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PMDA Perspectives on Oncology Panel

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- Regulatory Status of Oncology Panel in Cancer Genome Medicine in Japan
- Regulatory Perspectives on Oncology Panel
- CDx vs Comprehensive Genomic Profiling Test
Regulatory Status of Oncology Panel in Cancer Genome Medicine in Japan
Framework of Cancer Genome Medicine in Japan

11 Core Hospitals for cancer genome profiling for medicine

135 Cooperative Hospitals

CGP by Oncology Panel
- Draft Report
- Evaluation by Expert Panel
  - clinical evidence of variants
  - available therapies
- Final Report
- Primary Care Physician
Implementation of Oncology Panel in Japanese Medical Setting

DNA sequencing

Oncology Panel

DNA sequencer

Variant call

GeneX: c.2611C>T
GeneY: c.1652A>G
GeneZ: ...........

Software

SNV, Ins/De, CNV,SV

Draft Report

GeneA:L858R
GeneB: amplification...

Final Report

Patient #:

Draft Report

Interpretation by Expert Panel
Oncology Panel as a IVD Medical Device

DNA sequencing

Oncology Panel

GeneX: c.2611C>T
GeneY: c.1652A>G
GeneZ: ............

Variant call

Bioinformatics Pipeline

Software

SNV, Ins/Del, CNV,SV

Annotation

GeneA: L858R
GeneB: amplification ...

Draft Report

Final Report

Clinical Specimen

Physician

Interpretation by Expert Panel

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Promotion of Cancer Genome Medicine using Approved Oncology Panel

Center for Cancer Genomics and Advanced Therapeutics: C-CAT

Certified Labs for genomic testing
specimens
report
Core hospital
Sequence Data
Clinical info
Expert Panel
Cooperative Hospitals
CKDB report
cancer genomics info repository
Knowledge DB
Analysis using AI
Maximize treatment opportunity in collaboration with core and associated hospitals, Pharmaceutical companies, government
Secondary use
Development of Therapies, Dx system, and new BMs
Regulatory Perspectives on Oncology Panel
Proposed IVD Medical Device is reviewed on the following aspects:

- Analytical Performance
- Clinical Performance
- Clinical Utility
Clinical Utility is expected to be established through implementation of the approved or advanced medical care-covered oncology panel and accumulation of genomic and clinical data in CKDB.

Reference Database:
- Public DB: specified
- Proprietary DB: specified, DB procedures and operations are reviewed.
- Critical procedures to identify the clinically significant variants are subjected to the approved matter.
Analytical Performance

- Validation characteristics to be evaluated:
  - Accuracy, Precision (repeatability, intermediate precision), specificity, Detection Limit
  - Potentially interfering materials

- Representative validation approach:
  - Validation sample set should cover the variant categories (SNVs, indels, and others) that NGS panel intended to detect.
  - Scientific justification of representative set of variants are required.
Analytical Performance: Points to consider and Challenges

- **Accuracy**
  - By comparison to an orthogonal method
- **Test performance across tumor tissue types**

- **Challenges:**
  Availability of the validated orthogonal method other than approved CDx in Japan
<table>
<thead>
<tr>
<th>Ref DB</th>
<th>Proprietary DB</th>
<th>Public DB and proprietary DB</th>
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| What is reviewed? | • DB procedures and operations  
• Variant interpretation  
• Requirement and training for personnel involved in interpretation process.. etc. | • Procedures of variant interpretation using public and proprietary DB  
• Procedures and operations of proprietary DB  
• Requirement and training for personnel involved in interpretation process .. etc. |
| Approved Matters | • DB procedures and operations  
✓ Criteria of variant classification  
✓ Variant classification procedure  
✓ Variant re-classification criteria and procedure | • Procedures of variant interpretation using public and proprietary DB  
• Procedures and operations of proprietary DB |
| Approval conditions | QMS inspection  
• Variant classification operations following the approved SOP  
• Annual report on:  
✓ Newly identified variant  
✓ Reclassification of variant | Should be decided taking into consideration of:  
• Transparency and public accessibility of public DB  
• Clinical performance of panel is dependent on Expert Panel |
CDx vs CGP Test
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<th>CDx</th>
<th>Comprehensive Genomic Profiling Test</th>
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| **Analytical performance** | • In principle, evaluation for each specific BM  
• Representative validation approach is possible in some cases. | Representative validation approach is possible, if justified.                  |
| **Clinical performance** | Evaluated by -clinical study of the corresponding TP  
or -concordance study with the approved CDx                      | • Established by expert panel  
• Evaluated on whether it can appropriately provide necessary variant info for the expert panel to consider the best possible treatment for a patient. |
| **Clinical Utility**   | Established in the major efficacy trials of TP                             | Expected to be established through the implementation of oncology panel into clinical setting |
CGP test is reviewed on whether analytical report produced by the proposed MD could serve necessary information for expert panels to consider treatment possibilities for patients.

- Design of Panel Content
- Analytical Performance
- Detectability for possible driver genes

Clinical Performance

Expert Panel

Reference Database:
- Specified
- DB procedures and operations are reviewed for proprietary DB.
- Critical procedures to identify the clinically significant variants are subjected to the approved matter.