Ochsner Phase I Program
Louisiana Oncology Society Program

Marc Matrana, MD, MSc
Medical Director
Ochsner Targeted Cancer Therapies Program
## Disclosures

<table>
<thead>
<tr>
<th>Role</th>
<th>Companies</th>
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<tbody>
<tr>
<td>Research Support</td>
<td>Lilly, Genentech, Celgene, Astellas, Pfizer</td>
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<tr>
<td>Consultant</td>
<td>Pfizer, Bayer, EMD Sorono</td>
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<td>Speaker’s Bureau</td>
<td>Merck, Sirtex, Genentech, BMS, Eisai</td>
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Today’s Meeting

• Cancer in Louisiana

• Phase I Clinical Trails

• The Ochsner Targeted Cancer Therapies Program
  – Ochsner and TGEN

• Moving Forward… into the Future!
Cancer in Louisiana
Cancer in Louisiana

- 70 Louisianans receive the diagnosis of cancer every day.
- 23 Louisianans die from cancer every day.
- Despite mortality rates dropping for cancer, death rates for Louisianans with cancer is significantly higher than the national average.
- Cancer mortality rates for African Americans in Louisiana is about 30% higher than for their white counterparts.
Mortality Rates\(^1\) of All Cancers Combined
Louisiana vs. US,\(^2\) 2006-2010

<table>
<thead>
<tr>
<th></th>
<th>Rate Per 100,000</th>
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<tbody>
<tr>
<td>White Male</td>
<td>238</td>
</tr>
<tr>
<td>Black Male</td>
<td>317  277</td>
</tr>
<tr>
<td>White Female</td>
<td>157  150</td>
</tr>
<tr>
<td>Black Female</td>
<td>187  171</td>
</tr>
</tbody>
</table>

\(^1\)Age-adjusted to the 2000 US standard population.
\(^2\)Mortality data source: National Center for Health Statistics (NCHS).
* Mortality rate of Louisiana was significantly different from that of US.
Cancer Death Rate by State, 2010

United States: 172.8 cancer-related deaths per 100,000 population

Number of Cancer Deaths per 100,000 Population
- 133.7 – 163.4 (11 states)
- 165.5 – 172.4 (13 states)
- 172.5 – 183.4 (13 states including DC)
- 183.5 – 208.3 (14 states)


Ochsner Health System
Notes: The Cancer Alley consists of 11 parishes: East Baton Rouge, West Baton Rouge, Ascension, Iberville, St. James, St. John the Baptist, St. Charles, Jefferson, Orleans, St. Bernard, and Plaquemines.
Participation in Clinical Trials

• Only about 3% of adult cancer patients in the US participate in clinical trials

• Numbers are even less for patients in Louisiana
Phases of Clinical Research

### Preclinical
- Lab and animal studies
- Latest, most novel therapies
- More and more are relying on molecularly driven, targeted approaches matching patients to effective therapies
- Define dose, PKs, etc.
- Small number of subjects 20-30

### Phase I
- Builds on Phase I data
- Define efficacy
- Usually less than 100 patients
- More and more of these are combined with Phase I's

### Phase II
- Builds on Phase I and II data
- Define efficacy
- Usually less than 100 patients
- More and more of these are combined with Phase I's

### Phase III
- Builds on Phase I and II data
- Usually compare new therapy to SOC
- Often involve hundreds of institutions, and enroll 100s or 1000s of patients

### Phase IV
- Post approval analysis
- Real-world data
- Longer-term safety
Benefits of Clinical Trials

• Patients on trials tend to do better than patients off trials
• Early trials allow for patients to receive innovative therapy years before these therapies are available commercially
• May increase response rates and survival for selected patients
• Offers a treatment option for patients with good performance status who otherwise have progressed through standards therapies
• Advance science, leading to the approval of new therapies.
Barriers to Clinical Trial Participation

- Location – no clinical trials nearby
- Education – don’t understand the benefits
- Fear – afraid of placebos, being “experimented on,” etc.
- Financial – insurance or other hurdles
- Access – being treated by a center that doesn’t have trials, etc.
- Patients characteristics - doesn’t meet inclusion/exclusion criteria
Phase I Clinical Trials
What are Cancer Phase I trials?

• Clinical trial of a new agent/device usually in patients with advanced refractory cancer

• Many involve “first in man” agents

• Every agent on the market today went through a Phase I trial
History of Phase I Programs

- Experimental Therapeutics (early drug development) programs have been in place in major academic centers for about 4 decades.
- Originally in the early 1980s there were only 5 adult and 2 pediatric programs in the US and one in Europe – all sponsored by the NCI.
- As the number of major cancer centers in the US grew and cancer drug development became interesting to industry, so did the number of experimental therapeutics programs.
“Old” Phase 1’s

• Focused exclusively in dose-finding and toxicities

• Trials aimed across cancers

• No real efforts to pair patients with best therapies

• Few responders
“New” Phase 1’s

• Precision is key

• Great effort to match patient’s underlying biology (driving mutations, etc) to most appropriate therapy

• Function largely as Phase II studies and are often combined with Phase IIs

• Much higher response rates
Phase 1 – Response Rates

• Response rates in older trials ranged from 5-7% with CRs in 1% of patients (Von Hoff, 1991, Esty 1986)

• With more recent targeted agents responses closer to 20% with disease control rate >30% are routinely observed.
Molecular Profiling

• Studies have shown that between a quarter and a third of patients with advanced, refractory cancer can benefit from molecular profiling and precision therapeutics.

• Early trials allow patients the opportunity to potentially receive the most advanced, most novel therapies available.

• The availabilities of these types of therapies have been limited in the Gulf South.
Driving Mutations in Lung Cancer

- Unknown: 36.4%
- KRAS: 25%
- EGFR: 23%

Other mutations:
- NRAS: 0.2%
- MAP2K1: 0.4%
- ERBB2: 1%
- MET: 2%
- PIK3CA: 3%
- BRAF: 3%
- EML4-ALK: 6%
Activating ALK Mutations in NSCLC

- About 4% of NSCLC pts have a chromosomal rearrangement leading to ALK-EML4 fusion gene

- Adenocarcinoma, never or light smokers, younger pts.

- Crizotinib is a TKI targeting ALK and ROS1

- Nausea, vision disorder, vomiting, and diarrhea

- Pneumonitis cases reported
43 yo Male Never Smoker with Stage IV NSCLC Positive for EML4-ALK

Pretreatment

After 1 cycle
• Crizotinib has also been found to have profound efficacy in patients with ROS1 mutated lung cancers.
What Makes Phase I Trials Different?

• Unknowns – dose, toxicity
• Intense monitoring
• Demanding protocols
  – 12 EKGs/visit, for example
  – Intense pharmacokinetic measurements, q1 hr lab draws
  – Baseline and follow up tumor biopsies
  – Multiple consults required (eye exams, cardio, pulmonary, etc)
  – Intense imaging schedules
  – Nearly daily follow-up/checking on patient
  – Weekly visits and multiple other time intense functions.
What Makes Phase I Trials Different?

- Incredible amount of computer/paper work for on study adverse events and off study procedure

- Immense about of work to convince sponsors to bring their best new agents to our program

- The bottom line is still first of all delivering the best possible clinical care with lots of time spent with an individual patient (informed consent, weekly H+Ps)
What Infrastructure is Required

- Medical expertise
- Nursing expertise
- Regulatory affairs expertise
- Specimen processing expertise
- Experimental pharmacy (frequently audited)
- Dedicated physical facilities
- Administrative support
- Special equipment for specimen processing and labs
- Interventional radiology cooperating for specimen acquisition
- Budget and contracts
- Legal infrastructure who understand limits of intellectual property
- Networks of contacts and industry partners
Ochsner’s Targeted Cancer Therapies Program
Why Build a “Phase I” program?

- To fill an unmet need in our region, further the Ochsner mission
- The number of Phase 1 centers in the country is limited, because this is expensive, hard work with limited rewards… but, that doesn’t mean it shouldn’t be built!
Why Build a “Phase I” program?

• To fuel new and innovative partnerships, building on Ochsner’s success in the area

• To advanced science, and contribute to new drug development

• TO BENEFIT OUR PATIENTS NOW AND IN THE FUTURE!
What Makes Ochsner’s Targeted Therapies Program Different?

- **Powerful Partnerships:**
  - The Translational Genomics Research Institute (TGen)
  - Integrate, Translate, Accelerate!
  - Dr. Dan Van Hoff has more Phase I experience than anyone else on the planet, has led >500 phase I trials.
What Makes Ochsner’s Targeted Therapies Program Different?

• **Dedicated staff:**
  – Dedicated physician medical director and physician researchers
  – Full-time nurse supervisor
  – Dedicated scheduler/concierge/navigator
  – Phase I research nurses
  – Dedicated Phase I infusion center and Phase I infusion nurses
  – Phase I regulatory coordinator and a full time grants officer
  – Data analysis, lab techs

• **Dedicated Phase I lab space and research pharmacy space**
Progress

• Currently have a few Phase I trials open and enrolling

• Have about two dozen Phase I trials in various phases of opening (IRB, grants and contracts, etc)

• Working on a molecular “bucket” trial

• Anticipate many more through next year
Current Open Phase I Trials

• A Phase 1, Multi-center, Open-Label Dose Escalation Study of SYN004 in Patients with Solid Tumors to Evaluate the Safety, Immunogenicity and Pharmacokinetics of SYN004 following Administration of Eight Intravenous Doses.

  – SYN004 is a monoclonal antibody similar to cetuximab
Current Open Phase I Trials

- A Phase I/II Trial of X4P-001 as Single Agent and in Combination with Axitinib in Patients with Advanced Renal Cell Carcinoma
  - CXCR4 antagonist
  - CXCR4 binds CXCL12, which, through multiple divergent pathways, leads to chemotaxis, survival, proliferation, and gene transcription.
  - Blocking CXCR4 blocks these parallel processes
Current Open Phase I Trials

• A Phase I/II Trial of Brentuximab Vedotin in Combination with Gemcitabine for Pediatric and Young Adult Patients with Relapsed or Refractory Hodgkin Lymphoma

• A Phase I/II Study of Glembatumumab Vedotin in Patients with gpNMB-Expressing, Advanced or Metastatic Squamous Cell Carcinoma of the Lung
Current Open Phase I Trials

- A Randomized, Open-Label, Phase I/II Trial of Gemcitabine plus nab-Paclitaxel with or without FG-3019 as Neoadjuvant Chemotherapy in Locally Advanced, Unresectable Pancreatic Cancer

- A Phase I/II, Two-Part, Multicenter Study to Evaluate the Safety and Efficacy of M402 in Combination with nab-Paclitaxel and Gemcitabine in Patients with Metastatic Pancreatic Cancer
Moving Forward… into the Future!
Into the Future

• We want to accelerate the development of new, more effective, less toxic, more personalized therapies for cancer patients in Louisiana and beyond.
What’s Next?

• Continuing to build our team and identify the best talent at every level

• Working constantly to create new partnerships with sponsors and industry

• Identify additional philanthropic opportunities

• Polishing our molecular “bucket” trial protocol

• Working with Ochsner marketing and others to plan our opening event.
How can our program help you and your patients?

• We want to be your solution center for your patients!

• Discuss a referral:
  – mamatrana@ochsner.org
Questions, thoughts, ideas....