

# IMPACT OF DIRECT PHYSICIAN-TO-PHYSICIAN CONTACT ON ACCELERATING ONCOLOGY CLINICAL TRIAL ACCRUAL IN MULTIPLE TUMOR TYPES

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## BACKGROUND

The development of more effective oncology agents is critically dependent on the completion of clinical trials. Currently, >4000 oncology trials listed on www.clinicaltrials.gov are accruing pts in the United States, but no more than 5% of all adult cancer patients actually participate in a clinical trial during the course of their therapy. This number has changed little since the 1980s, forcing pharmaceutical companies to focus their enrollment initiatives overseas.<sup>1</sup> Barriers to participation in clinical studies remain two-fold: patient skepticism and lack of investigator engagement. Patient hesitancy has been associated with discomfort with or not understanding randomization, fear of being a "guinea pig," insurance difficulties, or concerns about cost and convenience.<sup>2</sup> These perceptions are exacerbated by a lack of patient understanding on what clinical studies specifically entail: the concepts of blinding, placebo controls, randomization, and clinical realities. It is therefore vital that clinical investigators, those bringing the study to patients, have a strong understanding of their studies, what they entail, and how best to convey their benefit to the patient in an easy to understand manner. Although nurses frequently oversee the formal consent process, patients look to physicians to guide their decision-making, and whether the physician implicitly or explicitly endorses the trial has a strong influence on cancer patients' choices. In fact, of all patients approached with a trial, 75% consented but no more than 20% of patients who were eligible were offered a trial – illustrating that in the vast majority of instances, it is the investigator who is the gatekeeper to successful clinical trial accrual.<sup>3</sup>

To overcome these barriers, DAVA Oncology initiated strategies to improve clinical trial accrual that optimize trial enrollment and engagement through direct physician-to-physician intervention.

<sup>1</sup>Lippman ME, Chabner BA: Overview of Proceedings of the NIH Consensus Development Conference on Adjuvant Chemotherapy and Endocrine Therapy for Breast Cancer, NCI Monographs No. 1. Bethesda, MD, National Cancer Institute 1986

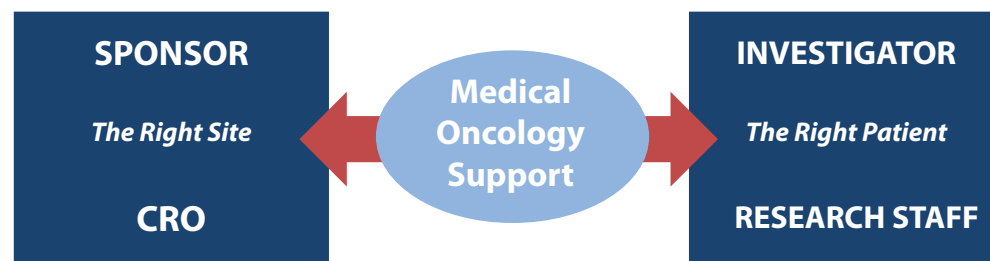
<sup>2</sup>Grant C, Cissna K, Rosenfeld L: Patients' perceptions of physicians communication and outcomes of the accrual to trial process. Health Commun 12:23-39, 200

<sup>3</sup>Siminoff LA, Ravdin PM, Colabianchi N, et al: Doctor-patient communication patterns in breast cancer adjuvant therapy decisions. Health Expect 3:26-36, 2000

## OBJECTIVE

As research has shown, investigators (and sub-investigators) are the most important drivers for patient accrual to oncology clinical trials. We have therefore implemented an investigator-focused strategy to increase patient enrollment to oncology clinical trials. Our goals are to overcome protocol and site-specific barriers to accrual through multiple enrollment strategies, primarily: site visits and phone interactions, direct peer-to-peer investigator education through accrual workshops, and increasing the pool of potential patients through referral network outreach.

## Maximizing Trial Enrollment



- Prioritization of sites based on protocol-specific accrual potential
  - » Access to targeted patient population
  - » Impact of concurrent studies in the same pt population

- Pro-active identification of pts potentially eligible for protocol
  - » Maintain interest in study and awareness of protocol
  - » Provide clarity on eligibility criteria and screening requirements

## METHODS

### Medical oncologist directed enrollment strategies to accelerate clinical trial enrollment.

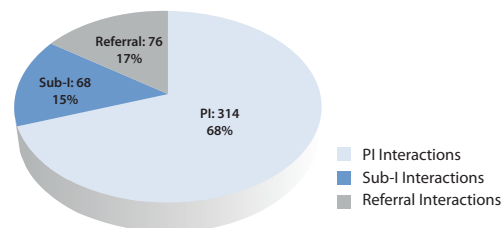
1. Implement site-specific strategies and tactics through peer-to-peer interactions, including:

- Frequent protocol-related discussions with investigators and research staff through on-site visits, conference calls, and individual phone conversations.
- Accrual workshops that highlight clinical and scientific rationale through case-based learning and, more importantly, provide a forum where investigators can reassess their stance on issues within the protocol after hearing from their respected peers and becoming more acutely aware of the standard of care.
- Maximizing the recruitment potential of each site on a trial by identifying, mapping and engaging key referring physicians in order to expand the pool of potential patients. Moreover, by increasing community awareness of a study and adding bandwidth to each site, DAVA reduces the amount of work individual investigators must expend to ensure that a clinical trial is successful. In a Phase III study, nearly one-third of total physician-to-physician interactions were made to sub-investigators and referral physicians in the vicinity of the participating site.

Figure 1: Physician-to-Physician Interaction Strategy: Expanding the Pool of Potential Patients

Interaction Type	Count	Percentage
PI Interactions	314	69%
Sub-I Interactions	68	15%
Referral Interactions	76	17%

### Physician-to-Physician Interaction



2. Track accrual performance of individual sites

- Correlate medical oncologist interactions with actual patient enrollment.
- Analyze changes in site-specific accrual rate.
- Adjust strategies and tactics to maximize enrollment.
- Implement updated site-specific enrollment plans – developed for each site, enrollment plans are a guide for where the site has been, where it is now, and where it is going. Patient tracking, referral flow & operations management are governed by these documents.

## RESULTS

The implementation of direct physician-to-physician intervention resulted in a measurable improvement in the monthly accrual to each of 7 oncology trials. In the two most recent phase III studies, enrollment increased 27.7% per site/month during a 15 month engagement, and 16.3% during an 18 month engagement, respectively.

Table 1.

Trial	Accrual Before*	Accrual After*	% Increase
1	0.11	0.14	27.7
2	0.23	0.27	16.3

\*Patients per site per month.

By stratifying each investigator based upon historical screening & enrollment performance, DAVA focuses its resources on those sites that have the highest patient enrollment potential. In a Phase III study, 34% of the participating sites enrolled 72% of the total patients on the trial. These sites were identified and prioritized to maximize patient yield for the study.

In regards to accrual workshops, attending investigators saw an average enrollment increase of 16%-86% with four accrual workshops over the course of a Phase III study.

Case Study 1: Accelerating Phase III clinical trial enrollment 246% above forecasted rate

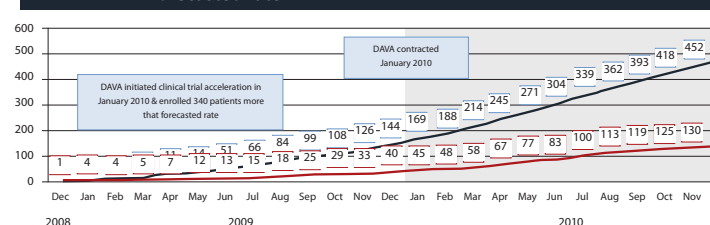
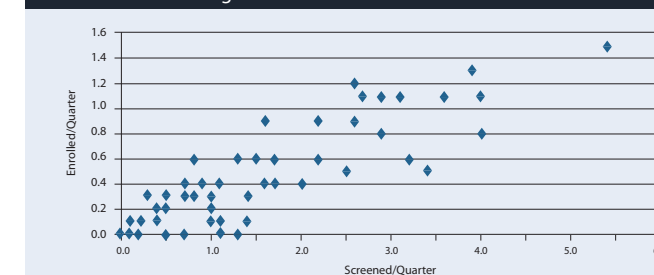


Figure 2: Performance Segmentation: Individualized Strategies for Each Investigator



Investigator Performance Segmentation	Investigators	Screening	Enrollment
High Performance	23 (34.3%)	324 (68.8%)	103 (71.5%)
Average Performance	18 (26.9%)	108 (22.9%)	27 (18.8%)
Below Average Performance	26 (38.8%)	39 (8.3%)	14 (9.7%)
Awaiting Initiation	1 (1.5%)	0 (0.0%)	0 (0.0%)
Total	68	471	144

## CONCLUSIONS

The tactful implementation of direct physician-to-physician contact and other site-specific strategies based upon performance potential, enrollment challenges and patient flow have been successful in significantly accelerating clinical trial accrual in 7 trials initiated to date. Expanding the pool of potential patients by focusing on referring practitioners & sub-investigators for one-third of total site interactions led to a phase III study enrolling 340 patients above its forecast.

## SUMMARY

Accrual to oncology clinical trials in the US is poor and significantly lagging behind the ROW. No factor has been as pivotal in this poor performance as the lack of investigator engagement due to limited buy-in to trial rationale, poor education on the intricacies of the study, and limited resources with which to carry out the study. An investigator-focused approach to identify and overcome site-specific barriers to accrual can significantly improve accrual and, ultimately, the timely completion of clinical trials in the US. DAVA Oncology's dedicated team of medical oncologists can oversee the operational aspects of increasing community awareness of a study and adding bandwidth to each site while decreasing the amount of work individual investigators must expend to ensure that a clinical trial is successful.

## Acknowledgments

The development of this poster was supported by DAVA Oncology, LP.

White Paper, 2011 ASCO Annual Meeting, June 4-8, 2011, Chicago, IL.