# Efficacy of Cladribine in the Treatment of Erdheim-Chester Disease

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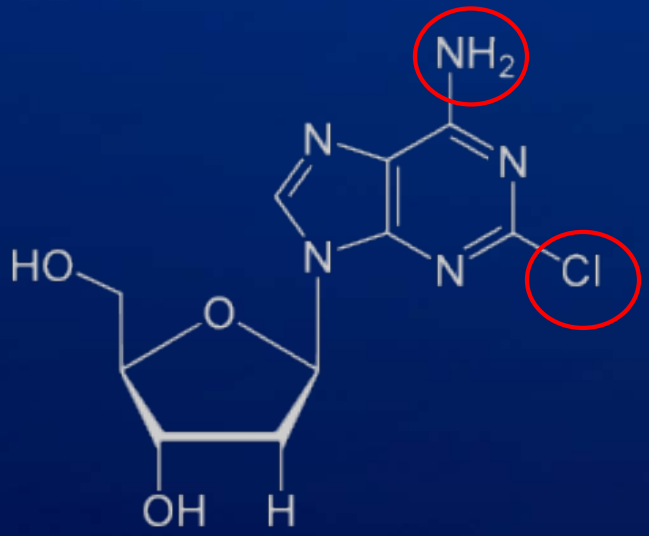
# Cladribine: Activity and Approval

- Synonyms
  - CdA, 2-CdA
  - 2-chloro-2'-deoxyadenosine
- Classification
  - Anti-metabolite
- Indication in US
  - Hairy cell leukemia

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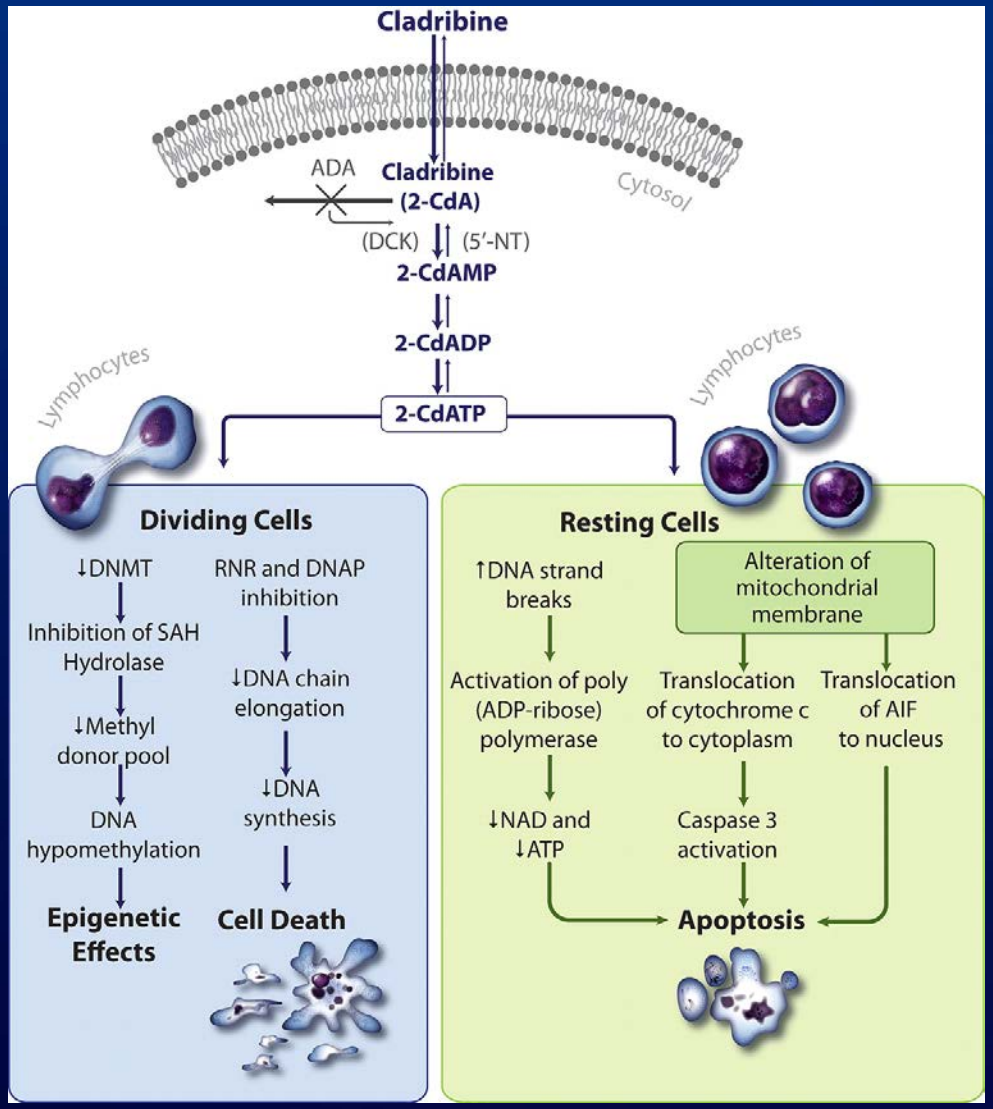
Sigal DS, et al. Blood. 2010 Oct 21;116(16):2884-96

# Cladribine: Mechanism of Action

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# Cladribine: Activity in Other Cancers

- Chronic lymphocytic leukemia
- Lymphoplasmacytic lymphoma
- Marginal zone lymphoma
- Mantle cell lymphoma
- Acute myelogenous leukemia
- Langerhans cell histiocytosis
  - 0.14 mg/kg/day x 5 days, Q4 weeks, up to 6 cycles
  - Response rate ~75%
  - Median response duration: 33 months (range, 1-65)

**Sigal DS, et al. Blood 2010;116:2884-2896.**
**Saven A, et a. Blood 1999;93:4125-4130.**

# Cladribine: Activity in Erdheim-Chester Disease (ECD)

- Limited to case reports with variable activity (N=17)
- Responded: 10 (60%)
- No response: 5
- Response not reported: 2

**Sheidow TG, 2000; Myra C, 2004; Aouba A, 2009; Alharti MS, 2010; Adam Z, 2011; Munoz J, 2014; Adam Z, 2014; Ho P, 2014; Mazor RD, 2014; Blomstrand L, 2016; Peric P, 2016; Azadeh N, 2016.**

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# Objective

- To retrospectively assess the efficacy of cladribine in ECD at our institution

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# Eligibility Criteria

- Seen at Mayo Clinic
- ECD patients - January 1998 to April 2016
- Diagnosis of ECD - histopathologic and clinical findings
- All biopsies reviewed at Mayo Clinic
- Received cladribine (at Mayo or in community)
  - 0.14 mg/kg days 1-5,  Q28 days x 4-6 cycles, or
  - 5 mg/m2 days 1-5,  Q28 days x 4-6 cycles

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# Response Criteria

- No uniform post-therapy assessment performed

| Clinical response criteria | |
|---|---|
| Complete response (CR) | Complete resolution of symptoms ≥3 months |
| Partial response (PR) | Incomplete resolution of symptoms ≥3 months |
| Stable disease (SD) | No change in symptoms ≥3 months |
| Progressive disease (PD) | Worsening of symptoms |
| **Radiological response criteria** | |
| Complete response (CR) | Complete resolution of proven or suspected lesions |
| Partial response (PR) | Incomplete resolution of proven or suspected lesions |
| Stable disease (SD) | No significant change in proven or suspected lesions |
| Progressive disease (PD) | Progression/worsening of proven or suspected lesion |

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# Patient Characteristics

| | |
|---|---|
| Total ECD patients (1998-2016) | 63 |
| Median age at diagnosis | 54 years (range, 18-80) |
| BRAF V600E tested | 23 (36%) |
| Positive | 12 (52%) |
| Patients treated with cladribine | 21 (33%) |
| Male to female ratio | 14:7 |
| Median age at time of treatment | 62 years (range, 40-78) |
| First line | 9 |
| Later line | 12 |
| Median # of cycles of cladribine | 2.5 (range 1-6) |
| Cladribine between 1998-2006 | 8 (38%) |
| Cladribine between 2007-2016 | 13 (62%) |

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# Results

| Clinical Responses* | |
|---|---|
| CR | 6% |
| PR | 46% |
| SD | 18% |
| PD | 30% |
| **Radiological Responses**** | |
| CR | 0% |
| PR | 54% |
| SD | 26% |
| PD | 20% |

*4 patients not evaluable; median duration of clinical response = 9 months (range 6+ to 129+)

**6 patients not evaluable

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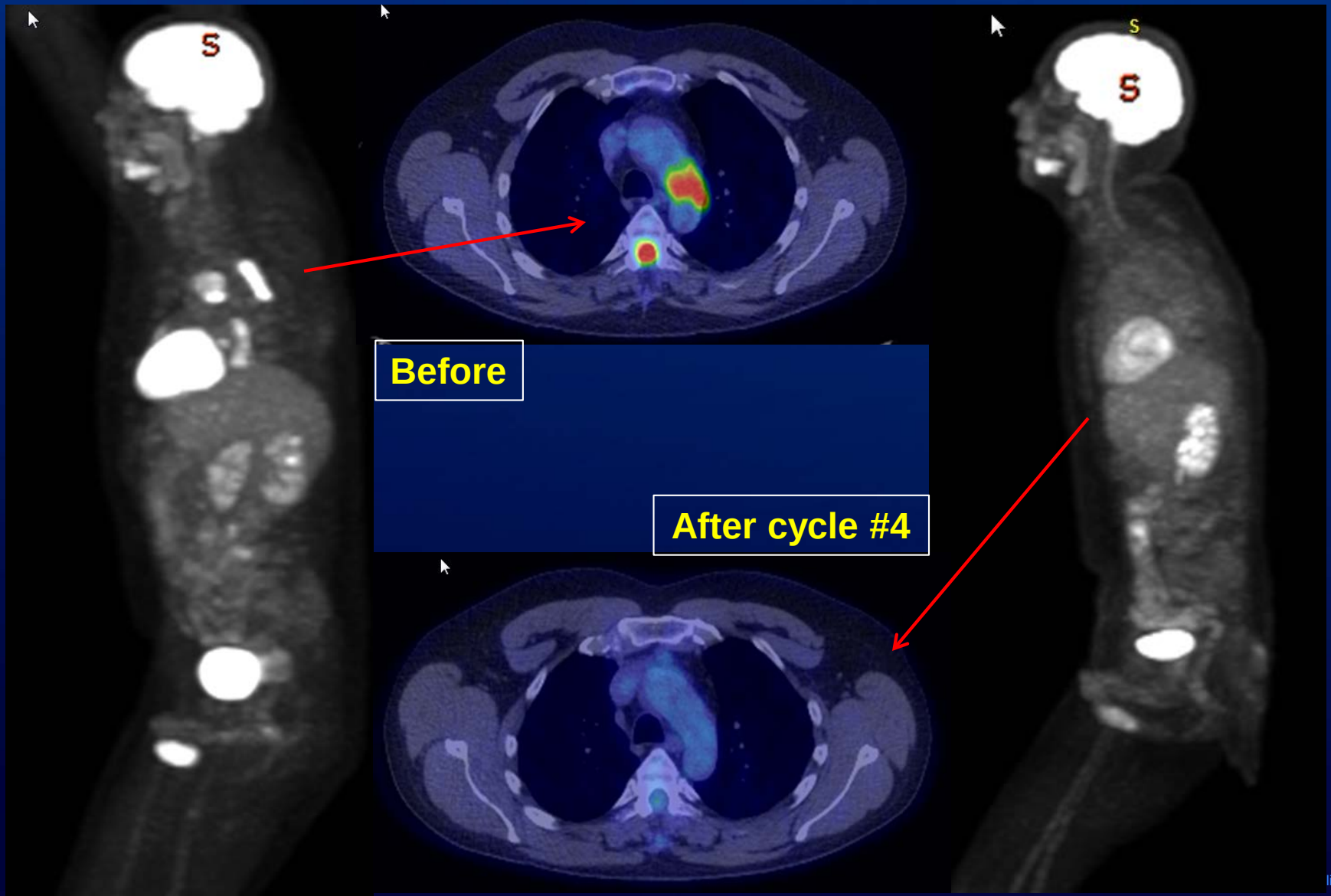
# 45-Year old male w/ T3-4, aortic, and testicular involvement; *BRAFV600E (-)*

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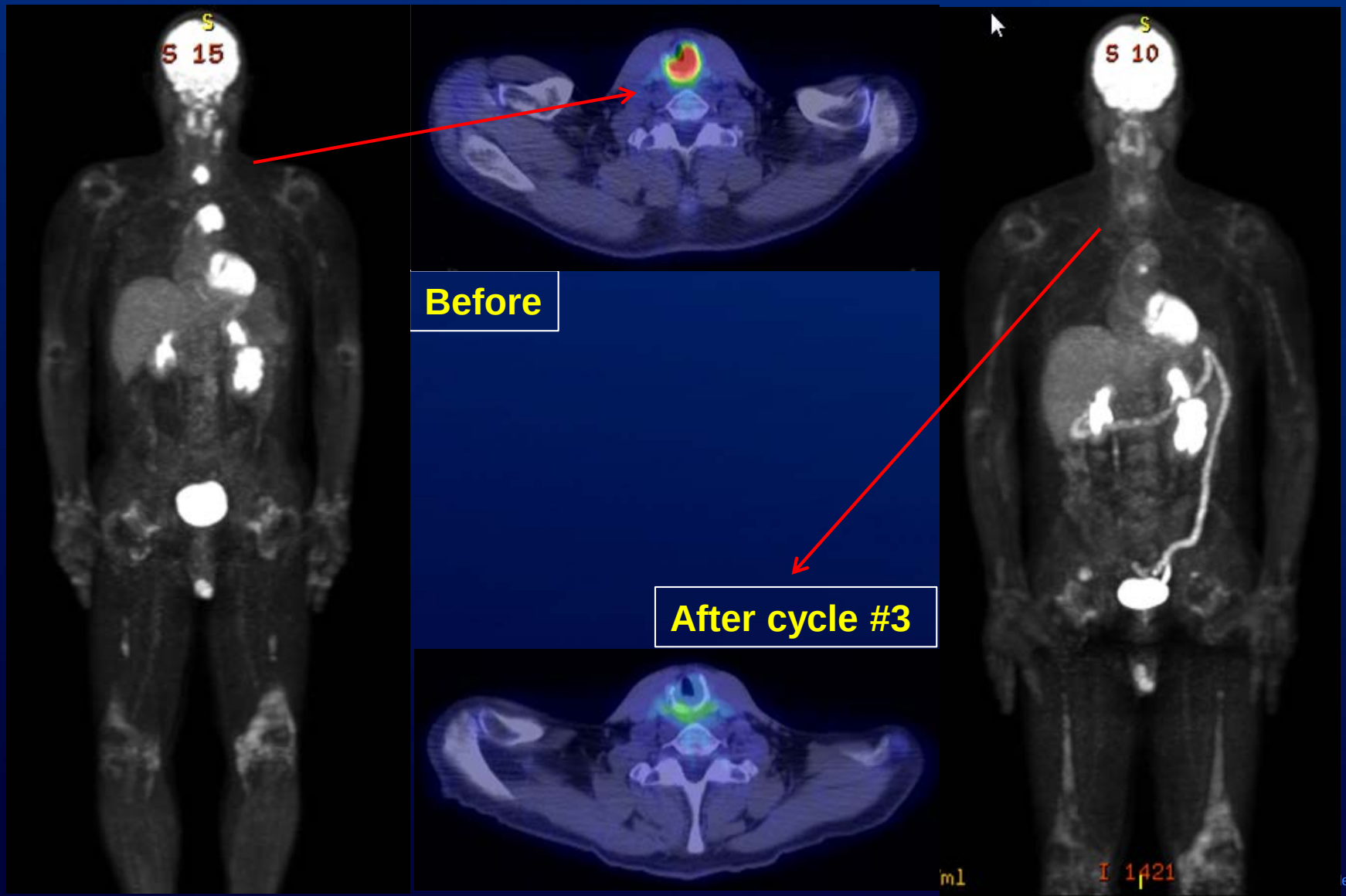
# 40-Year old male w/ orbital, sinus, tracheal, aortic, and splenic involvement; *MAP2K1 (+)*

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# Grade 3 Toxicities

- Infections (n=2)
  - Pneumonia
  - Central line infection
- Hematologic (n=2)
  - Neutropenia alone
  - Neutropenia and thrombocytopenia

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# Study Limitations

- Retrospective
- Spanned 18 years
- Response assessment not uniform and not always available

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# Conclusions

- Cladribine has moderate clinical activity in ECD
- It is generally well tolerated and may result in durable responses

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