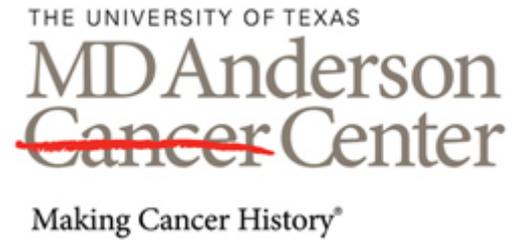




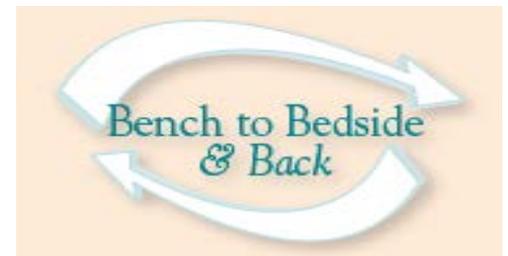
**ECD Global Alliance
Patient and Family Gathering
New York City
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ECD and Clinical Trials

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Why Do We Need Clinical Trials

- **Clinical trials answer two important questions**
 - Does the new treatment work?
 - Is the new treatment safe?
- **Clinical trials help**
 - To get new drugs approved
 - To get new drugs reimbursed

How Do We Do Clinical Trials

- Clinical trials are usually carried out in “phases”
 - **Phase I:** What is the safe dose?
 - **Phase II:** Does the treatment work?
 - **Phase III:** Is the treatment better than existing options?
- Timeline: 10-15 years

ECD

Clinical Trials: Pros

- **For mankind**
 - Increase knowledge about particular disease and therapy
 - Development of new therapies
 - Prove of efficacy or lack of thereof
 - Identification of potential 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**
 - Research is expensive, but other than that NONE
- **For individual patient**
 - Need to meet all qualifying criteria, which are usually not flexible
 - Less flexible and often more intense schedule
 - Travel, financial consequences and time commitment
 - Possible risk of unknown/unexpected side effects

Why Should I Consider Clinical Trials

- Results of clinical trials are important not only for developing new therapies and can provide access to medicines not otherwise available
- Clinical trials can provide necessary evidence to convince payers to reimburse new and effective therapies
- Clinical testing is necessary tool to make the progress happen

Strategies for Clinical Trials in ECD

- Prognosis and outcomes have dramatically improved; however, overall there is still room for improvement
- We have relatively limited therapeutic armamentarium
- We have limited resources (patients, finances) and large number of questions, which need to be answered

Strategies for Clinical Trials in ECD

- **Phase I:** Access for ECD patients to these studies, which are sometimes limited to conventional cancers
- **Phase II:**
 - “Basket studies”: clinical trials for patients with any cancer or histiocytosis with certain unifying feature
 - 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 approval
 - BRAF+: vemurafenib, dabrafenib/trametinib;
 - BRAF-: cobimetinib or trametinib
- **Phase III:** not feasible in ECD

Where Can I Learn About Clinical Trials?

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

Department of Investigational Cancer Therapeutics at MD Anderson

- The largest cancer drug development program in the nation and the world with more than 170 clinical trials on the priority list.
- The mission is to bring new drugs to cancer patients
- Clinical trial is an attractive option for patients with limited therapeutic options, who failed proven therapies

Examples of Clinical Trials for ECD Patients at MD Anderson

- *BRAF* mutation positive
 - Multicenter: my pathway (vemurafenib)
 - Multicenter: dabrafenib/trametinib
 - Multicenter: LXH254
 - Multicenter: LTT462
 - Multicenter: PLX8394
 - Multicenter: trametinib/ribociclib
- *BRAF* mutation negative
 - Multicenter: LXH254 (if RAS mutation is present)
 - Multicenter: LTT462 (if RAS or MAP2K1 mutations are present)
 - Multicenter: trametinib/ribociclib
 - Single Center: everolimus/anakinra

Take Home Message

- Clinical Trials are Part of Standard of Care in ECD
- Important recent clinical trials efforts
 - BRAF+: vemurafenib or dabrafenib/trametinib
 - BRAF-: cobimetinib (or trametinib?)