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Supplemental Appendix for:
Academic Cancer Center Phase 1 Program Development
Arthur Frankel et al.

ONLINE APPENDIX
SITE SUMMARY TEXT

Site #1 had an integrated phase 1 program in which individual physicians in hematology and oncology initiated studies and managed patients with their own research staff with the exception of a few "basket" trials. "Basket" trials refer to studies including several tumor types. The regulatory system provided continuous quality assurance—Q/A audits, approval of non-safety related deviations, and regular protocol management team meetings with principal investigators--PIs for adverse events or dose escalations. The Data and Safety Monitoring Committee--DSMC did quality control—Q/C audits on all phase 1 patients. Because of the excellence of the Q/A, protocol holds were very rare. Site #1 had an active marketing effort with a designated full-time employee, 4-5 community outreach talks/year, and E-blasts to 15,000 physicians/year. Philanthropy to phase 1 was $5 million last year. There were multiple certified and active cGMP facilities producing cell therapies, small molecule cytotoxic compounds, radioimmunoconjugates, and vaccines for phase 1 ISTs. Remarkably, site #1 held 57 INDs and had correlative laboratory or imaging studies for 53 trials.

Site #2 had a separate phase 1 program with physician leadership, assigned support personnel—nurse, administrative assistant, regulatory person, contracts person, coordinators, data managers, and pharmacology technicians. Site #2 used a "pod" system with a screening coordinator, treatment coordinator, data manager and pharmacology technician to handle 8 trials. No deviations of any kind were allowed. Q/C audits were performed on all ISTs after the first subject, after enrollment of 10% of the planned subjects and yearly. Study holds occurred occasionally. A special aspect of site #2 was the availability of advanced imaging resources such as 2-hydroxyglutarate magnetic resonance spectroscopy—2HG-MRS and arterial spin labeling magnetic resonance imaging—ASL MRI.

Site #3 had a partially integrated phase 1 program with some staff dedicated to "basket" trials. Site #3 had a large phase 1 program. The patient recruitment was among the highest observed. There was a pharmacokinetics—PK laboratory that performed institutional and contract PK assays. Regulatory oversight was supportive with permitted "deviations". PIs were able to present to the PRMC and IRB. The site #3 phase 1 program was remarkable for its size, successful patient recruitment, experienced and skilled research managers, and therapeutic vaccine research.

Site #4 had a separate phase 1 program in its first year of structured operation. The phase 1 unit had offices, exam rooms, patient waiting area, treatment rooms, an infusion area, and laboratory. There were full phase 1 facilities with adjacent offices, exam rooms, infusion area and laboratory. Q/C audits were performed quarterly and were constructive in nature. The program established a set of SOPs for on-boarding new investigators. Time to study initiation was 3.5 months. Some advertising and quarterly symposia were phase 1 directed. While the program was small, it had superb institutional support.

Site #5 had a separate phase 1 program for "basket" studies. There was a single dedicated physician leader with institutional support. There were 3 coordinators. There are no phase 1-directed offices, exam rooms, infusion rooms or laboratory. There was a tissue bank. Deviations were allowed. Q/A

audits by CRO personnel were done monthly, and Q/C audits by DSMC personnel were done 2-4 times per trial per year. There were weekly phase 1 meetings, and the median time to study initiation was 5 months. There were phase 1-specific SOPs. Remarkably, the small phase 1 team had 24 open trials and 89 accrued patients in 2015. This program stood out for its superb physician leadership.

Site #6 had a fully staffed independent phase 1 program with hematology, solid tumor, basket trials and ISTs. There was a dedicated physician leader and associate physician leader with very good institutional support. The program's administrator oversaw 16 coordinators, 4 regulatory coordinators, and 5 financial team members. There was a laboratory. The external Western IRB was employed with seven-day turnaround for pharma-sponsored trials. For ISTs, the local academic IRB was used. Minor deviations were allowed. CRO Q/A was done periodically, and DSMC Q/C audits were done once per trial per year. There were biweekly phase 1 meetings, and median time to study initiation was 4 months for industry trials and 6 months for ISTs. The program was rapidly growing with excellent physician and staff leadership, a robust portfolio of immunotherapy and immune checkpoint trials, targeted therapies, antibody-drug conjugates and novel cell therapies.

Site #7 was a new, expanding phase 1 program with basket trials, a dedicated physician leader and an enlarging staff including coordinators, research assistants, nurse, and manager. Impressively, they had staff participation in DSMC, PRMC and IRB meetings. Deviations occurred from time to time and did not lead to study interruption. Protocol exceptions were requested and approved by sponsors and IRB. There were guidelines for IRB reporting of deviations. Median time to study initiation was 3 months. Patient accrual was augmented by web-based and email communications. While currently small in number of trials and no ISTs, the program was growing rapidly with excellent patient accrual/trial. The program uniquely recruited patients from a wide geographic net—at least seven states.

Site #8 was an established, fully staffed phase 1 program with hematology, solid tumor, basket trials and ISTs. There was a single physician leader with excellent institutional support. There were 16 coordinators, 6 regulatory staff, and 4 data entry technicians. There was a dedicated phase 1 infusion area, office area and exam rooms. The director participated in PRMC and periodically DSMC and IRB meetings. The goal is to have zero protocol deviations, but if they do occur, they do not typically lead to study pause. There were periodic Q/A audits by the regulatory staff and quarterly audits by the DSMC Q/C staff of ISTs. Median time to study initiation was 4.5 months. There were a large number of industry trials and four ISTs. The program partnered with a fully integrated healthcare network including 40,000 providers, a quarter million "covered lives" through its health plan and a population base consisting of half of the state.

Site #9 had an integrated phase 1 program with 10 staff dedicated to "basket trials." Site #9 had the second largest number of phase 1 trials and ISTs and third highest patient accruals. Site #9 was outstanding for reversing delays for study activation.

Site #10 had a basket phase 1 program including hematology and solid tumors under new leadership with a dedicated physician leader with short study activation times, phase 1 program manager, clinical research coordinator, investigational pharmacist, navigator, funds for family lodging and travel, and

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identified nearby space for offices, exam rooms, infusion room, and laboratory. The institution provided prospective molecular genotyping of phase 1 patients.

Site #11 was a total phase 1 program with a devoted physician leader and growing staff including nurses and coordinators, a navigator, and two PhD level administrators to assist in protocol and grant writing. After the initial period of intense PK and toxicity assessments, patients were transferred to disease oriented team research management. There was access to regulatory and tissue processing personnel. There were phase 1 exam rooms and infusion chairs. The team focused on phase 1B studies with outstanding correlative science.

Site #12 was a one of the oldest phase 1 centers in the country with strong physician leadership and the highest ratio of phase 1 patients to total new cancer patients among all the sites. The site haa a high minority enrollment and had expertise on organ dysfunction, drug-drug interaction, and QTc monitoring.

Site #13 had a basket phase 1 program and has multiple phase 1B studies. The site offered patient tumor genomics through next generation sequencing without cost and uses the information to inform clinical trial selection.

Site #14 was a total phase 1 program with a single highly experienced physician leader assisted by three managers. This site had the highest number of phase 1 trials and ISTs and enrolled the most phase 1 patients of any of the studied sites. Importantly, the program had the second shortest trial activation time of any of the studied cancer centers. Startup time was reduced by prioritization of phase 1 trials over other trials at the PRMC and IRB and parallel work on contracts. This site had significant yearly philanthropy that facilitates special services including serial tumor biopsies during studies, rapid autopsies, a large dedicated staff and space for examinations, infusions and laboratory sample processing and storage.

Site #15 was a new, growing integrated phase 1 program with excellent institutional support and community outreach. There was very good accrual for the limited number of ISTs.

Site #16 had a fully integrated phase 1 program with outstanding institutional support, low costs, and extensive collaborations with basic science. They were one of three institutions to have early therapeutics-directed philanthropy and had the highest fraction of ISTs of any of the studied sites.