PDX USE IN CLINICAL TRIALS FOR TREATING COLORECTAL CANCER

Alexandra Deras, Scott Kopetz MD PHD, Preeti Marie Kanikarla PHD ,Melanie Wood, Maria Perez, April Vallian, Patricia Jensen loewe

The University of Texas MD Anderson Cancer Center GI, The University of Texas MD Anderson Cancer Center GI, The University of Texas MD Anderson Cancer Center GI, GSBS, University of Puerto Rico Medical, The University of Texas MD Anderson Cancer Center Gi, The University of Texas MD Anderson Cancer Center G

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center

Making Cancer History®

Introduction

- The third most commonly diagnosed cancer in men and women combined in the U.S..
- The second leading cause of cancer death in men and women combined in the U.S.
- 70% Of adults screened
- Colonoscopy at age 50 now lowered to age 45
- 30% of CRC diagnoses are under age 55.
- The 5-year relative survival rate for stage 1 and stage II colon cancer is 90%; the 5-year survival rate for patients diagnosed at stage III is 71% and stage IV is 14%.
- PDX:Tumor tissue that has been taken from a patient and implanted into mice for research purposes. Cancer drugs and other types of treatment may be tested on xenografts to see how well they work before they are given to the patient.

Objectives

- To analyze how PDX are turned into clinical trial for treating colorectal cancer. From tumors extracted from patient and implanted into immunocompromised mouse and treated with drugs to see if it viable for human testing. Afterwards clinical trial are started to test the drugs in colorectal cancer patients

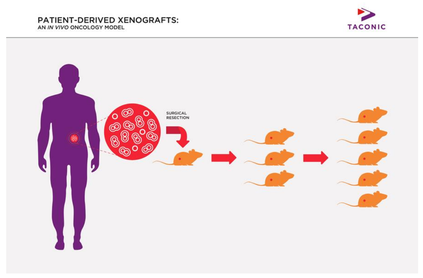


Fig. 1: Example of a PDX Model. Human tumor collected and surgically implanted into immunocomprised mouse and than removed. Removed tumor cut up and put into more mice.

Clinical Trial

- .The best does of LY3214996 with CETUXIAMB alone or with ABEMACIABLBE for patients with colorectal cancer that cannot be removed by surgery or has spread to other parts of the body.
- LY3214996/AMEMACICILB may stop the growth of tumor cells by blocking some enzymes needed for cell growth.
- Cextuxiamb is a monoclonal antibody that may infer with the ability of tumor cells to grow and spread

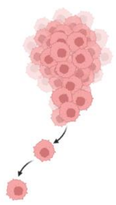


Fig. 3:. A 2D Model of a cells metastasis.

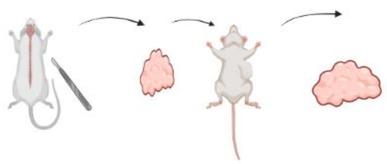
Methods

The methods of Protocol 2019-1016

1. Gets blood and tissues samples with the predictive biomarkers activity ad immune effects for the treatments.

.

2.Surgical implant them into immune comprised mouse Subcutaneous in matched patients it cetuximab refractory metastatic colorectal cancer. Remove the tumor and expand the tumor into more immune comprised mouse. Do some molecular profiling.



3.You can do pcr or western blots to test for DNA or rna in the drugs tested.

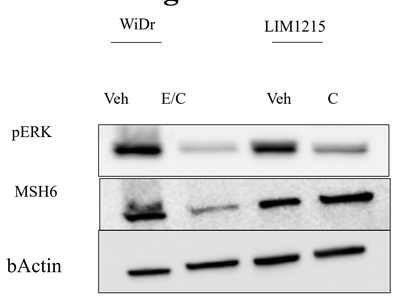
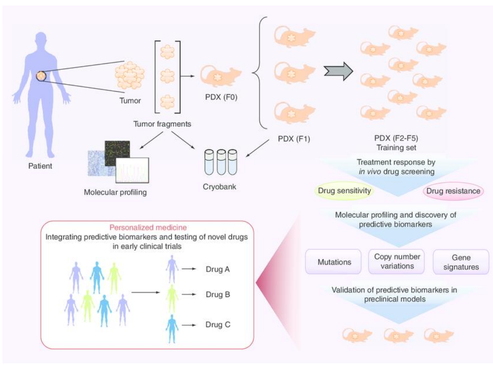
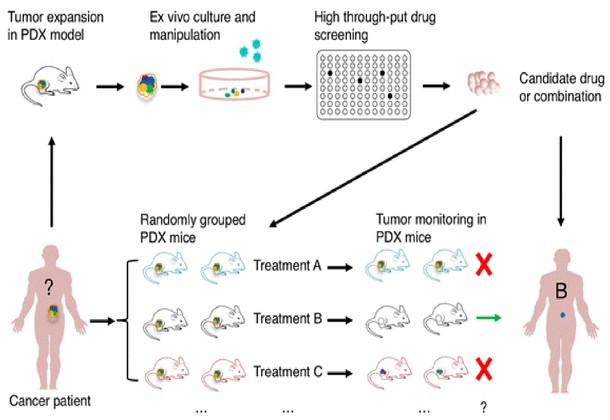


Figure 4: An example of Inhibition of MAPK pathway induces dMMR

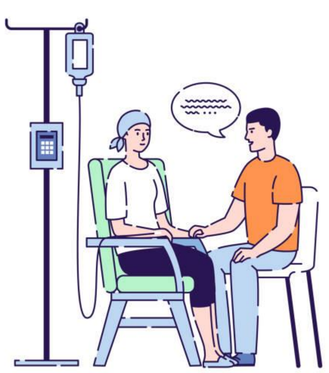
4.Expand the tumor into more mouse to test the combination of mouse with LY3214996 WITH CETUXIAMB alone or with ABEMACICLIB in two different mouse sets to test for biomarker response and mechanism of resistance in LY3214996 with CETUXIAMB and LY3214996 ,CETUXIAMB, and ABEMACICLIB.





.Clinical Trial: Patients

- 2 arms both start with 2 arms with dose escalation
- 1st arm: Erk ½ inhibitor LY3214996 orally and cetuxiamb over 1-2 hrs. Repeat every 28 cycle continuation depends on toxicity and progression
- 2nd arm b: Erk ½ inhibitor LY3214996 and cetuxiamble ABEMACILIB PO twice daily. Cycle evert 28 day depends on progression and toxicity.



Conclusions

- The PDX model is an effective way in treating patient with colorectal cancer as it mimic or somewhat predict the toxicity and its effectiveness.
- Protocol 2019-1016 I still ongoing therefore there is currently no results but its primary outcome measure is overall response and best response

References

1. Sia, Daniela & Moeini, Agrin & Labgaa, Ismail & Villanueva, Augusto. (2015). The future of patient-derived tumor xenografts in cancer treatment. Pharmacogenomics. 16. 10.2217/pgs.15.102.

2) Lai, Y., Wei, X., Lin, S. *et al.* Current status and perspectives of patient-derived xenograft models in cancer research. *J Hematol Oncol* **10,** 106 (2017). https://doi.org/10.1186/s13045-017-0470-7

3) Goto, Taichiro. 2020. "Patient-Derived Tumor Xenograft Models: Toward the Establishment of Precision Cancer Medicine" *Journal of Personalized Medicine* 10, no. 3: 64. https://doi.org/10.3390/jpm100300644)

Porta et al. Pain Digest Pain Pain

4) Porta et al. Pain Digest Pain Pain

6) Porta et al. Pain Digest Pain Pain

1) Porta et al. Pain Digest Pain Pain

2) Porta et al. Pain Digest Pain Pain

3) Porta et al. Pain Digest Pain Pain

4) Porta et al. Pain Digest Pain Pain

5) Porta et al. Pain Digest Pain Pain

6) Porta et al. Pain Digest Pain Pain