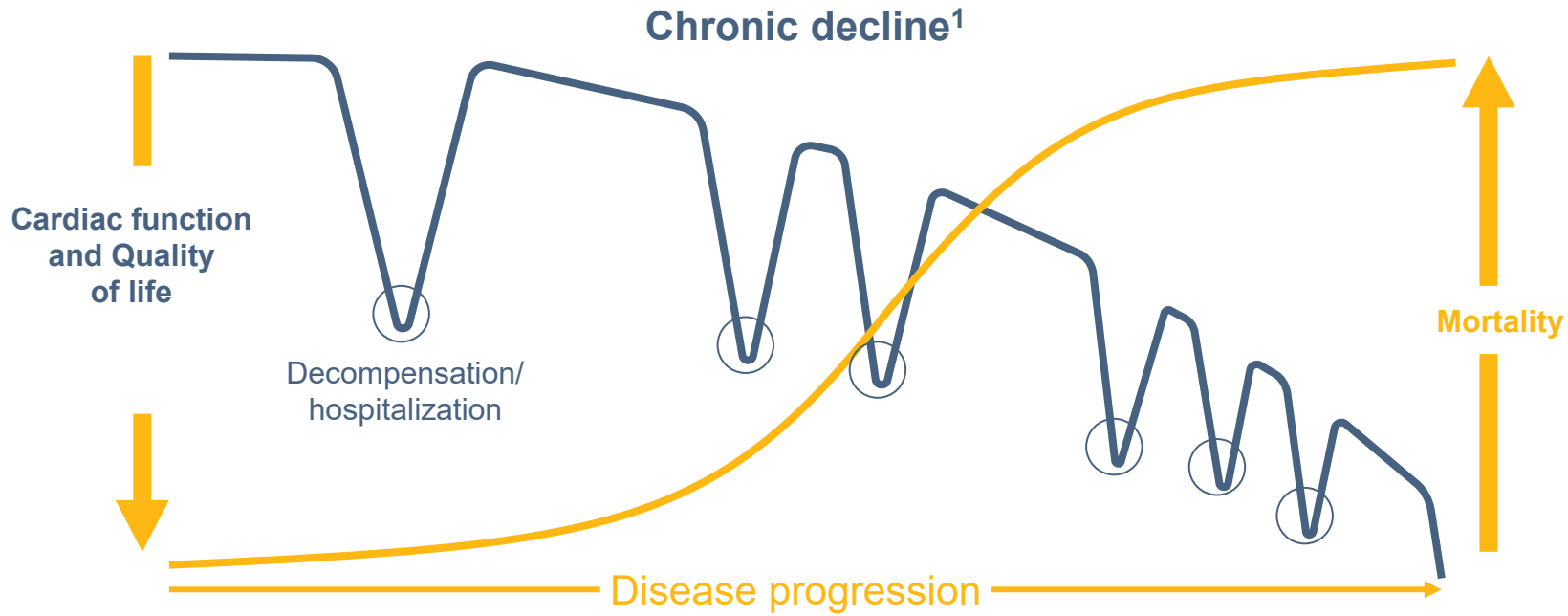
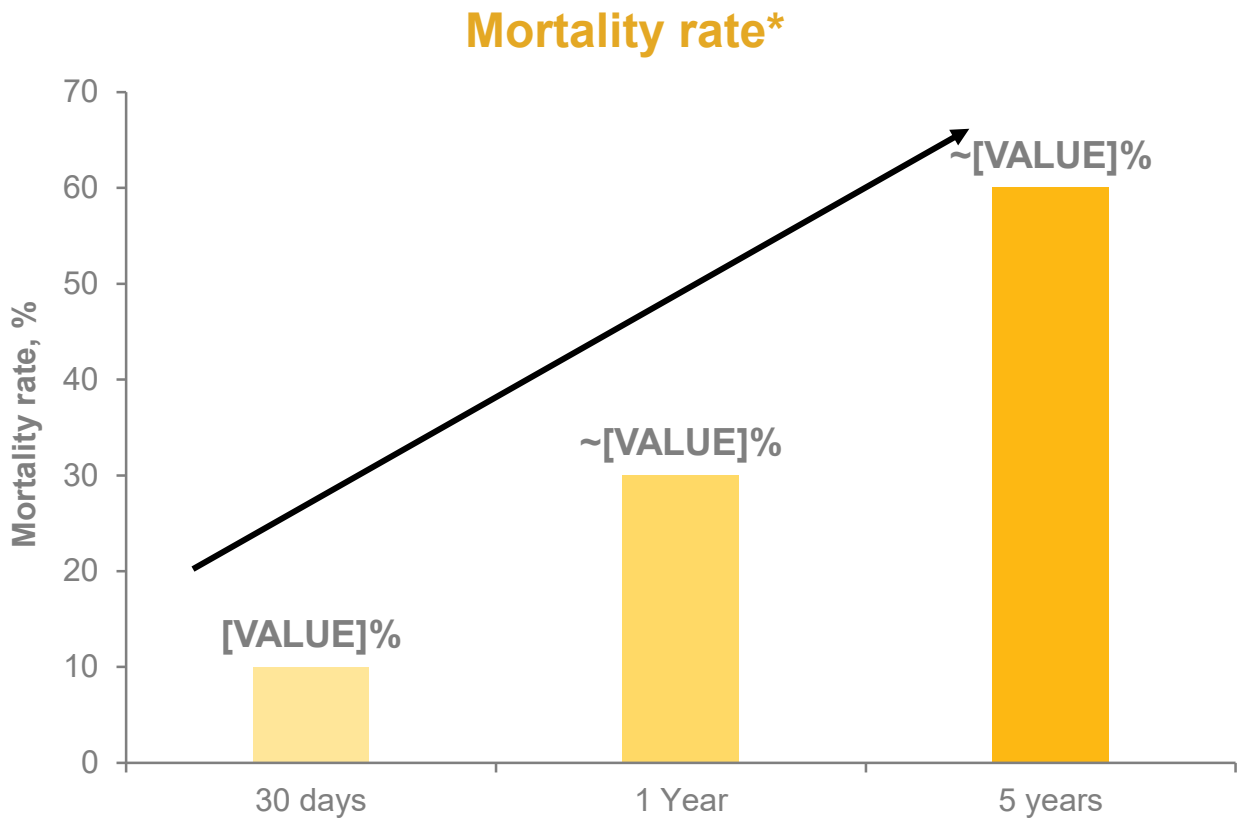
HF is a progressive disorder and can not be perceived as ‘stable’

Frequency of decompensation and risk of mortality increase,[1–3] with acute events and sudden death occurring at any time



HF, heart failure.
Ref: 1. Adapted from Gheorghiade et al. Am J Cardiol 2005;96:11G–17G; 2. Ahmed et al. Am Heart J 2006;151:444–50; 3. Gheorghiade and Pang. J Am Coll Cardiol 2009;53:557–73.

HF patients are at increased risk of mortality



*Based on the Framingham Heart Study, the mortality rate after diagnosis of HF in the USA was around 10% at 30 days, 20-30% at 1 year and 45-60% over 5 years of follow-up.
HF, heart failure.
Ref: 1. Bytyçi I, Bajraktari G. Anatol J Cardiol. 2015;15(1):63-68. doi:10.5152/akd.2014.5731.

Case study

Can GDMT reduce the risk of mortality in HFrEF patients?

Case discussion

Meet Kartik*, 61-year old marketing consultant.

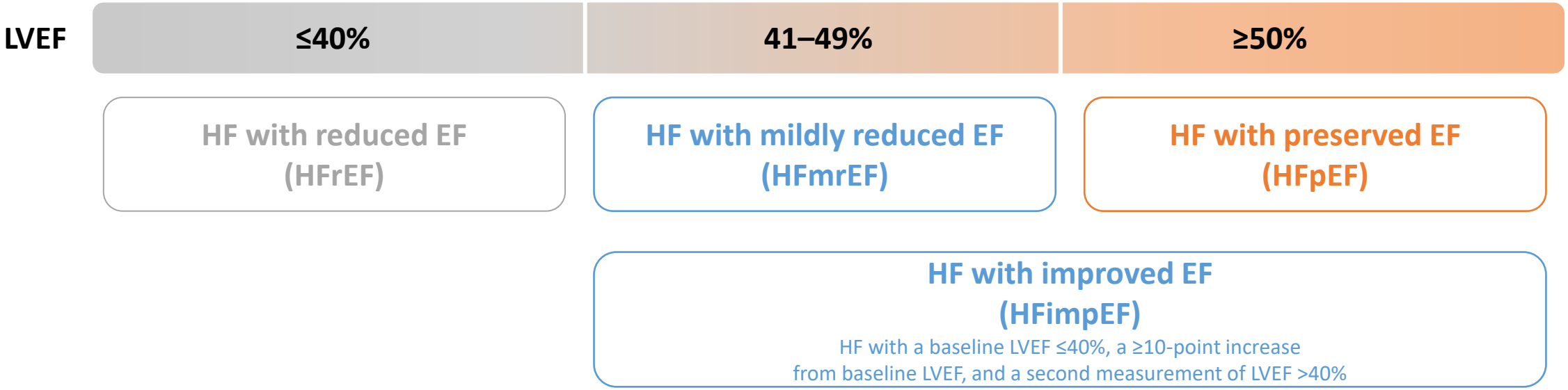
- A known case of HFrEF since 6 years.
- 3 months back, he was admitted in the hospital due to HF.

- He is on: ACEi/ARB, MRA and beta-blocker

““I am feeling much better than earlier, however, I still get tired easily occasionally get out of breath.”

*Stock photo, posed by model. Not a real/healed patient.
HFrEF: heart failure with reduced ejection fraction; HF: heart failure; MRA: mineralocorticoid receptor antagonists; ACEi: angiotensin converting enzyme inhibitor; ARB: Aldosterone receptor blocker.

The new universal definition of heart failure classifies the different phenotypes according to LVEF



EF, ejection fraction; HF, heart failure; LVEF, left ventricular ejection fraction.

Bozkurt B *et al. Eur J Heart Fail.* 2021;23:352.

Case discussion

Clinical investigation for Kartik* reveals:

- **LVEF:** 34%
- **Pulse rate:** 76/min
- **NT-proBNP:** 1743 pg/mL
- **SBP:** 124 mmHg
- **eGFR: 5**0 ml/min per 1.73 m^2
- **Sr. creatinine:** 1.56 mg/dL

Based on clinical examination, current therapy with ACEi/ARB is not showing clinical improvement in Kartik*

*Not a real patient. Image for illustration only.
NT-proBNP, N-terminal pro b-type natriuretic peptide; SBP, systolic blood pressure; Sr, serum; eGFR, estimated glomerular filtration rate; LVEF, left ventricular ejection fraction; ACEi, angiotensin converting enzyme; ARBs, aldosterone receptor blocker.

Do you feel that Kartik is at increased risk of mortality?

Dr Rajeev Rajput, Endocrinologist

Is Kartik with mild HF symptoms at increased risk of mortality?

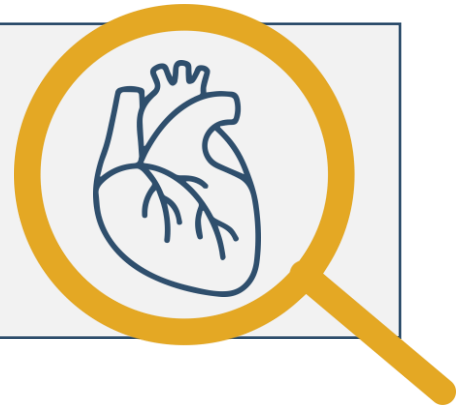
A	Yes
B	No

Heart failure: A growing public health concern

- Worldwide prevalence of heart failure is >37.7 million
- The burden is rapidly increasing by 2030, the number of HF patients would rise by 25%

Prognosis of heart failure

- Mortality rate is **~50% at 5 years** from the initial diagnosis of HF

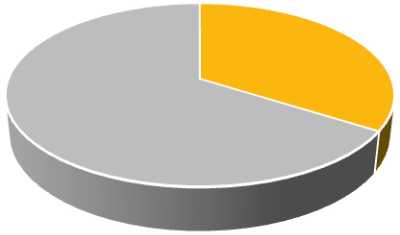


HF, heart failure.
Ref: Mishra S, et al. Indian Heart J. 2018 Jan - Feb;70(1):105-127.

Even mild to moderate patients are at high risk

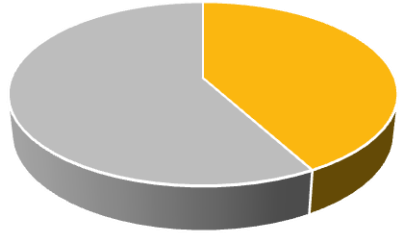
IN A CLINICAL TRIAL WITH MEDIAN FOLLOW-UP OF ~3 YEARS

34%



of NYHA class I and II patients died

42%



of NYHA class III and IV patients died

NYHA, New York heart association.

Ref: 1. Ahmed A. Am J Cardiol. 2007;99(4):549-553.

Indian patients typically differ from global population

Younger age of onset

RHD an important etiology

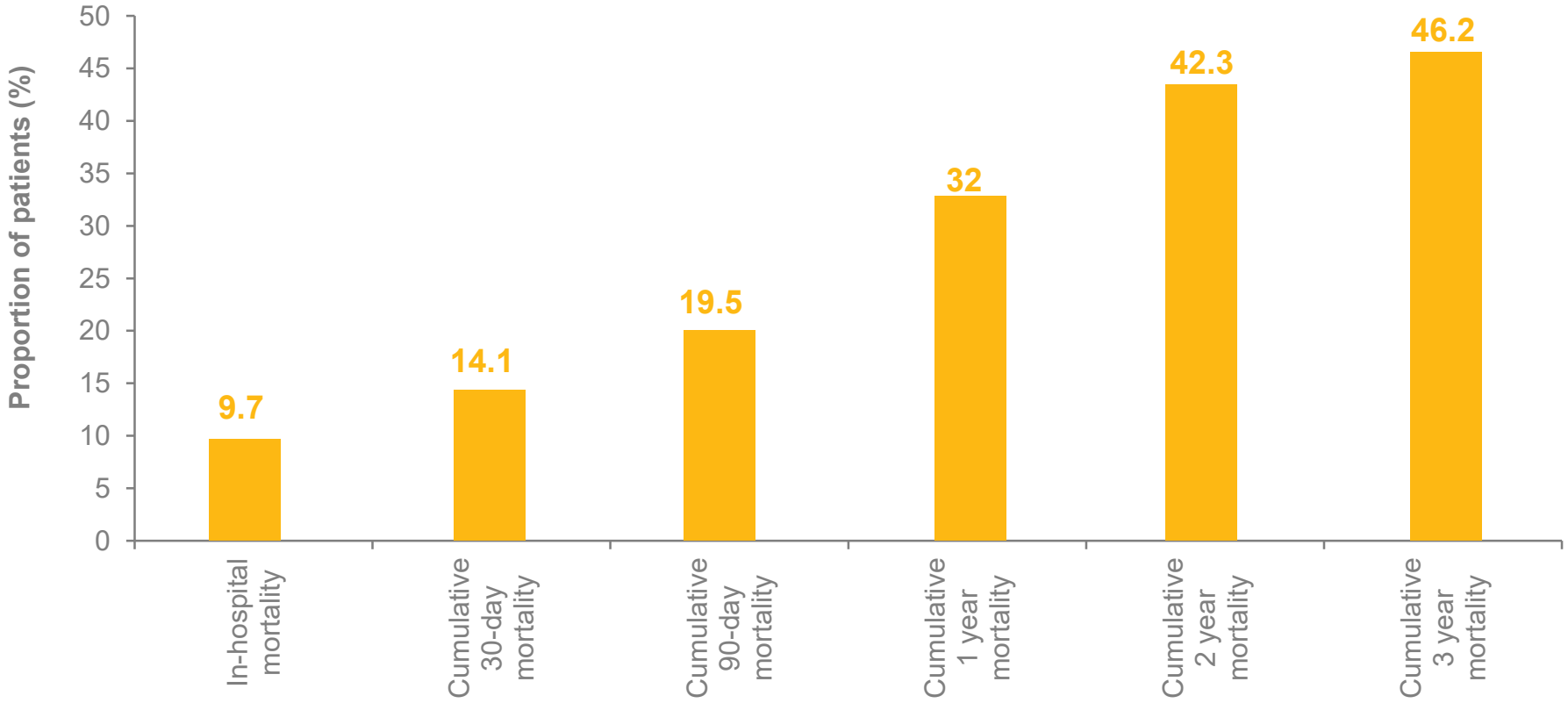
Males are predominantly affected than females (70:30)

Prevalence is higher in patients with diabetes

RHD, rheumatic heart disease.

Ref: 1. Kidambi BR, et al. J Pract Cardiovasc Sci. 2019;5:2-11.

In India, mortality rate in HFrEF patients increases with time[1]



Rates of morbidity and mortality are high in patients with heart failure (HF), but predicting prognosis is difficult[2]

HFrEF, heart failure with reduced ejection fraction; HF, heart failure.

Ref: 1. Sanjay G, et al. Journal of cardiac failure. 2018 Dec 1;24(12):842-8. 2. Simpson J, et al. JAMA Cardiol. doi:10.1001/jamacardio.2019.5850.

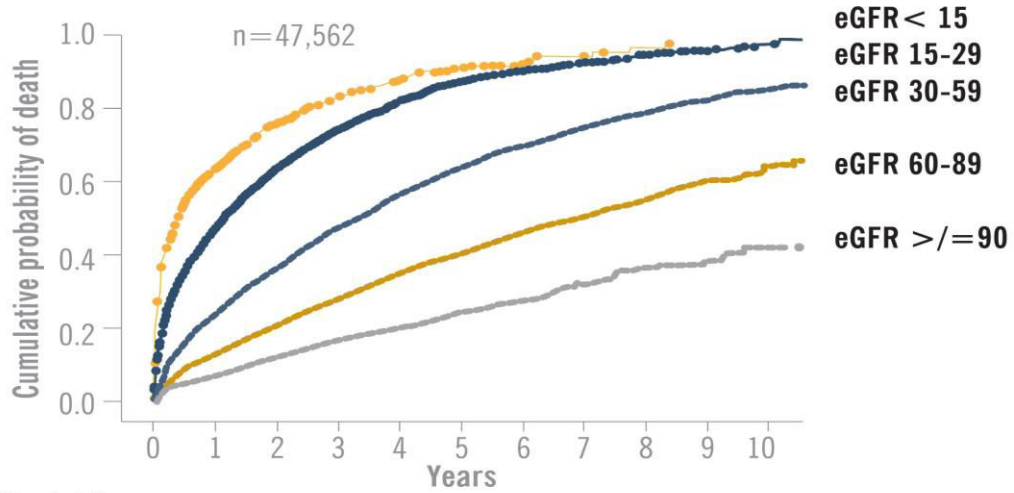
Is renal impairment quite common in HFrEF patients?

A	Yes
B	No

HFrEF, heart failure with reduced ejection fraction.

Renal failure is an independent predictor of mortality in heart failure patients[1,2]

Mortality risk with decreasing kidney function regardless of age, presence of diabetes, NYHA class, duration of heart failure and haemoglobin levels[2]



No. at risk

eGFR >/=90	5,235	3,385	2,072	820	189	16
eGFR 60-89	18,166	11,085	5,895	2,548	691	82
eGFR 30-59	19,102	9,711	4,822	1,863	506	68
eGFR 15-29	4,243	1,245	450	121	29	2
eGFR <15	811	151	54	12	3	

In HF patients with decreasing eGFR*:

- **13% increased risk of mortality with eGFR 30–59**
- **85% increased risk of mortality with eGFR 30–59:**
- **~3 fold increased risk of mortality with eGFR[2]**

*eGFR 60–89: 0.86 (0.79 to 0.95); eGFR 30–59: 1.13 (1.03 to 1.24); eGFR 15–29: 1.85 (1.67 to 2.07); and eGFR <15: 2.96 (2.53 to 3.47) compared to eGFR >90.
NYHA, New York Heart Association; HF, heart failure; eGFR, estimated glomerular filtration rate.
Ref: 1. Shamagiana LG, et al. Rev Esp Cardiol. 2006;59(2):99-108. 2. Löfman I, et al. s. Open Heart 2016;3: e000324. doi:10.1136/ openhrt-2015-000324.

Challenges in management of cardiorenal syndrome

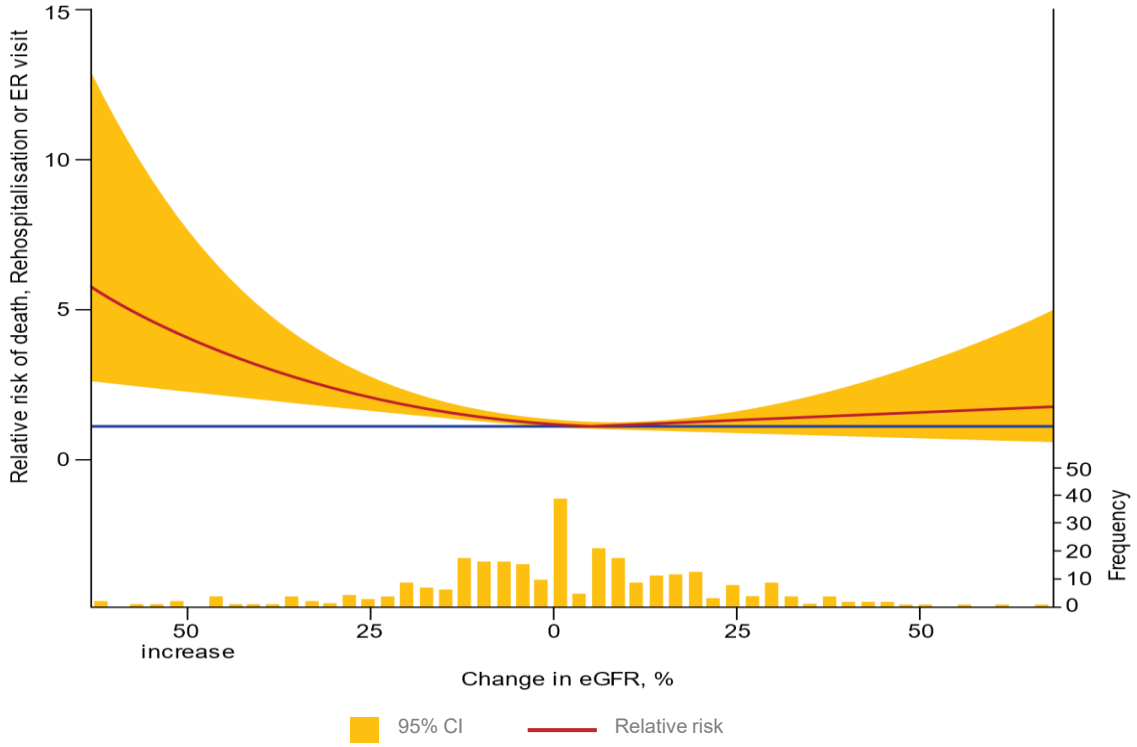
Managing the patient with cardiorenal syndrome frequently involves[1]

Making recommendations or choices of therapies that are commonly contradictory[1]	
While treating volume overload and congestion, the aggressive use of diuretics and volume depletion directly worsens renal function[1]	**ACEi/ARBs, while cardiorenal protective, can lead to temporary worsening of renal function[1]**

ACEi, angiotensin converting enzyme inhibitors; ARBs, aldosterone receptor blockers.

Ref: 1. Liu PP. Can J Cardiol 2008;24(Suppl B):25B-29B.

Use of ACEi/ARB increases the risk of mortality in patients with WRF



- 48% increase in risk of mortality with WRF in HFrEF patients
- 19% increase in risk of mortality with WRF on HFrEF patients on RAASi [ACEi/ARB]

WRF occurs more frequently in HFrEF patients on RAAS antagonists

HFrEF, heart failure with reduced ejection fraction; WRF, worsening renal function; RAASi, renin angiotensin aldosterone inhibitor; ACEi, angiotensin converting enzyme; ARB, aldosterone receptor blocker; eGFR, estimated glomerular filtration rate; ER, emergency room

Ref: 1. Testani JM, et al. Circ Heart Fail. 2017;10:e003835.

Need for newer therapy in managing HFrEF in CKD

Therapy for HFrEF can cause eGFR to vary, so when eGFR declines from >60 to <60 ml/min per 1.73 m^2 it can be unclear if this truly represents CKD versus a transient decline due to hemodynamic and neurohormonal factors[1]

Although strategies for treating HF are the same in patients with or without CKD, it is important to avoid medication toxicity and complications with cardiovascular or renal procedures[1]

Hence, the new therapy should focus on cardiorenal syndrome, and treat the whole patient, and treat for long term[2,3]

HFrEF, heart failure with reduced ejection fraction; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; HF, heart failure.

Ref: 1. House AA, et al. Kidney International (2019) 95, 1304–1317. 2. House AA, et al. International Journal of Nephrology. 2011;2011:doi:10.4061/2011/630809; 3. Liu PP. Can J Cardiol 2008;24(Suppl B):25B-29B.

ACEi/ARBs also reduce the risk of mortality due to HFrEF, what was the need of a new class of drug?

Rajiv Passey. Cardiologist

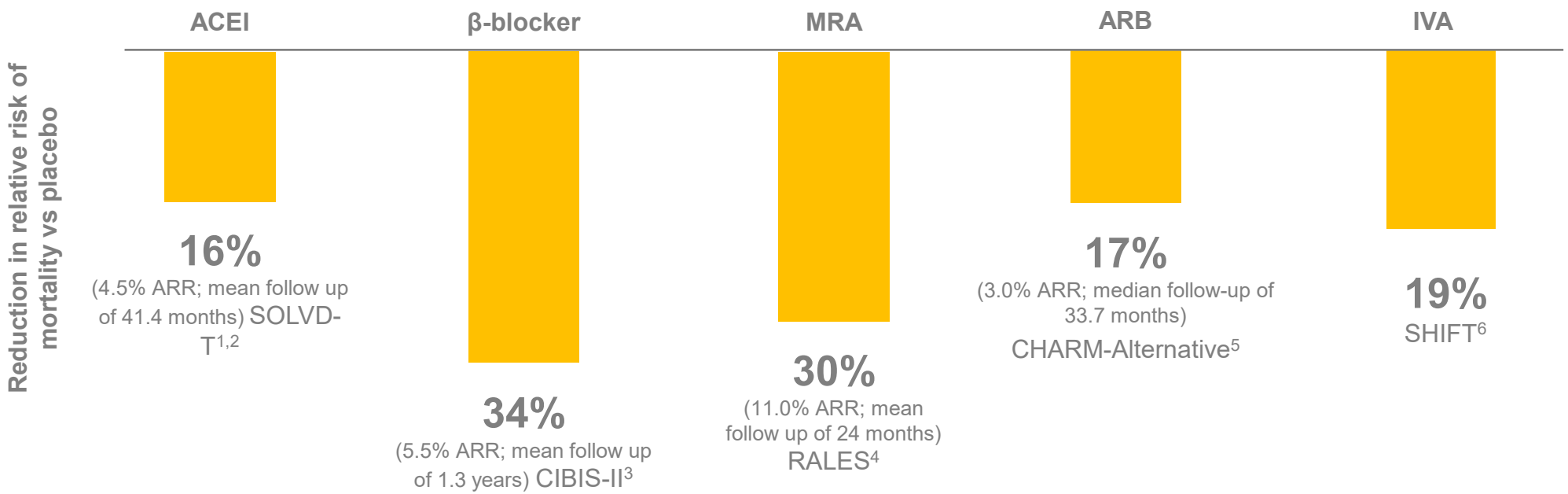
HFrEF, heart failure with reduced ejection fraction; ACEI, angiotensin converting enzyme; ARB, aldosterone receptor blocker.

What should be the next step in managing patients like Kartik?

A	**Yes**
B	**No**

ACEI, angiotensin converting enzyme; ARB, aldosterone receptor blocker; ARNI, angiotensin receptor neprilysin inhibitor.

Mortality in HFrEF remains high despite the introduction of therapies over the last 20 years



Despite conventional therapy, there is 50% mortality rate for HF patients at 5 years post-diagnosis[7-12]

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HFrEF, Heart failure with reduced ejection fraction, ACEi: Angiotensin converting enzyme inhibitor, ARB: Angiotensin II receptor blocker, MRA: Mineralocorticoid receptor antagonist, IVA: Ivabradine, SOLVD-T: Studies of left ventricular dysfunction trial, CIBIS-II: Cardiac insufficiency bisoprolol study II, RALES: Randomized aldactone evaluation study, CHARM: Candesartan in heart failure assessment of reduction in mortality and morbidity, SHIFT: Ivabradine and outcomes in chronic heart failure.

Ref: 1. McMurray JJV, et al. Eur Heart J 2012;33:1787–847; 2. SOLVD Investigators. N Engl J Med 1991;325:293–302; 3. CIBIS-II Investigators. Lancet 1999;353:9–13; 4. Pitt et al. N Engl J Med 1999;341:709-17;–50; 5. Granger et al. Lancet 2003;362:772–6; 6. Swedberg K, et al. Lancet. 2010 Sep 11;376(9744):875-85. 7. Owan et al. N Engl J Med 2006;355:251–9; 8. Roger et al. JAMA 2004;292:344–50; 9. Levy et al. N Engl J Med 2002;347:1397–402; 10. Yancy et al. Circulation 2013;128:e240–327; 11. Loehr et al. Am J Cardiol 2008;101:1016–22; 12. Askoxylakis et al. BMC Cancer 2010;10:105

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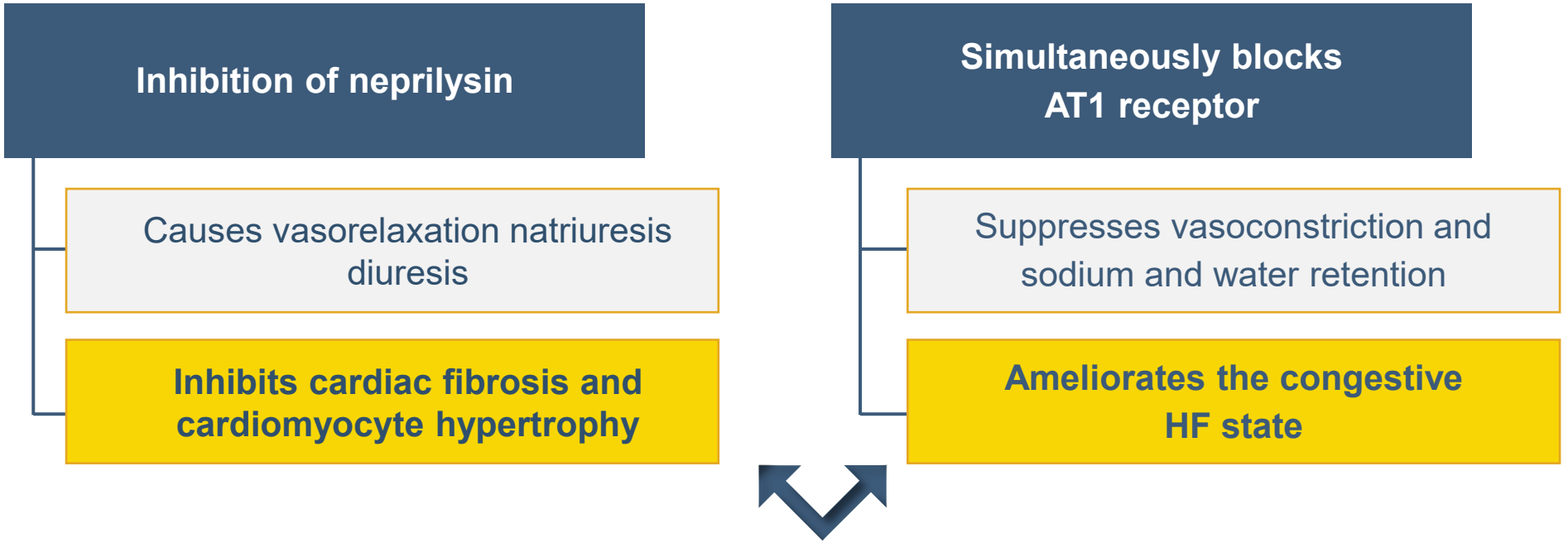
Advantages of sacubitril/valsartan over current therapies (ACEI or ARB)



Acts on underlying structural and molecular abnormalities which drive disease progression that is silent and life threatening

AT1, angiotensin II receptor 1; HF, heart failure; ACEI, angiotensin converting enzyme inhibitor; ARB: angiotensin-receptor blockers.

Ref: 1. Sabbah HN. Eur J Heart Fail. 2017;19:469-478.

ESC 2021 recommends sacubitril/valsartan as a first-line cornerstone therapy for all HFrEF patients

Sacubitril/valsartan may be considered as a first-line therapy instead of an ACEi in all HFrEF patients*

- Initiation of sacubitril/valsartan in recently hospitalized stable patients with HFrEF, including those who are ACEi/ARB naïve, is safe and may be considered

*Stage C HFrEF including *de novo*.
ESC, European Society of Cardiology; ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; HFrEF, heart failure with reduced ejection fraction.
Ref: McDonagh TA, et al. European Heart Journal (2021) 00, 1-128. doi:10.1093/eurheartj/ehab368.

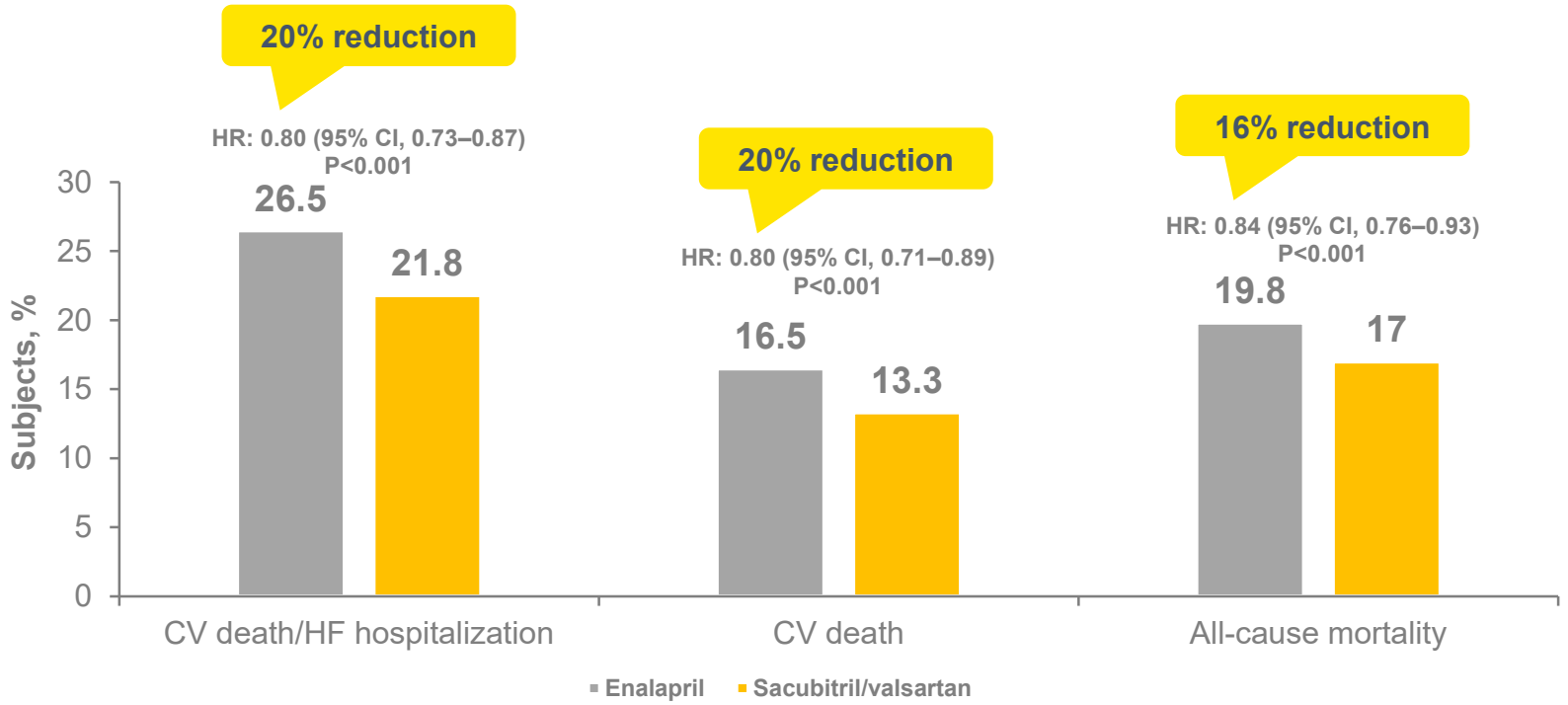
Even recent ACC 2022 guideline recommends sacubitril/valsartan as the first-line therapy for all HFrEF patients*

ARNI is recommended as the first-line therapy for HFrEF patients*

- In chronic symptomatic HFrEF NYHA class II or III who tolerate an ACEi or ARB, replacement by an ARNi is recommended
- ARNi is recommended as *de novo* treatment in hospitalized patients with acute HF before discharge

*Stage C HFrEF including *de novo* patients.
ACC, American college of cardiology; HFrEF, heart failure with reduced ejection fraction; ACEi, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blockers; ARNI, angiotenisn receptor-neprilysin inhibitor; GDMT, guideline directed medical therapy.
Ref: Heidenreich PA, et al. Circulation. 2022;145:00–00. DOI: 10.1161/CIR.0000000000001063.

Sacubitril/valsartan keeps HFrEF patients alive

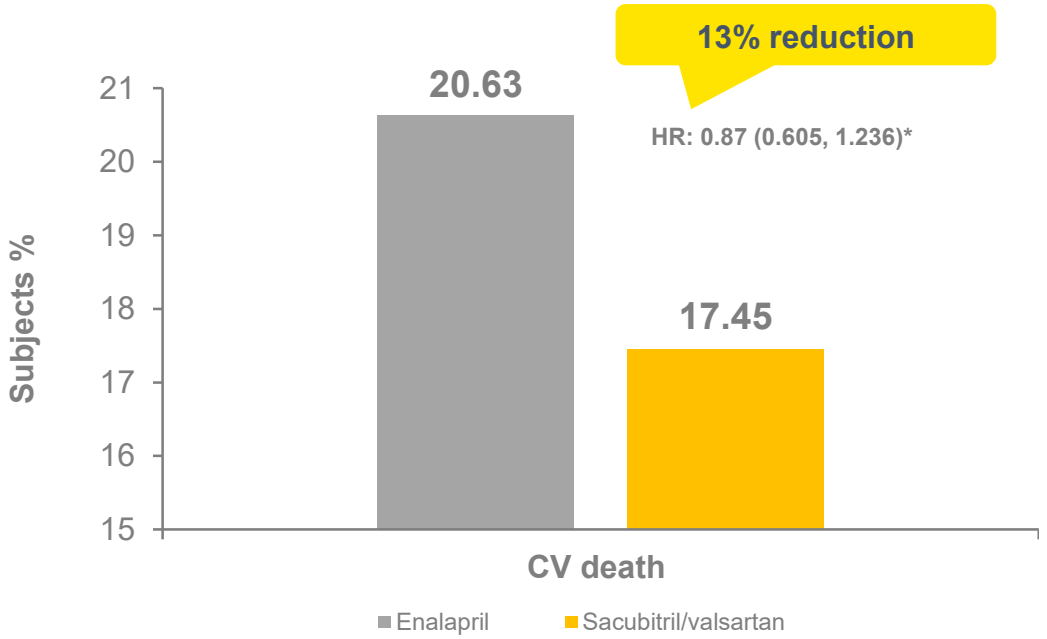


Sacubitril/valsartan significantly reduced the number of CV death/HF hospitalization, CV death and all-cause mortality

HR, hazrd ratio; HF, heart failure: CV, cardiovascular; CI, confidence interval; HFrEF, heart failure with reduced ejection fraction.

Ref: 1. McMurray et al. N Engl Med 2014;371:993-1004.

Sacubitril/valsartan has shown efficacy even in Indian HFrEF patients : CV death



13% reduction in risk of CV death in HFrEF patients with sacubitril/valsartan compared to enalapril

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*No significant difference was seen between the benefits of treatment in Indian and the total PARADIGM-HF cohort (p value for interaction > 0.05)
HR, hazrd ratio; CV, cardiovascular; HFrEF, heart failure with reduced ejection fraction.
Ref: 1. Jain AR, et al. Indian Heart Journal; 72;2020; 535-540.

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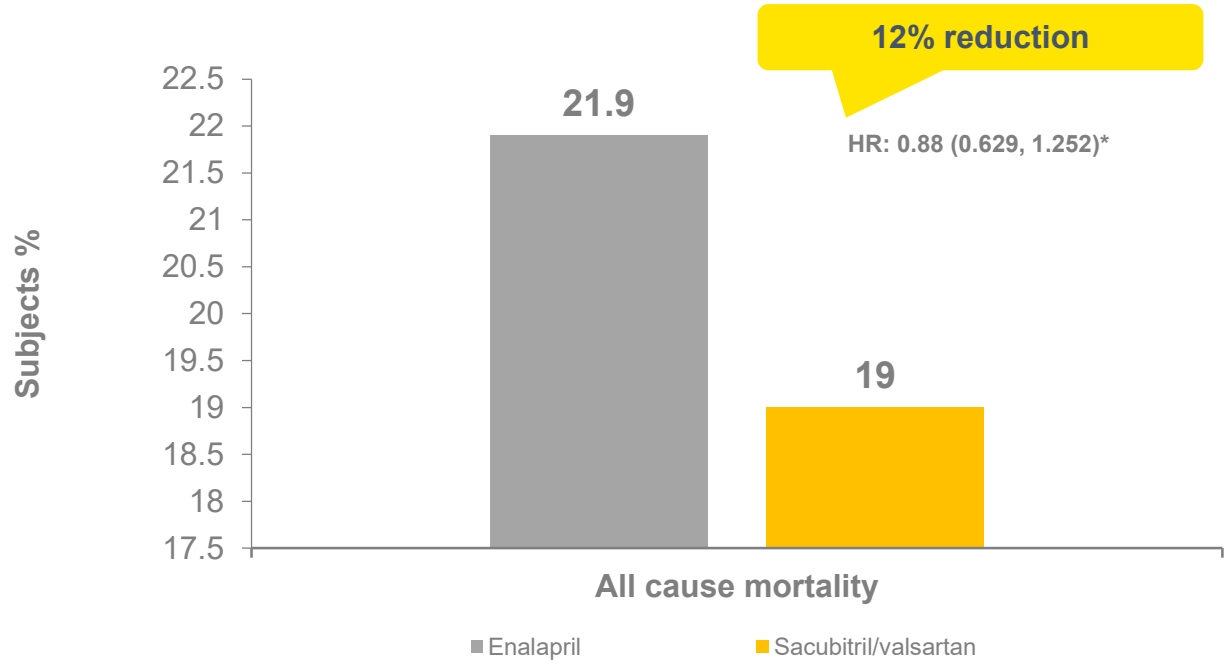
Sacubitril/valsartan has shown efficacy even in Indian HFrEF patients : All cause mortality



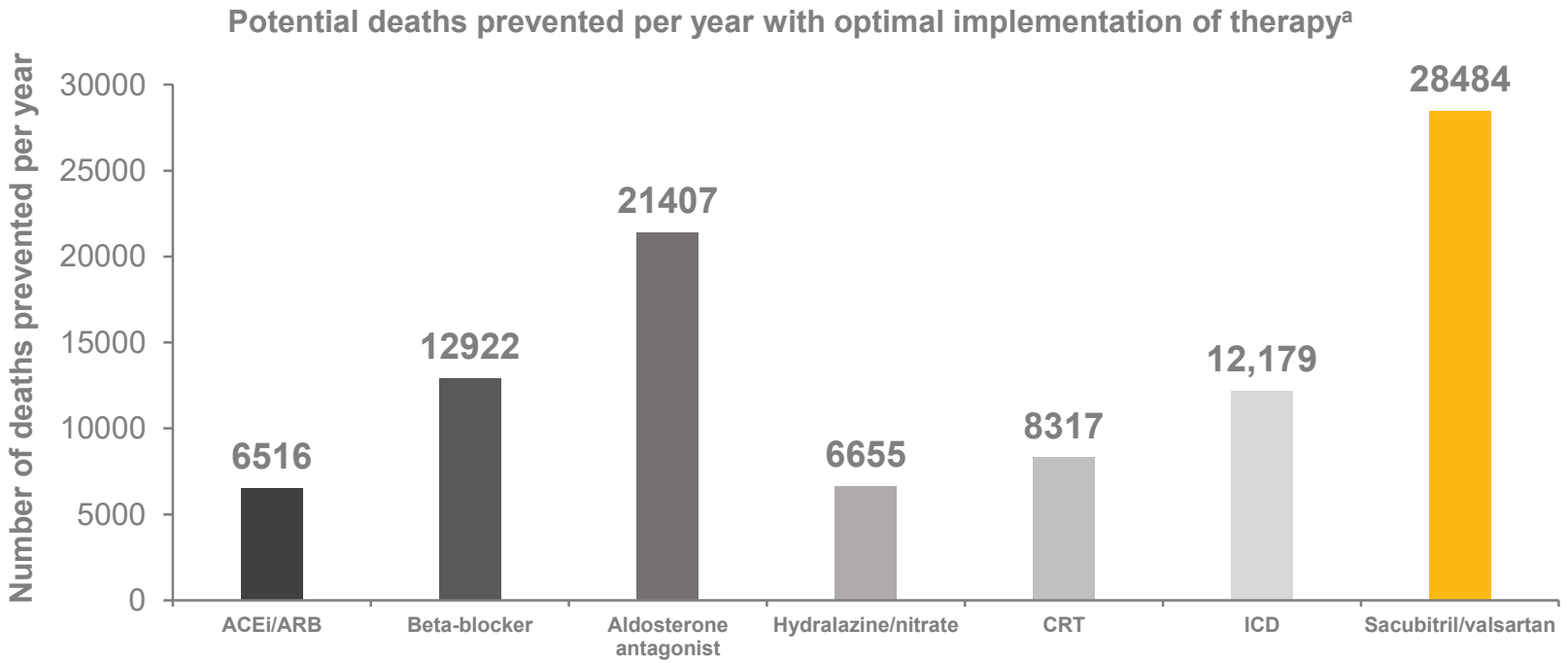
12% reduction in risk of all cause mortality in HFrEF patients with sacubitril/valsartan compared to enalapril

*No significant difference was seen between the benefits of treatment in Indian and the total PARADIGM-HF cohort (p value for interaction > 0.05)
HR, hazrd ratio; HFrEF, heart failure with reduced ejection fraction.

Ref: 1. Jain AR, et al. Indian Heart Journal; 72;2020; 535-540.

Sacubitril/valsartan can help reduce the mortality burden associated with HF

Estimated potential impact of optimal implementation of GDMT



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[a]Data are presented as n (%). Estimates are based on the number of patients with HFrEF in the USA (drawn from the 2010 American Heart Association Heart Disease and Stroke Statistics Update) and the number of patients with HFrEF who are potentially eligible for each of the guideline-recommended HF therapies (drawn from published HF registries).
HF, heart failure; GDMT, guideline recommended therapy; ACEi, angiotensin converting enzyme inhibitor; ARB, angiotensin II receptor blocker; CRT, cardiac resynchronization therapy; ICD, implantable cardioverter defibrillator.
Ref: 1. Anand I. Am J Cardiovasc Drugs. 2018;18:333–345.

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Besides Hazard ratio, are there any other outcomes measures that can be more relevant for clinicians and patients to understand therapy impact?

Rajiv Passey

Terms used in the analysis of time-to-event outcomes

Terms	Description
Hazard rate	The rate of an event (say, death or a cardiovascular disease) at a given time
Hazard ratio (HR)	The ratio of two hazard rates
Cox model	A statistical regression model that is used to analyse time-to-event outcomes. Its output is a time-constant HR, assuming that the hazard rates are proportional at all times
Restricted mean survival time (RMST)	The average survival time up to a given time point

HR, heart rate.
Ref: Stensrud MJ, et al. European Heart Journal. 2018:1–6.

Drawbacks of calculation based on HR

Hard to interpret due to selection bias

Not immediately relevant to individuals as causal effect

HR, heart rate.
Ref: Stensrud MJ, et al. European Heart Journal. 2018:1–6.

Understanding RMST measure and advantages

Restricted mean survival time (RMST) measure can be interpreted as the mean event-free survival time up to a prespecified, clinically important point[1]

Uses age at randomization instead of time[2]

Provides long-term estimates with a specific intervention across different age groups[2]

Provides an estimate of the effect of treatment in terms of time "free of an event," years of life gained, or both[2]

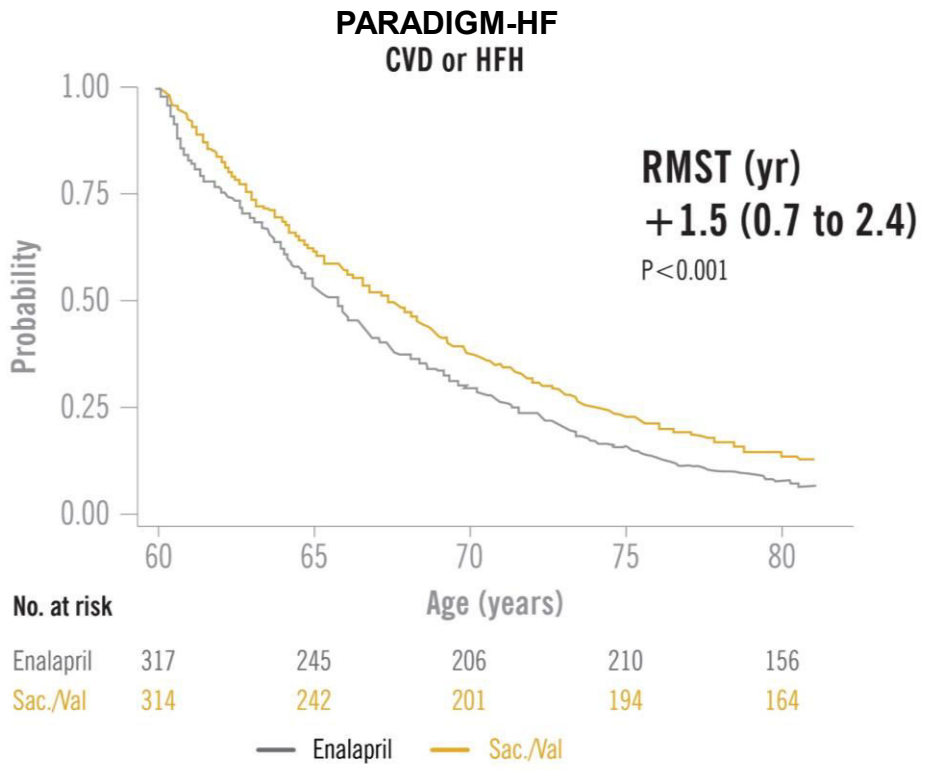
Such measures may be more readily interpretable and quantifiable for patients and clinicians[2]

RMST, restricted mean survival time.

Ref: 1. Kim HD, et al. JAMA Cardiology. 2017:E1-E2. 2. Ferreira JP, et al. JACC: HEART FAILURE. 2020;8(12): 984 – 95.

Sacubitril/valsartan extends life without primary event by 1.5 years compared to enalapril

RMST using age instead of time

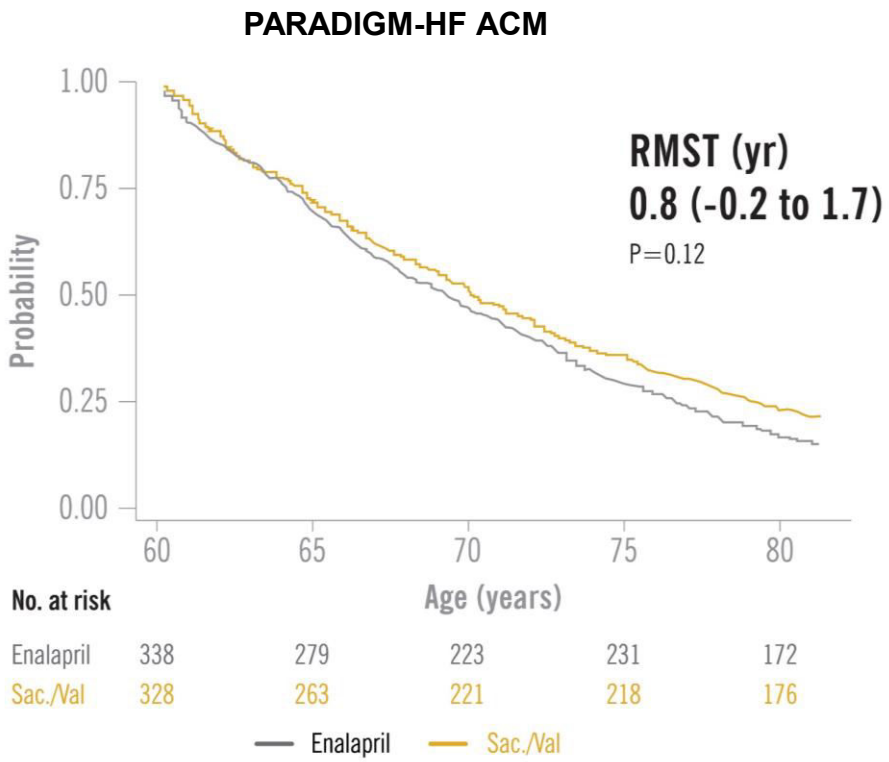


RMST days gained over this follow-up was +37 (23 to 52) days, and the potential extension of life without an event was estimated at +1.5 (0.7 to 2.4) years.

HF, heart failure; RMST, restricted Mean Survival Time; PARADIGM-HF, prospective Comparison of ARNI [Angiotensin Receptor–Neprilysin Inhibitor] with ACEI [Angiotensin-Converting–Enzyme Inhibitor] to Determine Impact on Global Mortality and Morbidity in Heart Failure Trial
Ref: Ferreira JP, et al. JACC: HEART FAILURE. 2020;8(12): 984 – 95.

Sacubitril/valsartan reduces all-cause death

RMST using age instead of time

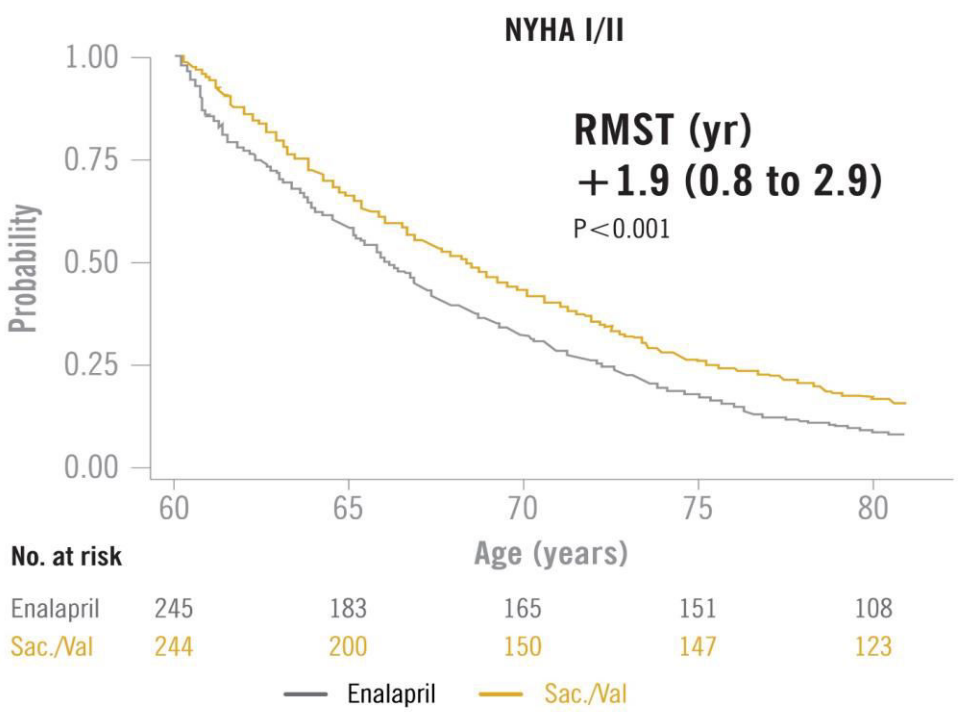


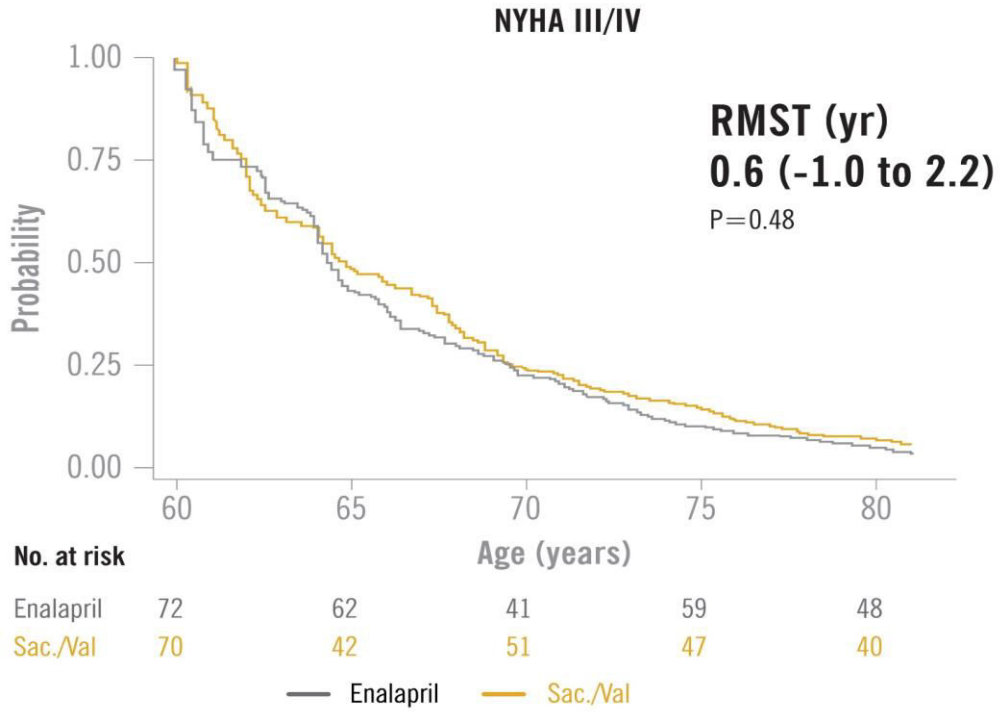
RMST days gained over this follow-up was +19 (7 to 31) days, and the potential extension of life without an event was estimated at +0.8 (-0.2 to 1.7) years.

ACM, all-cause mortality; RMST, restricted Mean Survival Time; PARADIGM-HF, prospective Comparison of ARNI [Angiotensin Receptor–Neprilysin Inhibitor] with ACEI [Angiotensin-Converting–Enzyme Inhibitor] to Determine Impact on Global Mortality and Morbidity in Heart Failure Trial.

Ref: Ferreira JP, et al. JACC: HEART FAILURE. 2020;8(12): 984 – 95.

Event free survival of ~6 months is achieved with sacubitril/valsartan, irrespective of NYHA functional class





The estimated extension of event-free survival was +1.9 (0.8 to 2.9) years

The estimated extension of event-free survival was +0.6 (1.0 to 2.2) years

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ACM, all-cause mortality; RMST, restricted Mean Survival Time; PARADIGM-HF, prospective Comparison of ARNI [Angiotensin Receptor–Neprilysin Inhibitor] with ACEI [Angiotensin-Converting–Enzyme Inhibitor] to Determine Impact on Global Mortality and Morbidity in Heart Failure Trial.

Ref: Ferreira JP, et al. JACC: HEART FAILURE. 2020;8(12): 984 – 95.

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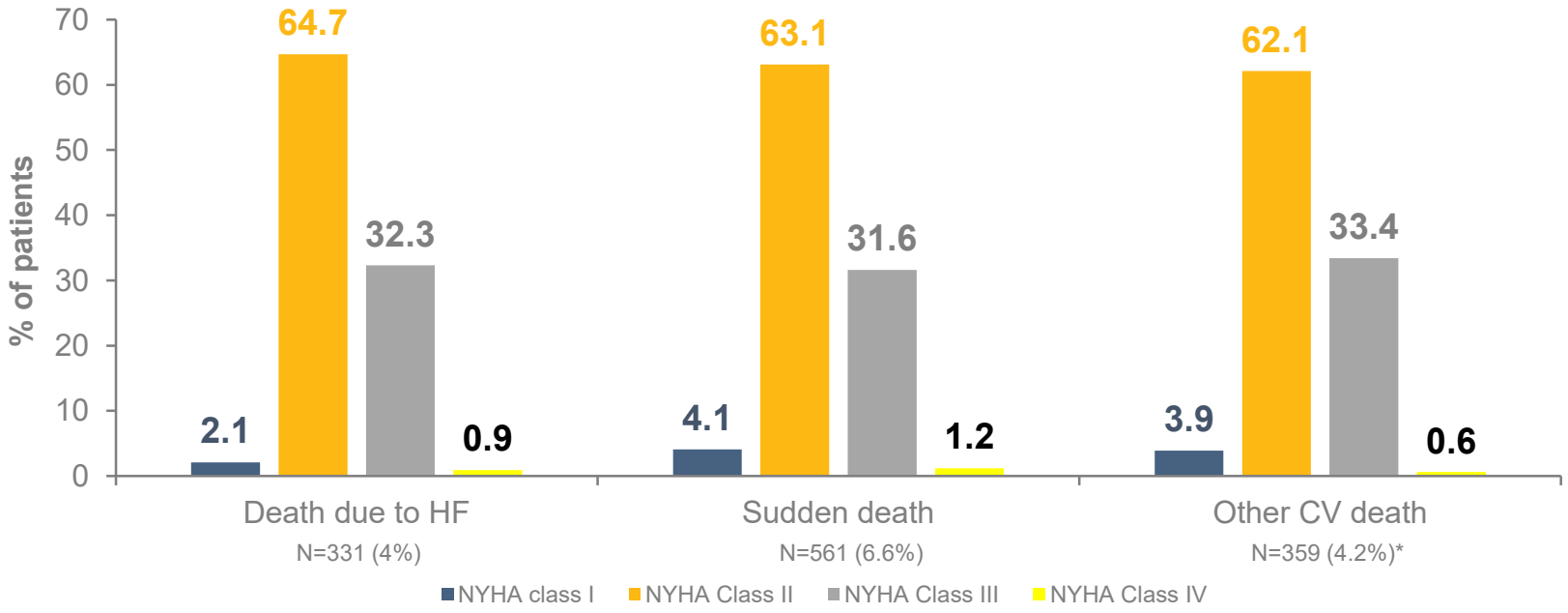
Sudden cardiac death can occur without worsening symptoms of HF, what is the role of sacubitril/valsartan in these patients?

Rajeev Rajput. Endocrinologist

Cause of death in NYHA Class II HFrEF Patients

PARADIGM-HF sub-analysis



6 out of 10 NYHA class II patients die due to SCD in PARADIGM-HF

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*Other CV death includes all CV deaths not ascribed to pump failure or sudden death.
NYHA, New York Heart Association; HFrEF, heart failure with reduced ejection fraction; SCD, sudden cardiac death; HF, heart failure; CV, cardiovascular.
Ref: Desai AS et al. Eur Heart J. 2015;36:1990–7

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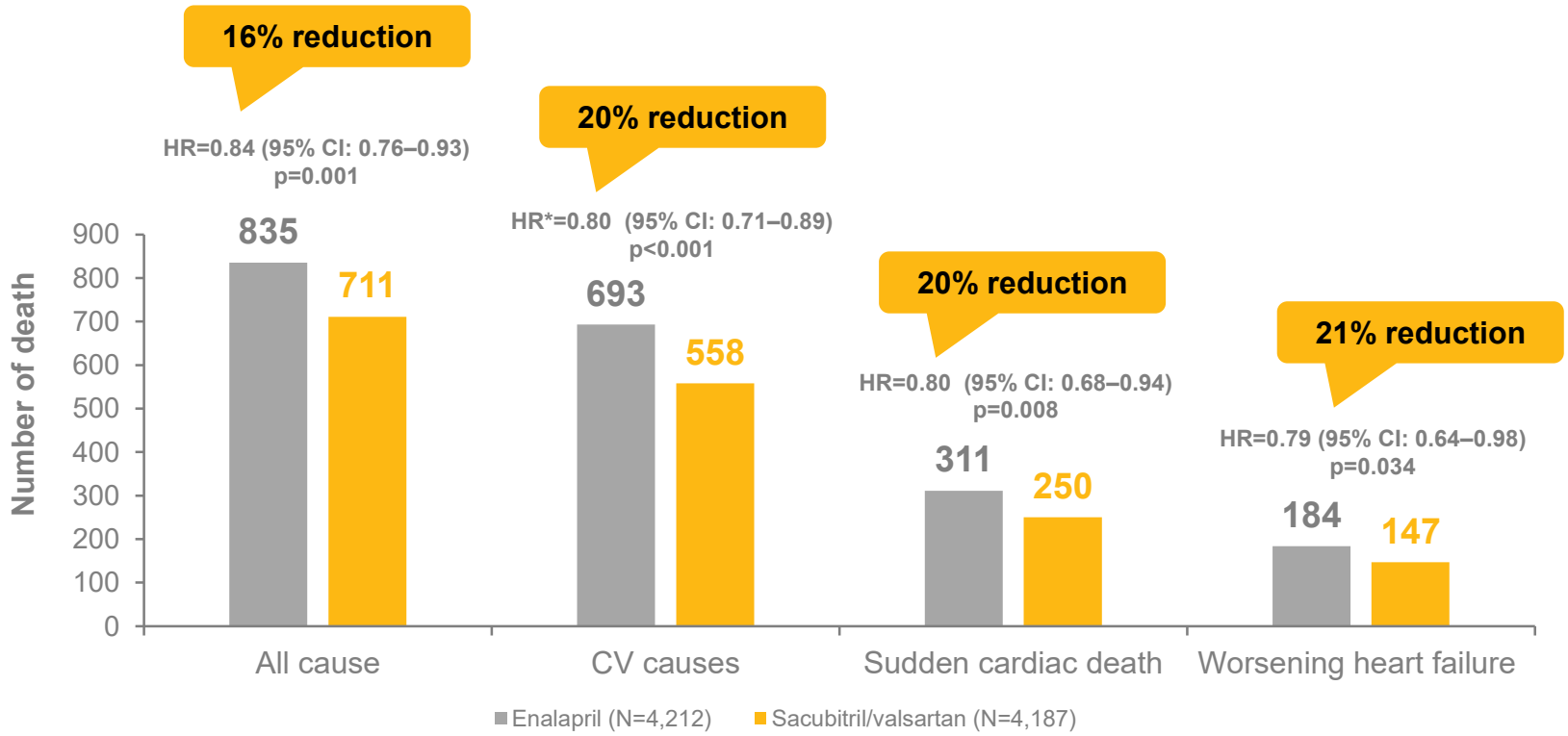
Sacubitril/valsartan impacts mode of death



Sacubitril/valsartan significantly reduced the number of sudden cardiac deaths and death due to worsening heart failure

CV, cardiovascular; HR, hazard ratio; CI, confidence interval.

Ref: Desai et al. Eur Heart J 2015; epub ahead of print: DOI:10.1093/eurheartj/ehv186.

Guideline recommendations - European society of cardiology 2016

Management of ventricular tachyarrhythmias in HF

Recommendations	Class[a]	Level[b]
Treatment with beta-blocker, MRA and sacubitril/valsartan reduces the risk of sudden death and is recommended for patients with HFrEF and ventricular arrhythmias (as for other patients)	I	A

Only Sacubitril/valsartan (not an ACEi/ARB) has been recommended for prevention of sudden cardiac death

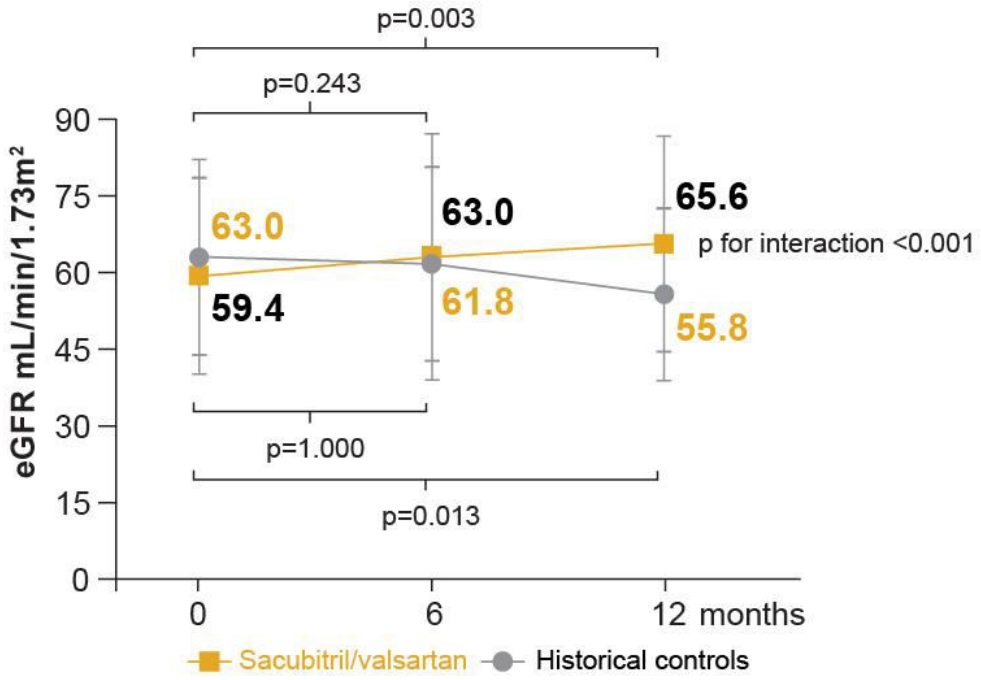
[a]Class of recommendation, bLevel of evidence.
MRA, mineralocorticoid receptor antagonist; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; HFrEF, heart failure with reduced ejection fraction.
Reference: Ponikowski P, et al. European Heart Journal (2016) 37, 2129–2200.

What is the effect of sacubitril/valsartan in HFrEF patients with CKD and dose recommendation?

Manish Aggarwal, Nephrologist

HFrEF, heart failure with reduced ejection fraction; CKD, chronic kidney disease.

Sacubitril/valsartan improves eGFR in HFrEF patients

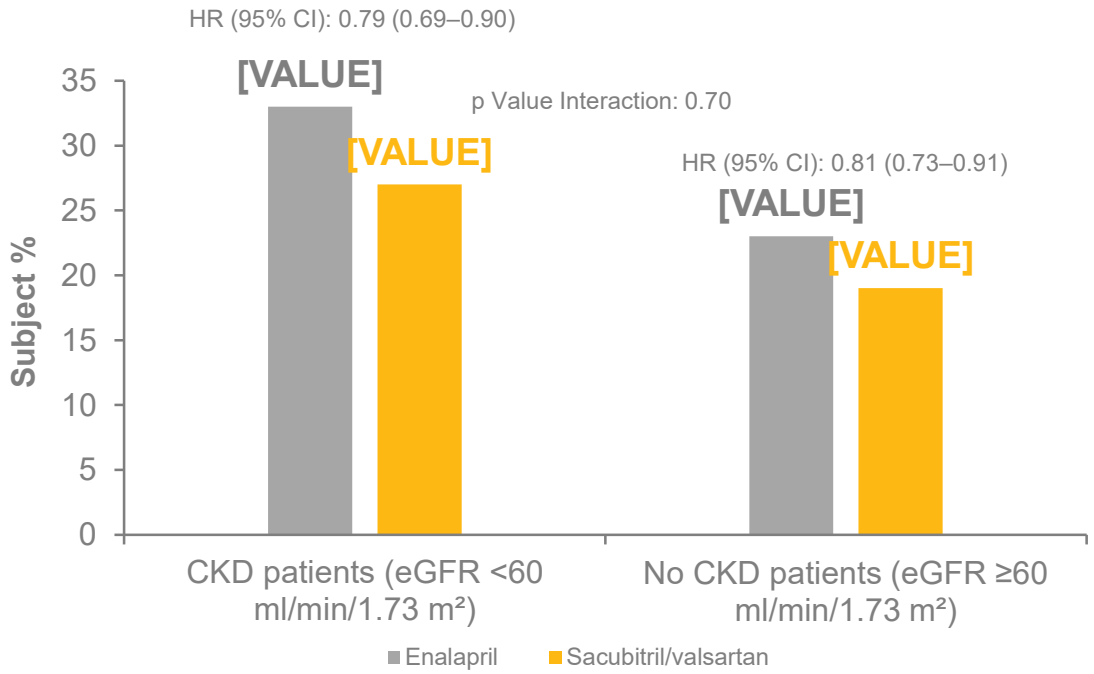


Significant improvement in eGFR with sacubitril/valsartan in real world setting in HFrEF patients[1]

eGFR, estimated glomerular filtration rate; HFrEF, heart failure with reduced ejection fraction.

Ref: Spannella F, et al. Intern Emerg Med. 2019. doi: 10.1007/s11739-019-02111-6.

Sacubitril/valsartan improves clinical outcomes in patients with HFrEF irrespective of CKD Status

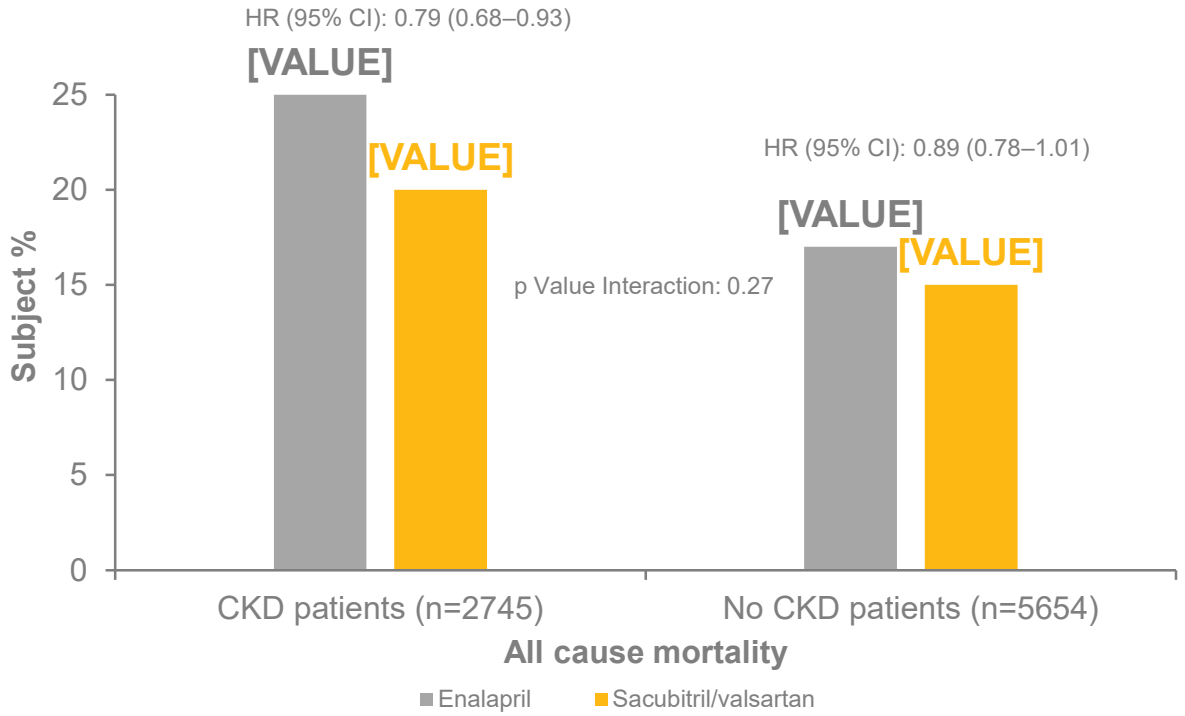


21% reduction in CV death and HF hospitalization with sacubitril/valsartan in patients with CKD

HFrEF, heart failure with reduced ejection fraction; CKD, chronic kidney disease; HR, hazard ratio; CI, confidence interval; CV, cardiovascular; eGFR, estimated glomerular filtration rate; HF, heart failure.

Ref: Damman K, et al. JACC Heart Fail. 2018 Jun;6(6):489-498.

Sacubitril/valsartan reduces all-cause mortality in patients with HFrEF and CKD patients



21% reduction in all cause mortality with sacubitril/valsartan in patients with CKD

HFrEF, heart failure with reduced ejection fraction; CKD, chronic kidney disease; HR, hazard ratio; CI, confidence interval.
Ref: Damman K, et al. JACC Heart Fail. 2018 Jun;6(6):489-498.

Dose initiation and optimisation based on eGFR levels

No dose adjustment for sacubitril/valsartan
is needed[1] when eGFR ≥30mL/min/1.73m^2

Dosing	Mild (eGFR ≥60 mL/min/1.73 m^2)	Moderate (eGFR 59-30 mL/min/1.73 m^2)	Severe (eGFR<30 mL/min/1.73 m^2)
Starting	No dose adjustment required	No dose adjustment required	50 mg
Duration			2-4 weeks
Target maintenance dose			200 mg

eGFR, estimated glomerular filtration rate; ACC, american College of Cardiology.
Ref: Maddox TM, et al. Journal of the American College of Cardiology. 2021 Feb 16;77(6):772-810. doi: 10.1016/j.jacc.2020.11.022.

To summarise…

Patients like Kartik with mild worsening HF symptoms are at increased risk of mortality and renal impairment further increases the risk of mortality[1-3]

Sacubitril/valsartan reduces the risk of mortality and improves survival in HFrEF patients[4]

HF, heart failure; HFrEF, heart failure with reduced ejection fraction.

Ref: 1. Ahmed A. Am J Cardiol. 2007;99(4):549-553. 2. Shamagiana LG, et al. Rev Esp Cardiol. 2006;59(2):99-108. 3. Löfman I, et al. s. Open Heart 2016;3: e000324. doi:10.1136/ openhrt-2015-000324. 4. McMurray et al. N Engl Med 2014;371:993-1004

We Are In 2022 and getting Soon into 2023
What else Besides What We Discussed So Far should be administerd ?

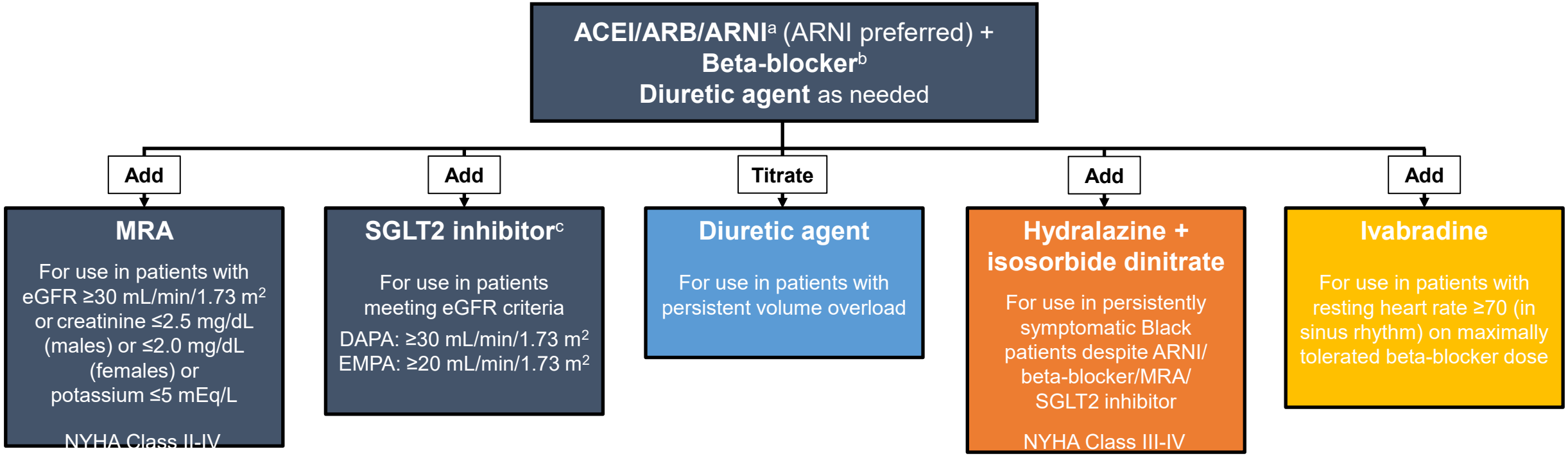
ARNI Came in 2017 (PARADIGM Trial) and should Replace ACE/ARB's

SGLT2 for HFrEF Came in 2019 (A very Important adjunct both in Diabetics and Non Diabetics) Esp in Renally compromised patients

Verciguat (Verquovo) came in 2020 (VICTORIA Trial) and have proven its benefit in WHF.

These benefits need to be realized and all useful group of drugs need to be administered.

2021 ACC Expert Consensus Now Includes Dapagliflozin as a Component of First-Line Treatment for Patients With HFrEF



- ARNIs, beta-blockers[b], MRAs and SGLT2 inhibitors are first-line medications for all patients with HFrEF.
- SGLT2 inhibitors should be added for patients with chronic HFrEF who are already receiving ARNI/ACEI/ARB, beta-blocker and MRA, if not contraindicated.
- Achieving target or maximally tolerated doses of other HFrEF therapies is not necessary before adding SGLT2 inhibitors.

Powered by HF Essentials Go with the guidelines

Blue boxes indicate first-line therapy.

[a]ACEI/ARB should only be considered in patients with contraindications, intolerance or inaccessibility to ARNI; [b]Evidence-based beta-blocker (carvedilol, metoprolol succinate, or bisoprolol); [c]DAPA is the only SGLT2 inhibitor with an FDA-approved indication for the treatment of HFrEF.

Maddox TM et al. *J Am Coll Cardiol*. 2021;77:772-810.

Conclusion

HFrEF patients, with mild symptoms are at increased risk of mortality and in India, mortality rate in HFrEF patients is increasing with time[1,2]

Mortality risk further increases in HFrEF patients with renal impairment. Renal failure is an independent predictor of mortality in heart failure patients[3,4]

Sacubitril/valsartan reduces risk of CV death and all-cause mortality in HFrEF patients, irrespective of CKD and extends survival time in HFrEF patients by 1 to 2 years[5-7]

HFrEF Patients in 2022/2023 need besides ARNI, Beta blockers, Aldosterone antagonists, SGLT2inhibitors (Dapagliflozin) and patients with WHF need Versiguat .

HFrEF, heart failure with reduced ejection fraction; CKD, chronic kidney disease; CV, cardiovascular; HF, heart failure

Ref: 1. Ahmed A. Am J Cardiol. 2007;99(4):549-553; 2. Sanjay G, et al. Journal of cardiac failure. 2018 Dec 1;24(12):842-8; 3. Shamagiana LG, et al. Rev Esp Cardiol. 2006;59(2):99-108. 4. Löfman I, et al. s. Open Heart 2016;3: e000324. doi:10.1136/ openhrt-2015-000324; 5. . McMurray et al. N Engl Med 2014;371:993-1004; 6. Damman K, et al. JACC Heart Fail. 2018 Jun;6(6):489-498; 7. Ferreira JP, et al. JACC: HEART FAILURE. 2020;8(12): 984 – 95.

Kartik is Luckier today than what he was in 2018!

Time is essential in your heart failure patients so, is initiating evidence based treatment in your HFrEF patients to reduce the risk of mortality

All the drugs should be on board within 4 weeks maximum

HFrEF Patients have much more for treatment for improving the quality of life, reducing hospitalizationsand improving survival

Thank you

Basic Succinct Statement (2/2)

Pregnancy: VYMADA must not be used during pregnancy. Patients should be advised to discontinue VYMADA as soon as pregnancies occur and to inform their physicians.
Females of child-bearing potential: Female patients of childbearing potential should be advised about the consequences of exposure to VYMADA during pregnancy and to use contraception during treatment and for 1 week after their last dose of VYMADA.
Breast-feeding: It is not known whether VYMADA is excreted in human milk. Because of the potential risk for adverse drug reactions in breastfed newborns/infants, VYMADA is not recommended during breastfeeding.
Adverse drug reactions:
Very common (≥10%)*:* Hyperkalemia, hypotension, renal impairment.
Common (1 to 9%): Cough, Dizziness, renal failure, diarrhea, hypokalemia, fatigue, headache, syncope, nausea, asthenia, orthostatic hypotension, vertigo.
Uncommon (0.1 to 1%)*:* Angioedemia, dizziness postural.
Unknown: Hypersensitivity (including rash, pruritus, and anaphylaxis).

Interactions: ♦***Concomitant use contraindicated***: aliskiren in patients with Type 2 diabetes, Use with ACE inhibitors. VYMADA must not be started until 36 hours after taking the last dose of ACE inhibitor therapy. ACE inhibitor therapy must not be started until 36 hours after the last dose of VYMADA. ♦***Concomitant use not recommended***: ARB, concomitant use of VYMADA with aliskiren, should be avoided in patients with renal impairment (eGFR < 60 mL/min/1.73 m2). ***Caution when used concomitantly*** with statins, sildenafil, lithium, potassium-sparing diuretics including mineral corticoid antagonists (e.g. spironolactone, triamterene, amiloride), potassium supplements, or salt substitutes containing potassium, non-steroidal anti-inflammatory agents (NSAIDs) including selective cyclooxygenase-2 inhibitors (COX-2 Inhibitors), inhibitors of OATP1B1, OATP1B3, OAT3 (e.g. rifampin, cyclosporine) or MPR2 (e.g. ritonavir).
Packs:
50 mg: Pack of 28 tablets (blister strip of 2 x 14).
100 mg: Pack of 28 tablets (blister strip of 2 x 14).
200 mg: Pack of 28 tablets (blister strip of 4 x 7).

Before prescribing, please consult full prescribing information available from Novartis Healthcare Private Limited, Inspire BKC, Part of 601 & 701, Bandra Kurla Complex, Bandra (East), Mumbai – 400 051, Maharashtra, India. Tel +91 22 50243335/36, Fax +91 22 50243010.
For the use only of a registered medical practitioner or a hospital or a laboratory.

India BSS dtd 28 Aug 17 revised on 19 Nov 18 based on international BSS dtd 10 Jul 17 effective from 19 Nov 18.

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