



# Long-term outcome and prognosis of 69 patients with mixed Erdheim-Chester disease and Langerhans Cell Histiocytosis

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# Disclosures

None



# Introduction and Background

## MYELOID NEOPLASIA

### Association of both Langerhans cell histiocytosis and Erdheim-Chester disease linked to the *BRAF*<sup>V600E</sup> mutation

Baptiste Hervier,<sup>1-3</sup> Julien Haroche,<sup>1-3</sup> Laurent Arnaud,<sup>1-3</sup> Frédéric Charlotte,<sup>2,4</sup> Jean Donadieu,<sup>5</sup> Antoine Néel,<sup>6</sup> François Lifermann,<sup>7</sup> Carles Villabona,<sup>8</sup> Bruno Graffin,<sup>9</sup> Olivier Hermine,<sup>10</sup> Aude Rigolet,<sup>1,2</sup> Camille Roubille,<sup>11</sup> Eric Hachulla,<sup>12</sup> Thierry Carmoi,<sup>13</sup> Maud Bézier,<sup>14</sup> Véronique Meignin,<sup>14</sup> Marie Conrad,<sup>15</sup> Laurence Marie,<sup>16</sup> Elise Kostrzewa,<sup>17</sup> Jean-Marie Michot,<sup>18</sup> Stéphane Barete,<sup>19</sup> Valerie Taly,<sup>20</sup> Karine Cury,<sup>19</sup> Jean-François Emile,<sup>21,22</sup> and Zahir Amoura,<sup>1-3</sup> on behalf of the French Histiocytoses Study Group

23 patients

Pre-targeted era



Hervier B, Blood 2014

9th Annual  
International Summit on  
Erdheim-Chester Disease

Fred Hutch  
Cancer Center



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# Methods

Retrospective analysis performed at two ECDGA referral centers

- Pitié-Salpêtrière Hospital, Paris (France)
- Meyer Children's Hospital, Florence (Italy)

Inclusion criteria:

- ECD diagnosed between 2000 and 2022 (consensus guidelines)
- Minimum follow-up 1 year

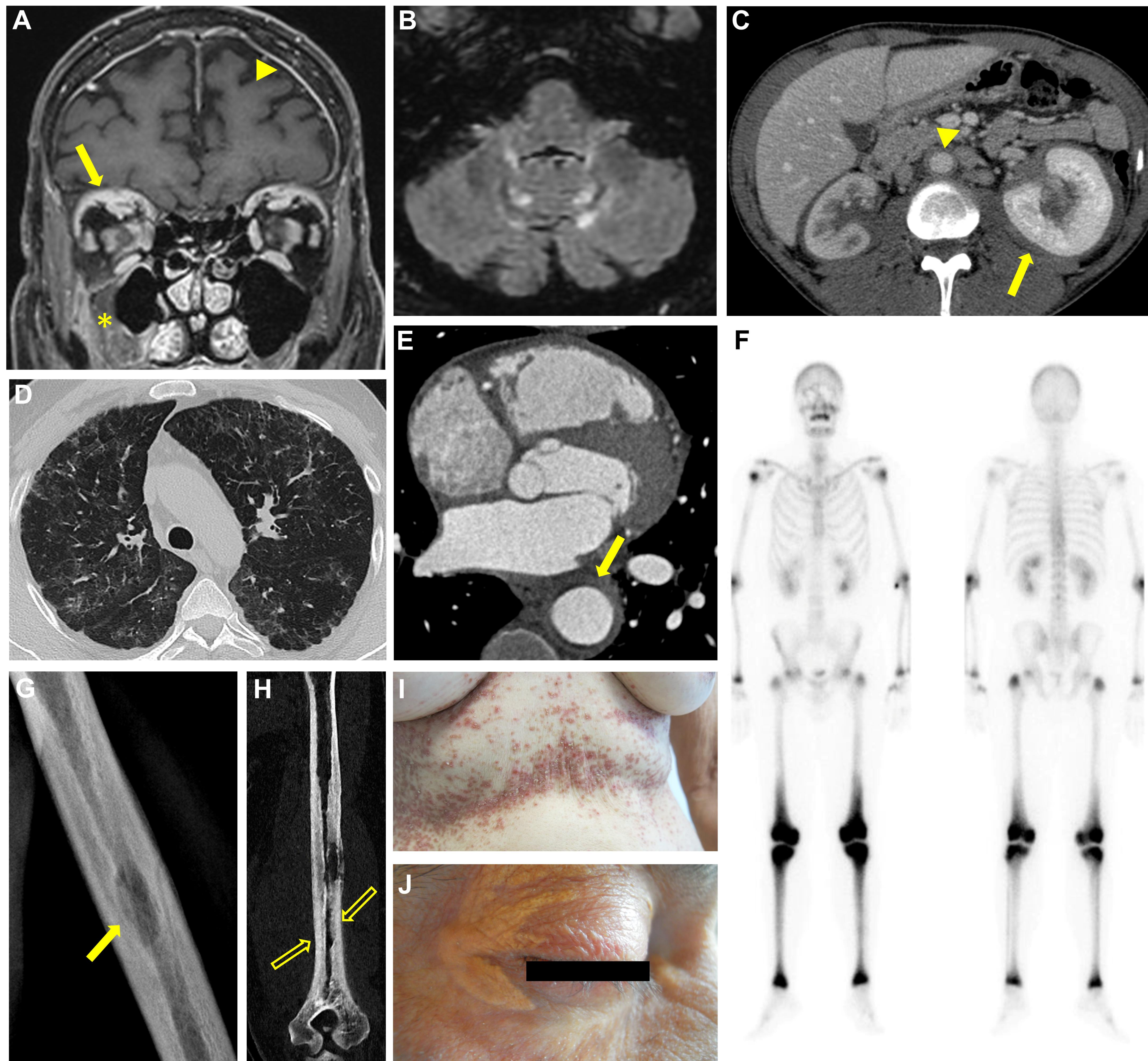
Patients selected based on associated LCH lesions (biopsy-proven)



# Results

502 ECD patients screened

69 patients (14%) with mixed ECD-

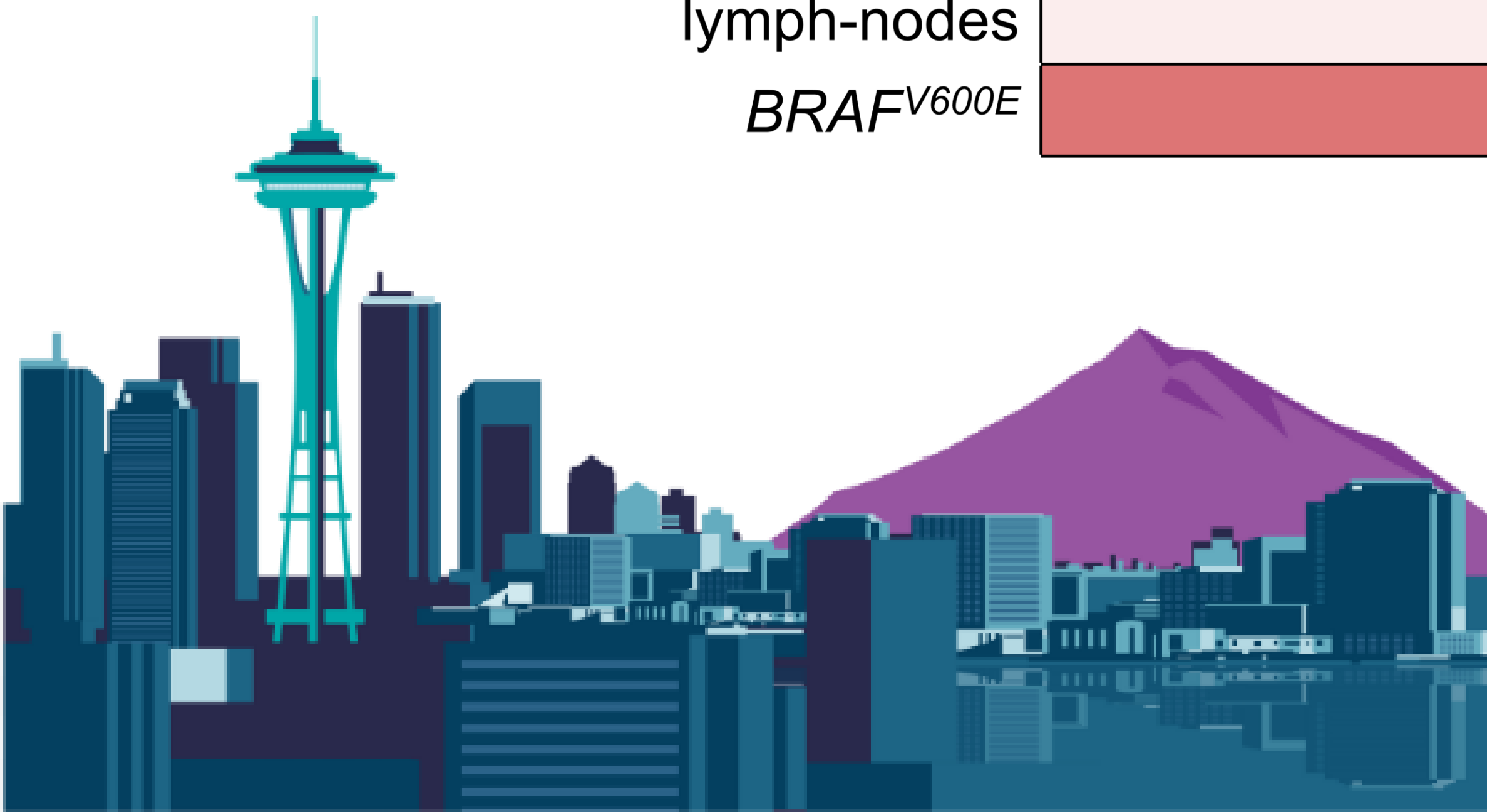


# Results

## Mixed ECD-LCH vs. isolated ECD

	ECD	ECD-LCH
male		
bone sclerotic		
bone lytic		
CNS		
facial/orbit		
heart		
peri-aortic		
lung		
peri-renal		
skin		
hypothalamic/pituitary		
lymph-nodes		
<i>BRAF</i> <sup>V600E</sup>		

	Mixed ECD-LCH	ECD alone (n=424)	p value
Age at ECD diagnosis (y)	55	60	0.040
Female	35 (51%)	109 (26%)	<0.001
Long bone	63 (91%)	334 (79%)	0.014
CNS	35 (51%)	144 (34%)	0.007
Neurodegeneration	21 (30%)	78 (18%)	0.021
Facial/orbit	36 (52%)	163 (38%)	0.031
Lung	30 (43%)	119 (28%)	0.009
Hypothalamic/Pituitary	35 (51%)	111 (26%)	<0.001
Skin	42 (61%)	123 (29%)	<0.001
Lymph nodes	10 (15%)	29 (7%)	0.028
≥4 involved sites	56 (81%)	275 (65%)	0.001
<i>BRAF</i> <sup>V600E</sup>	54/67 (81%)	227/387 (59%)	<0.001



# Results

## Treatment

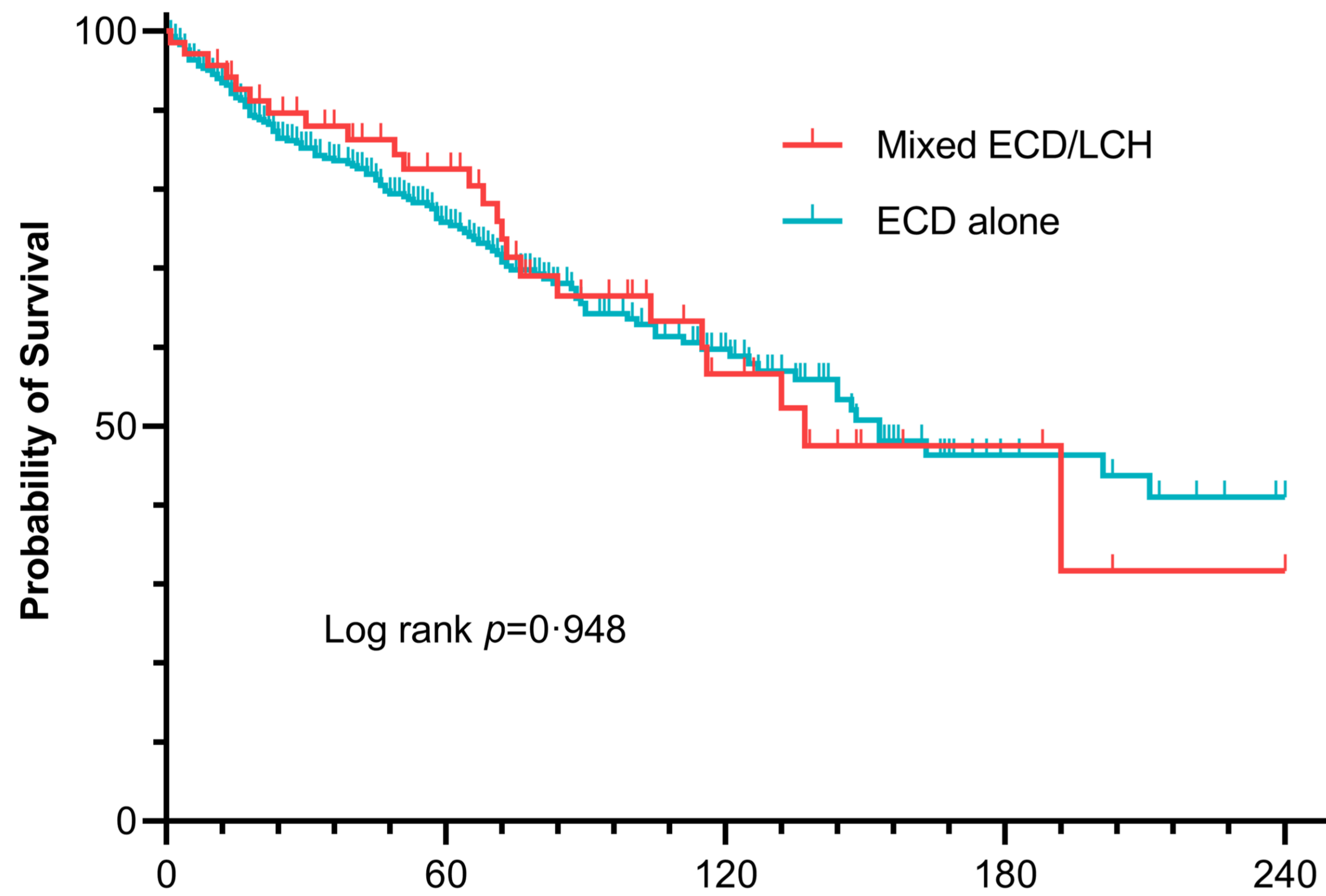
- First line: targeted (n=22, 33%); IFNa (n=25, 37%), CT (n=17, 25%)
- Best objective responses with targeted treatments
  - Targeted vs. conventional (first line): 77 vs. 29%,  $p < 0.001$
  - Targeted vs. conventional (any line): 75 vs. 24%,  $p < 0.001$
- Univariable predictors of treatment failure (negative association)
  - Sclerotic bone lesions
  - *BRAF*<sup>V600E</sup>
  - Targeted treatments



# Results

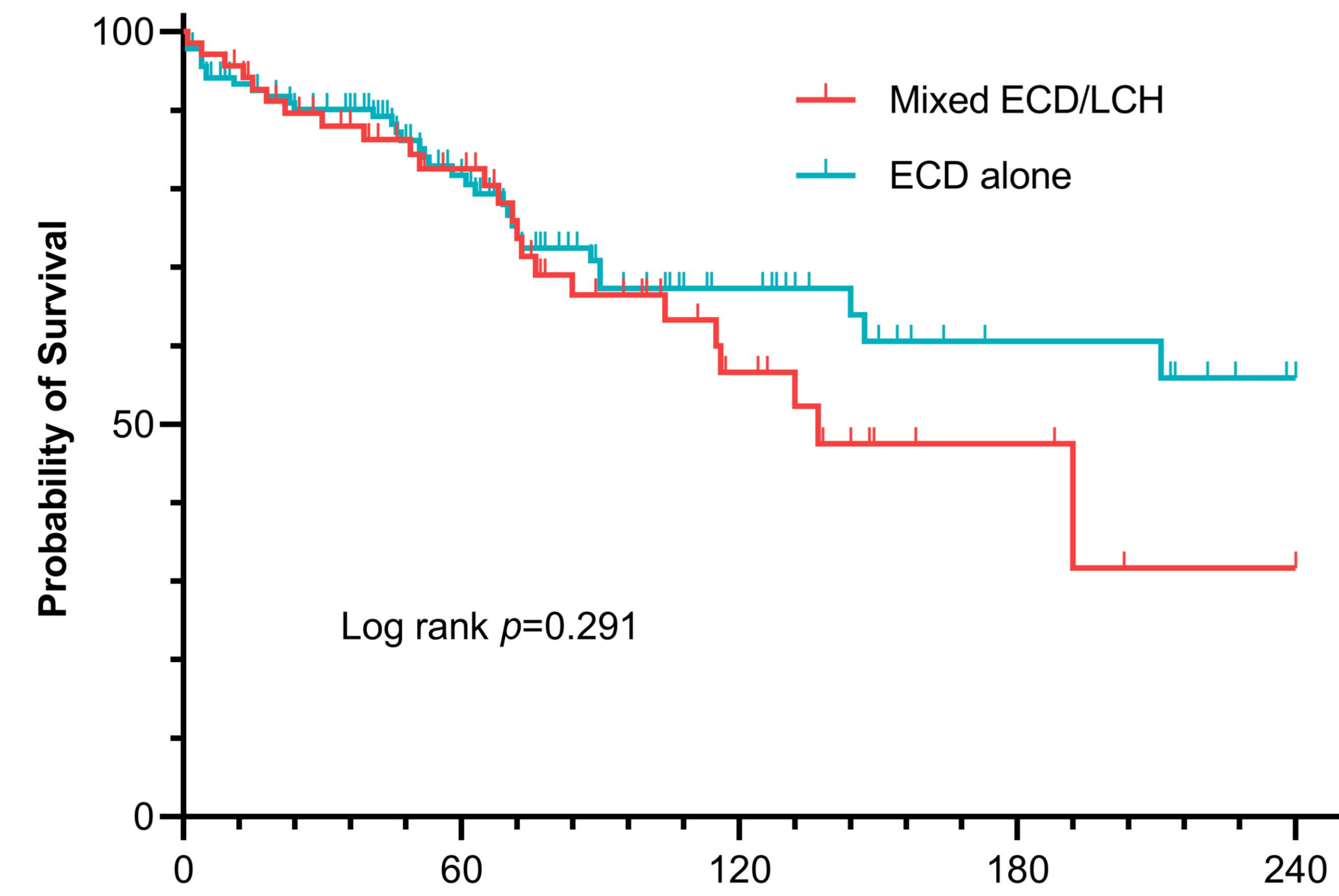
Survival 65% (median follow-up of 71 months)

**A** All patients



	Months of follow-up				
Number at risk	0	60	120	180	240
Mixed ECD/LCH	69	42	16	5	1
ECD alone	424	177	70	20	11

**B** Age- and gender-matched cohorts



	Months of follow-up				
Number at risk	0	60	120	180	240
Mixed ECD/LCH	69	42	16	5	1
ECD alone	138	70	29	14	7

No differences if compared to isolated ECD

- Age and gender correction (Cox regression)
- Age and gender matched cohort (n=138)



# Results

## Predictors of survival (multivariable analysis)

- Age at diagnosis: **HR 1.052** (95%CI 1.008-1.096)
- Lytic bone lesions: **HR 0.116** (95%CI 0.031-0.432)
- Associated hematologic neoplasms: **HR 3.030** (95%CI 1.040-8.827)
- Treatment failure: **HR 9.736** (95%CI 2.919-32.481)



# Conclusions

- Compared to ECD alone, mixed ECD-LCH is more frequently a **multisystem disease**
  - long bone, **CNS**, facial/orbit, **lung**, **skin**, and hypothalamic/pituitary involvement
- Mixed ECD-LCH is driven in most cases by the ***BRAF*<sup>V600E</sup>** mutation
- Patients are sensitive to **targeted treatments**
- Clinical features (type of bone involvement, associated neoplasms, age, response to treatment) are the main **predictors of outcome**



# For Additional Information

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**9th Annual  
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