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
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 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

• 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?)