Cardiac Resynchronisation Therapy Upgrade in Heart Failure with Right Ventricular Pacing: A Multicentre, Randomised, Controlled Trial

The BUDAPEST CRT Upgrade

On behalf of the BUDAPEST CRT Upgrade Committees and Investigators

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Background and Rationale



- Approximately 1 million conventional PMs or ICDs are implanted each year worldwide. Nearly 30% of these patients develop LV systolic dysfunction due to intraventricular dyssynchrony induced by RV pacing, can lead to HF hospitalisation and associated adverse clinical outcomes.
- In patients with HFrEF prior implanted a PM or ICD, the potential benefits of an upgrade to CRT, where an extra LV lead is implanted to the CS side branch, have not been established.
- Due to the lack of data regarding hard outcomes from large RCTs, the class/level of recommendations for CRT upgrade have been modified several times over the past decade in ESC and ACC/AHA/HRS guidelines (*IB in 2013, IIb B in 2016, IIa B in 2018, and IB in 2023*), showing an unmet need for more robust evidence.
- Moreover, the indicated upgrade procedures are frequently not performed or deferred to a later, undetermined date in over 60% of the candidates.
- BUDAPEST CRT Upgrade was the first trial powered to hard endpoints on efficacy and safety of a CRT-D upgrade, versus ICD alone, in HFrEF patients with intermittent or permanent RV pacing.

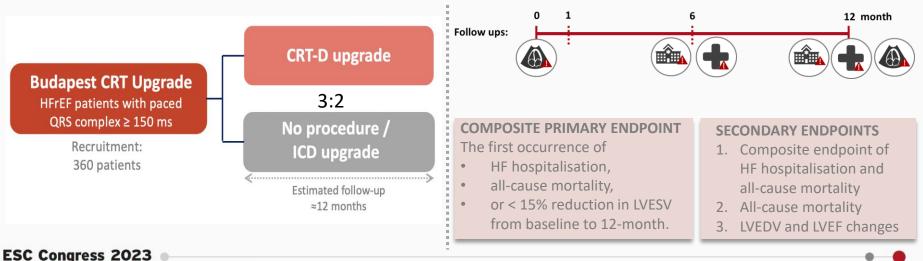
BUDAPEST CRT Upgrade - Study design



A Multicentre, Randomised, Controlled, Investigator-initiated Trial testing the hypothesis that CRT-D upgrade compared to ICD only would be associated with improved clinical outcomes

Key Inclusion Criteria: HFrEF patients with a prior pacemaker or ICD, RV pacing 20-100%, paced QRS complex ≥ 150 ms and GDMT

Key Exclusion Criteria: intrinsic QRS with LBBB morphology, severe renal dysfunction, severe RV dilatation, ACS events

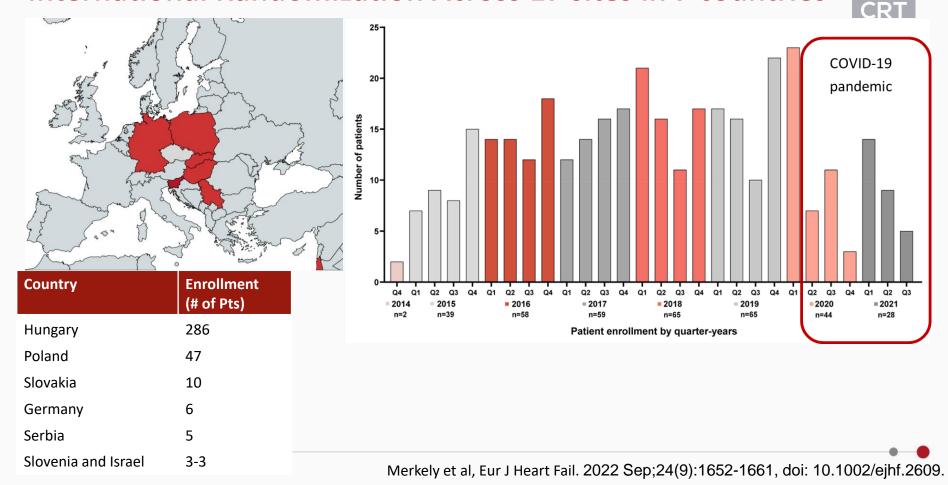


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Merkely et al, Eur J Heart Fail. 2022 Sep;24(9):1652-1661, doi: 10.1002/ejhf.2609.

International Randomization Across 17 sites in 7 countries

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BUDAPEST CRT Upgrade Baseline Characteristics



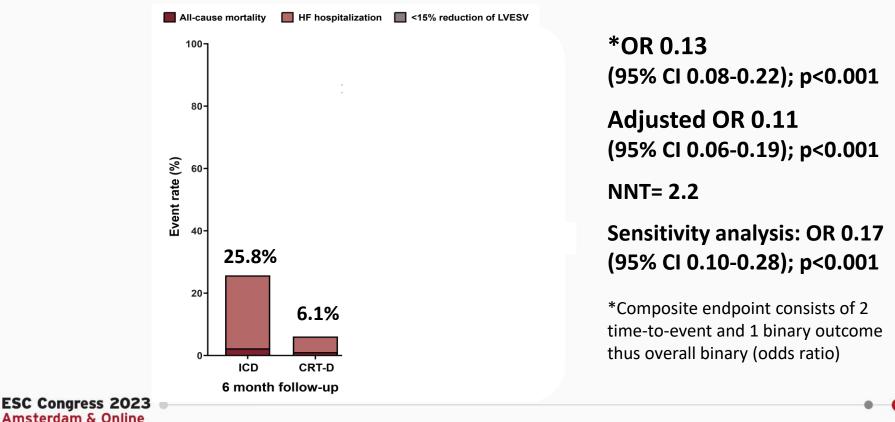
Advanced stage HF cohort	CRT-D N = 215	ICD N= 145 73 ± 8		
Age (years±SD)	73 ± 7			
Male sex – no. (%)	185 (86.1)	135 (93.1)		
NYHA class – no. (%) - II	105 (48.8)	64 (44.1)		
- 111	101 (47.0)	78 (53.8)		
- IVa	9 (4.2)	3 (2.1)		
Ischemic etiology – no. (%)	127 (59.1)	82 (56.6)		
Atrial fibrillation – no. (%)	116 (54.0)	87 (60.0)		
History of VT/ VF – no. (%)	47 (21.9)	37 (25.5)		
HF hospitalisation (12 months before) – no. (%)	101 (47.0)	77 (53.1)		
Echocardiographic parameters: LVEF– %	25 ± 7	25±6		
Prior Device type - no. (%): Pacemaker	150 (69.8)	94 (64.8)		
RV pacing rate prior to enrollment – %	85 ± 21	88 ± 19		

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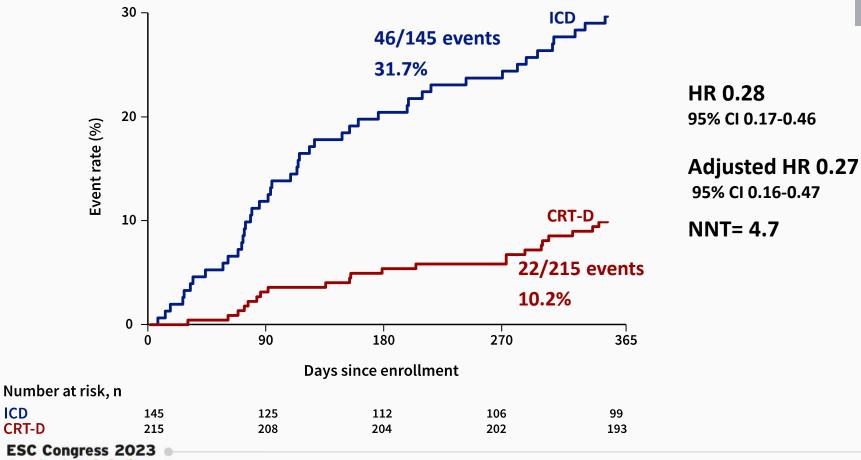
Primary Endpoint: All-cause mortality, HF hospitalisation or < 15% ESV decrease





Secondary Endpoint: All-cause mortality or HF hospitalisation





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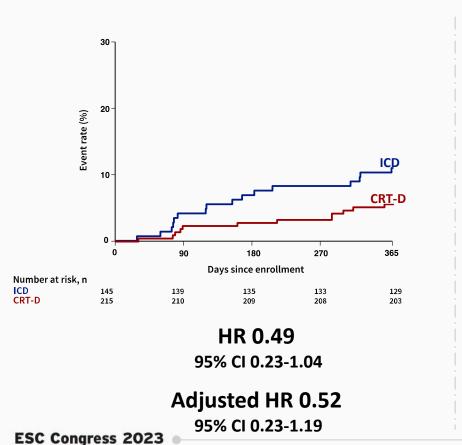
ICD

CRT-D

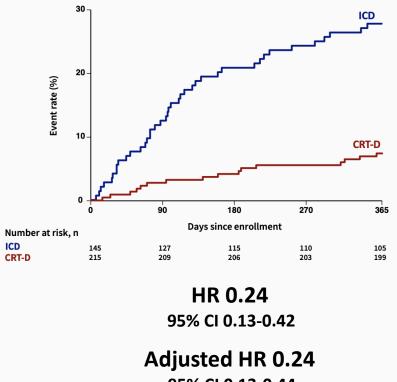
Secondary Endpoint: All-cause mortality

Heart Failure Hospitalisation (post-hoc outcome)





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95% CI 0.13-0.44

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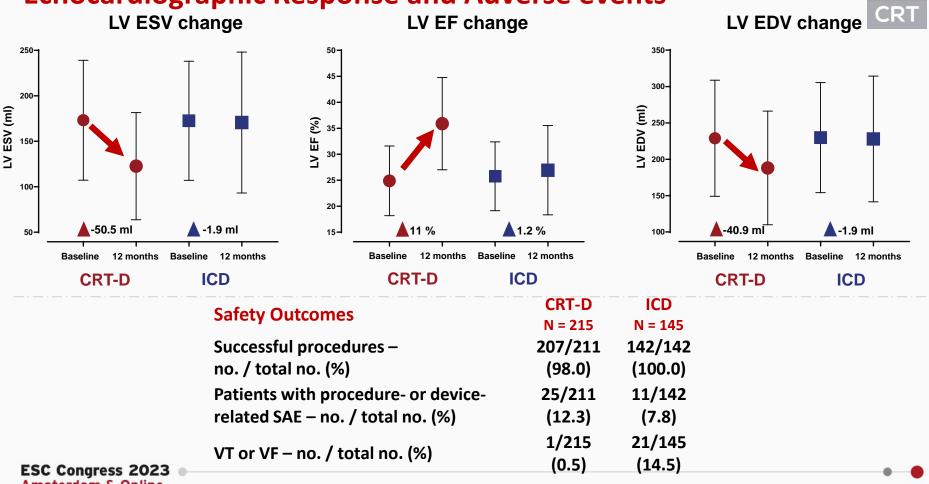
Primary Endpoint in Prespecified Subgroups Consistent, homogenous effect

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Subgroup	No. of patients with event/total no.		Odds ratio (95% CI)	Subgroup	No. of patients with event/tota	al no.	Odds ratio (95% CI)
All patients	159/307	_	0.11 (0.06 - 0.19)	History of diabetes mellitu No	IS 99/192	_	0.14 (0.07 - 0.28)
Age				Yes	60/115		0.07 (0.02 - 0.19)
≤ 75 years > 75 years	96/183 63/124		0.19 (0.09 - 0.38) 0.05 (0.02 - 0.14)	NYHA class at enrollment			
Percent RV pacing at enro ≤ median - 96.25 %	llment 87/151	_	0.18 (0.08 - 0.39)	ll III or IV	71/147 88/160		0.11 (0.05 - 0.25) 0.12 (0.05 - 0.27)
> median - 96.25 %	72/156		0.05 (0.02 - 0.13)	NT-proBNP at enrollment			
LVEF at enrollment			1 	≤ median - 2154 pg/ml	62/120		0.13 (0.06 - 0.31)
≤ 30 % > 30 %	119/233 40/74		0.11 (0.06 - 0.20) 0.17 (0.05 - 0.51)	> median - 2154 pg/ml	64/123	-	0.11 (0.04 - 0.27)
				Estimated GFR at enrollme			1
Atrial fibrillation or flutter				< 60 ml/min/1.73 m² ≥ 60 ml/min/1.73 m²	91/175 67/131		0.12 (0.06 - 0.26)
No Yes	94/195 65/112		0.13 (0.07 - 0.27) 0.06 (0.02 - 0.18)	2 00 mg/mm/1.73 m-	07/131	•	1 0.08 (0.05 - 0.21) 1 1
History of ischemic event			1 1	Body-mass index at enroll	ment		1
No	58/125		0.13 (0.06 - 0.29)	< 30	104/202		0.11 (0.05 - 0.21)
Yes	101/182		0.10 (0.05 - 0.22)	≥ 30	55/105		0.10 (0.03 - 0.29)
	0.01	0.05 0.1 0.25 0.5 CRT-D upgrade better	I 1.5 2 →→ ICD upgrade better			0.01 0.05 0.1 0.25 0.5 ≪ CRT-D upgrade better	I.5 2 →→ ICD upgrade better

Echocardiographic Response and Adverse events



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Conclusions



- In patients with HFrEF and significant RV pacing burden with a wide, paced QRS complex, CRT-D upgrade compared to ICD only treatment reduced the composite primary outcome of HF hospitalisations, deaths, and absence of reverse remodelling.
- Fewer hospitalisations for HF or reduced all-cause mortality favoured CRT-D which was accompanied by improved LV reverse remodelling compared to ICD alone.
- Moreover, the incidence of VT/VF events were significantly lower in CRT-D patients compared to ICD alone.
- The CRT-D upgrade proved to be a safe procedure in this sick patient population in experienced, high-volume centres.
- Overall, HFrEF patients with a PM or ICD should be strictly followed in clinical practice and in those with intermittent or permanent RV pacing, a CRT upgrade should be performed immediately without postponing the procedure to a later date to avoid or reduce the risk of further adverse events such as mortality, heart failure hospitalisation or LV remodelling.

Principal Investigator & Co-Principal Investigators

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Thanks all the Investigators and Participants!

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