



Team Progress Updates

Van Andel Research Institute-SU2C Cancer Epigenetics Dream Team:

“The Epigenetics Dream Team II”



The Van Andel Institute–Stand Up To Cancer Epigenetics Dream Team builds on the success of the previous SU2C Epigenetics Dream Team projects in lung cancer and colorectal cancer and expands its work by focusing on epigenetic agents in myelodysplastic syndrome (MDS) and acute myeloid leukemia (AML). The current VAI–SU2C Epigenetics Dream Team also is investigating the use of vitamin C in conjunction with epigenetic drugs.

Among the specific milestones of the team are:

June 2021

- The Team has treated more than 550 patients in 13 clinical trials.
- Enrollment has completed in 7 of 13 trials. These seven trials are in deep correlative analysis phase.
- The Team anticipates opening a single-arm pilot study in Copenhagen, Denmark using Metformin as a therapeutic option in CCUS and lower-risk MDS patients in November 2021.
- Dr. Benjamin Youngblood from St. Jude Children's Research Hospital joined the VAI–SU2C Epigenetics Dream Team.

December 2020

- The Team has enrolled over 533 patients in 13 trials; three trials are now complete.
- The clinical trial evaluating guadecitabine in combination with atezolizumab in high-risk MDS and chronic myelomonocytic leukemia (CMML) patients shows a median overall survival of 15.1 months in the total cohort treated in our study, compared to 5-6 months historically in patients with MDS for whom the primary hypomethylating agent has failed.

June 2020

- The Team has enrolled 489 patients across 13 clinical trials, with 3 trials having been completed.
- Analysis of the initial Legacy Lung trial shows that treatment with epigenetic drugs leads to upregulation of viral defense pathways in T-cell recruitment to tumors being treated in patients.
- The Team published a paper in *Nature* showing that epigenetic drugs are capable of modifying the tumor microenvironment and inhibiting the premetastatic niche. Low dose DNA demethylation inhibitor therapy might serve as an important adjuvant following surgical resection of tumors.





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December 2019

- Laboratory studies indicate that co-treatment with Talazoparib and Azacitidine results in immune activation, and suggest the potential to target the immune system in order to induce anti-tumor effects, enhance efficacy of our combination treatment and improve clinical outcomes in AML.
- The Team has reported three partial responses in patients enrolled on their clinical trial testing SGI-110 with irinotecan in metastatic CRC patients.
- The Team has activated their clinical trial investigating ASTX727, a combination of decitabine and cedazuridine in patients with solid tumors.

June 2019

- The Team has completed the serial dose phase for their AML trial testing the combination of talazoparib with decitabine, showing that the drugs can be given together at full doses and is well tolerated.
- The Team has preliminary results showing that lung cancer patients being treated with epigenetic and immunotherapies combined see an increase in effector T cells compared to immunotherapy alone.
- The Team is continuing to accrue patients onto all their clinical trials, including MDS, CRC and GI patients.

December 2018

- The Team has enrolled 64 patients in their amended Legacy Lung Cancer Project.
- The Team is testing the benefit of combining an epigenetic drug with an anti-PD-L1 antibody to treat patients with myelodysplastic syndrome. No dose-limiting toxicities and immune-related adverse events were observed in their Phase I study. The trial is now in Phase II.
- Promising results have been observed in their Phase II trial in colorectal cancer where they are testing whether an epigenetic drug can reverse resistance to the chemotherapy agent called irinotecan.
- 24 patients with Acute Myeloid Leukemia (AML) have been enrolled in a Phase I clinical trial (target for Phase I: 36) in which the safety of combining an epigenetic drug and a PARP inhibitor is being tested. Extended survival has been observed in a few patients.

June 2018

- The Legacy Lung Cancer Project continues. The protocol was modified to: 1) move checkpoint therapy up front for simultaneous administration with each cycle of epigenetic therapy, and 2) give six months of epigenetic therapy (instead of two) to patients who stay on trial. Almost all patients on combined therapy are tolerating the initial cycles.
- Myelodysplastic Syndrome (MDS) Project: Nine MDS patients have been enrolled in a clinical trial in which patients are treated with immunotherapy.
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- Multiple Solid Tumor (MST) Project: This trial is enrolling at USC, where three patients are on treatment; two additional clinical sites will soon be activated.
- The colorectal cancer (CRC) trial is almost fully accrued. Ninety-one of 96 patients have been enrolled.
- Eighteen patients with acute myeloid leukemia (AML) have been enrolled in a Phase I clinical trial to test the safety of combining an epigenetic drug and a PARP inhibitor.
- The EV-1 pilot trial in MDS/AML has reached the target patient accrual of 20 patients, and the team is analyzing blood samples.
- The EV-2 trial enrollment has begun for a cohort of subjects who have clonal cytopenia of undetermined significance, a precursor to MDS. So far, the trial has enrolled 22 patients.

December 2017

- Enrolled 67 patients with advanced colorectal cancer in a clinical trial testing the epigenetic drug guadecitabine.
- Enrolled 20 MDS/AML patients in the clinical trial combining an epigenetic drug with vitamin C. The Team has observed that a single 500 mg Vitamin C tablet given daily was sufficient to restore normal vitamin C blood levels in the patients.
- Enrolled 15 patients with AML in a Phase I clinical trial where the safety of combining an epigenetic drug and a PARP inhibitor, is being tested. Extended survival has been observed in four patients.
- Continued clinical trials in lung cancer and MDS.

June 2017

- Continued to enroll patients in clinical trials.
- Completed enrollment in EVITA pilot project of randomized vitamin C supplementation in combination with epigenetic therapy in MDS and AML patients.

December 2016

- Continued to move forward with clinical trials in lung cancer, MDS, colorectal cancer, and AML, and the EVITA project on Vitamin C supplementation.