



**2019 Patient Family Gathering
Milan, Italy
July 12, 2019**

THE UNIVERSITY OF TEXAS
MD Anderson
~~Cancer Center~~
Making Cancer History®

Clinical Trials in Erdheim-Chester Disease

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Why Do We Need Clinical Trials?

- Clinical trials answer important questions
 - Does the new treatment work?
 - Is the new treatment safe?
 - Can the new treatment be used as standard in clinical practice?

ORIGINAL ARTICLE

Vemurafenib in Multiple Nonmelanoma Cancers with *BRAF* V600 Mutations

David M. Hyman, M.D., Igor Puzanov, M.D., Vivek Subbiah, M.D., Jason E. Faris, M.D., Ian Chau, M.D., Jean-Yves Blay, M.D., Ph.D., Jürgen Wolf, M.D., Ph.D., Noopur S. Raje, M.D., Eli L. Diamond, M.D., Antoine Hollebecque, M.D., Radj Gervais, M.D., Maria Elena Elez-Fernandez, M.D., Antoine Italiano, M.D., Ph.D., Ralf-Dieter Hofheinz, M.D., Manuel Hidalgo, M.D., Ph.D., Emily Chan, M.D., Ph.D., Martin Schuler, M.D., Susan Frances Lasserre, M.Sc., Martina Makrutzki, M.D., Florin Sirzen, M.D., Ph.D., Maria Luisa Veronese, M.D., Josep Tabernero, M.D., Ph.D., and José Baselga, M.D., Ph.D.

JAMA Oncology | Brief Report

Vemurafenib for *BRAF* V600-Mutant Erdheim-Chester Disease and Langerhans Cell Histiocytosis
Analysis of Data From the Histology-Independent, Phase 2, Open-label VE-BASKET Study

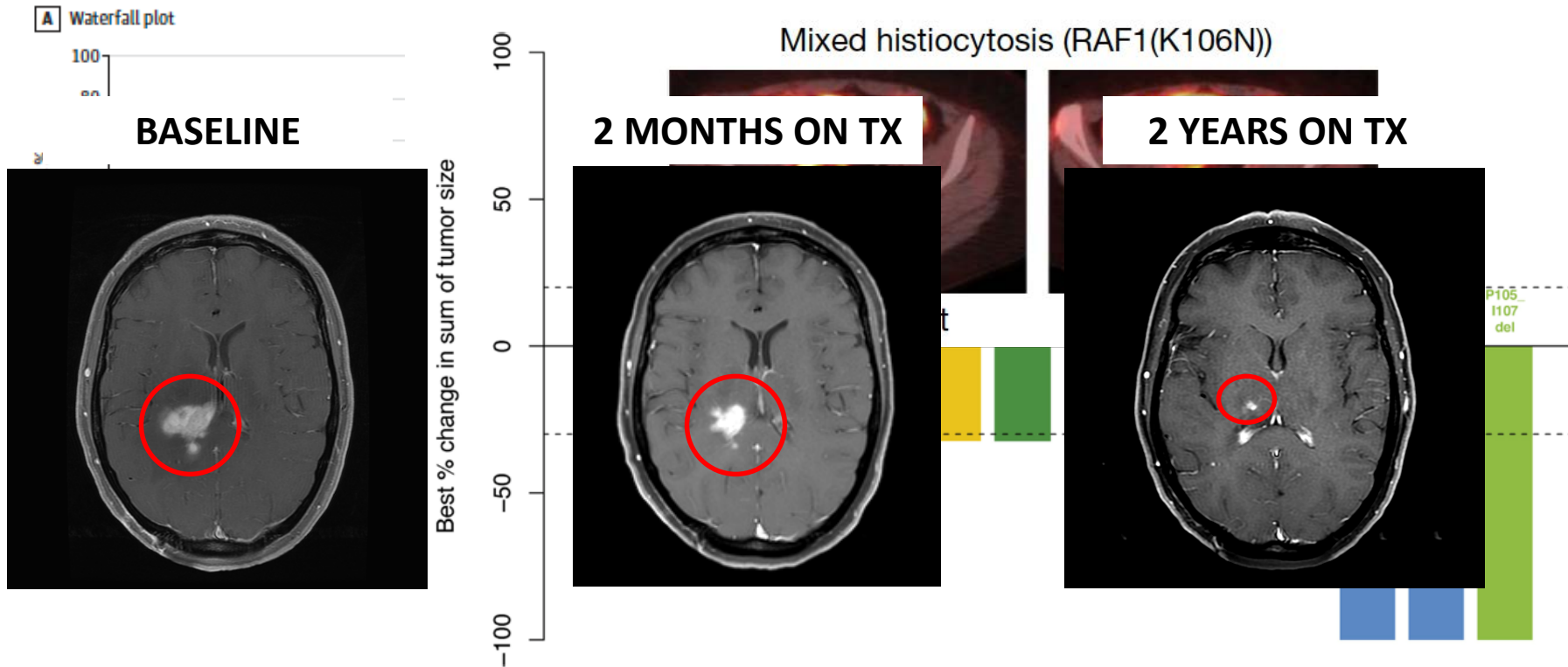
Eli L. Diamond, MD; Vivek Subbiah, MD; A. Craig Lockhart, MD; Jean-Yves Blay, Prof; Igor Puzanov, MD; Ian Chau, MD; Noopur S. Raje, MD; Jürgen Wolf, Prof Dr; Joseph P. Erinjeri, MD, PhD; Jean Torrisi, MD; Mario Lacouture, MD; Elena Elez, MD; Ferran Martínez-Valle, MD; Benjamin Durham, MD; Maria E. Arcila, MD; Gary Ulaner, MD, PhD; Omar Abdel-Wahab, MD; Bethany Pitcher; Martina Makrutzki, MD; Todd Riehl, PharmD, BCOP; José Baselga, MD, PhD; David M. Hyman, MD

Study enrolls 1st cancer patient
in April 2012

First ECD patient enrolls in
August 2012

On November 6, 2017 US FDA
approves vemurafenib for ECD
with *BRAF* mutations

Clinical Research Makes Difference



How Do We Do Clinical Trials?

- Clinical trials are usually carried out in “phases”
 - **Phase I:** What is the safe dose? **Variety of cancers**
 - **Phase II:** Does the treatment work? **ECD specific – resulted in FDA approval for vemurafenib**
 - **Phase III:** Is the treatment better than existing options? **Often not doable in rare disease**
- **Timeline: 10-15 years**
In case of vemurafenib for ECD: 5 years

Clinical Trials: Pros

For mankind

- Increase in knowledge about particular disease and its therapy
- Development of new therapies
- Prove of efficacy or lack of thereof
- Identification of potential significant side effects

For individual patient

- Access to new therapies, which are not commercially available
- Expansion of therapeutic options
- Standardized protocol-driven therapy
- Some studies in cancer patients suggested that patients on clinical trials tend to have better outcomes compared to patients treated outside of trials

Clinical Trials: Cons

For mankind

- none

For individual patient

- Need to meet all qualifying criteria, which are usually not flexible
- Less flexible and often more intense schedule
- Travel, financial and time commitments
- Possible risk of unknown/unexpected side effects

Why Should I Consider Clinical Trials?

- Results of clinical trials are important to confirm efficacy, safety and can help with patients advocacy efforts
- Clinical trials can provide necessary evidence to convince payers to reimburse new and effective therapies
- Clinical trial is a necessary tool to make the progress happen

2019 Reality Check in ECD

- Prognosis and outcomes have dramatically improved; however, ECD remains incurable
- Existing approved and off-label therapies transformed ECD to chronic and often manageable disease at the cost of long-term and costly treatment with possible side effects
- We still have relatively limited therapeutic armamentarium
- We have limited resources (patients, finances) and large number of questions, which need to be answered

Landscape of Clinical Trials in ECD

- **Phase I:** There is increasing number of cancer studies, which accept ECD patients
- **Phase II:**
 - “Basket studies”: clinical trials for patients with any cancer with certain unifying clinical or molecular characteristics (e.g. vemurafenib in patients with *BRAF* mutation)
 - ECD specific phase II studies: because of limited number of patients this approach should be reserved for promising therapies with high likelihood of FDA/EMA approval (BRAF+: dabrafenib/trametinib; BRAF-cobimetinib)
- **Phase III:** not feasible in ECD

Goals for Clinical Research in ECD

- Making clinical trials available to majority rather than minority of patients with ECD by curbing “geography discrimination” and other barriers
- Approval of a new therapy(therapies) for ECD without BRAF mutation
- Efforts to reduce side effects and improve efficacy of existing therapeutic strategies
 - Dabrafenib/trametinib (instead of vemurafenib)
 - Novel combinations
- Transformation of ECD from chronic disease to curable disease

Key Clinical Trials in ECD

➤ ***BRAF*** mutation **present**

➤ **Dabrafenib/Trametinib**

- **Available** at MD Anderson Cancer Center in Houston, TX (PI: Filip Janku).
- **Plan** to expand to other NCI Designated Cancer Centers/ECD Care Centers participating in the ETCTN (Experimental Therapeutics Clinical Trials Network).
- **Goal** - Approval for Clinical Use

➤ ***BRAF*** mutation present or **absent**

➤ **Cobimetinib**

- **Available** at Memorial Sloan Kettering Cancer Center, New York City, NY (PI: Eli Diamond)
- **Plan** to expand to one more NCI Designated Cancer Center/ECD Care Center.
- **Goal** - Approval for Clinical Use

Where Can I Learn About Clinical Trials?

- ECD Global Alliance Website
- [Clinicaltrials.gov](https://clinicaltrials.gov)
- Care Centers

MANY THANKS !!!

- YOU AND YOUR FAMILIES for teaming up with us to fight and defeat ECD
- ECD Global Alliance for making sure that we stay organized, communicate and deliver
- My colleagues all around the world, who dedicate their time, talent and intelligence to find better and safer therapies for ECD

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