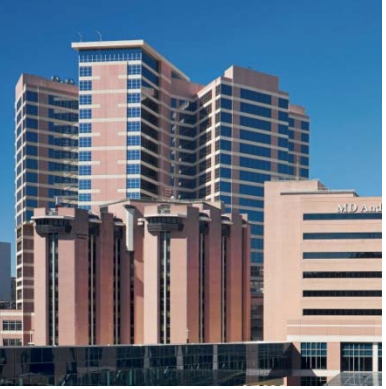

ECD Global Alliance
Patient and Family Gathering
Paris, France
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THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center
Making Cancer History®

Importance of Clinical Trials

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Bench to Bedside & Back

Department of Investigational Cancer Therapeutics at MD Anderson

- The largest cancer drug development program in the nation and the world with more than 150 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

Why Do We Need Clinical Trials

- Clinical trials answer two important questions
  - Does the new treatment work?
  - Is the new treatment safe?

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

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 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
- 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 often limited to conventional cancers

- **Phase II**:
  - "Basket studies": clinical trials for patients with any cancer or histiocytosis with certain unifying feature (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+: vemurafenib, dabrafein/trametinib; BRAF- cobimetinib or trametinib?)

- **Phase III**: not feasible in ECD

Where Can I Learn About Clinical Trials?

- ECD Global Alliance Website
- Clinicaltrials.gov
- Care Centers

Examples of Clinical Trials for ECD Patients at MD Anderson

- *BRAF* mutation positive
  - Multicenter: my pathway (vemurafenib)
  - Multicenter: dabrafenib/trametinib
  - Multicenter: BVD-523
  - Multicenter: PLX8394
- *BRAF* mutation negative
  - Multicenter: BVD-523 (if MAP2K1 mutation present)
  - Multicenter: PLX8394
  - Single Center: everolimus/anakinra

Take Home Message

Clinical Trials are Part of Standard of Care in ECD

Important clinical efforts

- BRAF+: vemurafenib or dabrafenib/trametinib
- BRAF-: cobimetinib? or trametinib?