Understanding and Navigating the Clinical Trial Landscape

July 27th, 2012
Robert Rutigliano, PhD
Director, Medical Information EmergingMed
What are cancer clinical trials?

- Final stages of medical research that are designed to answer specific scientific questions in an effort to better prevent, diagnose, or treat disease.

- Culmination of a long research process that moves testing from the lab to the clinic.
Why are clinical trials conducted in brain tumors?

- To contribute to our knowledge and progress
- To ensure that any treatments the health community recommends are both safe and effective
- To address the limitations of basic research in cell culture and animal models
- To secure a scientific, medical, evidence-based paradigm that successfully translates findings from the lab into better clinical outcomes
Types of clinical trials

• Treatment trials
• Prevention trials
• Early-detection trials/screening trials
• Diagnostic trials
• Quality-of-life studies/supportive care studies
• Genetic and biomarker studies
Phases of clinical trials

Phase 1

- These are the first studies in people (typically small groups) that evaluate the safety of a new experimental drug or procedure and seek to determine a safe dosage range, and identify any side effects
- How does the agent affect the human body?
- What dosage is safe?
Phases of clinical trials

Phase 2

• These studies continue to test safety, and begin to evaluate how well the new drug or procedure is working. Phase II studies usually focus on a particular type of cancer/tumor.

• Does the agent or intervention have an effect on the disease?
Phases of clinical trials

Phase 3

- These studies will test the effectiveness of the experimental drug or treatment in large groups of people and will compare the effectiveness to commonly used drugs and current standards of care.
- Is the new agent or intervention (or new use of a treatment) better than the standard?
- Participants have an equal chance to be assigned to one of two or more groups.
## Summary of phases 1-3

<table>
<thead>
<tr>
<th>Phase</th>
<th>Typical # of Enrollees</th>
<th>Typical Length</th>
<th>Purpose</th>
<th>% Drugs Successfully Tested</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase I</td>
<td>20 –100</td>
<td>Several months</td>
<td>Mainly Safety</td>
<td>70%</td>
</tr>
<tr>
<td>Phase II</td>
<td>Up to several 100</td>
<td>Several months- 2 years</td>
<td>Short term safety; mainly effectiveness</td>
<td>33%</td>
</tr>
<tr>
<td>Phase III</td>
<td>Hundreds- thousands</td>
<td>1-4 yrs.</td>
<td>Safety, dosage &amp; effectiveness</td>
<td>25-30%</td>
</tr>
</tbody>
</table>
The protocol

A study plan on which all clinical trials are based that is carefully designed by a principal investigator to safeguard the health of the participants as well as answer specific research questions.

A protocol will:

- Detail the rationale and goals of the trial
- Ensure the consistency of trial procedures
- Outline the duration and types of treatments, tests, and monitoring that will be given
- Define who is eligible for the trial
- Discuss what information will be collected and analyzed
What happens in a clinical trial?

You will meet your clinical care team who will:

- Check your health at the beginning of the trial
- Provide specific instructions for trial participation
- Offer guidance throughout
- Conduct tests and procedures if appropriate
- Continue to assess health through planned visits
- Coordinate frequent follow ups
How are patients’ rights protected?

Ethical and legal codes that govern medical practice also apply to clinical trials

• Informed consent
• Review boards
  • Institutional review boards (IRBs)
  • Data safety and monitoring boards
Informed consent

A document designed to detail important facts about the clinical trial prior to participation

• The research team will provide this document to outline details about the study--such as its purpose, duration, required procedures, and key contacts (understandable language)

• Informed consent includes information about the possible risks, benefits, and limits of the trial that help the participant decide whether or not to enroll in the study.

• The informed consent process does not end once the form is signed

• The informed consent document is not a contract, and the participant may withdraw from the trial at any time.
Institutional review boards (IRBs)

An IRB is defined as: "any board, committee or other group formally designated by an institution to review, to approve the initiation of, and to conduct periodic review of biomedical research involving human subjects“

- People qualified to evaluate new and ongoing trials on the basis of scientific, legal and ethical merit (often includes patient advocates)

- All institutions that conduct clinical trials must, by law, have a IRB that approves the protocol
Institutional review boards (IRBs)

- Review research to ensure that potential benefits outweigh risks & proper protection is in place for patients
- Develop and issue written procedures
- Review reports of unexpected adverse events received from the Investigator
- Continually monitor and review the integrity of the study
Data and safety monitoring boards:

- Ensure that risks are minimized
- Ensure data integrity
- Stop a trial if safety concerns arise or objectives have been met
Why should you consider clinical trials?

- To play an active role in your health care—informing decisions
- Clinical trials are often a natural part of the continuum of care
- Participation in advancing medical knowledge—a chance to help others and improve cancer care
- Quality treatment
Risks of participation in clinical trials

- New treatments or interventions under study are not always better than, or even as good as, standard care
- Even if a new treatment has benefits, it may not work for every patient
- Unpleasant or serious side effects
- May require more time and attention than a non-protocol treatment (e.g., more trips to study site, more treatments, etc.)
Barriers to participation in clinical trials—why do so few people participate?

- Lack of awareness--85% of patients unaware of clinical trials; 75% of these patients said they would have participated in trials (Harris Interactive 2001)
- Lack of access to trial information
- Fear, distrust, or be suspicious of research
- Have practical or personal obstacles
- Be unwilling to go against their physicians’ wishes
Barriers to participation in clinical trials

Physicians and other health professionals may:

• Be unaware of appropriate trials
• Be unwilling to lose control of patient’s care
• Believe that standard therapy is best
• Have concerns about the patient’s care or how the person will react to suggestion of clinical trial participation
What should you consider before joining a clinical trial

- What is the purpose of the study?
- Why do researchers believe the new treatment being tested may be effective?
- What kinds of tests and treatments are involved?
- How do the possible risks, side effects, and benefits in the study compare with my current treatment?
- How long will the trial last?
- Who will pay for the treatment?
- How will I know that the treatment is working?
- Can I leave the study after it has begun?
When should you consider joining a clinical trial?

Anytime you and your doctor are making new treatment decisions, it would be appropriate to consider clinical trials

- Before a biopsy (to study tissue from a tumor)
- Before the first surgery or radiation treatment (neo-adjuvant studies)
- After surgery or radiation treatment (adjuvant studies)
- When cancer has recurred or spread (metastasized)
- When cancer is spreading despite current treatment (refractory)
Clinical trials for brain tumors: assessing the landscape

Currently there are over 200 enrolling treatment trials across thousands of sites in the United States. These trials are:

• Testing over 100 new therapeutic agents with a wide range of molecular targets
• Seeking to improve the standard of care for the vast majority of tumor types and grades
• Seeking to improve quality of life by researching supportive care initiatives
• Seeking patients at all points throughout the treatment continuum
Clinical trials for brain tumors: assessing the landscape

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>Enrolling Treatment Trials</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acoustic neuroma (Schwannoma)</td>
<td>31</td>
</tr>
<tr>
<td>Anaplastic astrocytoma</td>
<td>170</td>
</tr>
<tr>
<td>Anaplastic oligodendroglioma</td>
<td>90</td>
</tr>
<tr>
<td>Astrocytoma</td>
<td>176</td>
</tr>
<tr>
<td>Central Nervous System (CNS) lymphoma</td>
<td>31</td>
</tr>
<tr>
<td>Chordoma</td>
<td>28</td>
</tr>
<tr>
<td>Craniopharyngioma</td>
<td>28</td>
</tr>
<tr>
<td>Ependymoma</td>
<td>52</td>
</tr>
<tr>
<td>Ganglioglioma</td>
<td>64</td>
</tr>
<tr>
<td>Germ cell tumor</td>
<td>34</td>
</tr>
<tr>
<td>Germinoma</td>
<td>29</td>
</tr>
<tr>
<td>Glioblastoma multiforme (GBM)</td>
<td>180</td>
</tr>
<tr>
<td>Glioma: mixed or not sure type</td>
<td>193</td>
</tr>
<tr>
<td>Gliosarcoma</td>
<td>103</td>
</tr>
<tr>
<td>Hemangioblastoma</td>
<td>28</td>
</tr>
<tr>
<td>Medulloblastoma</td>
<td>54</td>
</tr>
<tr>
<td>Meningioma</td>
<td>38</td>
</tr>
<tr>
<td>Oligoastrocytoma</td>
<td>67</td>
</tr>
<tr>
<td>Oligodendroglioma</td>
<td>80</td>
</tr>
<tr>
<td>Pilocytic astrocytoma</td>
<td>65</td>
</tr>
<tr>
<td>Pinealoma</td>
<td>33</td>
</tr>
<tr>
<td>Pituitary adenoma</td>
<td>27</td>
</tr>
<tr>
<td>Primitive Neuroectodermal Tumor (PNET)</td>
<td>41</td>
</tr>
<tr>
<td>Teratoma</td>
<td>29</td>
</tr>
</tbody>
</table>
Clinical trials for brain tumors: assessing the landscape

Regardless of how early or advanced there are significant research questions being addressed

<table>
<thead>
<tr>
<th>Adult - Tumor Grade</th>
<th>Enrolling Treatment Trials</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>111</td>
</tr>
<tr>
<td>II</td>
<td>116</td>
</tr>
<tr>
<td>III</td>
<td>150</td>
</tr>
<tr>
<td>IV</td>
<td>231</td>
</tr>
</tbody>
</table>
Clinical trials for brain tumors: assessing the landscape

<table>
<thead>
<tr>
<th>Treatment Status</th>
<th>Enrolling Treatment Trials</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer has been diagnosed but not yet treated</td>
<td>108</td>
</tr>
<tr>
<td>Cancer has been treated with surgery or radiation only-no drug therapy</td>
<td>150</td>
</tr>
<tr>
<td>Cancer has not responded to treatment</td>
<td>141</td>
</tr>
<tr>
<td>Cancer was successfully treated and patient is in remission</td>
<td>7</td>
</tr>
<tr>
<td>Cancer was successfully treated previously but has returned</td>
<td>209</td>
</tr>
<tr>
<td>On treatment; stable or results not yet known</td>
<td>16</td>
</tr>
<tr>
<td>On 'watch and wait'; not on treatment</td>
<td>18</td>
</tr>
</tbody>
</table>

Clinical trials are enrolling patients throughout the treatment continuum
TrialConnect is personalizing clinical trial options

54 year old male looking to explore clinical trials

GBM

Newly Diagnosed

Grade III

Heart Condition

258 Clinical Trials

148 Clinical Trials

43 Clinical Trials

21 Clinical Trials

13 Clinical Trials
### CLINICAL TRIALS MATCH RESULTS

We found 13 treatment trials that match your medical profile. Now what?

**Option 1:** Select trial(s) of interest, then click Submit to get more details.

**Option 2:** Call 1-877-709-4833 (toll-free) to discuss your results.

**Option 3:** Send an email with questions.

<table>
<thead>
<tr>
<th>Phase</th>
<th>Title</th>
<th>Intervention</th>
<th>Location</th>
<th>My Selection</th>
</tr>
</thead>
<tbody>
<tr>
<td>III</td>
<td>Fluorescence-guided Surgery for Low- and High-grade Gliomas (BALANCE)</td>
<td>Other</td>
<td>AZ - Phoenix - US (x2)</td>
<td>add to profile</td>
</tr>
<tr>
<td></td>
<td>(read more)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>Boswellia Serrata and Standard Treatment or Standard Treatment Alone in Treating Patients Who Have Undergone Surgery and Radiation Therapy for Newly Diagnosed or Recurrent High-Grade Glioma</td>
<td>Other</td>
<td>OH - Cleveland - US (x2)</td>
<td>add to profile</td>
</tr>
<tr>
<td></td>
<td>(read more)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>Stereotactic Ablative Radiotherapy for Comprehensive Treatment of Oligometastatic Tumors (SABR-COMET)</td>
<td>Radiotherapy</td>
<td>London - CA (x2)</td>
<td>add to profile</td>
</tr>
<tr>
<td></td>
<td>(read more)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>Crenolanib (CP-368,596), a Selective and Potent Inhibitor of PDGFR, for the Treatment of Adult Gliomas</td>
<td>Signal Transduction Inhibitor</td>
<td>TX - Dallas - US (x2)</td>
<td>add to profile</td>
</tr>
<tr>
<td></td>
<td>(read more)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
A closer look at results reveals diverse treatment opportunities.

- New surgical techniques
- New neoadjuvant therapies + stem cell transplants
- New signal transduction inhibitors (MDM2 antagonists, Proteasome Inhibitors)
- New radiation techniques
- New imaging technology
- New chemotherapy delivery methods
- Vaccine therapies

American Brain Tumor Association
Providing and pursuing answers™

2012 AMERICAN BRAIN TUMOR ASSOCIATION PATIENT AND FAMILY CONFERENCE
Targeted therapies for GBM

- **EGFR inhibitors**
  - Gefitinib
  - Erlotinib
  - Cetuximab
  - Nimotuzumab

- **PI3K-Akt-mTor-pathway**
  - Sirolimus
  - Temsirolimus
  - Everolimus
  - AP23573
  - perifosine

- **Ras-MAPK pathway**
  - Tipifarnib
  - Lonafarnib

- **Protein kinase C inhibitors**
  - Enzastaurin
  - Tamoxifen

- **Histone deacetylase inhibitors**
  - Vorinostat
  - Depsipeptide

- **PDGFR inhibitors**
  - Imatinib mesylate

- **VEGF and VEGFR inhibitors**
  - Bevacizumab
  - VEGF Trap
  - AZD2171
  - Vatalanib

- **Multitargeted TKIs**
  - Sunitinib (VEGFR2, PDGFR, C-Kit, FLT-3)
  - Sorafenib (Raf, VEGFR, PDGFR)
  - Lapatinib (EGFR, ERBB2/HER2)
  - Zactima (EGFR, VEGFR2)
  - Dasatinib (VEGFR, PDGFR, c-Kit, Src, EPHA2)

- **Integrin antagonists**
  - Cilengitide

- **Proteosome inhibitors**
  - Bortezomib
TrialConnect is personalizing clinical trial options

- 46 year old female looking to explore clinical trials
- Meningioma
- Newly Diagnosed
- Grade I
- 258 Clinical Trials
- 34 Clinical Trials
- 11 Clinical Trials
- 7 Clinical Trials
A closer look at results reveals diverse treatment opportunities

Proton Therapy x 2

Radiation techniques versus observation only

Testing approved APL drug as Chemo-protectant

New imaging technology for improved diagnosis

Biorepository to study molecular markers

mTOR inhibitor / immunosuppressant

Additionally, there are 12 supportive care studies to help with pain, fatigue, anxiety, nausea, and well-being

American Brain Tumor Association®
Providing and pursuing answers™

2012 AMERICAN BRAIN TUMOR ASSOCIATION PATIENT AND FAMILY CONFERENCE
Goals of the ABTA’s TrialConnect clinical trial information service

To create the opportunity for patients to make informed treatment decisions through:

- Increased access to accurate and verified information
- Increased awareness of the most current and up to date research
- Increased education on the basics of clinical trials through a free, personalized, and confidential call center
The TrialConnect CTIS identifies & removes addressable barriers for all trials

1. TrialConnect Infrastructure

2a. Ongoing Education, Navigation, Outcomes Tracking

2b. Dedicated Clinical Trial Navigator educates, matches to trial; brokers solutions to addressable barriers

3. Self referral directly to trial site; elects to join CTIS registry

Patient or healthcare provider seeks sponsor’s trial information

IRB-approved trial site initiates Informed Consent process

American Brain Tumor Association®
Providing and pursuing answers™
Patient-friendly questionnaire

Addresses basic information on diagnosis, staging and treatment history

Submit questionnaire to find clinical trials that match your unique situation
Responses Drive Results

Answers to questionnaire are related to the eligibility criteria of all trials to identify appropriate matches.

Select trials and sites of interest and call a clinical trial navigator to get connected to the appropriate staff.
Role of clinical trial navigators

Clinical Trials Navigators are there to:

• Learn about your condition
• Educate
• Provide detailed contact information for trial sites
• Provide additional resources
• Follow-up
Ongoing follow-up and benefits of a registry

- Provide access to clinical trials at the right times
- Guide families through a personalized search
- Fix addressable barriers
- Ensure system holds accurate, vetted information
- Keep families up to date on current research
Take home messages

- Clinical trials often yield important results that affect health and standards of care for patients
- Clinical trials follow specific guidelines & protocols and must ensure the well being of participants
- Patients have the right to make informed decisions—education is needed
- The clinical pipeline for brain tumors is robust
- Personalized matches and latest studies can be accessed via the ABTA’s TrialConnect
Discussion Questions??