

Frontline in Cancer Genomics,  
Novel Treatments  
and Precision Oncology

Proceedings of

**IAAO 2021**

INTERNATIONAL ACADEMY  
FOR ADVANCED  
ONCOLOGY



**C-FINDs**

CRISPR FOUNDATION  
FOR INNOVATIVE DRUG DISCOVERY SCIENCE

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## Opening Remarks

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Speaker:

**Osamu Nagayama**

President, Chugai Foundation for Innovative Drug Discovery Science (C-FINDs)

A handwritten signature in black ink, appearing to read 'O. Nagayama', written in a cursive style.

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Last year, due to the worldwide spread of COVID-19 infection, we unfortunately could not hold the International Academy for Advanced Oncology (IAAO) 2020. In consideration of the ongoing pandemic situation, we first planned to hold this year's forum in a hybrid format that combines online and on-site. However, because the local incidence of the infection is still high and a State of Emergency is ongoing through June, we decided to change to a full-remote format for IAAO2021. We are truly sorry that we cannot hold the forum on-site, but we are relieved to be able to hold it at all.

As president of C-FINDs (formerly Tokyo Biochemical Research Foundation), I would like to express my sincere gratitude to all of the distinguished guests, experts and investigators attending this conference from overseas and Japan.

Each year at IAAO, I am delighted to see that the size of our gathering continues to grow every year. This year, our eleventh meeting, is no exception, and even though it is an online event, more than 250 people will be in attendance. We are always encouraged by the positive feedback that we receive from participants, and are extremely happy and honored to know that more and more experts are interested in and value this event.

We are very fortunate to have here so many world-class experts who share their experience, knowledge, and insights. I am confident this year's forum will spark extensive and wide-ranging discussions. I encourage everyone to seize the opportunity provided by each session to actively engage in the discussions. Your comments and insights will be found truly valuable to others attending this forum.

The theme of this year's meeting is "Frontline in Cancer Genomics, Novel Treatments and Precision Oncology". The program focuses on cancer genomics and precision oncology, which have been rapidly progressing to the next stage of cancer biology and clinical practices. In the new molecular target session, we will hear expert lectures on novel biomarker strategies, RAS & other signaling pathways, hallmarks of pancreatic cancer, and challenges in targeted therapy. In cancer immunotherapy, the speakers will address the latest breakthroughs in clinical applications and new molecular mechanism insights of immune suppression in the tumor microenvironment.

This exceptional program was organized through active discussions and the hard work of the IAAO Advisory Board members, namely Dr. Chabner, Dr. Rosen, Dr. Tabernero, Dr. Hatake, Dr. Ishioka, Dr. Kitagawa, Dr. Miyazono, Dr. Mano, Dr. Toi and Dr. Ueda. I sincerely appreciate and respect the leadership and dedication of these eleven board members.

In closing, allow me to once again thank you for participating this year. C-FINDs' sincere wish is that this two-day event will be a highly informative and fruitful time for everyone. Our ultimate goal is for the IAAO forum to become an important venue for the exchange of information that advances the fight against cancer and, concurrently, empowers patients to deal with their treatment proactively and with hope.

Thank you very much for your attention.

# Session 1

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***Current Status of Cancer Drug R&D***

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**IAAO 2021**





Speaker:  
**Bruce A. Chabner, MD**  
Professor of Medicine, Harvard  
Medical School, USA  
Clinical Director, Emeritus,  
MGH Cancer Center,  
Massachusetts General Hospital,  
USA



Chairman:  
**Hitoshi Nakagama, MD,  
PhD**  
President, National Cancer  
Center, Japan

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## [Speaker's Biographical Sketch]

### Profile

Dr. Chabner is a professor of medicine at Harvard Medical School and director of clinical research at the Massachusetts General Hospital Cancer Center. He graduated summa cum laude from Yale College in 1961. He received his M.D. from Harvard University cum laude in 1965.

He has had extensive experience in the field of cancer drug discovery and development. After joining the National Cancer Institute (NCI) in 1971, he participated in the training of clinical and research fellows there for the following 24 years, including three years (1976-1979) as Chief of the Clinical Pharmacology Branch; two years (1979-1981) as Director of the Clinical Oncology Program; and in 1981, one year as Acting Director, and for 13 years as permanent Director of the Division of Cancer Treatment, NCI.

In 1995, he joined the Massachusetts General Hospital as Clinical Director of its cancer center and Chief of Hematology/Oncology. With the formation of the Dana-Farber/Harvard Cancer Center, he assumed responsibilities as Associate Director for Clinical Sciences of that consortium, which includes the Massachusetts General Hospital, Brigham & Women's Hospital, Dana-Farber Cancer Institute and Beath Israel Deaconess Medical Center. He has authored and edited the numerous textbooks of internal medicine, hematology, oncology and pharmacology.

He has received numerous awards, including Phi Beta Kappa, Alpha Omega Alpha, the Public Health Service's Distinguished Service Medal, the Karnofsky Award of the American Society for Clinical Oncology and the Bruce F. Cain Award for Drug Development of the American Association for Cancer Research. In 2006, he was the first recipient of the Bob Pinedo Award for Contributions to Improvement in the Care of Cancer Patients.

He is a senior editor for the *Oncologist* and serves on the executive advisory boards for some of the industry's leading innovators in drug development. In 2006, he received a presidential appointment to the National Cancer Advisory Board at the National Cancer Institute.

# Chemotherapy in the Age of Targeted and Immune Therapies: Learning New Tricks

Bruce A. Chabner, MD

## Current status of chemotherapy

This presentation is on chemotherapy in the age of targeted and immune therapies and how we are learning new ways of using chemotherapy in the context of the growing immunotherapy world.

I will start with exploring the current status of chemotherapy (Box 1). This is familiar to most of the medical oncologists attending this forum. Chemotherapy is the backbone of most current cancer treatments. We use it for induction maintenance therapy of acute leukemias. It's the basic regimen for the treatment of most metastatic solid tumors, and a component of adjuvant and neoadjuvant therapy for a number of solid malignancies including breast, colorectal, non-small cell lung, head and neck, and others. This adjuvant use of chemotherapy is of growing importance in allowing less surgery and better outcomes. It is also curative therapy on its own for lymphomas, childhood acute lymphoblastic leukemia (ALL), testicular cancer and

some adult leukemias. And finally, it is a necessary part of high dose therapy for regimens employing bone marrow transplantation for leukemia and lymphomas. Box 2 shows the advantages and obvious disadvantages of chemotherapy. The advantages are that it produces immediate systemic antitumor effects, the regimens are well established, and there is a predictable recovery of normal tissues. The disadvantages are equally apparent: there are no biomarkers for patient selection. Additionally, there is a rapid emergence of resistance to a single agent in most settings. The therapy suppresses the immune system and increases susceptibility to major infections, although this is usually temporary, and it produces late toxicity such as cancer and multi-organ damage.

There is a balance but the balance, particularly for solid tumors, is not obvious in some situations. There is also the inconvenience and expense of infusional therapy. Considering all of these aspects of the use of

- The "backbone " of most current cancer treatment
  - induction and maintenance therapy for acute leukemias
  - basic regimens for most metastatic solid tumors
  - basic component of adjuvant and neoadjuvant therapy for breast, colorectal, non-small cell lung, head and neck cancers
- Curative therapy for lymphomas, childhood ALL, testicular cancer, and some adult leukemias
- High dose therapy for bone marrow transplantation regimens for leukemias, lymphomas

### Box 1.

Current status of chemotherapy (CT).

- Advantages: Immediate systemic antitumor effects, well-established regimens, predictable recovery of normal tissues.
- Disadvantages: no biomarkers for patient selection, rapid emergence of resistance to single agents, immune suppression, late toxicities (cancer, multi-organ damage).
- Inconvenience and expense of infusional therapy.
- What is the future for CT?

### Box 2.

The balance: Advantages/disadvantages for chemotherapy.