

Don't Dish Out Old Therapies: Use of Pegylated-Interferon Alpha in a case of Erdheim-Chester Disease with congestive heart failure

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Disclosures

No financial disclosures to report

Background

PRINCIPLES OF SYSTEMIC THERAPY ^b

Erdheim-Chester Disease

- Regimens may be used in the first- or subsequent-line setting

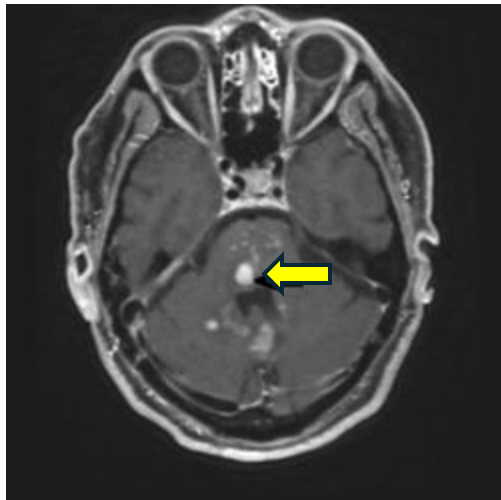
Preferred Regimens	Other Recommended Regimens
<p><u>BRAF V600E mutated disease</u></p> <ul style="list-style-type: none"> • Vemurafenib^{a,1,30} <p><u>MAP kinase pathway mutation, or no other detectable/actionable mutation, or testing not available</u></p> <ul style="list-style-type: none"> • Cobimetinib^{a,31} 	<p><u>BRAF V600E mutated disease</u></p> <ul style="list-style-type: none"> • Dabrafenib^{a,31,32} <p><u>MAP kinase pathway mutation, or no other detectable/actionable mutation, or testing not available</u></p> <ul style="list-style-type: none"> • Trametinib^{a,14,33} <p><u>Irrespective of mutation</u></p> <ul style="list-style-type: none"> • Cladribine³⁴ • Pegylated interferon alpha-2a and alpha-2b^{e,35} • Sirolimus + prednisone³⁶ • Methotrexate (oral)³⁷ • Anakinra^{a,38,39}

NCCN Guidelines Version 3.2024 Histiocytic Neoplasms
Goyal G, et al. *Blood*. 2020;135(22):1929-1945.

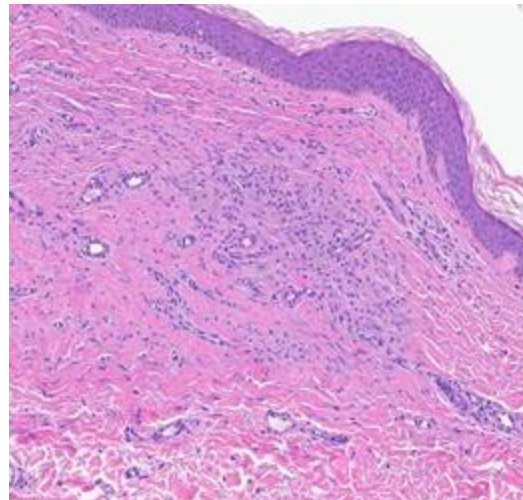
Case Presentation

Introduction

- 55 y/o Caucasian male
- Pmhx: colon cancer
- Dysarthria, ataxia
- Previous dx of multiple sclerosis (MS)
- Started on MEK inhibitor



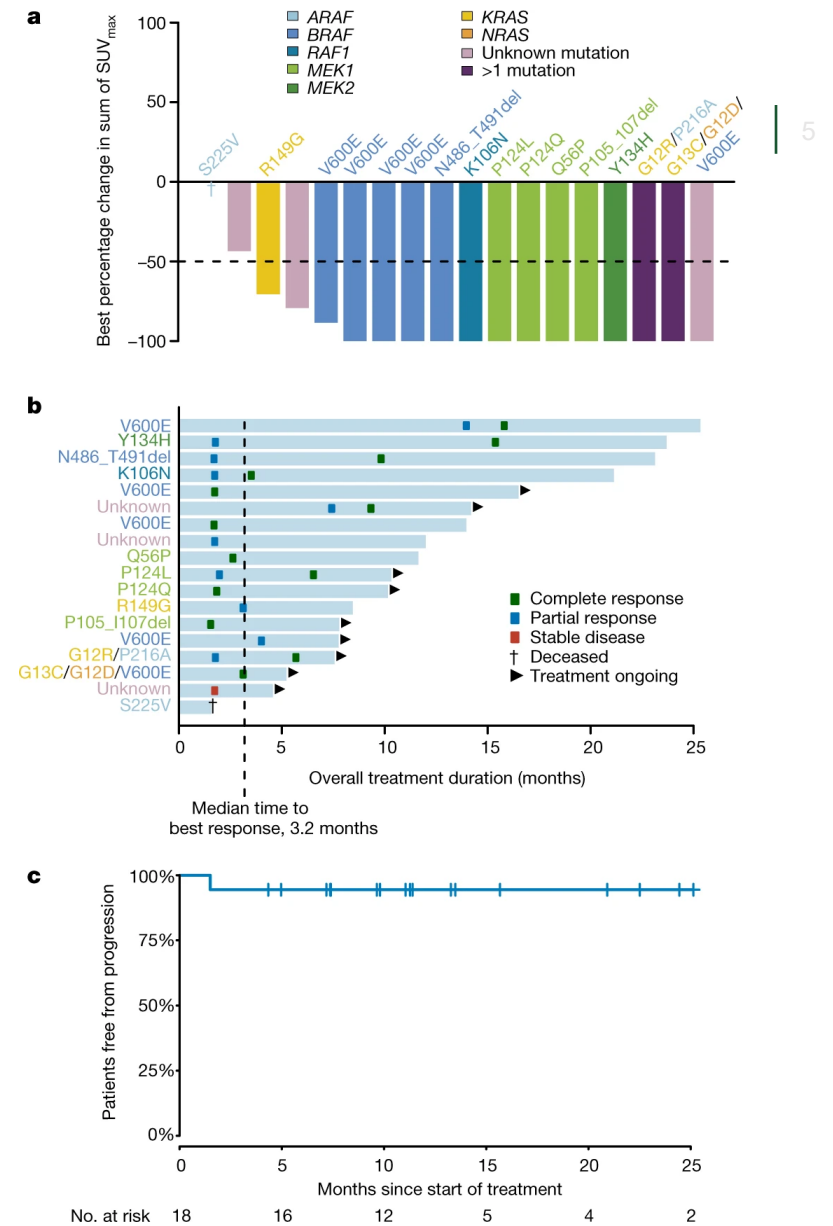
At diagnosis



Biopsy of skin lesion

MEK Inhibitors

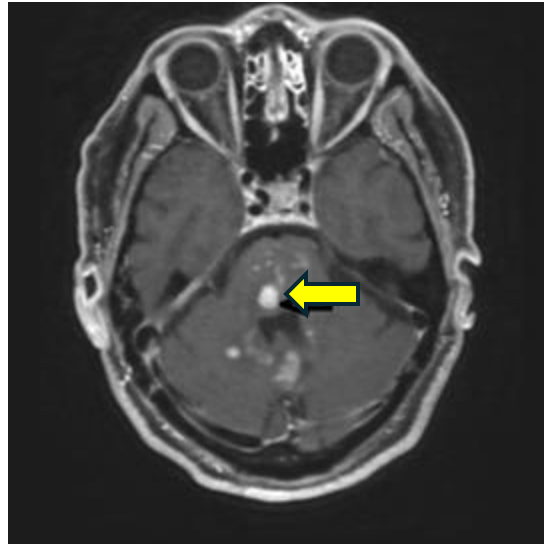
- Phase 2 trial (n=18) showing MEK inhibitors efficacy
- Overall response rate of 89%
- Dose reduction in 56%
- AEs leading to dose reduction : decreased ejection fraction (27.8%), rash (11.1%), diarrhea (11.1%), and fatigue & thrombocytopenia (5.6%)



Diamond EL et al. Nature. 2019 Mar ; 567 (7749): 521-524

Case Presentation

Introduction



At diagnosis



3 months on MEKi

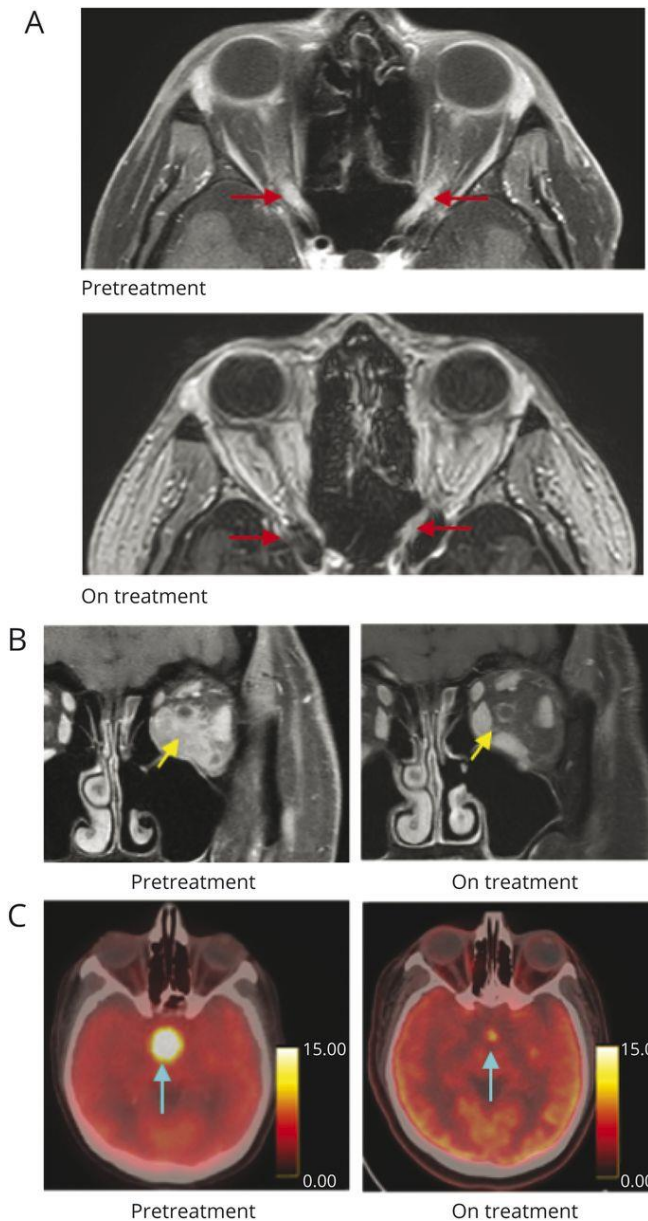
First & Second Line Treatment

- Cobimetinib → Trametinib
- Partial response
- AE: dyspnea, edema
- Decreased LVEF (25%), LBBB
- Discontinued 5 months after treatment start
- Next treatment: IA Melphalan

Intraarterial Melphalan

- 3 patients with neurologic non-Langerhans Cell Histiocytosis
 - No reported procedural AEs
 - Marked radiographic and clinical improvement

- 17 patients: 12 with tumorous disease and 5 with neurologic involvement
 - 75% response rate in 9/12 patients
 - No reported procedural AEs
 - 1 case each of neutropenia and melphalan hypersensitivity



Francis JH, et al. *Neurology*. 2021;96(23):1091-1093
Diamond E, et. al. *Neuro-Oncology*. 2023. 25. v166-v166

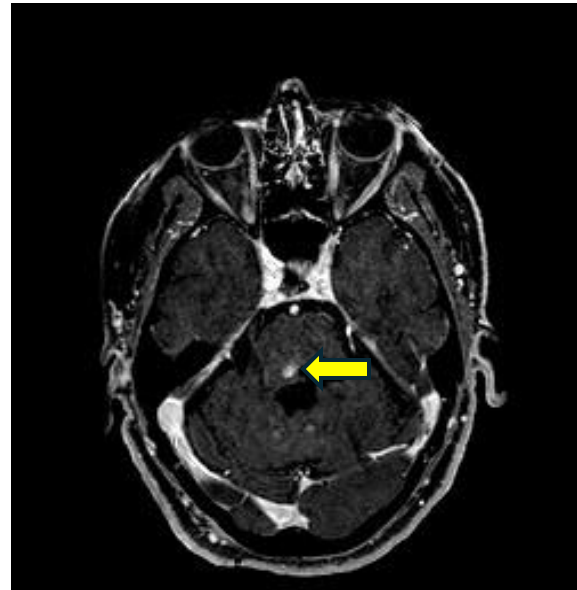
Case Presentation

Introduction

Third Line Treatment

- Intraarterial Melphalan
- AE: grade 3 vision loss
- Discontinued after single dose
- 2 months later, progressive disease on MRI
- Next treatment: subcutaneous Pegylated Interferon Alpha

First Line & Second Line Treatment



3 months on MEKi



2 months after IA Melphalan

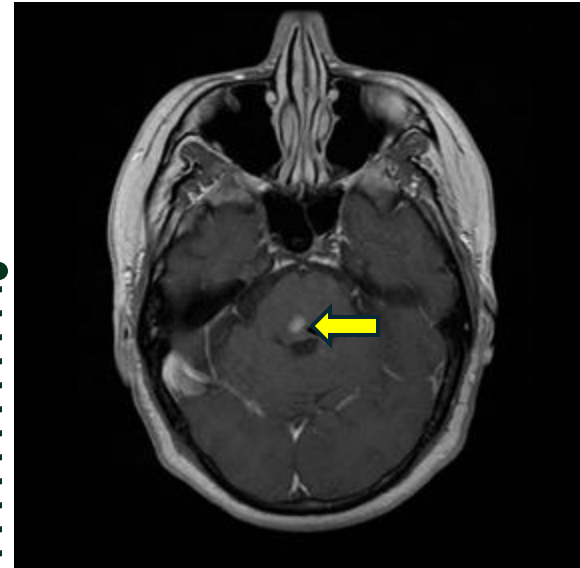
Interferon Alpha

Authors	Year of Publication	Type of Interferon used	Number of patients	Response Rates (%)	Progression Free Survival (%)	Patients with CNS involvement % (n)	CNS Involvement Response
Hervier B, et al.	2012	Interferon Alpha (58.3%) and Pegylated Interferon Alpha (41.7%)	24	67%	N/A	45.8% (11)	Improvement: 37% (n=4) Stabilization: 64% (n=7)
Cao XX, et al	2019	Interferon Alpha	32	80%	64.1%	34.4% (11)	Lower PFS and OS.

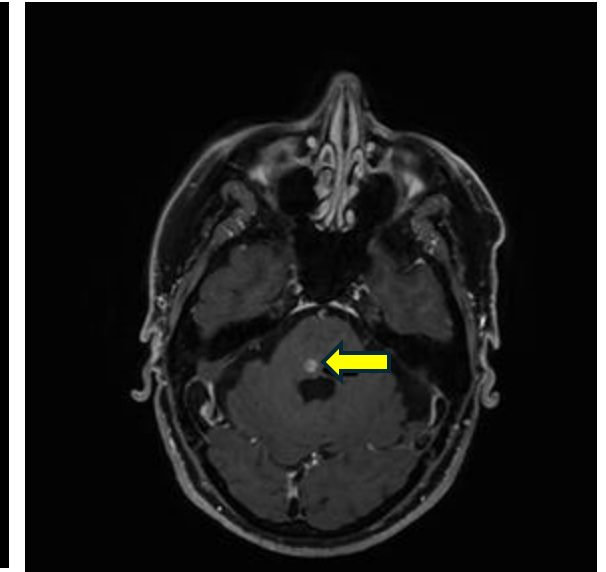
Case Presentation

Introduction

Third Line Treatment



2 months after IA
Melphalan



5 months on
Pegasys

First Line &
Second Line
Treatment

Fourth & Current Treatment Line

- Subcutaneous Pegylated Interferon Alpha (Pegasys)
- At 5 months persistent partial response
- Improvements in speech, balance, and mood
- AE: none

Overview of Treatment Costs

Treatment	Estimated monthly supply cost (\$USD)
Cobimetinib (40mg)	\$9,318
Trametinib (1mg)	\$10,248.75
Subcutaneous Pegylated Interferon Alpha (180 mcg/mL)	\$5,344.44
IV Cladribine (10mg/10mL)	\$210-\$260

<https://www.uptodate.com/contents/table-of-contents/drug-information>

Important Considerations & Conclusion:

- Thorough clinical evaluation when suspecting histiocytic neoplasm
- Novel therapies are not without side effects and pose substantial financial costs
- When novel treatments are contraindicated with side effects or inaccessible, interferon alpha and pegylated forms are still relevant treatments

Acknowledgements

- Patients/Families
- Dr. Gaurav Goyal
- UAB Histo Lab
 - Caroline Cannon
 - Elise Fitzgerald
 - Victoria Fennell
 - Vyshnavi Rallapalle
 - Tanvi Bhadkamkar
 - Lindsey Hageman