California Institute for Regenerative Medicine Grant to Fund Clinical Trial for Late-Stage Lung Cancer
We are excited to announce the receipt of a $12 million grant from the California Institute for Regenerative Medicine (CIRM), which will fund a new phase 1 clinical trial here at UCLA. This project, to be directed by Dr. Steven Dubinett in collaboration with the Thoracic Oncology Program’s Dr. Edward Garon, will investigate a new therapeutic combination for patients with previously untreated, advanced non-small cell lung cancer. Patients who are enrolled in the trial will receive the immunotherapy drug pembrolizumab in addition to CCL21 gene-modified dendritic cell (DC) therapy. This combination was devised in response to evidence that DCs expressing the CCL21 gene can encourage immune system cells called T cells to migrate into lung tumors, and increase anti-tumor T cell activity. However, Dr. Dubinett’s group has found that this CCL21 gene-modified DC therapy also increases expression of a molecule called PD-L1 in tumor cells, which has a negative effect on T cell activity. Since pembrolizumab operates by blocking the effect of PD-L1 on the immune system’s cells, it is possible that the combination of CCL21 gene-modified DC therapy with pembrolizumab will increase patients’ rate of response to therapy. The gene-modified DCs will be generated from patients’ own cells, and will be injected directly into their lung tumors on three separate occasions over a 42-day period. Patients will also receive pembrolizumab for up to one year after initiation of study treatment. We expect the trial to open to enrollment at UCLA Main Campus later this summer.

Those who are interested should contact Dr. Edward Garon for more information.

BMS CheckMate 817 Now Open for First-Line, High TMB NSCLC
Dr. Jonathan Goldman’s CheckMate 817 study is now open for previously untreated, stage IV or recurrent non-small cell lung cancer (NSCLC) patients who show a high tumor mutational burden (TMB). TMB is a measure of the prevalence of mutations in patients’ tumors, which may be associated with improved responses to treatment. Patients must not test positive for certain mutations called EGFR and ALK, which are sensitive to targeted therapies. Patients who are enrolled in this study will receive the immunotherapy drug nivolumab in combination with another immunotherapy drug called ipilimumab. This study is currently open to enrollment at UCLA Main Campus; UCLA’s satellite sites in Irvine and Porter Ranch; and the following TRIO-US sites: Bakersfield, CA, Grand Junction, CO, Hollywood, FL, Livingston, NJ, Redondo Beach, CA, San Luis Obispo, CA, Santa Maria, CA, SCORA, and Wichita, KS.

Those who are interested should contact Dr. Jonathan Goldman for more information.
Novartis CINC280A2201 Now Open to 2nd-Line Patients with cMET Mutation or High-Level Amplification

Dr. Edward Garon’s Novartis CINC280A2201 trial is now open for pre-treated, advanced non-small cell lung cancer (NSCLC) patients whose tumors are found to have either high-level amplifications or mutations in a gene called cMET. These patients must have received one prior line of systemic therapy for their cancer. The study also remains open for patients with either high-level amplification or mutation in the cMET gene, who have not received any prior systemic therapy for their cancer. All potential subjects must test negative for another targetable mutation called EGFR. Patients who are enrolled in the trial will receive treatment with a drug called INC280, which is an oral medication designed to target the cMET mutation. This study is currently open to enrollment at UCLA Main Campus.

Those who are interested should contact Dr. Edward Garon for more information.

ARRAY 382-201 Now Open for Advanced Solid Tumors

Dr. Jonathan Goldman’s ARRAY 382-201 study is now open for patients with advanced solid tumors, including those with lung tumors. In order to be eligible, patients must match one of the two following descriptions: 1) Patients with advanced solid tumors, who progressed on a PD-1/PD-L1 inhibitor-containing regimen as their most recent prior line of therapy. Prior treatment with a type of immunotherapy called a CSF-1R or CSF-1 inhibitor is allowed for these patients. OR 2) Patients with platinum-resistant ovarian cancer or pancreatic ductal adenocarcinoma, who have NOT received therapy with a type of immunotherapy drug called a checkpoint inhibitor. These patients also must NOT have received a prior CSF-1R or CSF-1 inhibitor therapy. All patients who are enrolled will receive treatment with ARRY-382, which is a CSF-1R inhibitor, in combination with the immunotherapy drug pembrolizumab. This study is open to enrollment at UCLA Main Campus.

Those who are interested should contact Dr. Jonathan Goldman for more information.

Novartis CPDR001C2101 Now Open for NSCLC Patients of Squamous Histology Only

Dr. Edward Garon’s CPDR001C2101 trial has reopened to enrollment for patients with advanced or metastatic NSCLC of squamous histology only. In order to enroll, subjects must not have received prior systemic therapy for their cancer. Patients who are enrolled will receive the chemotherapy drugs gemcitabine and cisplatin in combination with an immunotherapy drug called PDR001, followed by maintenance therapy with PDR001 alone. Along with Dr. Garon’s AstraZeneca POSEIDON trial, this study gives two options of immuno-chemotherapy for previously-untreated patients. Novartis CPDR001C2101 is open to enrollment at UCLA Main Campus and at UCLA’s satellite sites in Burbank, Pasadena, Torrance, Valencia, Ventura, and Westlake Village.

Those who are interested should contact Dr. Edward Garon for more information.
Our Program’s Dr. Aaron Lisberg is the lead author of a recent publication in the *Journal of Thoracic Oncology*, which was also co-authored by multiple members of the Thoracic Oncology team. The publication reports the results of Dr. Edward Garon’s Pembrolizumab Investigator Sponsored Trial (Pembro IST). Pembro IST was a clinical trial developed by our Program in response to our observation of improved clinical outcomes in non-small cell lung cancer (NSCLC) patients with EGFR mutations who were treated with an immunotherapy drug called pembrolizumab on a previous study at UCLA. Pembrolizumab has typically been less effective in NSCLC patients who have EGFR mutations than in the general patient population. However, we observed that EGFR mutated patients who had NOT previously received a type of drug called tyrosine kinase inhibitors (TKIs), which are targeted to EGFR mutated tumors, had improved clinical outcomes when treated with pembrolizumab. Based on this observation, Pembro IST was a study of pembrolizumab in TKI-untreated, EGFR mutant, advanced NSCLC patients who tested positive for a biomarker called PD-L1, which is used to predict patients’ likelihood of response to pembrolizumab.

Unfortunately, enrollment on this study was halted early due to an observed lack of efficacy of pembrolizumab treatment after 11 of 25 planned subjects were treated. Only 1 of these patients had an objective response to the treatment, and we found that this patient did not actually have an EGFR mutation as tests had originally indicated. Overall, observed treatment-related adverse events—meaning undesirable events experienced by the patient during treatment—were similar to those seen in prior studies with pembrolizumab, but 2 patient deaths within 6 months of enrollment were particularly concerning to the investigators. Due to the lack of efficacy of pembrolizumab in TKI naïve, PD-L1 positive, EGFR mutant advanced NSCLC patients in this study, the authors concluded that pembrolizumab is not an appropriate treatment choice for these patients.

**Journal of Thoracic Oncology Publication**