Oncology Basket Trials:

An Emerging Paradigm Shift in Trial Design & Treatment Approach?

Claire Dubuque, Paxton Major,
Sofia Suarez, Jillian Godfrey Scaife,
Vivian DeWoskin

May 2018

Introduction

Cancer treatment has made significant strides toward the promise of personalized medicine in recent years. Particularly with Keytruda's tissue-agnostic MSI-H and dMMR approval last year, basket trials have now become a viable registrational strategy to pursue such tissue-agnostic, biomarker-based indications. In this paper, we conduct an analysis of the mid-stage oncology clinical trial pipeline to determine the extent to which basket trials are being utilized as part of registrational strategies. In particular, we explore how many trials are likely to lead to tissue-agnostic indication approvals in the near-term. We ultimately identified 37 basket trials for further analysis; we categorized 2 as "Registrational," 9 as "Potentially Registrational," and 26 as "Exploratory." While truly registrational basket trials have been limited to-date, we may see an increase in the number of drugs approved for tissue-agnostic indications as interest in this regulatory pathway will likely grow. This paper also explores key questions to consider in a world where multiple oncology products are approved with tissue-agnostic indications.

Summary

In recent years, the treatment of oncology has made significant strides toward the promise of personalized medicine. Traditionally, tumor location and histology have been the primary drivers of treatment choice in oncology - this is even reflected in the organization of current treatment guidelines, such as NCCN guidelines, which are primarily outlined by the affected organ system (e.g., lung cancer, breast cancer, or colorectal cancer). The first major advance toward a more individualized approach to treatment was the introduction of targeted therapies, such as BCR-ABL tyrosine kinase inhibitors like Gleevec (imatinib) or VEGF inhibitors like Avastin (bevacizumab). Today, it is increasingly common to see therapy selection informed by the specific biomarkers or genetic characteristics of an individual patient's tumor.

Today, it is increasingly common to see therapy selection informed by the speci ic biomarkers or genetic characteristics of an individual patient's tumor.

Since 2016, advances in next-generation genomic sequencing (NGS) have raised the possibility of using tumor genetics alone to guide therapy choices.[1] Basket or bucket trials (referred to as basket trials throughout this paper) have increasingly been used in oncology as a potential means of providing the clinical data necessary to support such a shift in treatment approach.[i] Basket trials are designed to test a therapy in a genetically- or biomarker-defined patient population regardless of tumor type, and as such, they allow investigators and manufacturers to conduct "tissue-agnostic" or "pan-tumor" studies.[1]

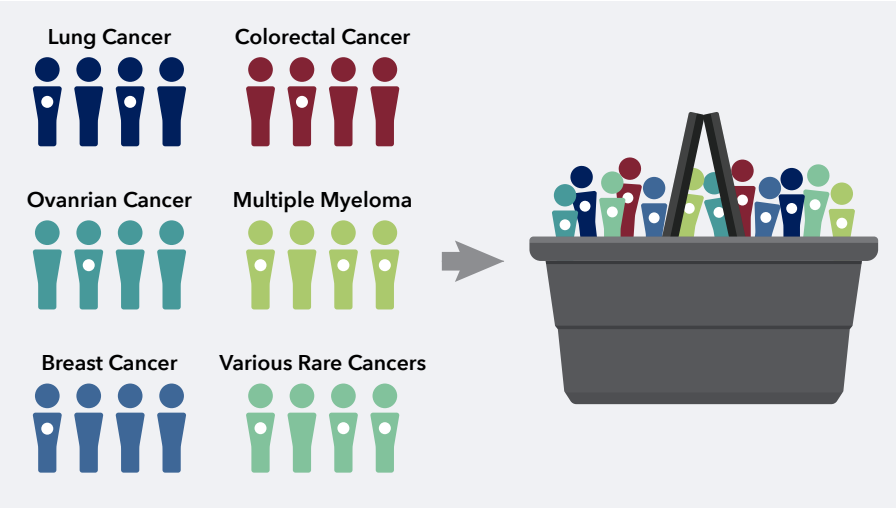

Figure 1: Basket trials test therapies for a specific genetic mutation (represented by white dots) regardless of tumor histology.[3]

[i] Basket trials have also been utilized outside oncology, however, our focus will be oncology specifically

Historically, basket trials have been used to explore multiple tumor types in one trial in order to prioritize the ones with the greatest response for further research.[ii,2,3,4] However, last year Keytruda became the first therapy to successfully use basket studies as a registrational strategy. In May 2017, Keytruda was granted accelerated approval of a second line treatment for adult and pediatric patients with microsatellite instability-high (MSI-H) or mismatch repair deficiency (dMMR) solid tumors irrespective of histology.

With Keytruda's MSI-H and dMMR approval, basket trials have now become a viable registrational strategy to pursue a tissue-agnostic indication. What does this mean for oncology treatment and for industry? Will this lead to a shift in the basic oncology treatment paradigm, as other therapies follow Keytruda's lead and pursue tissue-agnostic indications? Or will this remain a relatively uncommon approach to clinical study and regulatory approval? The prospect of additional tissue-agnostic indications raises a number of interesting questions for multiple stakeholders involved in oncology care.

With Keytruda's MSI-H and dMMR approval, basket trials have now become a viable registrational strategy to pursue a tissue-agnostic indication.

In this paper, we conduct an analysis of the oncology clinical trial pipeline to determine the extent to which basket trials are being utilized, and in particular, how many are likely to be registrational studies resulting in tissue-agnostic indications.

Our goals are to:

1. **Better understand whether and when there will be a tipping point in the oncology treatment paradigm as a result of these basket studies**
2. **Raise important questions that would accompany such a shift.**

[ii] For example, following Zelboraf's proof of efficacy in melanoma patients with BRAF mutations, Memorial Sloan Kettering conducted the first published report of a basket trial to determine whether Zelboraf monotherapy was efficacious in other tumor types. The trial included 122 BRAF positive patients regardless of tumor histology from 23 global centers. Results showed that Zelboraf had a response in a range of cancers, however, its effectiveness was mixed across types: strongest results were in non-small cell lung cancer, Erdheim-Chester disease, and Langerhans cell histiocytosis, with minimal effect in other cancers, including CRC.[4] Based on these results, Roche received approval for Zelboraf in Erdheim-Chester patients with BRAF V600 mutations.[4]

Materials & Methods

Clinical Trial Selection:

To answer these questions, we began by conducting a search (dated 3/14/2018) of ClinicalTrials.gov for registered studies that evaluated and/or will report on oncology therapies in development for tissue-agnostic indications. We applied keyword searches for relevant terms and set defined inclusion criteria to narrow down the list of trials to those of interest.

For our preliminary search the specific search terms were: "cancer," an active[iii] interventional study design, a Phase I/II or later trial, industry sponsored or a collaboration. After generating a comprehensive list of oncology clinical trials, we excluded trials with the following criteria:

I. **Trials with the following intervention types not studied in combination with a drug therapy: "behavioral," "radiation," "procedure," "device," "dietary supplement" or "diagnostic test"**
II. **Trials with completion dates before 2016 (those completed during 2016 were included)**
III. **Trials investigating greater than five interventions[iv]**
IV. **Trials studying ≤ 4 conditions[iv]**

As basket trials often include generalized oncology indications, we then added back studies with ≤ 4 conditions if they included the following general conditions: "solid tumors," "advanced cancer," "advanced malignancies," "oncology," "solid tumour," "solid malignancies," "advanced tumors," "neoplasm" or "cancer" as the only condition.

To supplement this database search, we conducted a hand search of "basket" and "bucket" clinical trials on ClinicalTrials.gov and Google Scholar.

[iii] Defined as "recruiting," "not yet recruiting," "active," "not recruiting," "completed," and "enrolling by invitation

[iv] Trials with >5 interventions and ≤4 conditions were excluded to attempt to limit the initial scale of the search. Trials with >5 interventions were deemed more likely to reflect umbrella trials, not the kind of basket trials this paper is investigating. And trials with ≤4 conditions were also unlikely to be studying a broad enough population to be considered a true basket trial

We initially identified 9,712 oncology clinical trials using our broadest search terms. After screening for intervention type, completion date, number of indications studied, among others noted above, we narrowed the list to 474 clinical trials which were individually reviewed. Utilizing prior knowledge of historical basket trial structure, design, and enrollment, we reviewed the list of clinical trials and excluded any trials that:

I. **Did not include a patient population with a specific biomarker or genetic mutation,**

II. **Did not include at least 1 study arm that was tumor-agnostic**

We then categorized each trial into three major segments: "Registrational," "Potentially Registrational," and "Exploratory" (as detailed below in Figure 2). "Registrational" trials are those intended to provide evidence for a drug seeking approval by the FDA while "Potentially Registrational" trials are those that are not clearly leading to a regulatory filing but could become registrational in the event of a positive readout. Meanwhile, "Exploratory" trials are those being conducted in a patient population that could possibly lead to a tissue-agnostic indication but are too early in development to be considered registrational.

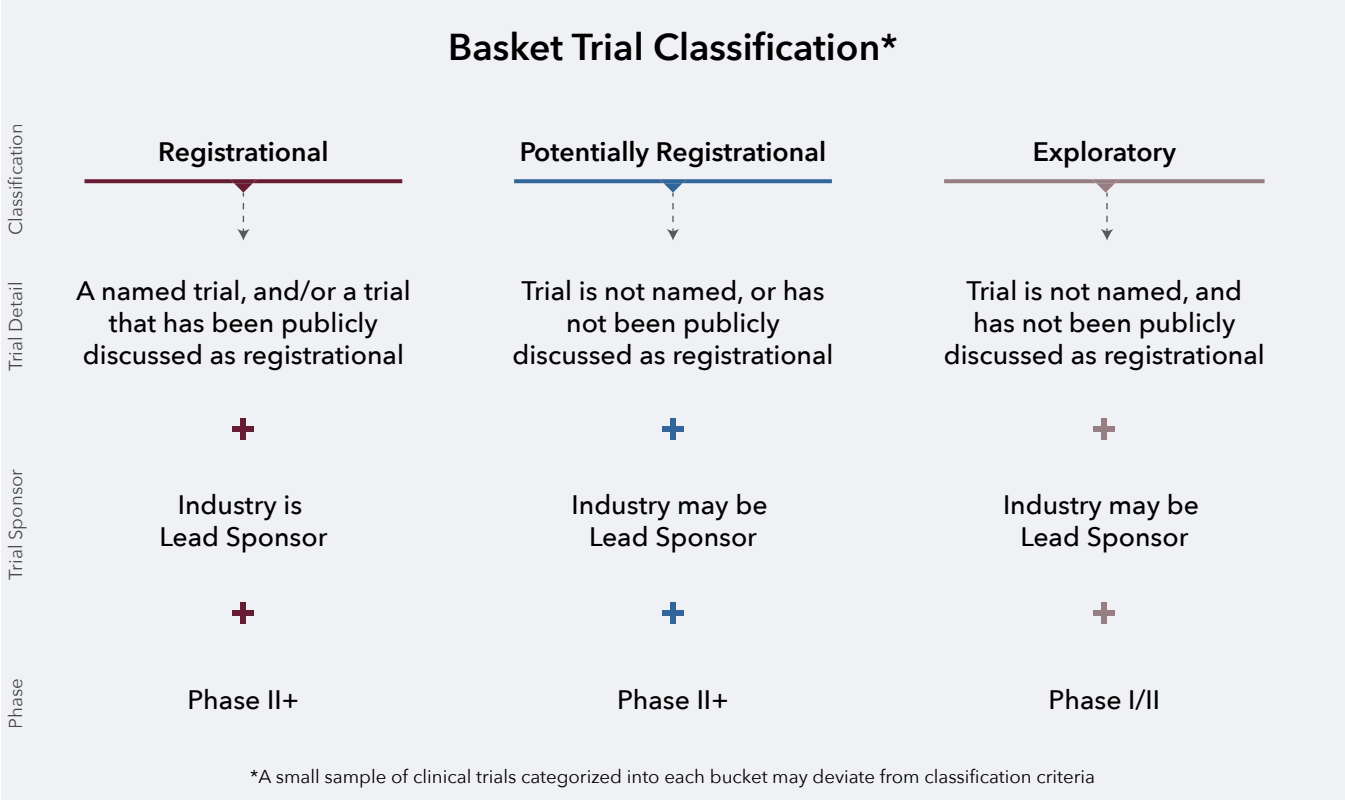

Figure 2: Basket Trial Classification Criteria

Results

We ultimately identified 37 basket trials for further analysis. Of these 37 trials, we categorized 2 as "Registrational," 9 as "Potentially Registrational," and 26 as "Exploratory".[v] Within these 37 basket trials, 31 unique therapies are currently being studied (as outlined in the table in Appendix).[v]

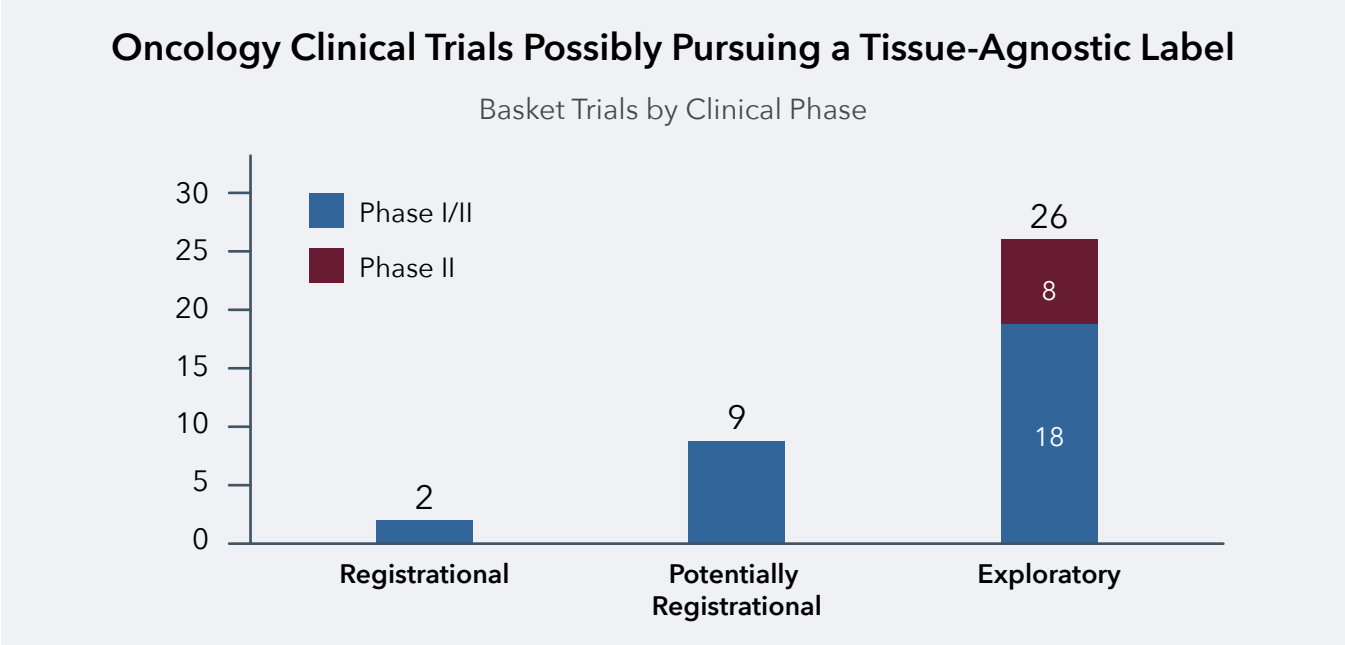

Figure 3: Oncology Clinical Trials Possibly Pursuing a Tissue-Agnostic Label by Clinical Phase

A few key takeaways emerge from a holistic review of the data:

I. ***Only a handful of trials are currently considered registrational:*** Given the current landscape of clinical trials and publicly available information, we identify only 2 trials that appear to clearly be pursuing a tissue-agnostic regulatory filing. Additionally, we find that there are no basket trials currently in Phase III.

[v] Appendix displays the details of the 37 included studies, including intervention, trial name, specific genetic mutation / biomarker tested, NCT number, and Industry sponsor / collaborator. These clinical trials are also categorized based on the registrational versus exploratory nature of the trial design.

II. ***Many current trials in the pipeline could lead to additional registrational trials in the next 1-3 years:*** Although many of the trials identified are not clearly linked to a planned regulatory filing for a tissue-agnostic indication (as shown in Figure 3), we expect that the results of these trials, if positive in the broad indication, could lead to future registrational trials in many cases.

III. ***Breadth of Biomarkers Studied:*** Across these 37 trials, 16+ types of biomarkers or genetic mutations are currently being studied as depicted in Figure 4. This broad scope verifies the growing trend of tumor-agnostic research across oncologic agents, regardless of biomarker studied.

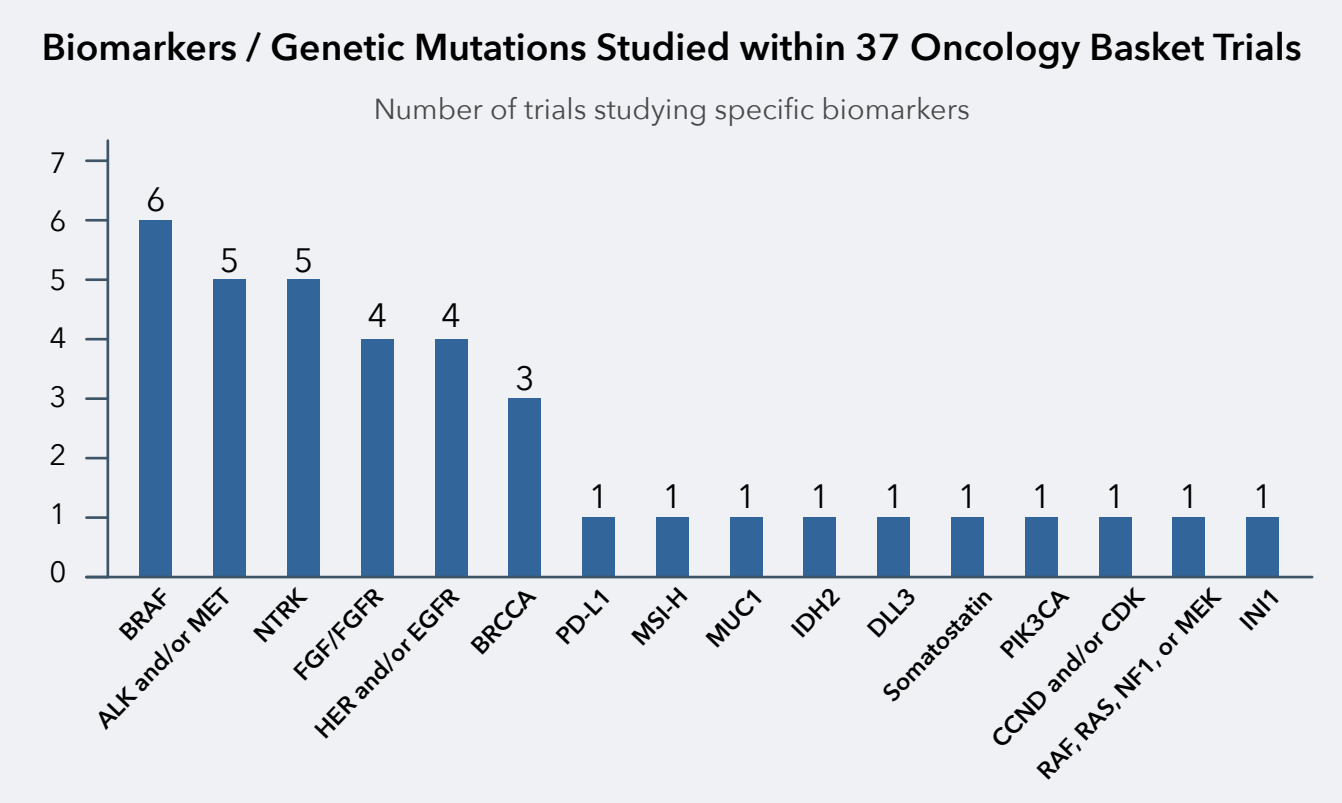

Figure 4: Number of Trials Studying Specific Biomarkers/Genetic Mutations

Our analysis identified only two assets currently being investigated in registrational Phase II trials: larotrectinib (LOXO-101; Loxo Oncology) and entrectinib (Ignyta, Inc.). Larotrectinib, a tropomyosin receptor kinase (TRK) fusion inhibitor being studied in tumors harboring TRK fusions, is the furthest along in development, having initiated a rolling NDA submission in December 2017. Loxo has partnered with Bayer to jointly develop larotrectinib, which has received Breakthrough Designation from the FDA.[5] Entrectinib is also in development for tumors with TRK fusions or ROS1 fusions, and is

partnered with Roche.[6] Together, these two agents could represent the next wave of tissue-agnostic approvals.

Even though the majority of the basket trials included in this analysis do not appear to be registrational, these findings nevertheless demonstrate the opportunity for growth in tissue-agnostic approvals. The process by which Keytruda gained approval provides a template for how these more exploratory trials could lead to tissue-agnostic approvals in the future. Keytruda was studied initially within an exploratory setting (i.e., within patients with MSI-H metastatic colorectal cancer) before being studied in broader tissue-agnostic cohorts that were MSI-H. Keytruda's MSI-H approval was ultimately based on results from five uncontrolled, open-label, single-arm trials and was comprised of N=149 patients with MSI-H or dMMR across a total of 15 cancer types. Merck stratified the primary efficacy outcome, overall response rate (ORR), by patients with colorectal cancer (N=90, ORR 36%) and patients without colorectal cancer (N=59, ORR 46%), as prevalence of MSI-H is notably higher in colorectal cancer.[7] Keytruda's approach validates the finding that many therapies, including the 26 "Exploratory" therapies noted above, may be primed to pursue a registrational trial in the future depending on initial clinical signals in those populations.

Even though the majority of the basket trials included in this analysis do not appear to be registrational, these findings nevertheless demonstrate the opportunity for growth in tissue-agnostic approvals.

Discussion

Keytruda's approval for MSI-H tumors serves as a proof of concept for tissue-agnostic development. Today, at least 31 unique therapies are conducting trials in various mutation- or biomarker-defined, tissue-agnostic indications. For manufacturers, this development approach could provide access to the greatest number of patients and the fastest route to market. While there are clear benefits, histological variance creates significant heterogeneity in tissue-agnostic, biomarker defined populations. Not only does this pose developmental risks (i.e. probability of success), but it may also impact how key stakeholders react to and incorporate such tissue-agnostic therapies into clinical practice. First, the FDA still requires tissue-agnostic trial data to be separated by tumor site in the product's label, allowing physicians, insurers, and other stakeholders to identify in which tumors the therapy works best. From an access and willingness to prescribe perspective, tissue-agnostic therapies may need tremendous efficacy and/or unmet need to encourage truly broad use and overcome small sample sizes compared to conventional histology defined trials. Patient identification may also be a challenge as universal testing for rare biomarkers could receive significant pushback from insurers due to cost considerations. Furthermore, many molecular targets may not be included in commonly used NGS panels.

For manufacturers, this development approach could provide access to the greatest number of patients and the fastest route to market. While there are clear benefits, histological variance creates significant heterogeneity in tissue-agnostic, biomarker defined populations.

It will likely be a challenge for a basket trial to produce data that is up to the statistical rigor required for conventional therapies to be incorporated into guidelines and/or clinical practice for a specific tumor type. Herceptin's registrational trials in HER2-positive metastatic breast cancer enrolled 220 patients while Keytruda was studied in 2 patients with MSI-H positive metastatic breast cancer. As such, Keytruda's use in MSI-H positive tumors has only been recommended by the NCCN for tumors with large sample sizes in its registrational trial, and tumors associated with Lynch Syndrome, which has long been linked to the MSI-H biomarker (i.e. biliary, endometrial, colorectal, gastric cancer and ovarian cancer). Specifically, the NCCN has added Keytruda as a category 2A option to the list of "other regimens" recommended for the treatment of these tumor types. For all other cancers, as specified in its label, Keytruda is indicated for MSI-H positive "solid tumors that have progressed

following prior treatment and who have no satisfactory alternative treatment options."[8] With minimal efficacy data and low biomarker prevalence, use in these other tumor types may be limited.

For a novel oncolytic that launches with a first approval for a tissue-agnostic indication, these clinical hurdles will likely be accentuated. At the time of its tissue-agnostic label approval, Keytruda's efficacy in many tumor types was well established. Without this type of supplemental tumor specific data, clinicians may be more hesitant to prescribe a new therapy. Second, testing for a novel biomarker may not be as easily incorporated into clinical practice as it was for MSI-H which was already being tested in routinely used immunohistochemistry assays. For a novel biomarker requiring the use of NGS, cost will be a significant barrier to patient identification. Private insurers may not be receptive to universal testing of patients for a rare biomarker. For indications like NSCLC, in which there are many actionable biomarkers and associated therapies available today, this may not be a significant barrier; however, for many indications, NGS may not be readily supported. Furthermore, there is no guarantee a novel biomarker will be included on commonly used NGS panels. MSI/MMR is now being reported on molecular profiling panels, but the level of efficacy and degree of unmet need required to drive widespread incorporation of a novel biomarker into NGS panels remains to be elucidated.

Beyond clinical barriers, the current tumor-site-oriented paradigm may also present many challenges from an access perspective. How payers will incorporate tissue-agnostic therapies into their formulary is still an unanswered question; however, it appears likely that in the near term, payers will continue to evaluate therapies based on tumor-site-specific data within the tissue-agnostic clinical data package. This may place restrictions on the use of tissue-agnostic therapies in the broadest possible eligible patient population.

Thus, we are left with a number of unanswered questions today, and even more questions in the future, if tissue-agnostic approvals gain significant traction:

From the clinical perspective: How will tumor-specific guidelines change in response to additional approval of tissue-agnostic therapies? Will they remain tumor-specific? Will clinical practice change in any fundamental way (e.g., genetic testing, treatment algorithms/pathways, operational changes in practice, etc.)? How will clinicians manage competing treatment algorithms in the practice setting? For example, for instances where there is overlap in tumor biomarkers (e.g., MSI-high and BRCA in Ovarian), how will clinicians use combination therapy, appropriate sequencing, or strict tradeoffs between targeted therapies?

From an access perspective: How will health technology assessments (HTAs) and agencies compare benefits across tumor types (e.g., a 2-month improvement in progression free survival is meaningfully different in hepatocellular carcinoma vs. prostate cancer)? How will payers manage a growing pool of tissue-agnostic therapies?

From an industry perspective: How will industry change forecasting and performance tracking of products approved across a broad range of tumor types? Will this trend result in a need for additional services (e.g., personalized genetic marker maps, machine-assisted treatment algorithms, real-world evidence and analytics, etc.)? What are the advantages and disadvantages of this development pathway relative to other clinical development options? Will these shift as tissue-agnostic therapies become more prevalent?

Thus far, the emergence of registrational basket trials has been limited (only 2 currently ongoing), perhaps due in part to the many short-term challenges associated with the development and commercialization of tissue-agnostic therapies enumerated above. However, we have identified at least 34 mid-phase and/or exploratory tissue-agnostic trials currently in the clinic. In the near term, pending the results of these trials, interest in tissue-agnostic basket trial development is likely to grow, especially as NGS continues to become more widespread in oncology. Whether the number of tissue-agnostic indication approvals will ever be substantial enough to drive a significant shift in treatment approaches remains an open question. The growing pool of mid-phase/exploratory tissue-agnostic trials suggests we could be headed in that direction, leading to many long-term implications on the clinical application, commercialization and development of targeted oncolytics in the next several years.

In the near term, pending the results of these trials, interest in tissue-agnostic basket trial development is likely to grow, especially as NGS continues to become more widespread in oncology.

References

1. Redig, A. J., & Janne, P. A. (2015, June 10). The Basket Trial: An Evolving Clinical Trial Design. The ASCO Post. Retrieved April 9, 2018, from www.ascopost.com

2. Beckman, R., Antonijevic, Z., Kalamegham, R., & Chen, C. (2016). Adaptive Design for a Confirmatory Basket Trial in Multiple Tumor Types Based on a Putative Predictive Biomarker. Clinical Pharmacology & Therapeutics, 100(6), 617-625. doi:10.1002/cpt.446

3. Clinical Trial Shows Promise of "Basket Studies" for Cancer Drugs. (2015, August 20). Retrieved April 09, 2018, from https://www.mskcc.org/blog/clinical-trial-shows-promise-basket-studies-drugs

4. Roche. (2017, November 07). FDA approves Zelboraf (vemurafenib) for Erdheim-Chester disease with BRAF V600 mutation [Press release]. Retrieved April 9, 2018, from https://www.roche.com/investors/updates/inv-update-2017-11-07b.htm

5. Loxo Oncology Announces Global Development and Commercialization Partnership with Bayer for Larotrectinib and LOXO-195. (2017, November 14). Retrieved April 12, 2018, from https://ir.loxooncology.com/press-releases/loxo-oncology-announces-global-development-and-commercialization-partnership-with-bayer-for-larotrectinib-and-loxo-195

6. Roche and Ignyta reach definitive merger agreement. (2017, December 22). Retrieved April 12, 2018, from https://www.roche.com/media/store/releases/med-cor-2017-12-22.htm

7. FDA Approves Merck's KEYTRUDA® (pembrolizumab) for Adult and Pediatric Patients with Unresectable or Metastatic, Microsatellite Instability-High (MSI-H) or Mismatch Repair Deficient (dMMR) Solid Tumors. (2017, May 25). Retrieved April 12, 2018, from http://www.mrknewsroom.com/news-release/prescription-medicine-news/fda-approves-mercks-keytruda-pembrolizumab-adult-and-pediatr

8. Keytruda (pembrolizumab) [package insert]. Whitehouse Station: Merck Sharp & Dohme Corp, NJ, 2014

Appendix

Intervention	Trial Name	Genetic Mutation/ Biomarker Studied	Industry Sponsor/ Collaborator	NCT Number	Phase	Designation
LOXO-101	LOXO-101 (Larotrectinib) in Subjects With NTRK Fusion Positive Solid Tumors (NAVIGATE)	NTRK1, NTRK2 or NTRK3	Loxo Oncology, Inc.	NCT02576431	Phase 2	Registrational
Entrectinib	Entrectinib (RXDX-101) in Patients With Solid Tumors Harboring NTRK 1/2/3 (Trk A/B/C), ROS1, or ALK Gene Rearrangements (Fusions) (STARTRK-2)	NTRK1/2/3, ROS1, or ALK	Ignyta, Inc.	NCT02568267	Phase 2	Registrational
Crizotinib	Cross-tumoral Phase 2 With Crizotinib (CREATE)	ALK and/or MET	Pfizer	NCT01524926	Phase 2	Potentially Registrational
Tazemetostat	EZH2 Inhibitor Tazemetostat in Subjects With INI1-Negative Tumors	cohort 1: MRT, RTK, or ATRT l cohort 3: EZH2 GOF mutation	Epizyme, Inc.	NCT02601950	Phase 2	Potentially Registrational
Talazoparib Tosylate	BMN 673 in Advanced Cancer Patients With Somatic Alterations in BRCA1/2	BRCA1 or BRCA2	Pfizer	NCT02286687	Phase 2	Potentially Registrational
Veliparib	Response to PARP Inhibitor Predicted by the RAD51 Assay (REPAIR)	BRCA 1/2	AbbVie	NCT03044795	Phase 2	Potentially Registrational
ado-trastuzumab emtansine	Ado-Trastuzumab Emtansine for Patients With HER2 Amplified or Mutant Cancers	HER2	Genentech, Inc.	NCT02675829	Phase 2	Potentially Registrational
Vemurafenib	Vemurafenib for Patients With Tumors Harboring BRAF Genomic Alterations	BRAF V600	Hoffmann-La Roche	NCT02304809	Phase 2	Potentially Registrational
AMG 337	QUILT-3.036: AMG 337 in Subjects With Advanced or Metastatic Solid Tumors	MET or METex14del mutations resulting in MET exon 14 skipping	NantPharma, LLC	NCT03147976	Phase 2	Potentially Registrational
Dabrafenibl Trametinib	Dabrafenib and Trametinib in Subjects With BRAF V600E-Mutated Rare Cancers	BRAF V600E	Novartis Pharmaceuticals	NCT02034110	Phase 2	Potentially Registrational
Vemurafenib	Vemurafenib in Participants With BRAF V600 Mutation-Positive Cancers	BRAF V600E	Hoffmann-La Roche	NCT01524978	Phase 2	Potentially Registrational
Neratinib	Neratinib HER Mutation Basket Study (SUMMIT)	HER2, HER3 or EGFR	Puma Biotechnology, Inc.	NCT01953926	Phase 2	Exploratory
Merestinib	Merestinib In NSCLC And Solid Tumors	NTRK1, 2, or 3	Eli Lilly and Company	NCT02920996	Phase 2	Exploratory
LGX818	LGX818 for Patients With BRAFV600 Mutated Tumors (SIGNATURE)	BRAF V600	Array BioPharma	NCT01981187	Phase 2	Exploratory

Appendix

Intervention	Trial Name	Genetic Mutation/ Biomarker Studied	Industry Sponsor/ Collaborator	NCT Number	Phase	Designation
Avelumab lTalazoparib	Javelin Parp Medley: Avelumab Plus Talazoparib In Locally Advanced Or Metastatic Solid Tumors	BRCA or ATM	Pfizer	NCT03330405	Phase 2	Exploratory
BGJ398	BGJ398 for Patients With Tumors With FGFR Genetic Alterations	FGFR	Novartis Pharmaceuticals	NCT02160041	Phase 2	Exploratory
MEK162	MEK162 for Patients With RAS/ RAF/MEK Activated Tumors (SIGNATURE)	RAF, RAS, NF1 or MEK	Array BioPharma	NCT01885195	Phase 2	Exploratory
Abemaciclib	Abemaciclib in Solid Tumors Harboring Genetic Alterations in Genes Encoding D-type Cyclins or Amplification of CDK4 or CDK6	CCND1, CCND2, CCND3, CDK4, or CDK6	Eli Lilly and Company	NCT03310879	Phase 2	Exploratory
Lenvatinib	Lenvatinib in Patients With Advanced Cancer and Aberrations in FGF/FGFR Signaling	FGF/FGFR	Eisai Co., Ltd.	NCT02846766	Phase 2	Exploratory
Crizotinib	Crizotinib in Patients Harboring an Alteration on ALK, MET or ROS1	ALK, MET, RON and ROS1	Pfizer	NCT02034981	Phase 2	Exploratory
Apatinibl Pembrolizumab	Apatinib With Pembrolizumab in Previously Treated Advanced Malignancies (APPEASE)	MSI-H	LSK BioPartners Inc.	NCT03407976	Phase 1, Phase 2	Exploratory
TAS0728	TAS0728 in Patients With Solid Tumors With HER2 or HER3 Abnormalities	HER2 or HER3	Taiho Oncology, Inc.	NCT03410927	Phase 1, Phase 2	Exploratory
TPX-0005	TPX-0005 in Patients With Advanced Solid Tumors Harboring ALK, ROS1, or NTRK1-3 Rearrangements (TRIDENT-1)	ALK, ROS1, NTRK1, NTRK2, or NTRK3	TP Therapeutics, Inc.	NCT03093116	Phase 1, Phase 2	Exploratory
TAS-120	TAS-120 in Patients With Advanced Solid Tumors With FGF/FGFR-Related Abnormalities	FGF/FGFR	Taiho Oncology, Inc.	NCT02052778	Phase 1, Phase 2	Exploratory
PLX8394	PLX8394 in Patients With Advanced Unresectable Solid Tumors	BRAF	Plexxikon	NCT02428712	Phase 1, Phase 2	Exploratory
LOXO-195	LOXO-195 in Patients With Previously Treated NTRK Fusion Cancers	NTRK	Loxo Oncology, Inc.lBayer	NCT03215511	Phase 1, Phase 2	Exploratory
INCB054828	INCB054828 in Subjects With Advanced Malignancies	FGF/FGFR	Incyte Corporation	NCT02393248	Phase 1, Phase 2	Exploratory
PEN-221	PEN-221 in Somatostatin Receptor 2 Expressing Advanced Cancers	Somatostatin-R2	Tarveda Therapeutics	NCT02936323	Phase 1, Phase 2	Exploratory

Appendix

Intervention	Trial Name	Genetic Mutation/ Biomarker Studied	Industry Sponsor/ Collaborator	NCT Number	Phase	Designation
Rovalpituzumab tesirine	Rovalpituzumab Tesirine in Delta-Like Protein 3-Expressing Advanced Solid Tumors	DLL3	Stemcentrx	NCT02709889	Phase 1, Phase 2	Exploratory
anti-MUC1 CAR-pNK cells	CAR-pNK Cell Immunotherapy in MUC1 Positive Relapsed/ Refractory Solid Tumor	MUC1	PersonGen BioTherapeutics (Suzhou) Co., Ltd.	NCT02839954	Phase 1, Phase 2	Exploratory
AG-221	AG-221 in Subjects With Advanced Solid Tumors	IDH2	Celgene Corporation	NCT02273739	Phase 1, Phase 2	Exploratory
Sym015	Sym015 (Anti-MET) in Patients With Advanced Solid Tumor Malignancies	MET	Symphogen A/S	NCT02648724	Phase 1, Phase 2	Exploratory
Pembrolizumab	Pembrolizumab (MK-3475) in Patients With an Advanced Solid Tumor or Lymphoma (MK-3475-051/KEYNOTE-051)	PD-L1	Merck Sharp & Dohme Corp.	NCT02332668	Phase 1, Phase 2	Exploratory
HerinCAR-PD1 cells	PD-1 Antibody Expressing CAR-T Cells for EGFR Family Member Positive Advanced Solid Tumor	EGFR	N/A	NCT02873390	Phase 1, Phase 2	Exploratory
OMO-1	OMO-1 in Solid Malignancies	MET	Octimet Oncology N.V.	NCT03138083	Phase 1, Phase 2	Exploratory
LGX818, MEK162, LEE011	LGX818 in Combination With MEK162 in Patients With BRAF Dependent Advanced Solid Tumors	BRAF V600	Array BioPharma	NCT01543698	Phase 1, Phase 2	Exploratory
BYL719lAMG 479	Combination of BYL719 Plus AMG 479 in Patients With Selected Solid Tumors	PIK3CA	Novartis Pharmaceuticals, NantCell, Inc.	NCT01708161	Phase 1, Phase 2	Exploratory