



2019-2020

Impact Statement

So much has happened in the world since last April when we launched **Battle Osteosarcoma**, and we hope that through all of it, you and your families are safe and well. While it's hard to keep up, it's even harder to keep us down.

Likewise the past year has been a series of ups and downs for our Osteowarriors Charlotte and Dylan. In superhero fashion, both are rebounding from relapses this past year, which only more sharply draws into focus the urgent need for treatment options for relapsed osteosarcoma.

And that is where you have made a tremendous impact.



Impact of Donor Support

Because of the incredibly generous support of our Battle Osteosarcoma donors, the Sweet-Cordero Lab at UCSF has made meaningful strides toward this goal. Dr. Sweet-Cordero's research lab is investigating genetic alterations of osteosarcoma that are specific to patients with relapsed and metastatic disease, and is focused on studying the quickest ways to find the most effective drugs to treat these genetic alterations in osteosarcoma patients.

Battle Osteosarcoma has raised \$607,548 to date, which has accelerated Dr. Sweet-Cordero's research.

\$607,548 HAS FUNDED THE FOLLOWING:

- Developed new cell lines & PDX models
- Tested new drugs & promising drug combinations
- Evaluated biomarkers to match patients to therapy
- Created rapid pipeline to clinical trial



Impact of Donor Support

1 DEVELOPED 8 NEW CANCER CELL LINES AND 22 PDX MODELS

Historically, new cell lines have been difficult to establish, so developing eight new lines is an incredible accomplishment. Cell lines are integral to research, and once established, they provide an indefinite source of biological material for experimental purposes.

Research based on newer cell lines is considered more reliable, relevant and easier to replicate than research that relies on older, existing cell lines. Drawing conclusions based on older cell lines proves difficult due to lack of patient treatment history and outcomes, and inadequate representation of the vast heterogeneity of genetic mutations in osteosarcoma.

These new cell lines have also been reproduced in 22 PDX (patient derived xenograft) models, enabling more reliable drug testing and an enduring resource to propel research for all scientists working on osteosarcoma research.

22 PDX Models Grown

16 With WGS/RNA Sequencing

14 Implanted/Waiting

8 New Cell Lines Generated

RESEARCH BASED ON NEW CELL LINES = RESULTS THAT ARE MORE RELIABLE RELEVANT & REPLICABLE

Impact of Donor Support

2

TESTED 45 DRUGS AND IDENTIFIED 3 PROMISING DRUG COMBINATIONS

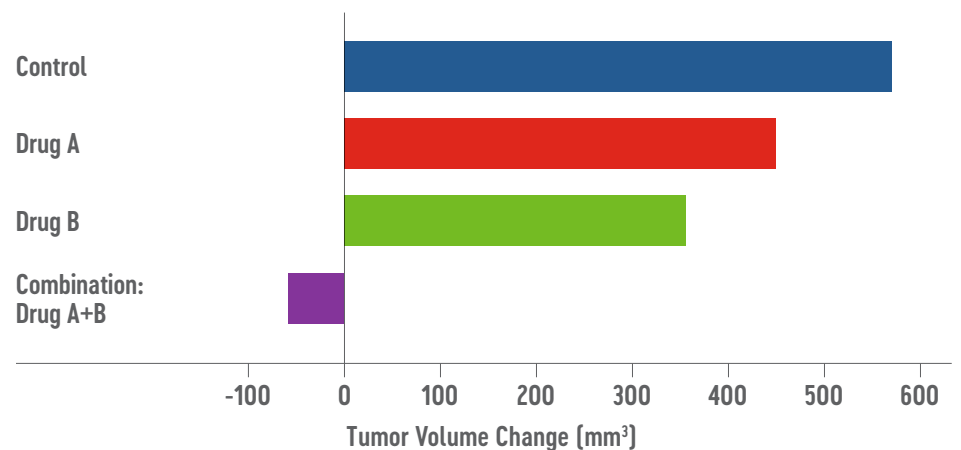
With the new cell lines and PDX models established, Dr. Sweet-Cordero has made progress on testing both single agent drugs and combinations.

To date, the Sweet-Cordero Lab has tested 45 drugs against the panel of eight cell lines. Due to the heterogeneous nature of osteosarcoma, using a single drug is not likely to significantly impact a patient with osteosarcoma. However, combining drugs has yielded far superior results. The completed phase of testing single agent drugs has generated valuable data to inform a strategy for finding effective drug combinations. So far, the research has identified three very promising drug combinations. And due to his research over the past year, Dr. Sweet-Cordero now has a blueprint for conducting combination experiments.



DRUG COMBINATIONS -VS- INDIVIDUAL DRUGS

Change in Tumor Volume after Treatment

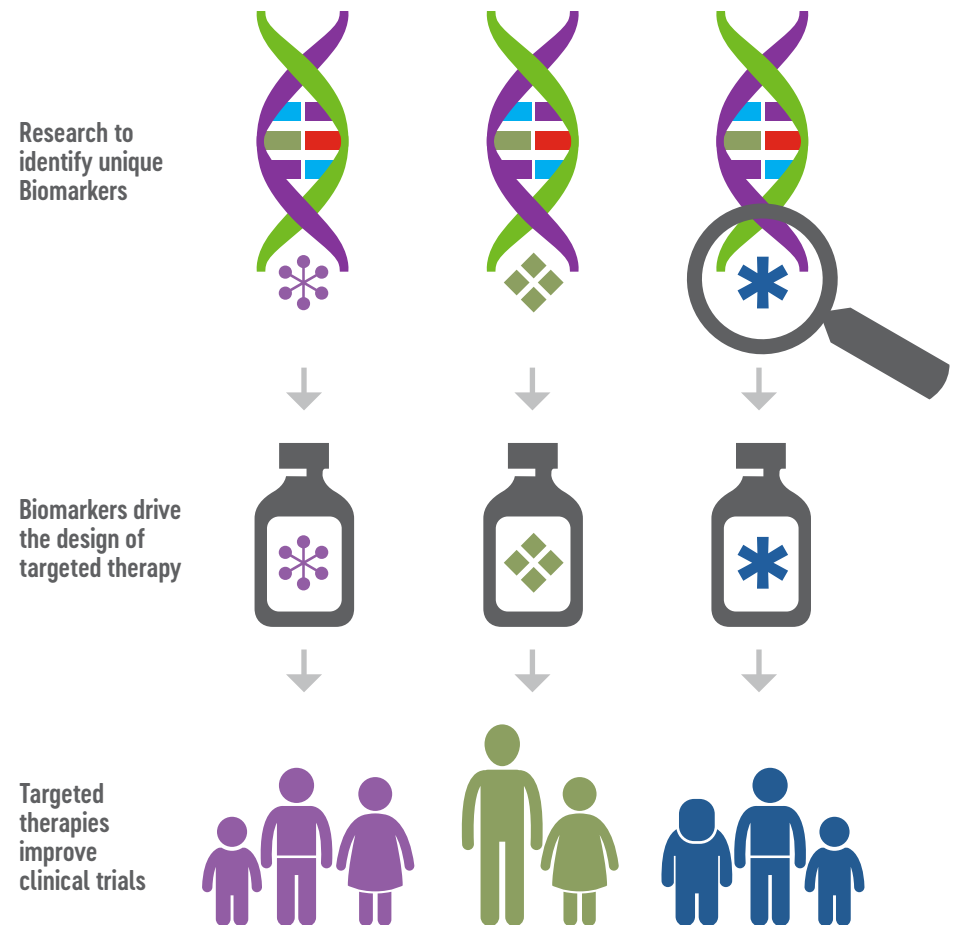


Impact of Donor Support

3

PROGRESS ON IDENTIFYING PREDICTIVE BIOMARKERS

Biomarkers are measurable indicators of how likely or unlikely a patient is to respond to a given treatment. Currently, osteosarcoma lacks good biomarkers, so all patients are treated with the same drugs, which is an ineffective approach given the heterogeneity of genetic mutations. By identifying biomarkers, Dr. Sweet-Cordero is laying the groundwork to execute on the promise of precision oncology. This research will drive the design and proper use of targeted therapy and improve clinical trial design. So far, they have evaluated 7 cell lines in vitro and will be evaluating biomarkers of response to the ATR/PARP clinical trial.



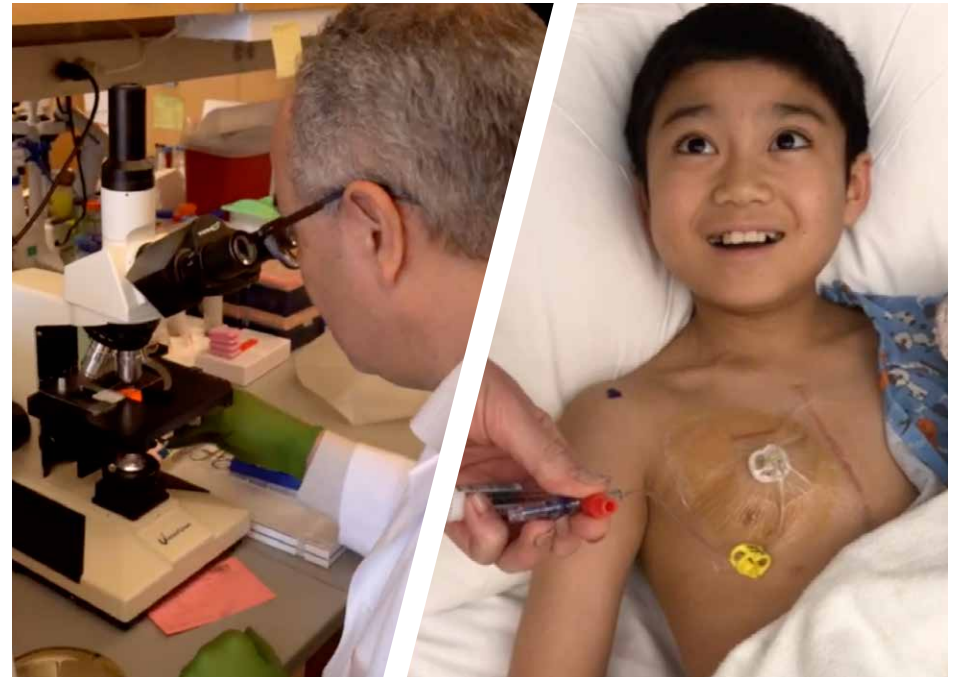
Impact of Donor Support

4

CREATED A RAPID PIPELINE FROM LAB TO CLINICAL TRIAL

A unique aspect of Dr. Sweet-Cordero's research is that his lab has already established a framework for tandem development of clinical and preclinical efforts with real time evaluation of clinical trial results via collaboration with Dr. Katie Janeway at Dana Farber Cancer Institute in Boston. With this unique partnership, promising drug combinations in the lab can be rapidly transitioned into clinical trials within 12 to 18 months to potentially benefit patients. This is a process that normally takes several years, sometimes even a decade.

Using gene sequencing, Dr. Sweet-Cordero and Dr. Janeway plan to better define what combination therapies are best for patients with osteosarcoma. As a direct result of lab tests this past year, the first clinical trial featuring a PARP inhibitor + ATR inhibitor is slated to open in the Summer of 2020.



All of the progress in the first year of this grant has established the foundation and framework for finding more effective treatment options for relapsed osteosarcoma, creating critical building blocks that have far-reaching benefits in osteosarcoma research, even beyond the Sweet-Cordero Lab.

What's Next...

With some major foundational milestones met in year one, there is still much more work to do:

- Establish more cell lines and PDX models to better represent heterogeneous genomic mutations in osteosarcoma patients - especially cell lines for genomic mutations that are under-represented
- Procure and screen more drugs to identify additional promising drug combinations
- Test these promising drug combinations and make them available to patients in clinical trials

The Battle Osteosarcoma grant has funded 45% of the total research budget for Dr. Sweet-Cordero's four year research proposal, with another \$742.5K needed to fully fund more cell lines, further drug testing, and support additional clinical trials in the next three years. To keep battling osteosarcoma with us, please consider continuing to support this work.

We're 45% of our way to our funding goal!



WATCH DR. SWEET-CORDERO DISCUSS HOW THE BATTLE OSTEOSARCOMA GRANT HAS IMPACTED HIS WORK.



Thank you for your generous contribution and we hope you will continue to support this work.

Donate Now

Osteowarrior Update



Charlotte Murdoff: Last April 2019, when we kicked off our Battle Osteosarcoma campaign, Charlotte was in remission. After a relapse in February 2020 in her right lung, Charlotte had a thoracotomy and began out-patient chemotherapy in March 2020. She's currently on a combination regimen, getting infused twice each week at UCSF. She completed her sophomore year via distance learning, which worked out well since she likely wouldn't have been able to attend school with her compromised immune system. Charlotte's summer will be filled with chemo infusion days, online biology class, time with family and friends, swimming, sewing and golfing. Much of Charlotte's genetic testing and analysis was delayed due to lab closures from COVID-19, but her team is back to actively working on a targeted therapy for Charlotte's metastasis.



Dylan Toma: When the Battle Osteosarcoma campaign launched last April 2019, Dylan had no evidence of disease and had been on an oral maintenance targeted therapy. While on therapy, he had minimal side effects and enjoyed his first year in middle school with his classmates. After a third relapse in September 2019 in his right lung, he had a thoracotomy and started out-patient chemotherapy from October 2019 to February 2020. Post chemotherapy, he currently has no evidence of disease and is on another oral maintenance targeted therapy regimen. He was able to fully participate in the school year with minimal interruptions and finished up 7th grade in our strange new world via distance learning. This summer, he looks forward to success with his sourdough starter, honing his cooking skills, connecting virtually with his friends on the Xbox, building puzzles and Legos in his offline time, and someday beating his mom at pingpong.



Thank You

