北京市希思科临床肿瘤学研究基金会

SOCIETY FOR TRANSLATIONAL ONCOLOGY®

Satellite Roundtable: Biomarkers in Cancer

卫星圆桌会议：癌症生物标志物

-- By invitation only --

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Satellite Roundtable: Biomarkers in Cancer
卫星圆桌会议：癌症生物标志物

Convener: **Martin J. Murphy**
Co-Chairs: Yi-Long Wu & Richard L. Schilsky

Task Force Agenda
-- By invitation only --

Time	Subject	Speakers
7:00 – 7:45	Breakfast	
7:45 – 8:00	Welcome and introductions	Martin J. Murphy, Convener
8:00 – 8:15	Contemporary role of biomarkers in clinical oncology	Richard L. Schilsky
8:15 – 8:30	Concepts in biomarker development and validation	Lillian Siu
8:30 – 9:00	Regulatory framework for molecular testing	Guest Commentators
9:00 – 9:15	Current status of biomarker testing in China	Xu-Chao Zhang
9:15 – 10:15	Description of cancer biomarker tests offered commercially in China	10-15 minutes each
10:15 – 11:00	Biomarker testing needs in China	Open discussion (all attendees)
11:00 – 11:45	Potential biomarker testing solutions for China	Open discussion (all attendees)
11:45- 12:00	Next steps; adjourn	Richard L. Schilsky & Yi-Long Wu

Mission

The purpose of the **Satellite Roundtable: Biomarkers in Cancer** is to discuss the pathway forward in China for biomarker-driven targeted drug development that will enable multicenter clinical trials to be conducted, the results of which will be evaluable by the three regulators represented: CFDA, US FDA and EMA.

Session Overview

Test developers from the commercial and academic spheres will engage with Chinese clinical oncologists and international oncology experts in a discussion and planning exercise to identify needs for biomarker testing in China and discuss potential commercial and academic solutions to meet these needs.

Statement of Need

Biomarkers are molecular, biological or physical attributes of cells, tissues or organisms that characterize a physiological state and can be objectively measured to detect or define disease progression or predict or quantify therapeutic responses. Biomarkers are increasingly used in contemporary clinical oncology to assess cancer risk, refine prognosis, select optimal therapy and monitor response to treatment. Biomarker tests that are used to inform clinical decisions must be analytically validated and performed in highly qualified laboratories according to rigorous performance standards. Ideally, all biomarker tests should have clear clinical utility, that is, use of the biomarker in clinical

management should improve patient outcomes. The most common uses of biomarkers in clinical oncology are to refine prognosis of patients (prognostic biomarkers) and to aid in selecting treatment (predictive biomarkers). Increasingly, predictive biomarkers are co-developed with targeted therapies and used to identify patients most likely to benefit from treatment with the targeted agent. Tests for Braf V600E mutation in melanoma or EML4-ALK translocation in NSCLC are recent examples. Tests that provide inaccurate results can be harmful to patients if they result in a patient receiving a toxic and expensive drug that is not likely to be beneficial (false positive test) or if they exclude a patient from receiving a potentially beneficial treatment (false negative test). With the rapid introduction of molecular testing of cancer into the marketplace, clinicians are increasingly challenged to understand what test(s) to order in what clinical scenario, to understand the test results and to take appropriate action based on the test. In China, a need exists to develop a plan to for nationwide testing of tumors for those molecular abnormalities that are likely to impact patient care. An approach needs to be developed to determine the tests to be performed in each tumor type, the assay methodology to be employed, the biospecimen type to be studied and the optimal ways to insure widespread access to high quality testing with acceptable turnaround time and cost in a large a diverse country. The purpose of this workshop is to bring together clinical oncologists and test developers to develop a plan for cancer biomarker testing in China.

Commentary*

Max Ning, MD, PhD
US Food and Drug Administration

Development and routine use of tests for predictive tumor biomarkers become increasingly necessary for selection of patients appropriate for targeted therapies in order to achieve best treatment outcomes. Traditional tumor biomarkers such as specific chromosomal abnormalities and hormone receptor's positivity were tested prior to the development of cancer treatments targeting the biomarkers or related pathways. With a large number of emerging new tumor biomarkers in the last decade, co-development of targeted therapies with companion diagnostics to detect predictive biomarkers has considerably increased in recent years. Since 2011, six targeted oncologic products have been approved by the US FDA for the treatment of tumors with biomarkers as detected by FDA-approved companion diagnostics. To help understand how efficiently to co-develop a companion diagnostic for detection of clinically significant tumor biomarkers, the first approval (vemurafenib along with its diagnostic for BRAF V600E mutation test) of the six products will be used as an example to discuss key elements and challenges involved in the successful development of tumor biomarker testing. (*The views Dr. Ning expressed in the meeting represent his own scientific opinions based on his best knowledge and experience, and have no association with his official duty).

Biographies

Chenyan GAO, MD
China State Food and Drug Administration (CFDA)

Dr. Gao is currently Chief Pharmacist, Senior Reviewer, and Deputy Director of Office of Clinical Evaluation I.
Dr. Gao attended the Capital University of Medical Science in Beijing from 1980 – 1985 and was an Ophthalmologist at Beijing Juxianqiao Hospital from 1985 – 1988.
In 1988, she joined China's State Food and Drug Administration in the Center for Drug Evaluation. From 1988 – 2004, she was a Reviewer and responsible for evaluating the data of clinical trials of new drugs. From 2005 – 2011, she was Director of Division VII where she was responsible for evaluating the applications of cardiology (hypertension, angina etc.) and surgery (prostatitis, organ transplanting, etc.) drugs.
Since 2011, she has been the Deputy Director of office of Clinical Evaluation and is responsible for evaluating the data of clinical trials of oncology and hematology new drugs.

Francesco Pignatti, MD
European Medicines Agency (EMA)

Dr. Pignatti graduated as medical doctor at the University of Rome La Sapienza.
In 1995 he became research fellow at the EORTC Data Center, Brussels, Belgium, where he was involved in numerous activities including clinical trial design, conduct, analysis, and reporting.
He became Medical Advisor for the Gastrointestinal Tract Cancer Cooperative Group, and Brain Tumor Cooperative Group in 1997.
In 1997 he obtained a Master of Science degree in Biostatistics from the University of Limbourg, Belgium.
In 1999 he joined the European Medicines Agency (EMA) in London. Since 2009 he holds the position of Head of Oncology, Haematology and Diagnostics in the Human Medicines Evaluation Division.

Yangmin Max Ning, MD, PhD
US Food and Drug Administration (US FDA)

Dr. Ning is a board-certified medical oncologist and serves as a senior reviewer in the Office of Hematology and Oncology Products, Center for Drug Evaluation and Research, US Food and Drug Administration (FDA). He also is an active associate investigator, conducting clinical trials at the National Cancer Institute.

He has conducted clinical reviews of 10 new oncology drug applications and helped design a number of key trials leading to regulatory approvals. He has received several awards including the 2012 FDA Scientific Achievement Award for Excellence in Review Science.

Dr. Ning received his M.D. from Beijing Medical University and his Ph.D. from the Medical College of Ohio with research in steroid receptors' signaling. He had his post-doctoral training in genetic regulation at the University of Michigan and completed his residency in internal medicine at Wayne State University, followed by a clinical oncology- hematology fellowship at the National Cancer Institute and National Naval Medical Center. He is a recipient of National Research Service Award, has authored a number of well-cited publications and book-chapters based on his original research and review activities, and has presented at national and international meetings.

Satellite Roundtable Attendees

Yi-Long Wu President, CSCO & CSCO Executive Committee Deputy Director, Guangdong People's Hospital Director, Guangdong Lung Cancer Research Institute	**Shu-Kui Qin** Chairman, Xi Si Ke Deputy Director, Chinese PLA 81st Hospital Director, PLA Cancer Center Past President, CSCO	**Tony Mok** Vice-Secretary General, CSCO President, IASLC Professor, Chinese University of Hong Kong
Jin Li Secretary General, CSCO Executive Committee Director, Division of Medical Oncology, Fudan University Cancer Hospital	**Shun Lu** Deputy Secretary General, CSCO Executive Committee Director, Lung Cancer Clinical Center, Shanghai Chest Hospital	**Qing Zhou** Deputy Secretary General, CSCO Executive Committee Guangdong Lung Cancer Research Institute
Rong-Cheng Luo Deputy Secretary General, CSCO Executive Committee Vice Director, Nanfang Hospital affiliated with Southern Medical University	**Ying-Cheng** President, CSCO Expert Committee on Small-Cell Lung Cancer Director, Jiling Oncology Hospital	**Ji-Wei Liu** Vice President, CSCO Expert Committee on Small-Cell Lung Cancer Director, Division of Medical Oncology, No.1 Hospital Affiliated to Dalian Medical University
Xu-Chao Zhao Guangdong Lung Cancer Institute, Guangdong Academy of Medical Sciences	**Bi-Yun Wang** Physician, Fudan University Cancer Hospital	
Richard L. Schilsky Chief Medical Officer, ASCO Visiting Faculty, ACT China	**J. Jack Lee** MD Anderson Cancer Center Visiting Faculty, ACT China	**Lillian L. Siu** Princess Margaret Hospital Visiting Faculty, ACT China
Chen-Yan Gao China Food and Drug Administration (CFDA)	**Max Ning** United States Food and Drug Administration (US FDA)	**Francesco Pignatti** Head of Oncology, Haematology and Diagnostics European Medicines Agency (EMA)
Helena Zhang Quintiles	**Yu-Mei Yang** Quintiles	**Susan Wang** BTG International Canada Inc.
Svetlana Kobina Bayer Healthcare Pharmaceuticals	**Zhihui (Zig) Lang** Bayer Healthcare Pharmaceuticals	**Mo Chen** Sanofi
Jiang Peng Sanofi	**Martin J. Murphy** Convener, ACT-China Member, Fourth CSCO Steering Committee	**Ann Murphy** Board Chairs Delegate, STO

Roundtable Executive Summary

November 22, 2013, Guangzhou, China

*In advance of the third annual **Advanced Clinical Trials – China** workshop (**ACT China III**), held under the auspices of the **Chinese Society of Clinical Oncology** (CSCO), the **Beijing CSCO Clinical Oncology Research Foundation** (Xi Si Ke), and the **Society for Translational Oncology** (STO) in association with the **American Society of Clinical Oncology** (ASCO), a **Biomarker Satellite Roundtable** was convened in Guangzhou on November 22, 2013. The purpose was to discuss the status of biomarkers in relation to targeted anti-cancer drug development including target and companion diagnostic validation.*

Martin J. Murphy: Dr. Murphy, Convener of *ACT China* and its *Biomarker Satellite Roundtable*, opened the meeting and provided general information about ACT China, CSCO, STO and ASCO. He discussed the reasons to hold this first *Biomarker Satellite Roundtable* along with remarks about the attendee profile and the mission and agenda. He welcomed all invited speakers and guests, especially **Dr. Chenyan GAO** (China FDA), **Dr. Francesco Pignatti** (EMA), and **Dr. Max Ning** (United States FDA). Dr. Murphy also acknowledged his appreciation to those who helped support this first *Biomarker Satellite Roundtable* and encouraged all to have a productive discussion that will advance cancer drug discovery and development in and for China. He then introduced the Roundtable Chairman, **Professor Yi-Long WU**.

Yi-Long Wu: Dr. Wu welcomed everyone to Guangzhou and thanked them for joining the Roundtable and introduced Dr. Richard Schilsky, ASCO's chief medical officer, who has also been an adviser to the US FDA on the validation and use of biomarkers in the development and registration of oncology products in the United States.

Richard L. Schilsky: "*Contemporary Role of Biomarkers in Clinical Oncology*".

Dr. Schilsky began with a definition of biomarkers by the NIH as molecular, biological or physical attributes that characterize a physiological state that can be objectively measured to detect or define disease progression or predict or quantify therapeutic responses.

He discussed the following topics, providing pertinent definitions, as warranted:

- *Potential use of biomarkers*: Risk Assessment, Detection, Prognosis, Prediction/therapy selection, Response assessment, Monitoring for recurrence.

- *Prognostic and Predictive Markers need to be differentiated.* ***Prognostic marker:*** a characteristic associated with the disease natural history; best assessed in a randomized trial with a no treatment control group. ***Predictive marker:*** a characteristic associated with treatment effect; best assessed in a randomized trial where the treatment of interest is the variable.

- *Biomarkers in Clinical Cancer Care:* Sequencing, expression arrays, FISH, IHC can be used to detect the biomarker and the clinical information such as imaging studies and serum markers, e.g. PSA and CA125, are also considered as biomarkers. Pharmacokinetics and PD biomarkers in tumor or normal tissue such as blood, hair and skin can be the biomarkers too. The newest technologies such as functional imaging, circulating tumor cells (CTCs) and circulating endothelial cells (CECs) can also be used as biomarkers.

- *Increasing Reliance on Biomarkers:* When a *cancer prevention clinical trial* is conducted, the most important goal is to use biomarkers to identify high-risk patients, estimate risk reduction and make an early

diagnosis. In a *therapy trial* the prognostic biomarkers can identify the risk of recurrence and avoid the toxicity of adjuvant therapy for low risk patients or recommend more intensive adjuvant therapy for high risk patients. *Predictive markers* can be predictors of toxicity, drug sensitivity or relapse/resistance and can enable selection of the least toxic therapy and most efficacious therapy.

Schema of Personalized Medicine: A genome-based vision for personalized cancer medicine will require a paradigm shift in both diagnosis and treatment. Traditionally, tumors are classified by site of origin and histology. In the future, tumor nucleic acids will be profiled for a wide array of genomic alterations with a view to specific, tailored treatment options for each individual patient.

Increasing Complexity of Molecular Diagnosis: For the histomorphologic diagnosis we performed clinical & histology-based therapy and use clinicopathologic factors to select available drugs for an individual patient. For the molecular diagnosis we need to obtain FFPE or fresh tumor specimens, then macro- or micro-dissection of tumors and extract tumor nucleic acids. Current personalized medicine (Target-Based Therapy V1.0) uses single gene-based molecular tests to select specific drugs for an individual patient. Evolving Personalized Medicine (Target-Based Therapy V2.0) uses multiplexed molecular tests for an individual patient. Future Personalized Medicine (Patient-Base Therapy) will use an integrated genomic profile from high-throughput next-generation sequencing to tailor targeted treatment for an individual patient based on aberrations in molecular pathways or networks.

For single biomarker tests, Sanger DNA sequencing or pyrosequencing, RT-PCR, FISH and IHC can be used. For multiplex hotspot mutation tests PCR-based SNapShot, PCR-based Mass Array SNP Sequenom can be used. With High-Throughput technologies SNP/CNV, DNA microarray, RNA microarray and epigenetic modifications can be assessed. For next-generation sequencing whole genome or exome capture sequencing (DNA), whole or targeted transcriptome sequencing (RNA) and epigenetic profiling can be used.

Biomarker Validation: A biomarker needs to be validated. Demonstration of clinical utility requires that health outcomes be improved when the biomarker is used compared to when it is not used. The clinical validity demonstrates that the biomarker identifies clinically relevant phenotypes and includes clinical specificity, clinical sensitivity, prevalence, PPV/NPV, penetrance. The analytic validity includes assay robustness, quality control, analytic specificity and analytic sensitivity.

Omics-based Test Development Process: During the discovery phase, the candidate test is developed on a training set, followed by the lock-down of all computational procedures and confirmation of candidate omics-based test using an independent sample set if available (preferred) or a subset of the training set not used during training (less preferred). Consultation with the FDA is needed in the test validation phase. We need to define the clinical test method, analytical validation and clinical/biological validation using blinded sample sets. Then we define, validate and lock down the test (intended use, assay, computational procedures and interpretation criteria). After the discovery and test validation stage there is the evaluation for clinical utility and use stage. There are three potential pathways: prospective/retrospective study with archived specimens, prospective clinical trial (test does not direct patient management) and prospective clinical trial (test directs patient management). After the evaluation stage, if IDE is needed, then FDA approval/clearance or LDT process for clinical test needs additional high quality evidence to evaluate clinical utility of the test and practice guidelines and reimbursement. Finally, the test goes into clinical use.

What is “Actionable”? Classification of the clinical effect of the variant taking into account the type of effect, strength of the evidence, and the size of the effect. Variants in the top right quadrant should have the highest priority with respect to actionable clinical decisions.

Implementing Personalized Cancer Care needs biospecimens and molecular pathway analysis, biomarker validation and multiplex assays, instrumentation and informatics, clinical decision support and patient monitoring.

Discussion:

Yi-Long Wu: In gastric cancer or breast cancer we don't talk about the driver gene. Only in lung cancer we talk about it. Why?

Richard Schilsky: In breast cancer, the HER2 may be a driver pathway.

Tony Mok: I want to know the definition of "clinical validity."

Richard Schilsky: Clinical validity means that the test reliably defines a specific patient population. Any time we perform a test to guide a clinical decision, the test procedure needs to be well described and the test should be reproducible and reliable. Different sponsors may choose different methods.

Max Ning: Safety and efficacy of biomarker based product development and use are also considered for clinical validation.. Examples were erlotinib with the EGFR detection and crizotinib with the ALK detection.

Lillian L. Siu: "Concepts in Biomarker Development and Validation"

To develop an ideal biomarker during the drug discovery phase, we explore the biomarker during preclinical and clinical development phases. Most targeted drugs, however, usually had no biomarkers during their drug discovery phase; only after drug approval or during the drug's marketing phase were biomarkers established (e.g., anti-EGFR, MAb and KRAS).

Stages of Biomarker Discovery and Development: When the target identification biomarker was discovered and during lead identification the assay was developed, biomarker validation was performed with preclinical evaluation. With IND and phase I/II/III trials, biomarkers were test developments, clinical validation and regulatory submission. Finally, when the drug was marketed the diagnostic test was approved.

Types of Biomarkers:

Prognostic Biomarkers: provide information about the patient's overall cancer outcome regardless of therapy. *Examples:* ECOG status in lung cancer, LDH in non-Hodgkin's lymphoma, cytogenetics in AML.

Predictive Biomarkers: provide information regarding the probability of benefit or toxicity from a specific therapy. *Examples:* HER2 overexpression in breast cancer (trastuzumab), K-RAS mutational status in colorectal cancer (anti-EGFR antibodies), ALK translocation in NSCLC (ALK inhibitors).

Pharmacokinetic (PK): provide information about the absorption, distribution, metabolism and elimination (ADME) of the drug and/or its metabolites in the patient and/or tumor. *Examples:* Cmax (peak concentration), Cl (clearance), t1/2 (half-life), AUC (exposure = area under concentration x time curve).

Pharmacodynamic (PD): provide information about the effect of a therapeutic intervention on the patient and/or tumor. *Examples:* neutrophil count, skin rash, tumor expression of a downstream marker (e.g., pERK post administration of a MEK inhibitor), decrease in FDG uptake on PET scan post treatment.

Integral Markers are essential for conducting the study, being used for patient enrollment, treatment stratification or for measuring outcomes (e.g., prognostic, predictive biomarkers).

Integrated Biomarkers are used when testing a hypothesis based on preclinical data (e.g., pharmacodynamic, predictive biomarkers).

Exploratory Biomarkers are used to generate a hypothesis (e.g., pharmacodynamic, predictive biomarkers).

Trial Designs for Predictive Marker Validation was then introduced.

Even if you have the ideal biomarker, several issues should be considered.

Assay Related: Assay development, optimization, reproducibility and validation, CLIA-certified lab. Tissue Related: Type of tissue specimens: Archival vs. fresh, Paraffin-embedded vs formalin-fixed vs. fresh frozen. Tissue blocks vs. slides. Diagnostic/therapeutic specimens vs. samples obtained for research purpose only (retrospective vs. prospective), Primary tumors vs. metastases, FNA, core needle biopsy, resection specimens, Realistic assessment of amount of tissue available for biomarker analysis.

Target Assessment: What is the status of the target in tissues (tumor or surrogate) pre-treatment? Present vs absent/Activated vs inhibited/Gene amplified vs not/Wild-type vs mutated, etc. What happens to the target in tissues (tumor or surrogate) during treatment? If there is a "change"? How can you validly measure and quantitate the "change"? Is the assay reproducible? When do you measure the "change"? How do you report the "change"? Does the "change" in surrogate tissues reflect same "change" in tumor tissues? Does the "change" correlate with clinical outcome?

The Key Players: Pathologists and translational scientists/Lab technicians/Correlative studies coordinators/Interventional radiologists/Biostatisticians/Bioinformatics experts/Clinical trial nurses and coordinators/Clinical investigators/Patients – who give informed consent.

Discussion:

Tony Mok: How do you define the cut-off value of quantitative biomarkers?

Lillian Siu: For a biomarker with positive and negative, it's easy to define the status of the biomarker. While for the quantitative biomarker, the pre-clinical model was important to define the cut-off value of the biomarker.

Max Ning: Cut-off of quantitative determination is really dependent on the pre-clinical data. For quantitative data, if a 10% positive cut-off can have a response and the response is durable, the cut-off would be defined as 10% positivity. For the quantitative biomarker, some tissue was tested and some was not, so it may affect the result.

Richard Schilsky: If you want to make a cut-off value to determine a biomarker you have to consider the incidence of the marker. If the incidence is low, you need to screen more patients. If the incidence is high, then fewer patients are needed to be screened.

Lillian Siu: For the quantitative biomarker, the biological feature is another aspect to consider.

Tony Mok: When should a biomarker not be a biomarker? There are so many biomarkers and I think most of them will die. So how to design and when to decide a biomarker is dead?

Yi-Long Wu: For example of the cMET clinical trial, 2++ or 3+++ of the IHC result for the cMET may be both are OK as a biomarker. But when we performed the trial we chose the 3+++ patients because it was high enough. When the trial is finished and develop the market, we can try 2++ patients.

Max Ning: No biomarker has yet been found even though Avastin has biological activities. If there was a perfect biomarker, it would even be better. But so far we have no biomarker for use of the drug..

Yi-Long Wu: Another example is cetuximab. Almost all the trials in lung cancer of cetuximab were a failure. If they look back of the trials, maybe they would have chosen 3+ IHC patients.

Tony Mok: This may not be science but commercial.

Jin Li: We performed the phase I study of cetuximab in colorectal cancer. The data found that while patients did not respond to the cetuximab, the reason may be the BRAF pathway. The cancer cells activate the EGFR. When the BRAF was activated the downstream of EGFR was activated. So we needed to consider the interaction of the signal pathway.

Xu-Chao Zhang: "Current status of tumor biomarker testing in China".

Biomarkers include three types: **Diagnostic** - to indicate if an individual is ill or carrier of defective genes, **Prognostic** - to show the effects of tumor on the outcome of a patient, with no relationship with intervention, **Predictive** - to show the effects of intervention on the tumors.

Cancer disease model shifts from common disease, common variations to common disease with many rare variations. Lung cancer is the most heterogeneous disease. Multi-gene needs multi-platform: NGS for all mutations, expression, CNV and SV, IHC for altered proteins.

In 2012 EGFR testing rate was about 20%. In Taiwan it was 85%. In the mainland until April 2013, total of 58 hospitals had established the EGFR testing platform. In 2012, only 16 high-level hospitals participated on the NHFPC PQCC EGFR EQA program. Results from 68 hospitals' feedback showed that 59 hospitals passed the quality control. Concordance got up to 87%. 7 hospitals did not up-load their results. EGFR mutation testing had been written into the 2010 China lung cancer guidelines, the 2011 diagnosis and prognosis standards for primary lung cancers, expert consensus on the management of EGFR mutant patients, and expert consensus on EGFR testing for Chinese lung cancer.

ALK testing status in China: ALK was only tested in high-level hospitals and third-party service, Ventana IHC approved, yet Vysis FISH were under application for CFDA approval. QRT-PCR was approved by the CFDA, Pfizer and Roche Ventana, who are jointly pushing forward the clinical use of IHC testing, which is the CTALK program by CTONG.

CSCO biomarker committee: Affiliated with CSCO, a non-profit and academic organization, has proposed a path of biomarker identification, validation and application in clinic. Collaboration will be achieved more in biomarker-driven practice and trials. This will make the Experts Consensus of ALK testing in NSCLC (China).

Burgeoning market in China: There is faster growth in the China market of personalized diagnostics, which includes >20 Molecular Diagnostic Companies mainly in high-tech areas like Beijing, Shanghai and Guangzhou. There are more and more companies in infectious disease moving into this tumor Dx field.

Features of China products for tumor molecular Dx: DNA/RNA as material, which are different technologies, but PCR were most often used. One company may have several kinds of platforms. Domestic companies will set up their brands gradually.

Application Status of personalized tumor Dx products: In mainly middle-, or big- cities and high-level hospitals, Dept. of Pathology (67%), and third-party service centers, several PCR products were approved by the CFDA. Several tumor types were involved, like cancers of lung, colon and rectum, breast, lymph node, and gastric. Specimen's types: mainly FFPE and other small biopsies and pleural effusions.

CFDA-approved Dx products: Cover Lung Cancer, breast cancer, CRC, melanoma and leukemia. This includes point mutation, insertion, deletion, rearrangement, and CNV. EGFR and KRAS kits are most common. Sequencing has not been approved for a special kit.

Future directions: Quality improvement, testing rate to be promoted, Multi-gene, multi-platform, Strengthen to support trial patient selection, Re-biopsy and Liquid biopsy.

Multi-gene testing: ongoing and promising, Snapshot technology: home-brewed assays.

Summary: Consensus-guided tumor marker testing: key markers like EGFR and ALK. These are preferable for more sensitive methods, ROS1, RET, MET, FGFR, PIK3CA, BRAF, HER2 testing for trial patients, from tissue to circulating blood and are chaotic for other markers: a muddy water! Some markers are not useful at the moment, esp. for chemotherapy, ERCC1 / RRM1 /TUBB3, etc. Molecular alterations of drugable targets might be encouraged to facilitate patient screening for trial enrollment. China is a burgeoning market for tumor biomarker testing but it needs quality improvement in assay standardization, quality control and accreditation, and consensus development.

Future directions: Multi-gene multi-platform methods should be developed and standardized, e.g., NGS + IHC

Jin-Li: In China the tissue bank of the association was impossible, even the tissue between the hospitals was controversial.

Shun Lu: There is no cancer registration system. In Shanghai a database based on clinical information was established but there is no tissue data in it.

Comment from pharmaceutical representatives: Companies are developing a plan of tissue banking in China.

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