Insights From Building a New National Cancer Institute Community Oncology Research Program Site

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ABSTRACT

Background: The new National Cancer Institute (NCI) Community Oncology Research Program (NCORP) went live August 1, 2014; 34 sites were selected for the program, including 7 new sites that previously did not have a research grant from the NCI. This report describes the first year of a new program site.

Methods: Accrual, investigator and site participation, and number of open studies by the program over the first 12 months of the grant were compared to performance at our institution over the prior 12 months.

Results: During the pre-NCORP period, 84 patients were accrued to NCI-sponsored trials and 106 patients to non–NCI-sponsored trials. In year 1 of the new program, 140 were accrued to NCI-sponsored trials—a 66% improvement, and 109 patients to non–NCI-sponsored trials ($P = 0.013$ when comparing corresponding increases for NCI vs non-NCI trials). Success of the NCI-sponsored trials was associated with increased accrual to both treatment trials ($P = 0.03$) and Alliance for Clinical Trials in Oncology-sponsored trials ($P = 0.0001$).

Conclusions: NCORP implementation was associated with a significant ($P = 0.013$) improvement in accrual to NCI-sponsored trials that was immediate (1 year) and large (a 66% increase in accrual). In year 2, the intention is to increase cancer control studies; foster inclusion of radiation, surgical, gynecologic, and neurologic oncologists; and focus on minority outreach. Studies that accrue poorly will be assessed, and those accruing poorly on a national basis will be considered for closure. Studies accruing well nationally will be evaluated for barriers to local accrual.

INTRODUCTION

In recent years, the National Cancer Institute (NCI) has been challenged to do more research with less funding. Its cooperative groups were merged and all trials consolidated under the National Clinical Trials Network. In addition, the NCI's 2 community programs, the Community Clinical Oncology Program (CCOP) and the NCI Community Cancer Centers Program were replaced by the NCI Community Oncology Research Program (NCORP).[1,2] In August 2014, the NCI announced 34 institutions selected to receive NCORP community site grants. Most of these grants were awarded to sites that previously had a CCOP grant (n = 20) or mergers of multiple sites that previously had CCOP grants (n = 7). However, grants also were awarded to 7 new sites including the Aurora NCORP,[3] which is affiliated with the Milwaukee-based health provider Aurora Health Care.

Prior to being awarded the grant, Aurora was a main site for the National Surgical Adjuvant Breast Project and the Gynecologic Oncology Group and an affiliate site for the Radiation Therapy Oncology Group, 3 national groups that subsequently merged to form NRG Oncology. Aurora also was an affiliate site for Eastern Cooperative Oncology Group—American College of Radiology Research Network. Limited availability to trials from other cooperative groups was available through the Clinical Trials Support Unit.

In this report, the first year of the Aurora NCORP was compared to the year prior to its implementation to determine if there was any change in accrual patterns. The program's first-year performance also was compared to NCI expectations and the American Society of Clinical Oncology guidelines for excellence in community research.

METHODS

Terminology and Definitions: "NCI-sponsored trials" were defined as trials from any of the NCI-sponsored research bases. "Non–NCI-sponsored trials" were industry-sponsored studies, investigator-initiated studies, and registries managed by the Aurora Research Institute (Milwaukee, Wisconsin) requiring institutional review board (IRB) approval and patient consent.

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"Investigators" were identified as physicians who had completed human subjects training in accordance with Aurora IRB requirements and were registered NCI investigators. This report includes investigators who met these requirements any time during the interval specified.

An "open clinical trial" was a trial open to accrual for any portion of time during the interval specified.

Time Intervals: August 1, 2013, to July 31, 2014 was the year "prior to NCORP;" "year 1" of the program was August 1, 2014, to July 31, 2015.

S*oftware and Statistical Analysis:* Via Oncology™ (Via Oncology, Pittsburgh, Pennsylvania) is a clinical decision support program[4] that was added to the electronic health record (Epic Systems, Verona, Wisconsin).[5] It prioritizes treatment choices by efficacy, followed by toxicity and then cost, and assists medical oncologists with treatment options. The system, which went live at our organization on November 3, 2014,[6,7] is configured to prioritize clinical trial options when available.

Patients with cancer were recorded and classified by the Aurora Health Care Cancer Registry. The accrual of patients to clinical trials was calculated based on the total number of new analytical cases recorded for the last complete year.

All categorical variables were described as frequencies and percentages, and comparisons across categories were made using chi-square or Fisher's exact test as appropriate. When expected frequencies were less than 5, including zero, Fisher's exact test was used. All continuous variables were described as mean, median, standard deviation (SD), and range of minimum-to-maximum values. Multivariate logistic regression was used to identify predictors of the NCORP accrual. For all statistical tests, alpha ≥ 0.05 was used as level of significance. All statistical analysis was done using SAS version 9.4 (SAS Institute, Cary, North Carolina).

Monthly Reports: The NCORP Update is a monthly report e-mailed to all investigators and other members of the clinical trials community (Appendix). It provides accrual metrics categorized by investigator, site, study, research base, and by oncology specialty. It also includes a summary of accrual for month- and year-to-date. The NCORP Open Trials document is updated monthly and sent with the NCORP Update. Both documents are restricted to a single page to encourage routine readership. The monthly program meeting is attended by principal investigators, the program administrator, the clinical trials director and the oncology clinical trials manager. The purpose of the meeting is to provide a forum of regular dialogue regarding program successes, challenges, and needs.

Research Bases: Prior to the NCORP, Aurora was a member of Eastern Cooperative Oncology Group – American College of Radiology Research and NRG Oncology. During year 1 of the program, Aurora added the following research bases: Alliance for Clinical Trials in Oncology (Alliance), University of Rochester Cancer Center, and Wake Forest University. The Cancer and Leukemia Group B, American College of Surgeons Oncology Group, and North Central Cancer Treatment Group merged to form the Alliance, whereas the University of Rochester Cancer Center and Wake Forest are research bases with special interest in cancer control research.

RESULTS

Aurora Tumor Registry: The total number of cancer patients seen from August 1, 2013, to July 31, 2015, was 15,114. Non-Hispanic/non-Latino whites numbered 13,208; minority patients totaled 1,906 (12.6%). Prior to the NCORP, 7,065 new cancer patients were seen compared to an estimated 8,049 new patients in year 1.

Number of Trials Open, Investigators: Prior to NCORP, there were 49 NCI-sponsored trials and 30 non–NCI-sponsored trials. During year 1, NCI-sponsored trials increased to 63 and non-NCI-sponsored trials increased to 45. The number of NCI trials open as a percentage of all open trials was not significantly different between the 2 periods ($P = 0.61$). There were 63 investigators prior to the NCORP and 65 during year 1.

Accrual Rate to NCI Clinical Trials: Of the 7,065 patients in the tumor registry, 84 (1.2%) were accrued to NCI-sponsored trials prior to the NCORP vs 140 of 8,065 (1.7%) during year 1.

Accrual to NCI vs Non-NCI: Prior to the NCORP, 84 patients were accrued to NCI-sponsored trials and 106 patients to non–NCI-sponsored trials. During year 1, 140 were accrued to NCI-sponsored trials and 109 to non–NCI-sponsored trials. This change was a 66% improvement in accrual to NCI-sponsored trials, which is statistically significant compared to the corresponding increase in non–NCI-sponsored trials ($P = 0.013$).

Accrual by Minority Status: Eight of 84 accruals (10%) prior to the NCORP were minority patients, while 15 of 140 accruals (11%) during year 1 were minority patients ($P = 0.8$).

Accrual by Treatment or Cancer Control: Accrual to treatment trials increased from 72 to 132 after year 1; accrual to cancer control trials dropped from 12 to 8 ($P = 0.03$), respectively.

Accrual by NCORP Research Base: There has been a significant change in accrual by research base ($P < 0.0001$), except for Wake Forest, which experienced no increase during the study period. The Alliance experienced the greatest increase (from 7 to 46), and the University of Rochester Cancer Center accruals rose from 0 to 5 (Table 1).

Accruals by Oncology Specialty: During year 1, medical oncologists increased accruals from 72 to 119; radiation oncologists from 7 to 9, surgical oncologists from 0 to 6, and neurologic oncolo-

gists from 0 to 3. In contrast, gynecologic oncologists decreased accruals from 5 to 3. There was no difference in accrual by specialty from the year prior to the NCORP to year 1 ($P = 0.1$).

Accrual by Investigator: The Aurora program included 61 investigators: 37 accrued 1 or more patients; 24 accrued no patients. Mean accrual per investigator was 2.3 (SD: 3.2, range: 0-17). The median was 1 accrual per investigator; the mode was 0 accruals (Figure 1).

Accrual by Site: There were 19 program sites. Mean accrual by site was 7 (SD 6, range: 0-22). Both the median and mode were 5 accruals per site.

Accrual by Study: During year 1, there were 63 open NCI-sponsored clinical trials; 39 accrued at least 1 patient, and 24 trials had no accruals. Eight studies had no accrual for more than a year, and 5 trials had no accrual for 2 years. Mean accrual per study was 2.2 patients (SD: 3.1, range: 0-14).

Accrual by Oncology Specialty: For NCI-sponsored open studies, mean number of accruals per study was 2.2. Medical oncology had the highest number of accruals (3.3), while gynecologic oncology had the fewest accruals (0.3) (Table 2).

Table 1. Accrual by Research Base

Research Base	Accrual Prior to NCORP	Accrual in NCORP
ECOG-ACRIN	35	38
NRG Oncology, NSABP, RTOG and GOG	26	24
Alliance, CALGB, NCCTG and ACOSOG	7	46
University of Rochester Cancer Center	0	5
Wake Forest	0	0
Southwestern Oncology Group (SWOG) through CTSU	16	27
Total	**84**	**140**

Abbreviations: ACOSOG, American College of Surgeons Oncology Group; CALGB, Cancer and Leukemia Group B; CTSU, Clinical Trials Support Unit; ECOG-ACRIN, Eastern Cooperative Oncology Group – American College of Radiology Research Network; GOG, Gynecologic Oncology Group; NCCTG, North Central Cancer Treatment Group; NSABP, National Surgical Adjuvant Breast Project; RTOG, Radiation Therapy Oncology Group.

Figure 1. Accrual By Investigator in the Aurora NCORP

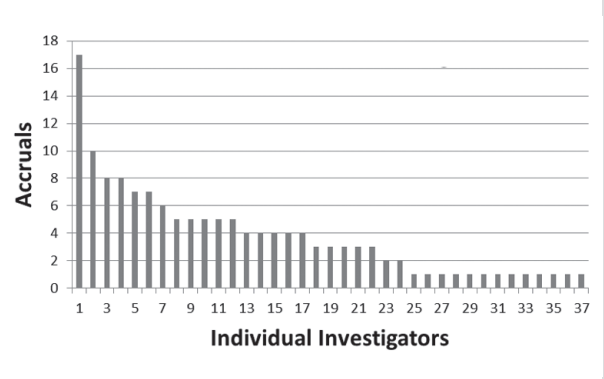


Table 2. Ratio of Accrual to Studies Open by Oncologic Specialty

Oncologic Specialty	Accrual	Number of Studies Open	Ratio
Medical oncology	119	36	3.3
Radiation oncology	9	7	1.3
Gynecologic oncology	3	11	0.3
Surgical oncology	6	7	0.9
Neurologic oncology	3	2	1.5
Total	**140**	**63**	**2.2**

DISCUSSION

Accrual to NCI-sponsored trials increased 66% with formation of the Aurora NCORP. This increase was significantly greater than accrual to non–NCI-sponsored trials open during the same period. These findings are consistent with the observations of other community sites that received NCI grants for community cancer research.[8,9]

The 140 Aurora program accruals fall short of the 200 total accruals required to meet NCI's definition of a "high-performing" community site.[10] Accrual as a percentage of patients seen improved from roughly 1% to 2% in our program. This contrasts with the total accrual goal set by the American Society of Clinical Oncology (ASCO) of 10% of patients to all clinical trials[11,12] and implies that an accrual of approximately 800 patients at our institution is required to achieve excellence, as defined by ASCO.

Accrual improvement was associated with increased accrual to treatment trials as opposed to cancer control trials. NCI anticipates that a program site should accrue equally to cancer treatment and cancer control studies,[10] and aggregate data from all NCORPs demonstrated this to be typical.[10] This implies that accrual to treatment trials was acceptable at this site and that there is an opportunity for increased accrual in cancer control trials.

Increased accrual also was associated with increased accrual to Alliance-sponsored trials. It is likely this is related the availability of practical trials for common cancers from the Alliance and increased awareness of these trials after the Aurora program added the Alliance research base.

Increased accrual of minority patients was proportional to increased accrual in general. Relative accrual to minority trials was stable. The percent of minorities enrolled in clinical trials was 10%, while the percent in Aurora's tumor registry was 12%. This suggests that the highest minority accrual the program is likely to achieve is 12%, and published strategies for improvement of

Appendix. The NCORP Update, A Monthly Report E-mailed to All Investigators and Other Members of the Clinical Trials Community

August 19, 2015

NCORP update

Dear colleagues,

Welcome to the **year-end NCORP update.** As you know, the first year of the NCORP grant ended July 31, 2015. All totaled, 140 patients were enrolled in NCORP trials **– 70% toward our goal of accruing 200 patients to NCI sponsored trials**. While this fell short of our target, it was an incredible 66% improvement over the prior year's enrollment (84 accruals from August 1, 2013 to July 31, 2014). We're excited to take this momentum forward in the second year.

Special thanks to all the physicians who enrolled patients into NCORP trials this year. Dr. Mike Mullane finished the grant year as the top investigator, with 17 enrollments. Aurora Cancer Care-Racine was our highest enrolling site, with 22 patients accrued.

We look forward to updating you as we enter year two as an NCORP community site.

Sincerely,

Tom Saphner, MD, FACS
Mike Thompson, MD, PhD

Jan DeBartolo, Manager, Clinical Trials
Neha Glandt, NCORP Administrator

PHYSICIAN	
Mullane	17
Bandealy	10
Halaweh	8
Shamah	8
Nawaz	7
Ruggeri	7
Santosh-Kumar	6
Haider	5
Maul	5
Patel	5
Tjoe	5
Virani	5
Jeffreys	4
Qamar	4
Sanchez	4
Saphner	4
Thompson	4
Choucair	3
Flejsierowicz	3
Jella	3
Kamelle	3
Naida	3
Davis	2
Gautam	2
Bastin	1
Gould	1
Matthaeus	1
McGartland	1
Mikkelson	1
Oesterling	1
Peliska	1
Pincus	1
Rodrigues	1
Rohde	1
Vanderwall	1
Yetter	1
Ziaja	1
Total	140

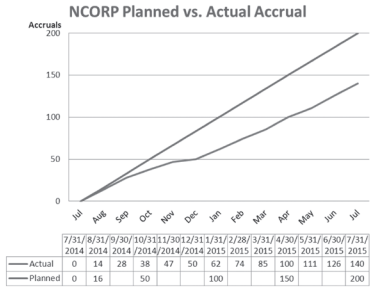
LOCATION	
Racine	22
St. Luke's	19*
BayCare	18
Kenosha	11
Grafton	10
Marinette	8
Sinai	8
Lakeland	7
Sheboygan	7
Burlington	5
Oshkosh	5
Two Rivers	5
West Allis	4
Good Hope	3
Waukesha	3
Summit	2
Menomonee Falls	1
Total	140

SPECIALTY	
Medical	118
Radiation	10
Surgical	6
Gynecologic	3
Neurology	3
Total	140

STUDY TYPE	
Treatment	132
Cancer Control	8
CCDR	0
Total	140

*St. Luke's and South accruals are now combined

STUDY NAME	
E5508 - M Lung	14
C80702 - M Col.	12
A031201 - M Pros.	11
C90203 - Neo Pros.	8
E1912 - CLL	7
E1A11 - Myelo.	6
S0931 - A Kid.	6
AO41202 - CLL	5
S1207 - A Br.	5
S1304 - R/R MM	5
B43 - A. BrCA	4
E1412 - Lymph.	4
R1203 - A. End/Cerv.	4
S1007 - A Br.	4
A011104 - Br	3
A071102 Neuro	3
B47 - A Br.	3
GOG 0274 - A. Cerv.	3
SWOG S1216 - M.Pros	3
A011202 - A Br.	2
B52 - Neo Br.	2
E2112 - M Br.	2
R0924 - Pros.	2
S1211 - Myelo.	2
AZ11102 - Neo Br.	1
B51 - Neo Br.	1
B55 - A Br.	1
E2108 - M Br.	1
E2810 - M Kid.	1
E2905 - MDS	1
E3A05 - HR MM	1
E3A06 - Myelo.	1
GOG 0213 - M Ov.	1
GOG 0238 - M Ute.	1
S1400B Lung	1
Total	140



	7/31/2014	8/31/2014	9/30/2014	10/31/2014	11/30/2014	12/31/2014	1/31/2015	2/28/2015	3/31/2015	4/30/2015	5/31/2015	6/30/2015	7/31/2015
Actual	0	14	28	38	47	50	62	74	85	100	111	126	140
Planned	0	16		50			100			150			200

Aurora Health Care

minority involvement[13-17] may not result in a decisive increase in accrual. Identification and quantification of minority patients who are not documented in the Aurora tumor registry may be an opportunity for improved minority accrual.

Accrual by investigator was highly variable; 24 of 61 total investigators had no accrual at all. The observation that physicians commonly complete registration to become an investigator and complete human subjects training but fail to accrue patients to trials is not new.[9] Medical oncologists accrued the most patients, followed by radiation oncologists and surgical oncologists, but the changes in accrual pre- and post-NCORP by specialty were not significant at this institution. This distribution of accrual by oncologic subspecialty is consistent with the literature.[9] It has been suggested that a minimum of 4 accruals to NCI-sponsored trials be required to maintain clinical investigator status.[18]

Accrual by study also was highly variable. Eight of the NCI studies had no accrual for a year, and 5 NCI studies had no accrual for 2 years. Two of these trials are accruing well nationally, and investigation of local barriers is underway. Three of the trials are not accruing well locally or nationally and are candidates for closure.

The mean number of accruals for an open trial at our program was 2.2, but the number of accruals for each open study varied greatly by oncologic subspecialty (range: 0.3-3.3). This could be interpreted as a guide to the types of trials to open to maximize accrual, or as a clue to the specific subspecialties that may have the greatest potential for increased accrual in the future.

Many activities were initiated during year 1 that likely improved accrual, including the initiation of Via Oncology—a clinical decision support program that prioritizes clinical trials, the NCORP Monthly Update, the NCORP Open Trials list, the monthly program meeting, and many others.[19,20] These activities were described qualitatively in the Methods section because it is likely they related to increased accrual, but they were not mentioned in the Results section because it was not possible to individually quantify their effects.

The NCORP grant was associated with a large (66%), significant, and immediate ($P=0.013$ at 1 year) improvement in accrual. Now in its second year, the Aurora NCORP acknowledges the following observations and opportunities:

- Cancer treatment studies historically have been the most successful at Aurora NCORP, but the greatest opportunity for increased accrual is cancer control studies.
- Medical oncologists are central to a successful community research program, but the greatest opportunity for enhanced accrual lies with radiation oncology, surgical oncology, gynecologic oncology, and neurologic oncology trials.
- Minority accrual is close to expected based on our registry data but if there are patients not captured in the registry, they may be a potential source of accrual growth.
- Studies that accrue poorly at the Aurora program and nationally will be closed. Studies that accrued poorly at Aurora but accrue well nationally will be evaluated for local barriers, as they may be a potential source of increased accrual.

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