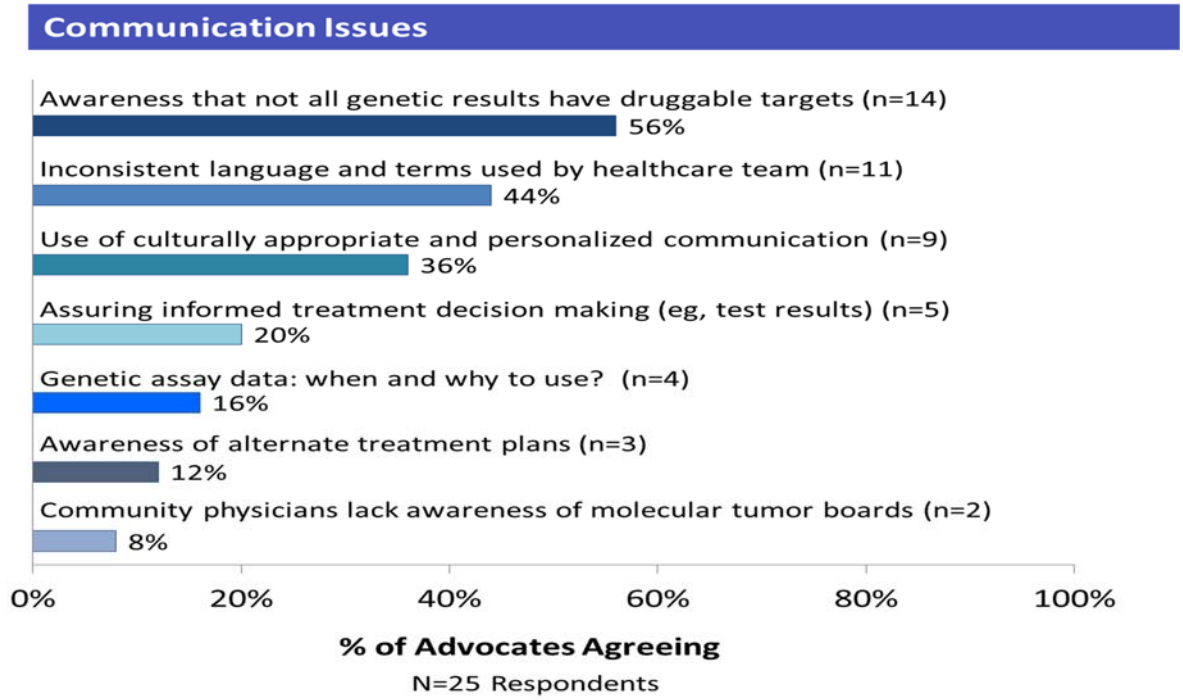
Think Tank

A Think Tank was convened on the final day of the Symposium to explore ideas from advocates for future precision medicine trials. Advocates were broken out into small groups to address 3 major issues in precision medicine trials: Communications, Logistics, and Clinical Trial Design. Prior to break out, advocates were polled on subtopics within each major topic area to prioritize them; results of this polling are presented at the end of this section.

Communications Group



Among communication issues considered, the awareness that not all genetic results have drugable targets was identified as the highest priority for discussion, followed by the inconsistent language and terms used by the healthcare team. These two topics were selected for more detailed consideration in the Think Tank by the Communications team.

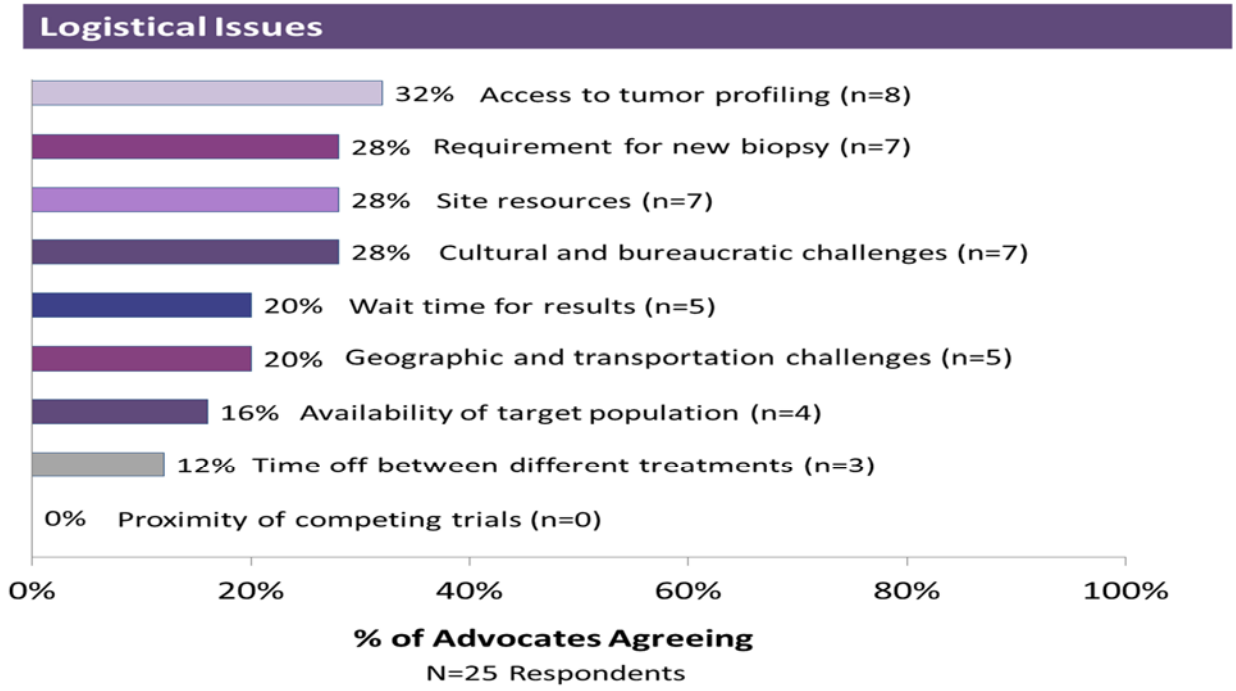
- Awareness that not all results will have actionable mutations

Patients in precision medicine clinical trials are not always aware that their cancers may not have actionable mutations. Although consent forms include this information, it is easy for patients to overlook. Informed consent documents should include a checklist or bullet points to bring this information to patients' attention and the trial should include additional educational material in multimedia formats, such as CDs or DVDs. Different formats would also help patients more fully understand the meaning of actionable mutations and why not everyone has one.

- Inconsistent language and terms used by the healthcare team

Definitions in precision medicine vary, as demonstrated by the speakers in this Symposium—even experts do not agree. Additionally, healthcare team members do not all use the same terms to mean the same thing. Advocates can urge organizations such as the NCI, SWOG, and Alliance to use consistent language, as well as researchers and the medical community. Although it may be difficult to achieve consistent language among all of these groups, the general consensus is that we need to start somewhere. Lungevity conducted a language audit (https://www.lungevity.org/sites/default/files/file-uploads/testing-terminology-world-lung-2016-poster.pdf) about what patients hear about biomarker testing that may be a useful place to begin. Moreover, patients need language that is understandable. A glossary would be helpful to patients and their families and could be made available in print and other formats, such as CDs and DVDs. Development of a glossary can be done by different organizations and is not solely the responsibility of the trial organizers.

Logistical Issues



Among logistical issues, access to tumor profiling was the highest priority issue, followed by a 3-way tie between requirement for new biopsy, site resources, and cultural/bureaucratic challenges. A tie-breaking vote identified site resources as the second highest priority topic for consideration.

- Access to tumor profiling

Access to tumor profiling includes several aspects. First, patients may not know that tumor profiling exists and second, physicians may not know how or where such tests can be performed. For this reason, access to tumor profiling may need to be addressed at both the patient and physician levels.

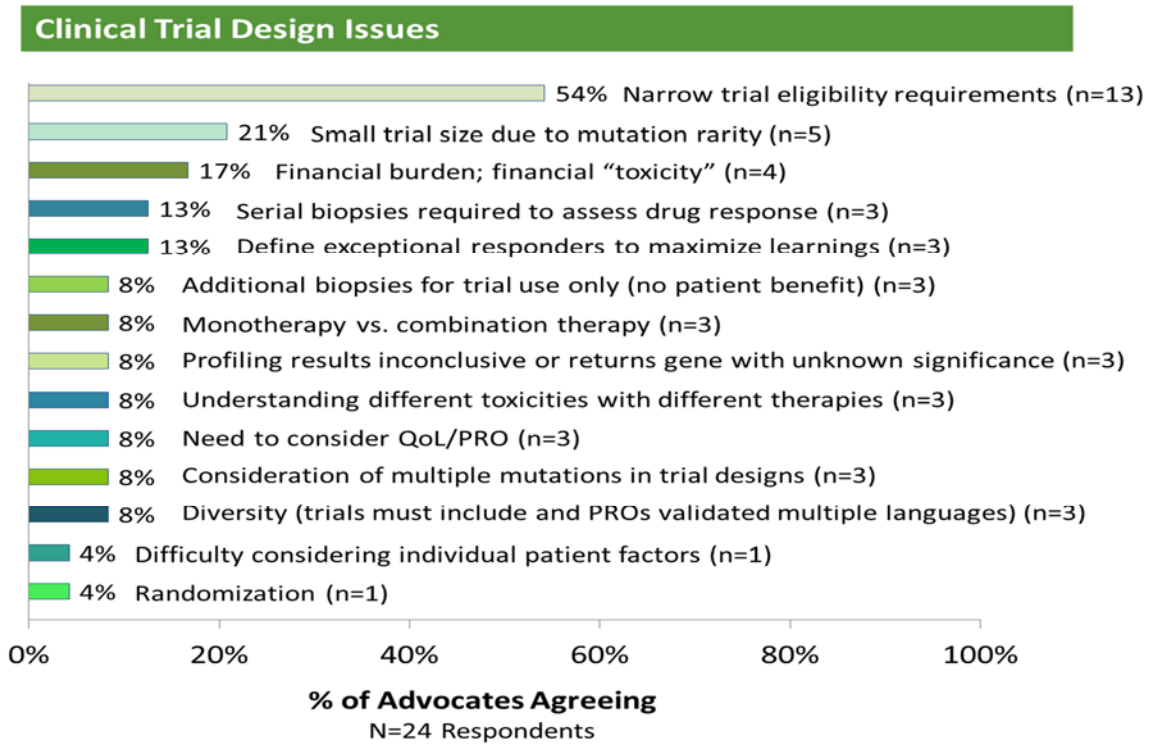
- Site resources

Site resources include physical resources, financial resources, and staff skills, among other things. Centers of excellence should be recognized within communities or cancer networks so that patients know where to go for tumor profiling, as well as to obtain information about the process for themselves and their families. Sites outside the centers of excellence should be identified that can prepare tumor tissue for profiling, and staff should be skilled in handing and storing tumor tissue. Third party vendors should be included to manage tissue handling and storage to promote consistency.

In many cases, patients do not have control over their own tumor tissue once it is removed. This may be problematic if patients later seek to have their tumor tissue profiled to determine whether they might benefit from a certain treatment. However, at the time of tumor removal, patients are not focused on the fate of their excised tumor tissue, but rather on the current treatment and their own recovery. Patients need education regarding the fate of the removed tumor tissue and need contact information for the surgical center that removed it.

Patient consent to use the tissue for research can be an issue. Each state has its own laws regarding how long tumors are held in pathology laboratories. The Common Rule in the Code of Federal Regulations governing human research protections recently changed to allow broad consent for use of tumor tissue. Patients can opt out, but many do not. Patients who opt out of broad consent retain the ability to consent to each individual study that seeks to include their tumor tissue. It's also important to note that cooperating institutions may not cooperate well when it comes to tumor tissue samples. One institution may allow the other institution to take the tissue they need from the biospecimen block, whereas other institutions provide a certain amount of tissue that may or may not be enough for the second center to use.

Financial resources are also a critical consideration, even in clinical trials. Patients may require preapproval from their insurance company to start a clinical trial treatment and may need reimbursement for out of pocket expenses. Private parties may be able to help with this need.



Among clinical trial design issues, narrow trial eligibility requirements was selected as the highest priority discussion topic, followed by the small size of precision medicine studies and the consequent implications for clinical practice.

- Trial has narrow eligibility requirements and even those with actionable mutations may be denied entry

Many precision medicine (and other) clinical trials have narrow eligibility requirements, such that patients with the mutation under study, who stand to benefit from the treatment, may not qualify for enrollment. Any exclusion criteria must be specifically justified, and exclusion criteria must be removed if not clinically or scientifically supported.

- Small size of precision medicine trials precludes influence on clinical practice

Precision medicine studies can be quite small due to the rarity of individual mutations. This leads to a low number of patients in each mutation group, even though the overall number enrolled in the trial may be quite large. The low number of patients with each mutation may preclude statistically significant results that would support changes in practice recommendations. In these trials, it is important to analyze differences between responders and nonresponders to potentially identify variables that influence outcomes. Additionally, precision medicine studies in which small groups show strong positive results should be able to influence clinical practice recommendations.

Another alternative for achieving statistically significant outcomes despite the small numbers of patients in precision medicine trials is to reconsider endpoints when designing trials. Typical endpoints in cancer

studies are progression free survival and overall survival, but statistical significance in these outcomes can be difficult to achieve with small patient numbers. Endpoints should be continually evaluated and modified as scientifically and clinically indicated. Even relatively small improvements may add up for patients. For example, if one treatment extends progression free survival by 10 months, patients may then opt for another treatment that again adds 10 months, and so forth. Projects evaluating endpoints are currently underway and the results may influence clinical trial design.