

BACKGROUND

The development of more effective oncology agents is critically dependent on the completion of clinical trials. Currently, >4000 oncology trials listed in www.clinicaltrials.gov are accruing pts in the United States

- Only 3-5% of new cancer pts participate in clinical trials
- Most trials do not meet their projected accrual timelines
- Enrollment problems delay more than 70% of clinical trials from one to six months in the United States¹

For faster and less expensive trial completion, industry and government sponsors move their clinical trials to less developed countries

- Number of countries serving as trial sites outside the United States more than doubled in the past 10 years
- Number of investigators based outside the United States has grown by 15% annually, while the number of US-based investigators has declined by 5.5%²

Hurdles to patient enrollment in the US

- 60% of newly diagnosed cancer patients are not told about clinical trials as a treatment option¹
 - » Increased standard treatment options available
- Patients concerns about participation in research trials
 - » Fear of randomization to placebo
- Practice concerns about increased investment in time and resources to allow trials to open at their sites

Barriers to accrual^{3,4}

Site-specific barriers to accrual

- Perception of protocol unavailability
- Actual protocol unavailability
- Protocols competing for similar pt population

Protocol-specific barriers to accrual

- Perception of pt ineligibility
- Complex inclusion/exclusion criteria
- Cumbersome screening process

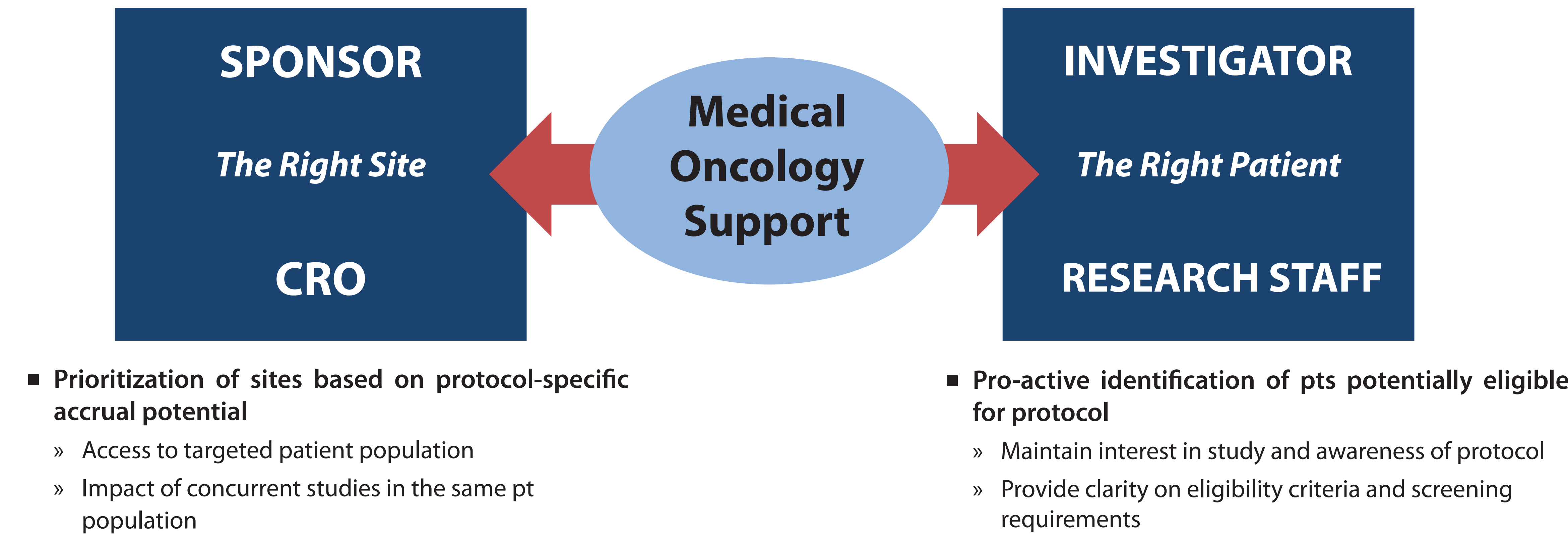
OBJECTIVE

Investigators (and sub-investigators) are the most important drivers for patient accrual to oncology clinical trials.

We implemented an investigator-focused strategy to increase patient enrollment to oncology clinical trials. Our goals were to overcome protocol and site-specific barriers to accrual through:

- Site prioritization: site-specific enrollment strategies
- Site engagement: medical oncologist-mediated communication strategies

OVERCOMING ACCRUAL CHALLENGES



METHODS

Site Prioritization

- Diagnosis of current accrual performance, protocol-specific barriers, and investigator interest and attitude
- Develop site-specific strategies and tactics to overcome accrual barriers and accelerate enrollment

Table 1: Assessment of accrual potential for study sites

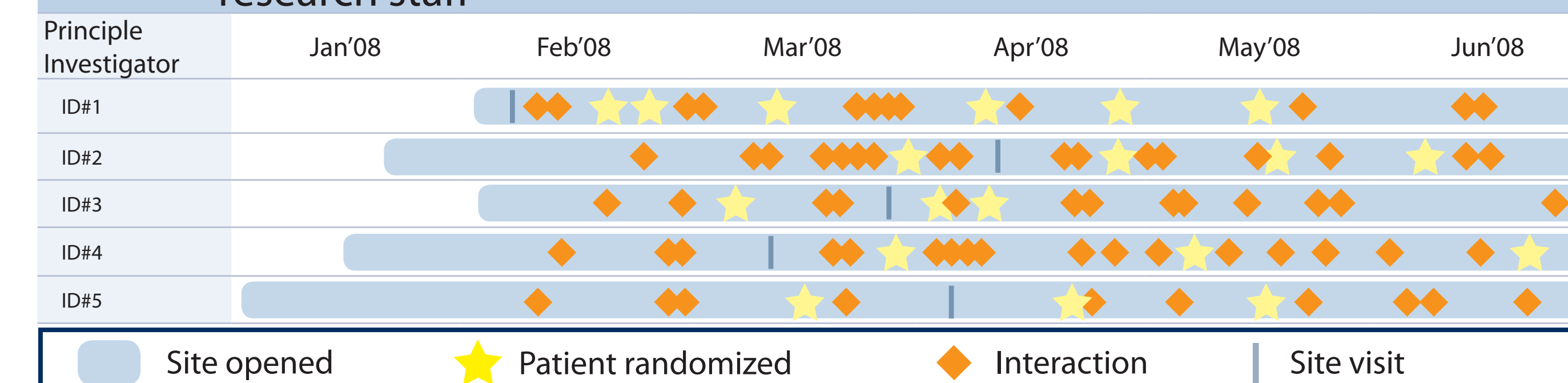
Patient Potential	Site Infrastructure	Active Studies in Selected Indications
<ul style="list-style-type: none"> Location Setting Reputation 	<ul style="list-style-type: none"> IRB Laboratory Study coordinator 	<ul style="list-style-type: none"> Potential for competition Eligibility criteria Target enrollment Priority

Site Engagement

Medical oncologist directed accrual intervention as defined in a site-specific enrollment plan

- Implement site-specific strategies and tactics through peer-to-peer interactions, including:
 - Accrual workshops to highlight clinical and scientific rationale through case-based learning
 - Frequent protocol-related discussions with investigator and research staff through on-site visits, conference calls, and individual phone conversations
- Track accrual performance of individual sites
 - Correlate medical oncologist interactions with actual patient enrollment
- Analyze and adjust
 - Analyze changes in site-specific accrual rate
 - Adjust strategies and tactics to maximize enrollment
 - Implement updated site-specific enrollment plan

Figure 1. Example of tracking number of interactions with investigators and research staff



RESULTS

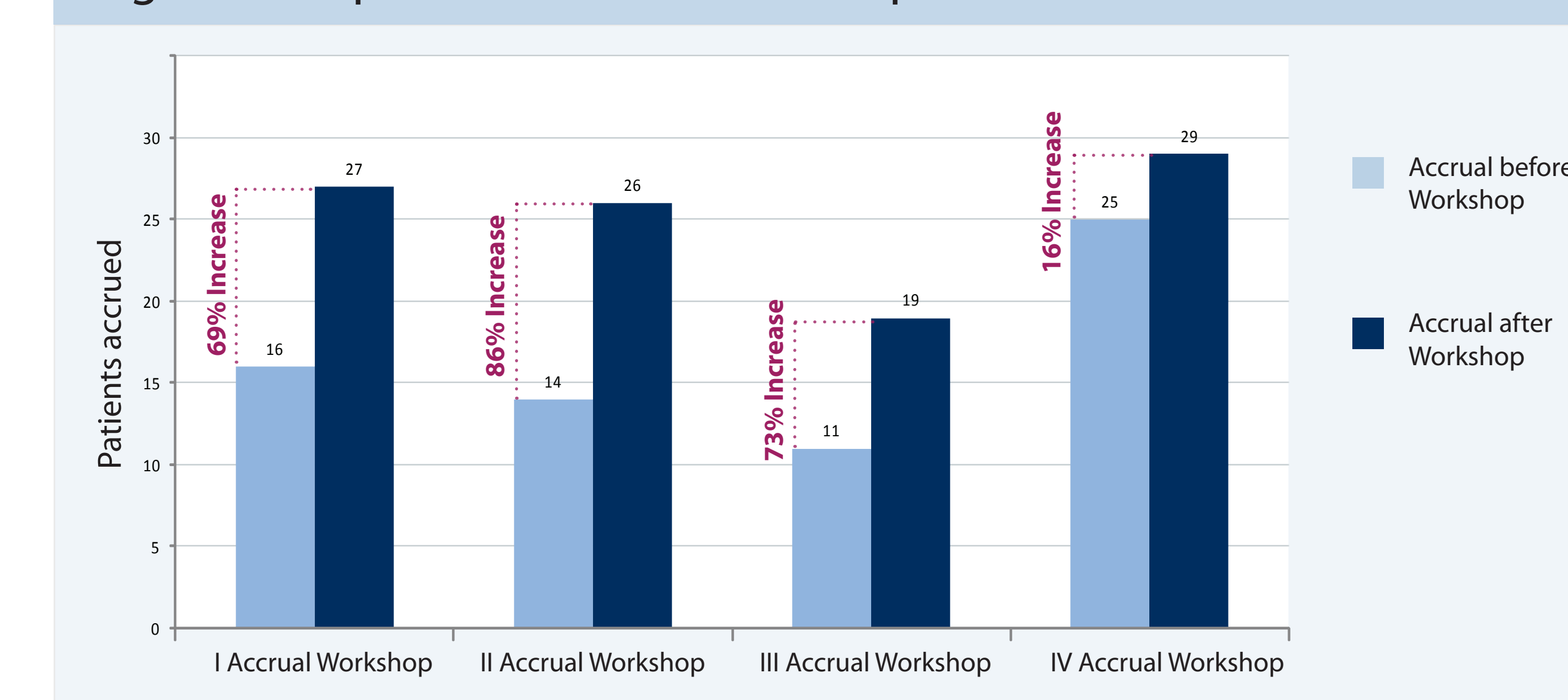
We evaluated the performance of our investigator-focused strategy in five different oncology clinical trials over a 12 month period:

- Trials included single arm as well as randomized oncology trials in four different tumor types; all trials were considered to be behind projected accrual timelines
- Trials had been open and accruing between 6-16 months before our intervention
- Impact of the interventions were measured by comparing the monthly accrual rates before and after implementation of our investigator-focused strategy

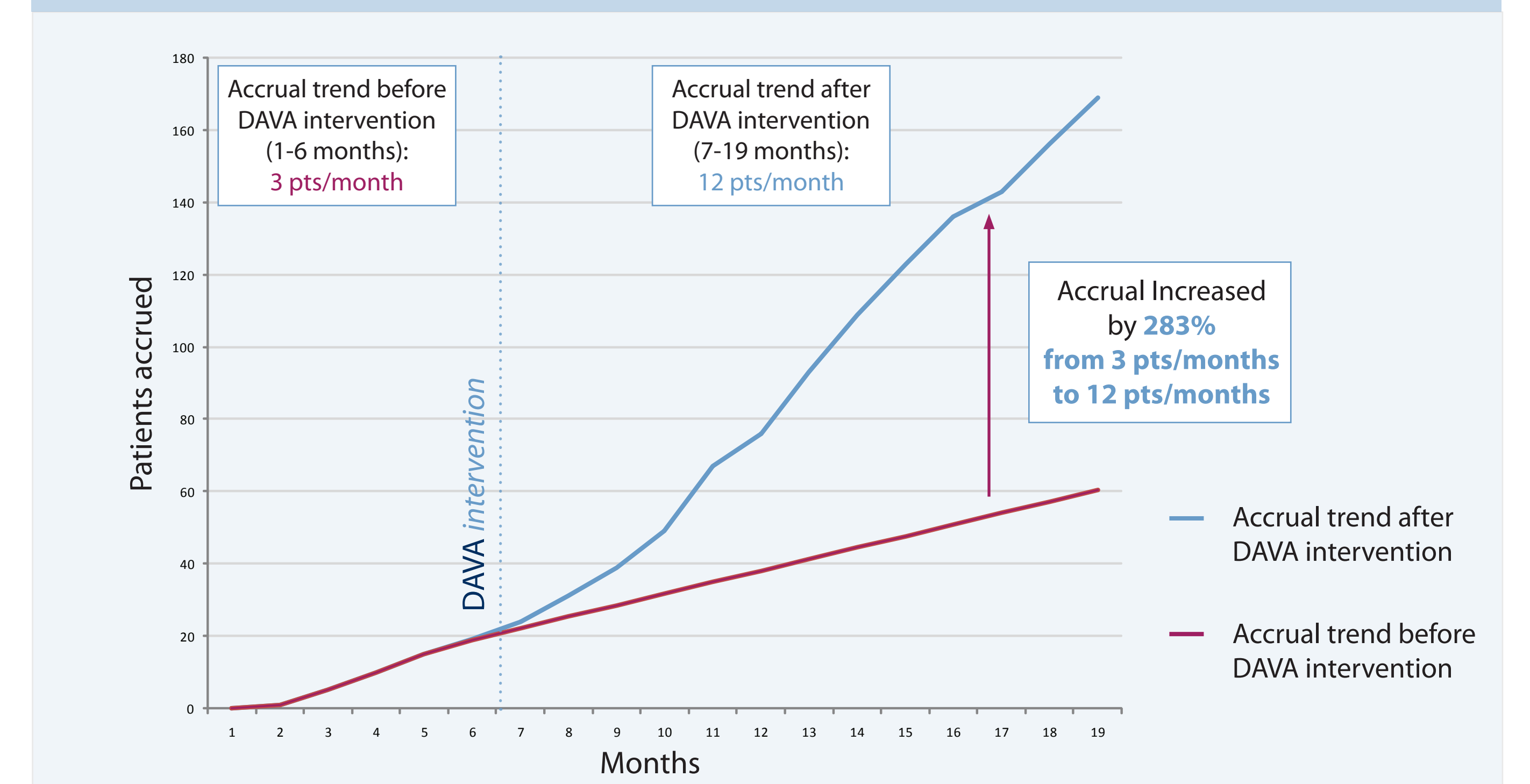
Table 2. Impact of DAVA Intervention

	Average number of patients accrued per month		Increase %	Trial accrual (months)	
	Before DAVA	With DAVA		Before DAVA	With DAVA
TRIAL #1	2	3	50%	16	5
TRIAL #2	3	5	67%	14	5
TRIAL #3	3	6	100%	12	6
TRIAL #4	2	6	200%	10	5
TRIAL #5	3	12	283%	6	13
TOTAL	13	32	142%		

Figure 2. Impact of Accrual Workshops



Case Study 1. Acceleration of an international, Phase III trial



- Sponsor goal of 25% US accrual to this global trial; however, accrual trajectory was only 12% of total enrollment
- DAVA goal of >50% US accrual
- Actual US enrollment to date with DAVA intervention is 53% of total accrual.
- The accrual in the US has surpassed the sponsor's projection of 12% as well as the sponsor's goal of 25%

CONCLUSIONS

- Our current model of investigator-focused interventions, which develops and implements site-specific accrual enhancement strategies, has been successful in significantly accelerating clinical trial accrual in 5/5 trials
- Direct medical oncologist to medical oncologist interactions resulted in a measurable improvement of 50 - 283% in the monthly accrual to each of the five trials

SUMMARY

- Accrual to oncology clinical trials in the US is poor and significantly lagging behind the ROW
- This slow accrual in the US has been attributed to various causes; however, no universal cause can be identified
- An investigator-focused approach to identify and overcome site-specific barriers to accrual can significantly improve the accrual and, ultimately, the timely completion of clinical trials in the US

References

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Acknowledgments

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