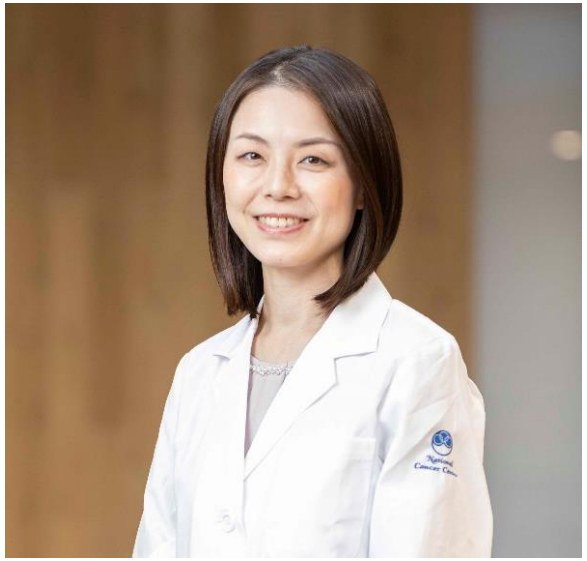
Cancer Genomic Medicine System (Status in Japan)



Yayoi Ando

Headings

I. Cancer Genomic Medicine System

II. Expert Panel

III. Actual Operations

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Basic Plan to Promote Cancer Control Programs (3rd term) (Summary)

Section 1 : Overall goals

"People including cancer patients, To understand cancer, To overcome cancer"

(1) Improvement of cancer prevention and cancer screening based on scientific basis
(2) Realization of patient-oriented cancer treatment
(3) Establishment of a society in which cancer patients can live peacefully while maintaining dignity

Section 2 : Specific areas

1. Cancer prevention

(1) Primary prevention
(2) Early detection, Cancer screening (Secondary prevention)

2. Improvement of cancer treatment

(1) Cancer genomic medicine
(2) Surgical therapy, Radiotherapy, Pharmacotherapy, Immunotherapy
(3) Team-based cancer treatment
(4) Rehabilitation
(5) Supportive care
(6) Rare cancer, Intractable cancer (According to the characteristics of each cancer)
(7) Cancer among children, adolescent and young adult, and elderly
(8) Pathological diagnosis
(9) Cancer registry
(10) Promotion of early development and authorization of medical products and equipment

3. Living with cancer

(1) Palliative care appropriately provided after diagnosis
(2) Counseling support and information service
(3) Cancer control and provision of patient support founded on social collaboration
(4) Social issues including employment of cancer patients
(5) Cancer control according to the life stages

4. Development of foundation to support above

(1) Cancer research
(2) Human resource training
(3) Cancer education and awareness-raising activities

Section 3 : Necessary items to promote cancer control comprehensively and systematically

1. Further strengthening collaboration among relevant organs
2. Prefectures formulate prefectural cancer control plans
3. Endeavor of people included cancer patients
4. Cooperation with the patient community
5. Implementation of necessary financial measures Efficiency and prioritizing of budget
6. Assessment of the goal achievement status
7. Reviewing Basic Plan to Promote Cancer Control Programs

Third phase of the Basic Plan to Promote Cancer Control programs

Key elements of Cancer Genomic Medicine

①Establish a body of providing CGM

- Designate core hospitals for CGM throughout Japan
- Establish a body of CGM cooperating with designated cancer hospitals

②Establish a body to aggregate and utilize genomic and clinical information

- Establish the Center for Cancer Genomics and Advanced Therapeutics (C-CAT) as a new hub for cancer genomic medicine.

③Consider approval and insurance coverage of genomic tests and related pharmaceuticals.

- Consider an appropriate position of genomic tests (Ex. genomic panel testing, etc.) under the national health coverage.
- Promote expansion for pharmaceuticals with conditional early approval system.

④Develop human resources in CGM

- Develop and deploy human resources in CGM (Ex. genomic counseling, etc.)

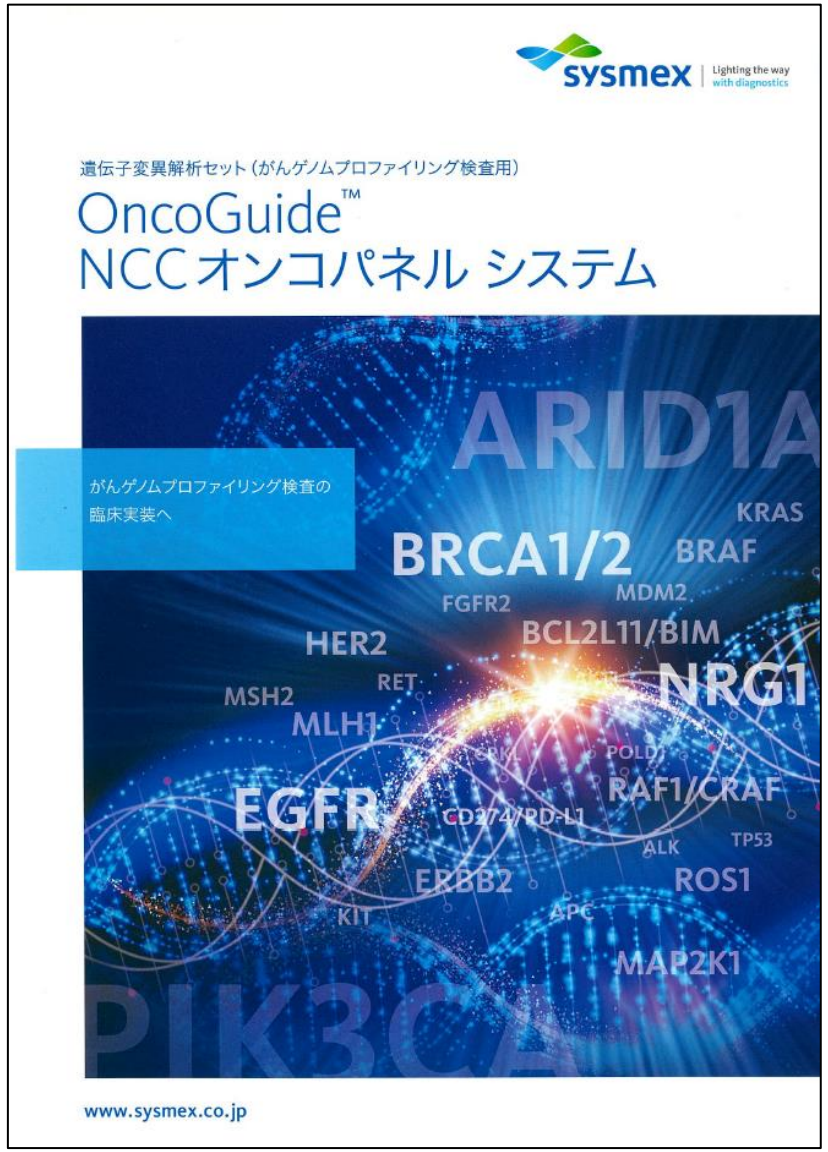
⑤Promote research in cancer genomics

- Promote research, especially in clinical genomic medicine and immune therapeutics
- Analyze collected information in C-CAT and promote research strategically.

⑥Build up the consortium with experts, patients and citizens.

- Build up the consortium of Cancer genomic medicine promotion consortium

Gene Panel Tests Covered By Insurance In Japan



The Outline of Cancer Genomic Medicine in Japan

National Cancer Center Japan

Regulatory authority

Academic societies etc.

Cancer Genomic Medicine Promotion Consortium

Council

Scientific evaluation for CGM from a standpoint of a third party
Providing opinions to MHLW based on scientific evaluation.
- Collecting opinions from citizens and providing appropriate information to citizens about CGM

Decision about the direction of CGM in Japan

Patients・People

Center for Cancer genomics and Advanced Therapeutics (built in National Cancer Center)
- Collecting, storing and managing data
- Contracting with hospitals, research institutes or industries
- Storing patients' data and receiving consultancy

- Genomic information
- Clinical information

CKDB

Research institute
- Strategic promotion of research including Liquid biopsy or Immunotherapy, etc.

Industry
- Drug development
- Medical Device Development

Collecting and managing information

Private companies
- Quality- and efficiency-assured genomic analysis

Information registry

Reports

Entrustment contract

Designated Core Hospitals for CGM
- Quality-assured genomic panel testing
- Annotation of genomic panel testing
- Implementing and supporting genomic counseling
- Implementing and introducing clinical trial
- Collecting, storing and managing quality information

Samples・Clinical information

Reports

Designated Hospitals for CGM
Cooperative Hospitals for CGM

MHLW: Ministry of health, labour and welfare
CGM: Cancer Genomic Medicine
NGS: New generation sequensing

Designated core hospitals for cancer genomic medicine

Driving force of cancer genomic medicine

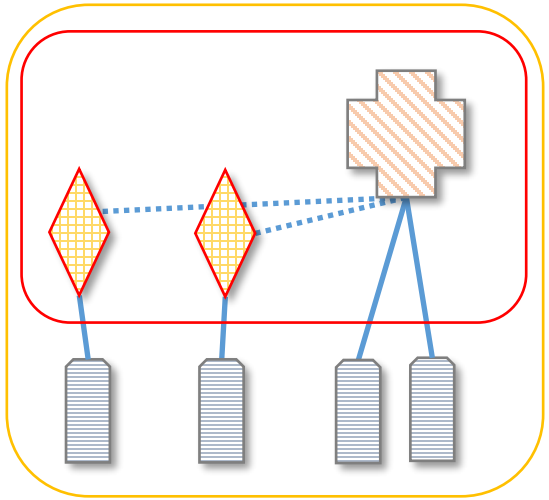
ICRweb: https://www.icrweb.jp/icr_index.php?lang=en

Functions of the Designated Core Hospitals for CGM

Designated Core Hospitals: DCH

Designated Hospitals: DH

Cooperative Hospitals: CH



Consent about tests → Specimen preparation → Sequencing → Create Reports → Expert panel → Result Explanation → Treatment → Research and developments

	Consent	Specimen	Reports	Expert Panel	Result	Treatment	Research
DCH	Required	Required	Required		Required	Required	Required
DH	Required	Required	Required		Required	Required	Cooperation
CH	Required	Required	・Taking part in expert panels held in DCH or DH		Required	Required	Cooperation

Designated Core Hospitals, Designated Hospitals, and Cooperative Hospitals for CGM cooperate to ensure that people can undergo oncogene panel tests at any location in Japan and can be treated based on the results.

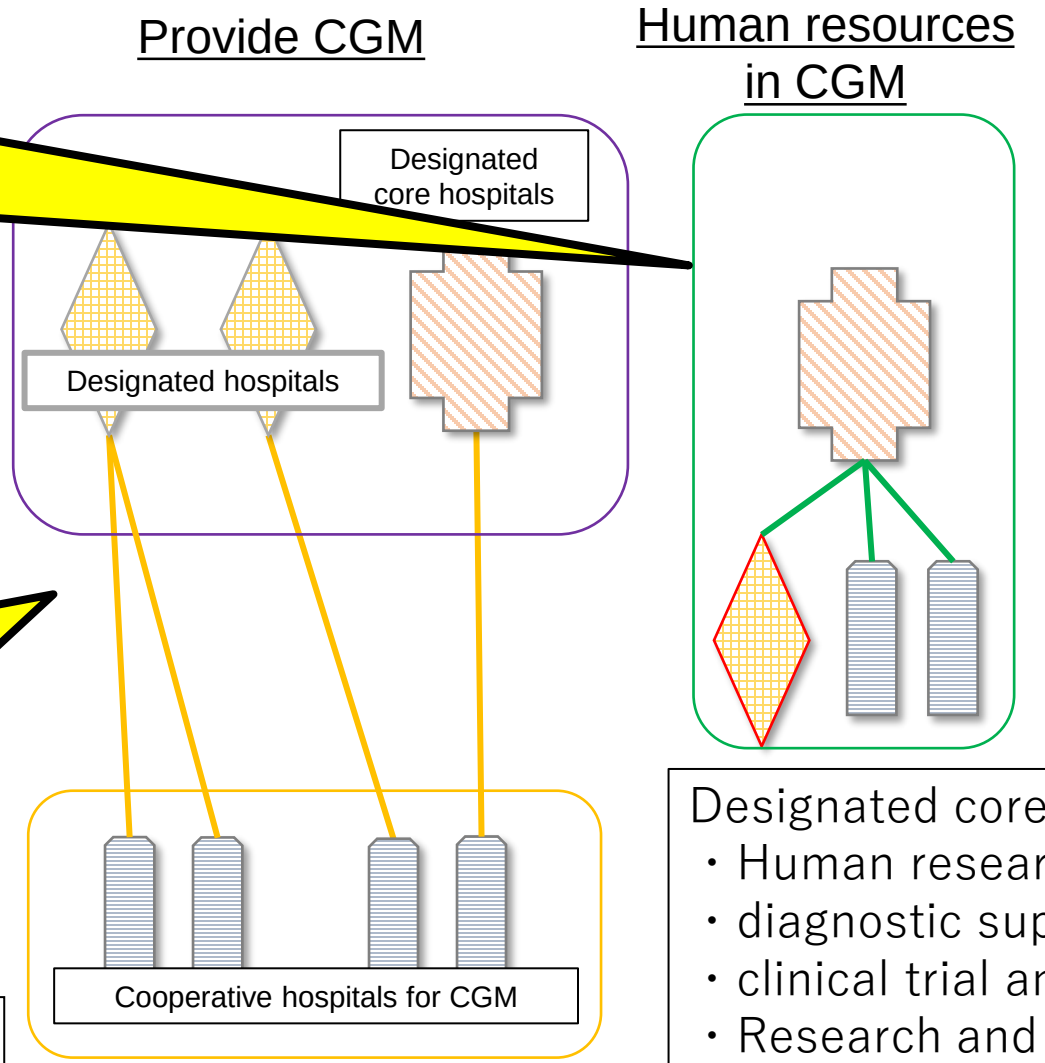
Cooperative System For Designated Core Hospitals For CGM

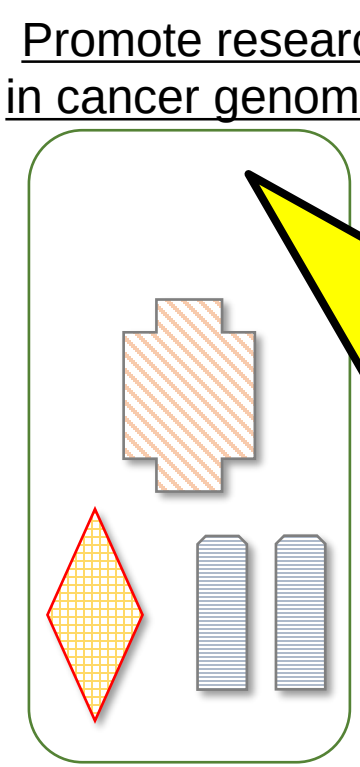
Designated Core Hospitals are mainly responsible for the development of human resources related to oncogenes.

Analyze the results of genomic panel testing in their own institutes.

Cooperative Hospitals collaborate with Designated Core Hospitals or Designated Hospitals to provide cancer genomic medicine.

Provide CGM cooperating with DCH or DH





Although Designated Core Hospitals are leading the way in treatment, clinical research, clinical trials, and research and development of new drugs based on oncogene information, the nation is working together to achieve these goals.

Designated core hospitals play a core role in;
- Human research management
- diagnostic support
- clinical trial and advanced medical care
- Research and development

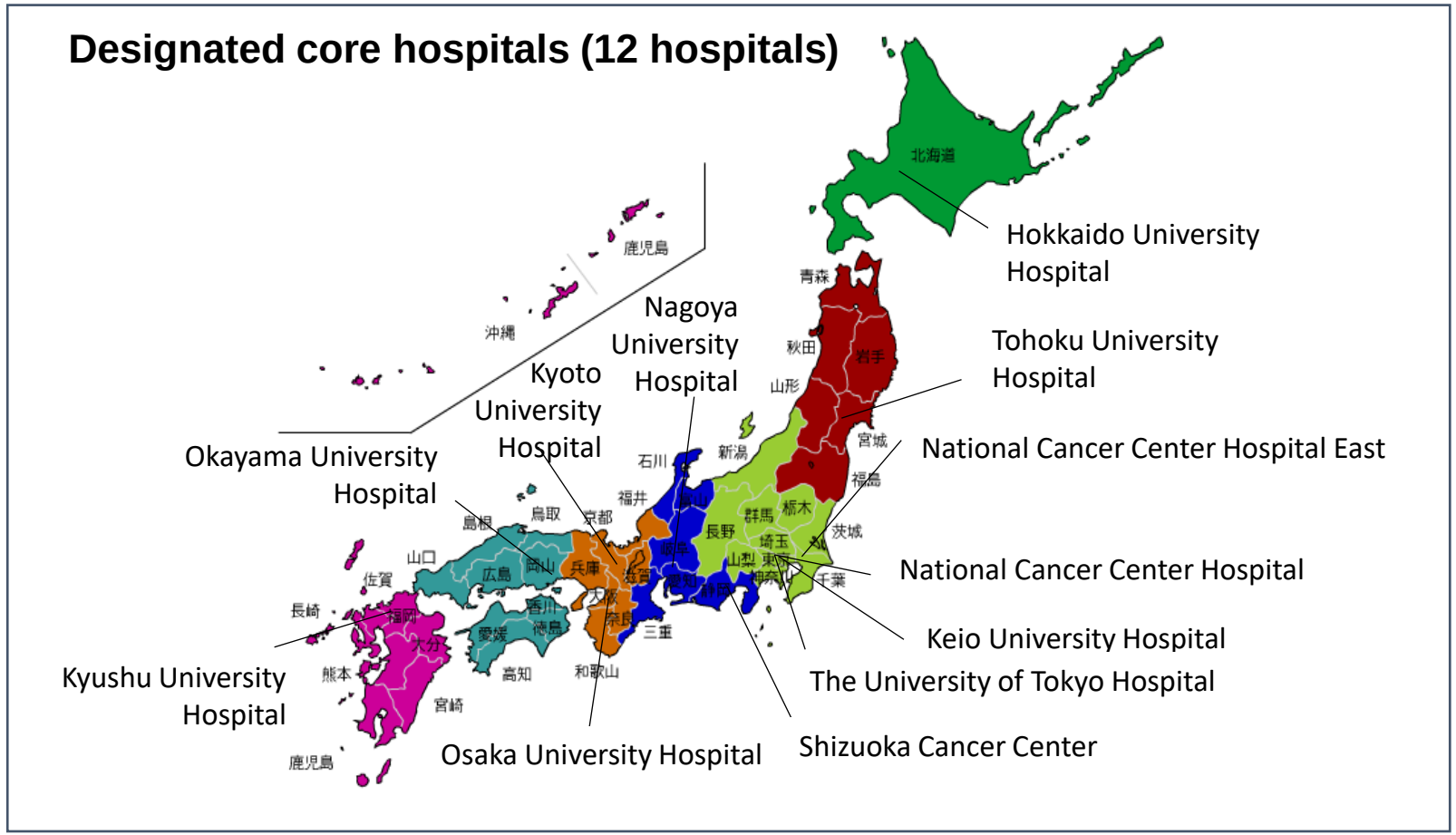
ICRweb: https://www.icrweb.jp/icr_index.php?lang=en

Designation Requirements For Designated Core Hospitals For CGM

①	A system for conducting panel tests (including outsourcing to external organizations)
②	A group of experts able to medically interpret the results of panel tests (including responding by collaborating with other organizations in some clinical areas)
③	Able to provide expert genetic counseling to patients, including those with hereditary tumors
④	More than a certain number of cases requiring panel tests
⑤	Able to collect and manage panel tests results and clinical information using an appropriate, security-assured method, and the required information is registered with the Center for Cancer Genomics and Advanced Therapeutics
⑥	A system able to store biological samples with fresh cryopreservation, including surgical specimens.
⑦	An appropriate system in place for conducting clinical studies and clinical trials, including advanced medicine, physician-led clinical trials, and international joint studies, and has a track record of conducting trials
⑧	A contact point that is easy for patients to understand and access regarding utilization of medical information and provision of clinical trial information

Partially revised from Guidelines for Maintenance of Designated Core Hospitals for CGM. HPB Notification No.0719/3

Designated Core Hospitals for CGM



Designated Core Hospitals and Designated Hospitals select the affiliated Cooperative Hospitals with whom they want to collaborate

<u>The system is built to ensure that cancer patients can receive cancer genomic medicine anywhere in Japan</u>

ICRweb: https://www.icrweb.jp/icr_index.php?lang=en

Guidelines for the Maintenance of Designated Core Hospitals for CGM

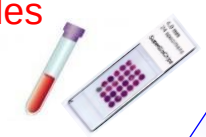
(omitted)
The National Cancer Center Hospital Center for Cancer Genomics and Advanced Therapeutics (hereinafter referred to as C-CAT) maintains a system where the **clinical information** of patients treated with cancer genomic medicine (as stipulated in the “Oncogene Information Repository Clinical Information List” established by the liaison conferences of such establishments as Designated Core Hospitals for CGM). **Genomic information** (original base sequence data (FASTQ or BAM) and a **list of genetic mutations** (VCF or XML) can be properly registered with the patient’s consent.

Guidelines for Maintenance of Designated Core Hospitals for CGM. HPB Notification No.0719/3

Center for Cancer Genomics and Advanced Therapeutics (C-CAT)

Certified laboratories for genomic testing

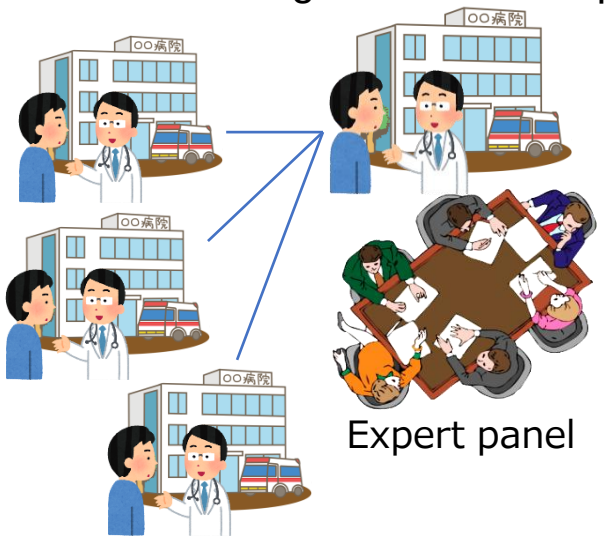
Samples



Reports

Sequencing data

Designated core hospitals

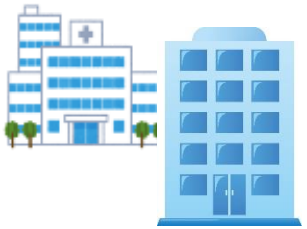


Expert panel

Cooperative hospitals

Clinical information

CKDB report annotating clinical significance



Secondary use

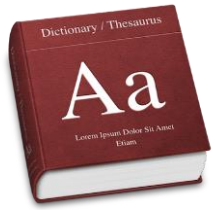
C-CAT

Repository for CGM

AI analysis

Development of new drugs, etc.

Cancer Knowledge Data Base



Sharing and research use of cancer genomics data

ICRweb: https://www.icrweb.jp/icr_index.php?lang=en

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What Is An Expert Panel?

An expert panel is a multidisciplinary panel to medically interpret the results of gene panel tests (comprising professionals, such as doctors with expert knowledge and skills in cancer drug therapy, doctors with expert knowledge and skills in medical genetics, and individuals with genetic counseling skills)

Guidelines for Maintenance of Designated Core Hospitals for CGM. HPB Notification No.0719/3

Members of an Expert Panel

- Cancer drug therapy specialist
- Medical genetics specialist
- Individuals with genetic counseling skills
- Pathologist
- Expert in molecular genetics and cancer genomic medicine
- Expert in bioinformatics
- Pediatrician who examines patients in your own facilities
- Patient's attending physician

Guidelines for Maintenance of Designated Core Hospitals for CGM. HPB Notification No.0719/3 (Partially revised)

Requirements For Conducting Expert Panels

(Designated Core Hospitals for CGM, Designated Hospitals for CGM)

- Meetings are held at least once per month.
- The results of gene panel tests requested by Cooperative Hospitals for CGM are considered, and the information is provided appropriately.
- Request additional information as needed from other knowledgeable Designated Core Hospitals for CGM or Designated Hospitals for CGM when discussing pediatric cases, or other cases that require greater expert knowledge.

Guidelines for Maintenance of Designated Core Hospitals for CGM. HPB Notification No.0719/3 (Partially revised)

Requirements For Conducting Expert Panels

(Cooperative Hospitals for CGM)

- Request expert panels at an affiliated Designated Core Hospital for CGM or Designated Hospital for CGM

- The attending physician participates in the referred patient's expert panel so that the physician can explain the presented content to the patient.

Guidelines for Maintenance of Designated Core Hospitals for CGM. HPB Notification No.0719/3 (Partially revised)

Matters Considered By Expert Panels

Overall test	Quality of specimens and data
Regarding each genetic change	Biological significance of genetic change
	Existence of candidate therapeutic drugs corresponding to the genetic change
	Genetic change, specific candidate drugs, and clinical studies/trials corresponding to the change
	Interpretation of evidence related to diagnosis and prognosis
	When secondary findings are discovered (or suspected), the significance and response to these findings in accordance with the related guidelines, guidance, and recommendations

Guidance for Cancer Diagnosis based on Gene Panel Tests using Next-generation Sequencers (Japan Society of Medical Oncology, Japan Society of Clinical Oncology, Japanese Cancer Association, May 15, 2020 Ver. 2.1)

ICRweb: https://www.icrweb.jp/icr_index.php?lang=en

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Actual Expert Panel

(in this hospital)

1. Receipt of results	Receipt of test results and C-CAT survey results
2. Preliminary examination	Each member of the expert panel performs the respective preliminary preparations
3. Progress of expert panel	• Presentation of clinical information • Panel members (molecular biology experts) explain each detected genetic abnormality • If necessary, panel members (clinical genetic specialists, certified genetic counselors) explain and consider responses to (possible) germline mutations • Recommended candidate therapeutic drugs are listed and summarized based on the opinion of the attending physician

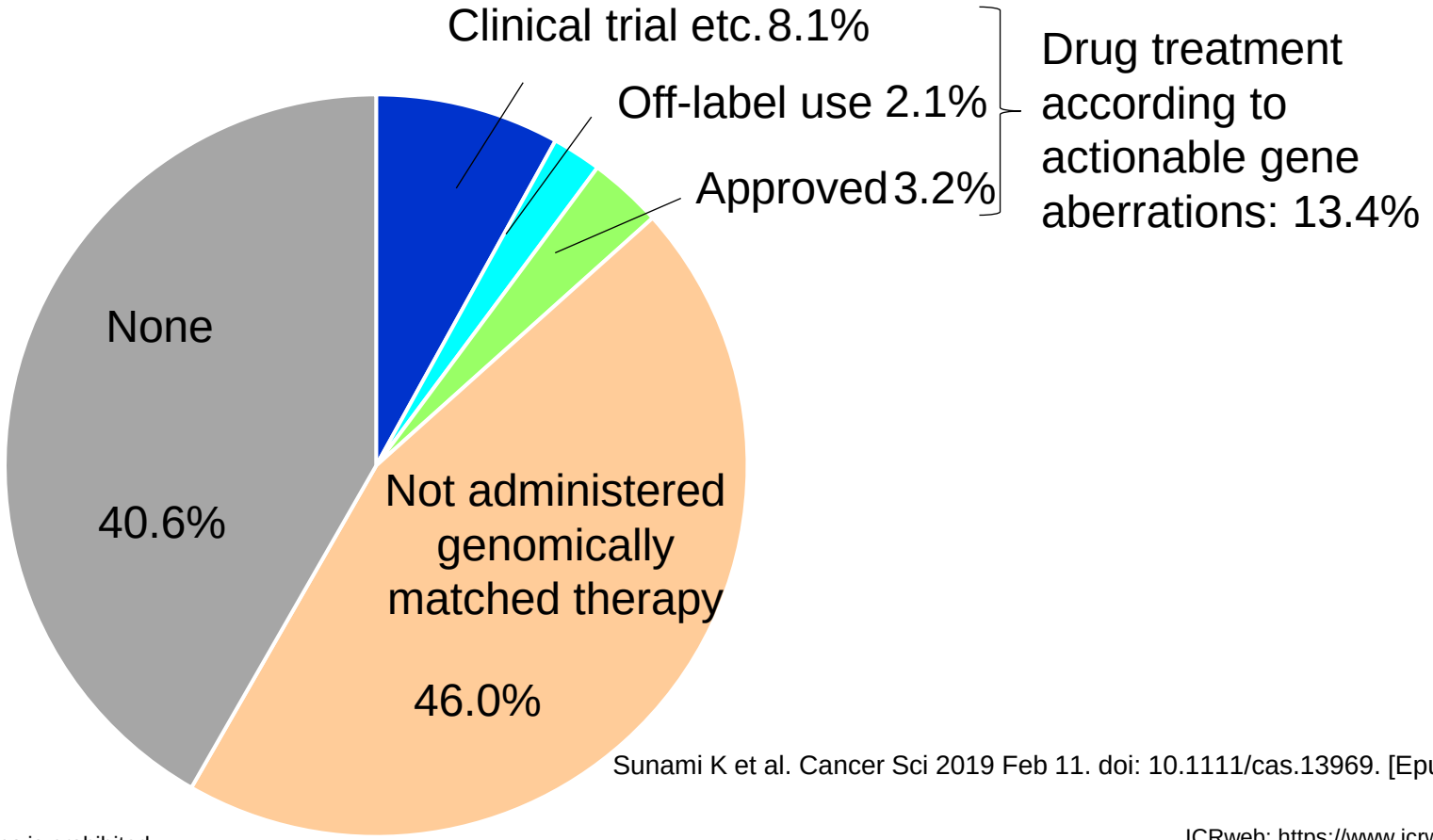
Cancer genomic medicine gene panel tests – Implementation guide (Igaku Shoin – Modified citation)

ICRweb: https://www.icrweb.jp/icr_index.php?lang=en

Result of TOP－GEAR project

2016.5_2017.5

- **1 ≤ alternations: 156/187 (83.4%)**
- **1 ≤ actionable alternations and/or high TMB: 111 (59.4%)**
- **Patients with a TMB ≥10/Mb: 17(9.1%)**
- **Drug treatment: 25/187 (13.4%)**



Sunami K et al. Cancer Sci 2019 Feb 11. doi: 10.1111/cas.13969. [Epub ahead of print]