Longitudinal assessment of cardiac involvement in Erdheim-Chester disease using cardiac magnetic resonance imaging

Levi-Dan Azoulay, MD

Julien Haroche, MD, PhD

Sorbonne Université, Assistance Publique-Hôpitaux de Paris, Service de Médecine Interne 2, Centre National de Référence des Histiocytoses, Hôpital Pitié-Salpêtrière, 47-83 Boulevard de l'hôpital, 75013 Paris, France

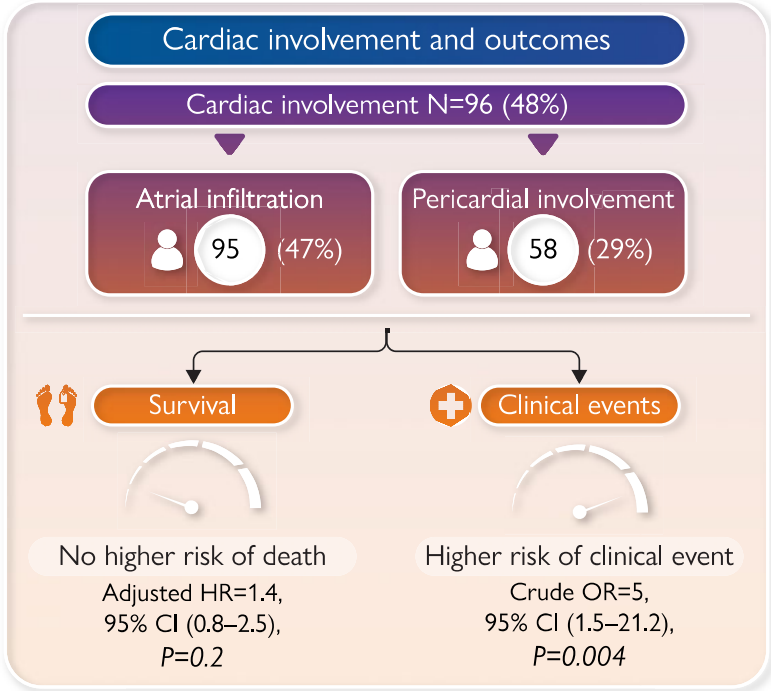
ASSISTANCE PUBLIQUE HÔPITAUX DE PARIS

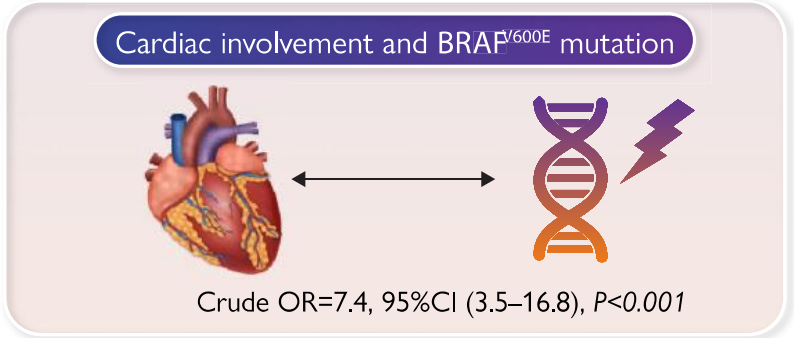
HÔPITAUX UNIVERSITAIRES PITIÉ SALPÊTRIÈRE

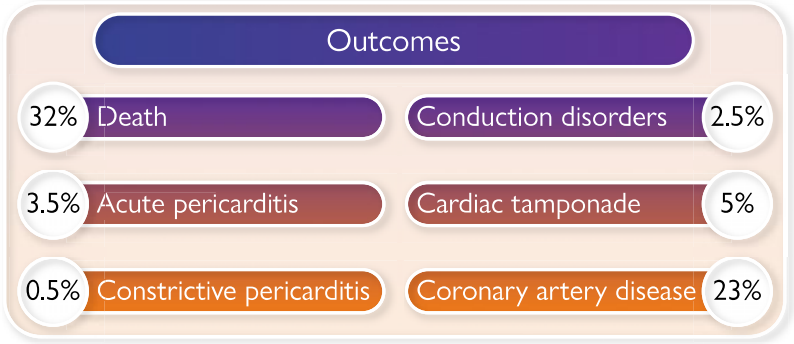
SORBONNE UNIVERSITÉ CRÉATEURS DE FUTURS DEPUIS 1257

Background

- Erdheim-Chester disease (ECD) is a rare multi-systemic histiocytosis that affects the heart in nearly **half of patients**[1].
- **Atrial infiltration** and **pericardial effusion** are the hallmarks of cardiac involvement and can lead to clinical complications (conduction disorders, coronary artery stenosis, tamponade, constrictive pericarditis)[2–4].
- Evolution under treatment is poorly studied.







1. Emile J-F, Cohen-Aubart F, Collin M, et al: Histiocytosis. *The Lancet*, 2021 Jul 10;398(10295):157-170. doi: 10.1016/S0140-6736(21)00311-1. Epub 2021 Apr 23.

2. Azoulay L-D, Bravetti M, Cohen-Aubart F, et al: Prevalence, patterns and outcomes of cardiac involvement in Erdheim–Chester disease. *Eur Heart J* ehac741, 2022

3. Morita S, Watanabe M, Morita S, et al: Dip and plateau pattern in a patient with Erdheim–Chester disease. *Eur Heart J - Cardiovasc Imaging* jeab083, 2021

4. Alharthi MS, Calleja A, Panse P, et al: Multimodality imaging showing complete cardiovascular involvement by Erdheim–Chester disease. *Eur Heart J - Cardiovasc Imaging* 11:E25–E25, 2010

Purpose

- To investigate the evolution of cardiac involvement in ECD using cardiac magnetic resonance (CMR) imaging.

Methods

Inclusion criteria:

- All ECD patients with a CMR imaging
- With a cardiac involvement
- Who underwent at least one follow-up CMR imaging between 2005 and 2020
- At a French tertiary center

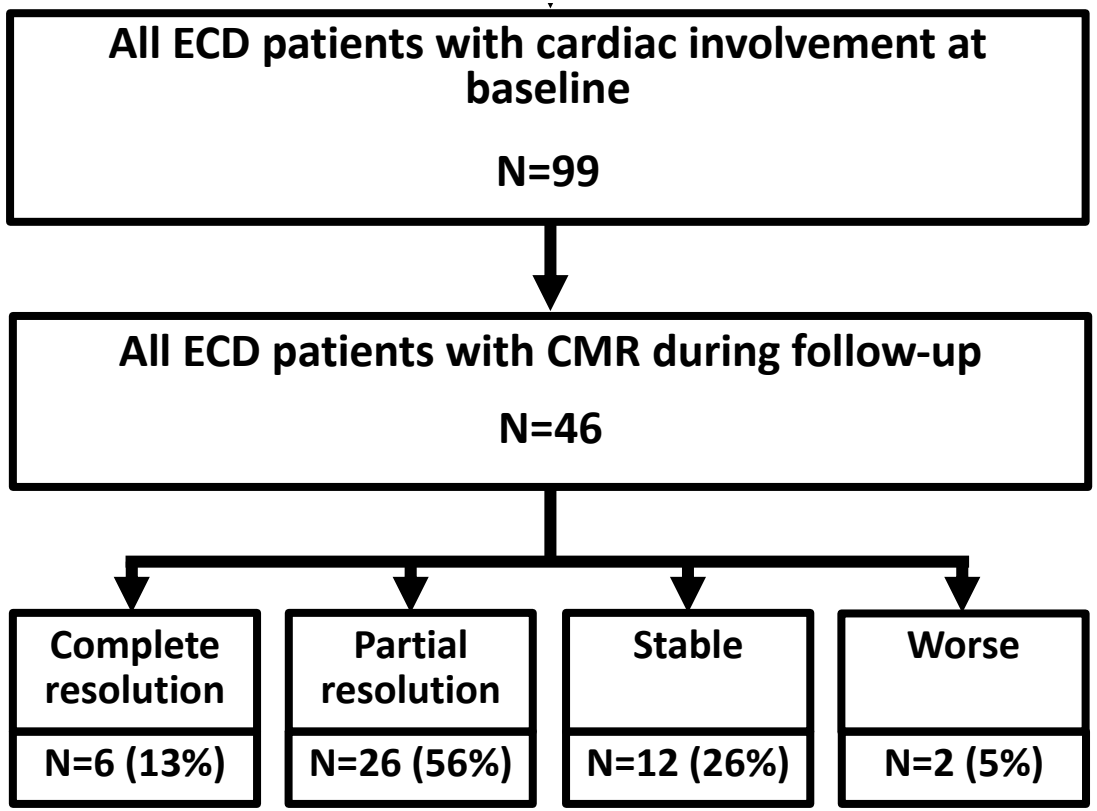
Data analysis:

- First and last CMR imaging were compared.
- Multivariable analysis was performed to search for independent predictors of cardiac involvement resolution. Variables were included in the model if their *P*-value was < 0.1 on univariable analysis.

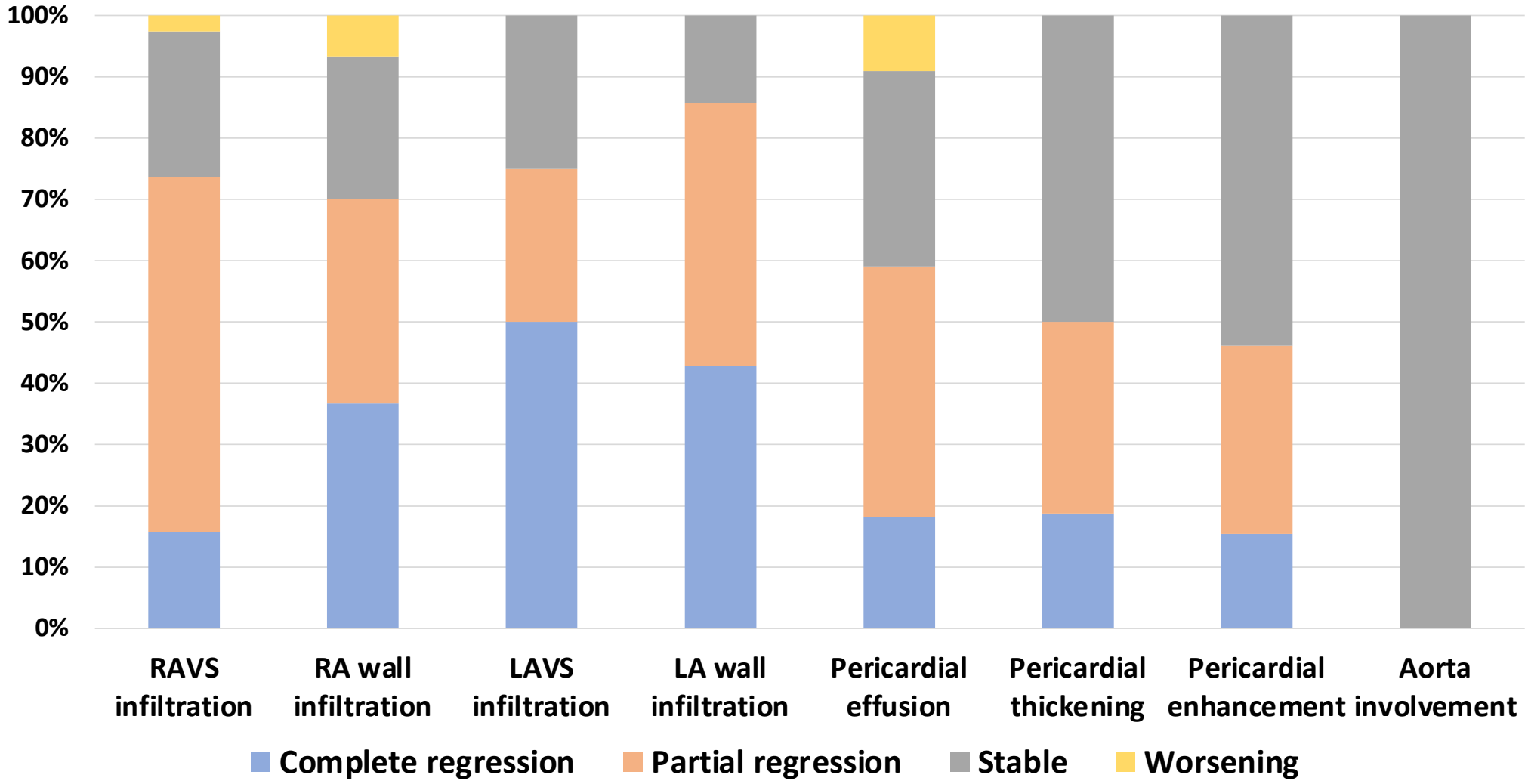
Results

- Overall, 46 patients were included.
- Median age at first imaging was 63 years [53-69].
- Median delay between the first and the last imaging was 4 years [2-7].
- *BRAF*^{V600E} mutation was present in 43 patients (94%).
- Patients received a median of 2 [1-3] treatments. All patients (100%) had cardiac involvement at baseline.

Results


All ECD patients with cardiac involvement at baseline
N=99
All ECD patients with CMR during follow-up
N=46
Complete resolution
N=6 (13%)
Partial resolution
N=26 (56%)
Stable
N=12 (26%)
Worse
N=2 (5%)

Results – Over 50% of complete or partial resolution



Results – Similar age and imaging delays

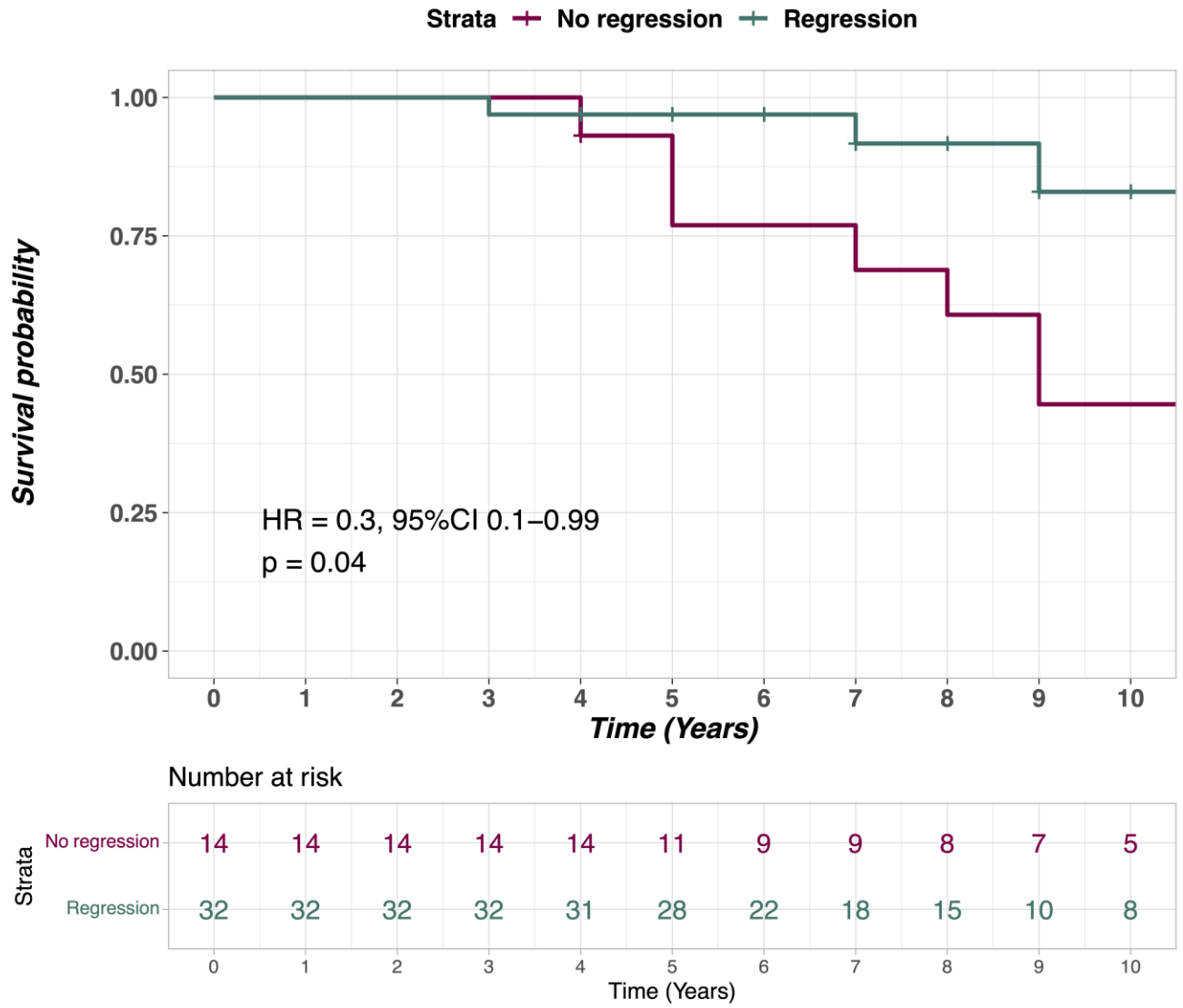
	Regression (partial or complete) N=32	No regression (stable or worsening) N=14	P-value
General features			
Median age at first symptom, y (IQR)	56 [46-63]	54 [44-68]	0.8
Median age at diagnosis, y (IQR)	60 [49-65]	61 [54-70]	0.5
Median age at first imaging, y (IQR)	62 [51-68]	65 [56-72]	0.3
Median age at last imaging, y (IQR)	67 [58-72]	68 [64-78]	0.3
Median delay between imaging, y (IQR)	5 [3-6]	3 [2-7]	0.5

Results – Uni and multivariable analysis

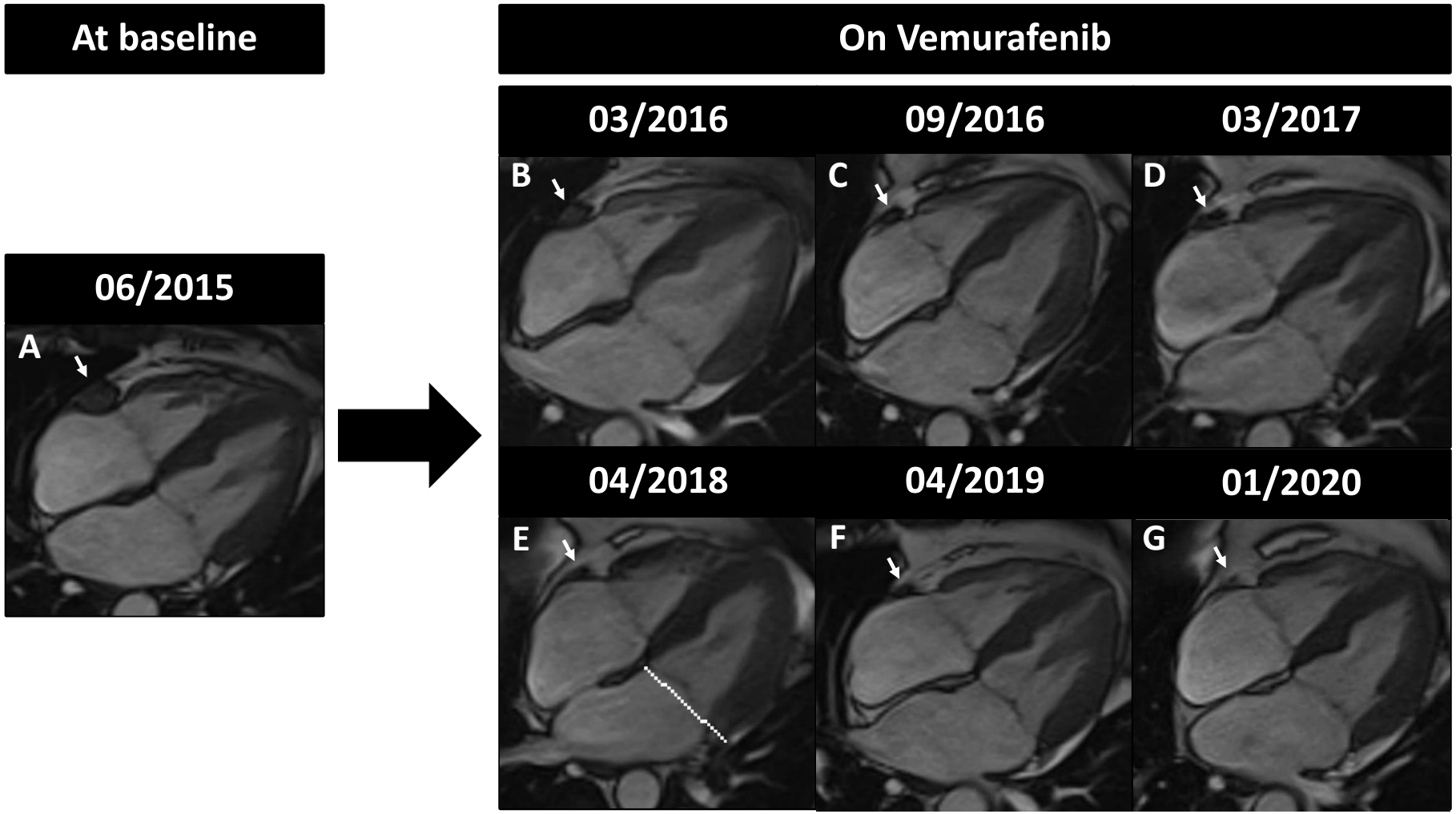
- **<u>On univariable analysis</u>**, patients with **regression** of their infiltration had a lower rate of **death** (16% versus 64%, *P*=0.002), a higher rate of atrial infiltration **late gadolinium enhancement** (LGE) (97% versus 71%, *P*=0.01), a higher rate of **hydronephrosis** (50% versus 14%, *P*=0.03) and a lower rate of **interferon** prescription (69% versus 100%, *P*=0.02). A similar rate of vemurafenib use was observed in both groups (69% versus 54%, *P*=0.3).

- **<u>On multivariable analysis</u>**, **death remained significantly associated with follow-up imaging status (ß=-2.3 *P*=0.01),** while atrial infiltration LGE (ß=2.7, *P*=0.06), hydronephrosis (ß=1.6, *P*=0.1) and treatment with interferon (ß=-16, *P*=1) were no longer significantly associated with imaging status.

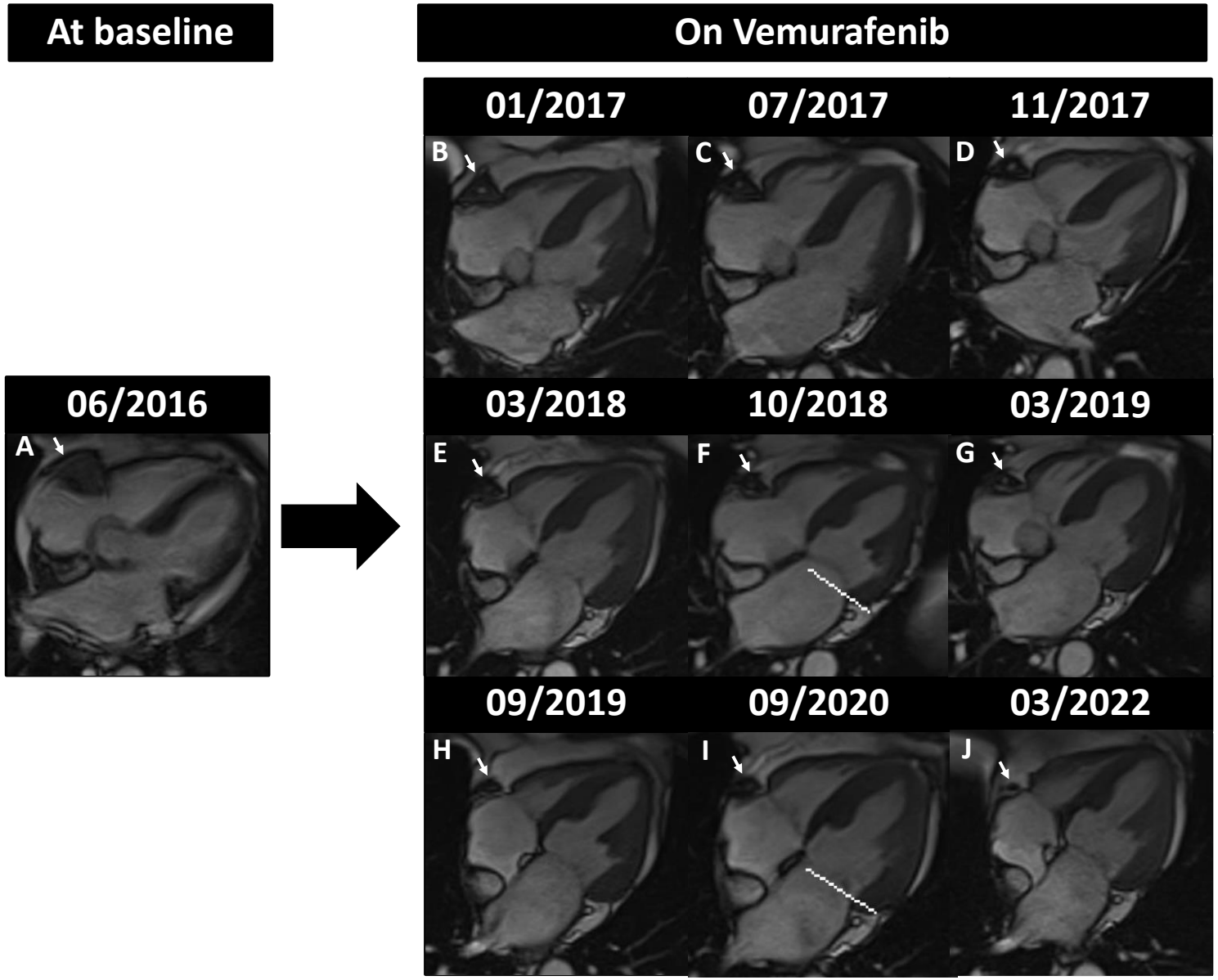
Results – Survival analysis



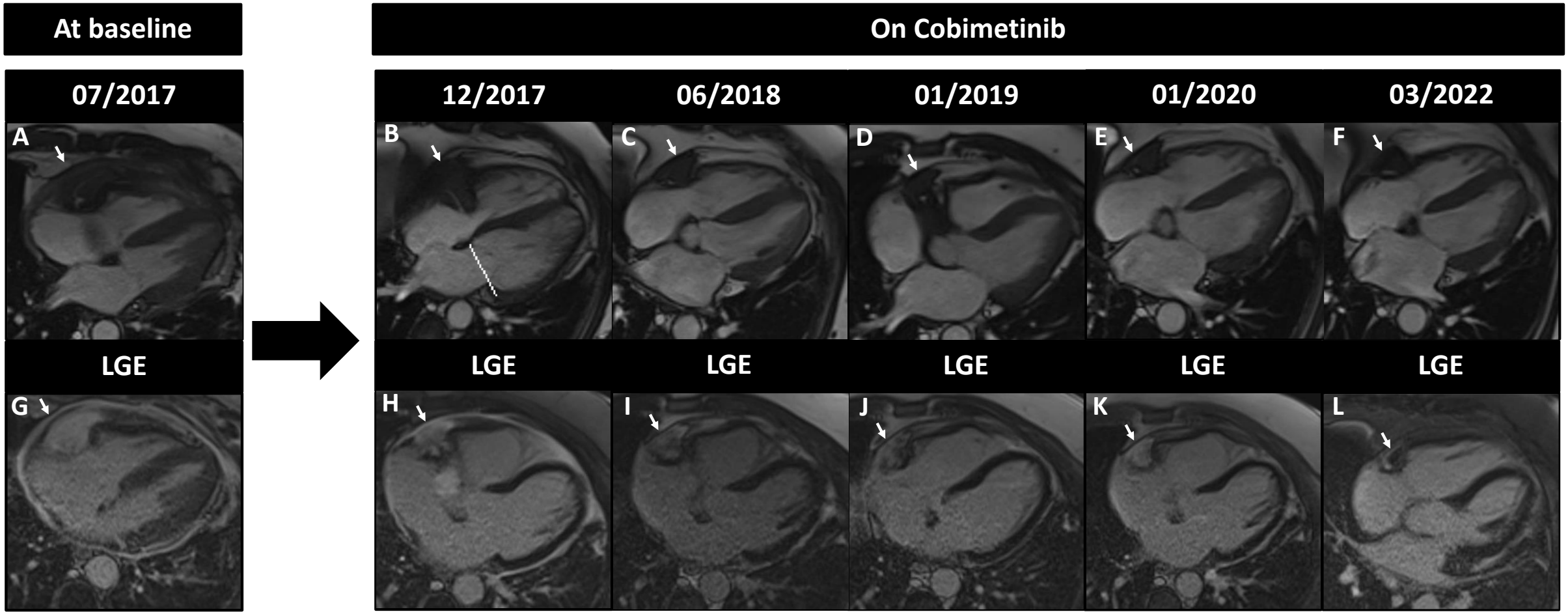
Results – Resolution takes time (few months or years)



Results


At baseline
On Vemurafenib
06/2016
A
01/2017
B
07/2017
C
11/2017
D
03/2018
E
10/2018
F
03/2019
G
09/2019
H
09/2020
I
03/2022
J

Results


At baseline
On Cobimetinib
07/2017
12/2017
06/2018
01/2019
01/2020
03/2022
A
B
C
D
E
F
LGE
LGE
LGE
LGE
LGE
LGE
G
H
I
J
K
L

Conclusion

Partial or complete resolution of cardiac involvement was observed in 69% of patients with ECD and was significantly associated with a lower rate of death on multivariable analysis.

Thank you

Lévi-Dan Azoulay,

Marine Bravetti,

Fleur Cohen-Aubart,

Zahir Amoura,

Philippe Cluzel

All the patients and the ECD Global Alliance